HIGH-YIELD ANTIBIOTICS

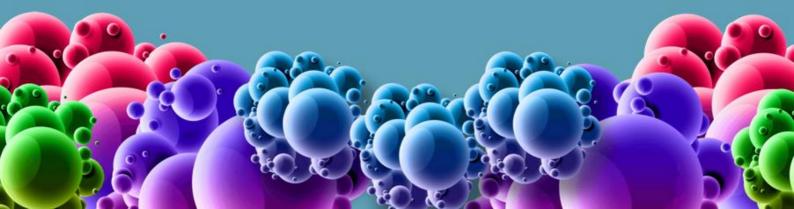
for USMLE, NBDE, FMGE, NEET

500+ High-yield points 50+ Illustrations & Mnemonics

References and updates from Goodman Gilman's 13/e, Katzung & Trevor 13/e, Harrison's 19/e, CMDT 2018 & Standard journals

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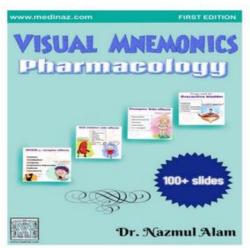
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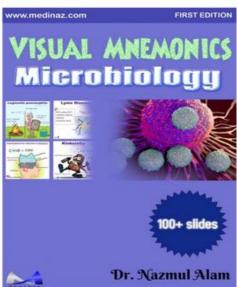
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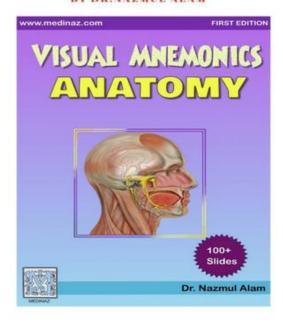








BY DR.NAZMUL ALAM







Penicillin

Penicillin G (IV and IM form), penicillin V (oral).

Mn.Penicillin G destroys with Gastric acid



D-Ala-D-Ala structural analog. Bind penicillin-binding proteins (transpeptidases). Block transpeptidase cross-linking of peptidoglycan in cell wall.Activate autolytic enzymes leads to osmotic burst.

Extend spectrum penicillin — Ampicillin, Amoxicillin, Carbenicillin, Ticarcillin, Mezlocillin, Azlocillin, Piperacillin

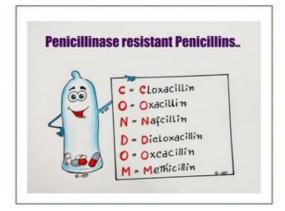
Mn. A CT MAP



Acid resistant penicillin



Penicillinase resistant penicillin







Extended spectrum penicillin prevent H influenzae, H pylori, E coli, Listeria monocytogenes, Proteus mirabilis, Salmonella, Shigella, enterococci.

Mn. HHELPSS



Aqueous penicillin G is DOC for neurosyphilis

Methicillin resistance is developed due to the formation of alternative penicillin binding proteins that have less affinity for the drugs

Ampicillin is DOC for Listeria meningitis

Side effects:

Methicillin - interstitial nephritis

Oxacillin - hepatitis

Nafcillin - neutropenia

Carbenicillin high dose - bleeding

Nafcillin = Neutropenia

β-lactamase inhibitors - Include Clavulanic acid, Avibactam, Sulbactam, Tazobactam.

Mn. CAST



Anti-pseudomonal penicillin







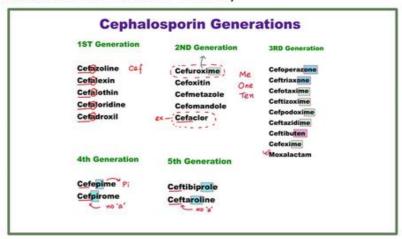
- Benzathine penicillin is the longest acting penicillin and it does not cross BBB
- If a patient develops severe hypersensitivity to penicillin, all other beta lactam antibiotics are contraindicated except Aztreonam
- Procaine penicillin can cause Seizures in high dose







Excreted via kidney through tubular secretion (Ceftriaxone & Cefoperazone are secreted in bile)



- 4 th generation cephalosporins Cefpirome, cefepime
- 5 th generation cephalosporins Ceftobiprole, Ceftaroline
- Ceftazidime (max) & Cefoperazone are active against Pseudomonas
- Organisms typically not covered by 1st-4th generation cephalosporins are Listeria, Atypicals (Chlamydia, Mycoplasma),
 MRSA, and Enterococci (treated by ceftaroline).

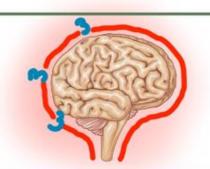






 - 3 rd generation cephalosporin can cross bloodbrain barrier (BBB)

 $\frac{BBB}{3} = \frac{3}{3}$ letters $\frac{3}{3}$ rd generation



- 5 th generation cephalosporins are useful against MRSA
- Most nephrotoxic Cephaloridine

CephaloRIdine = Renal Impairment



- Cefazoline is DOC for surgical prophylaxis
- Ceftazidime is DOC for melioidiosis
- Ceftazidime has maximum antipseudomonal activity
- Cefoperazone is active against pseudomonas, secreted in bile, doesn't cross BBB
- Important side effects disulfiram-like reaction,
 vitamin K deficiency, increase nephrotoxicity of
 aminoglycosides.





Carbapenems

Doripenem, Imipenem, Meropenem, Ertapenem (DIME antibiotics are given when there is a 10/10 [life-threatening] infection).



Always administered with cilastatin (inhibitor of renal dehydropeptidase I) to decrease inactivation of drug in renal tubules.



Only beta-lactam which are reliably efficacious against Extend spectrum beta lactamase.





- Newer carbapenems include ertapenem (limited
 Pseudomonas coverage) and doripenem.
- Meropenem has a lower risk of seizures and is stable to dehydropeptidase I





Monobactams

 Aztreonam is the only beta-lactam antibiotic that can be used in patients having severe allergy to penicillin or cephalosporin.

Aztreonam in Allergy



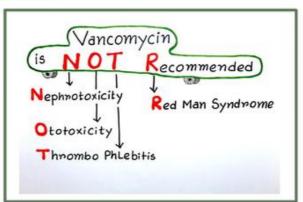
- Gram -ve rods only - no activity against gram + ve rods or anaerobes



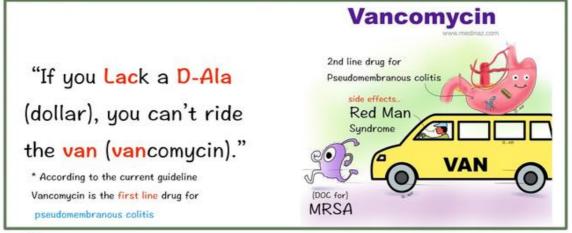


Vancomycin

- Bactericidal glycopeptide antibiotic that inhibit cell wall synthesis by inhibiting transglycosylase enzyme
- DOC for MRSA and Clostridium jeikeium
- Bacteriostatic against C difficile
- Rapid IV infusion can cause "Red Man Syndrome"
- Other side effects Nephrotoxicity, Ototoxicity,
 Thrombophlebitis



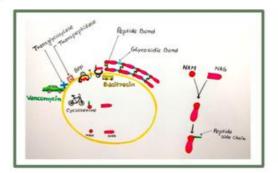
- Resistance - Occurs in bacteria (eg, Enterococcus) via amino acid modification of D-Ala-D-Ala to D-Ala-D-Lac.







- Bacitracin Only for topical use because of nephrotoxicity
 Inhibits cell wall formation by interfering with
 dephosphorylation in cycling of the lipid carrier
 that transfer peptidoglycan subunits to the growing cell wall.
- Cycloserine can cause neuropsychiatric symptoms Inhibit cell wall synthesis

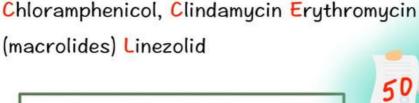


- All protein synthesis inhibitors are bacteriostatic, except aminoglycosides (bactericidal) and linezolid (variable).

30S inhibitors

Aminoglycosides, Tetracyclines

50S inhibitors



"Buy AT 30, CCEL (sell) at 50."







Aminoglycosides

- Bactericidal, 30S inhibitor
- Post antibiotic effect and concentration dependent killing is seen
- It is ineffective against anaerobes
- Curare like effect is seen. Neomycin & Streptomycin should not be used with d-TC
- Do not cross BBB / CSF
- Streptomycin is not used in TBM (Tuberculous Meningitis)
- Streptomycin is the DOC for Plague & tularemia
- Neomycin can be used orally for hepatic encephalopathy
 & gut sterilisation
- Side effects Nephrotoxicity, Neuromuscular blockade,
 Ototoxicity (especially when used with loop diuretics).

Teratogen

Nephrotoxicity

Neuromuscular blockade,

Ototoxicity

Teratogen



- Neuromuscular blockade is due to inhibition of presynaptic release of ACh which can cause severe respiratory depression (Reversed by IV calcium)





Tetracyclines

- Bacteriostatic & binds with 30S ribosome
- All tetracyclines undergo enterohepatic circulation
- Demeclocycline is used in SIADH, the most potent inhibitor of V2 receptors in kidney
- Use

TETracyclines
T
R - Rickettsia, Relapsing fever
A - Atypical pneumonia
C - Cholera
Y - LYme's disease
C - Chlamydia
L - LGV
I
N
INguinale (granuloma)

E - Epidemics of plague

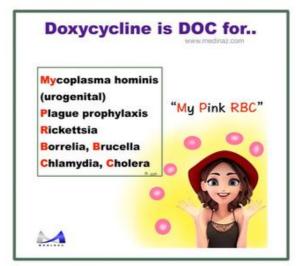




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 Doxycycline is DOC for - Mycoplasma hominis (urogenital), Plague prophylaxis, Rickettsia,
 Borrelia, Brucella, Chlamydia, Cholera



- Contraindicated in pregnancy as it can cause fetal tooth enamel hypoplasia and discoloration and irregularities in the fetal bone growth.
- Minocycline specifically produce vestibular toxicity and brown discoloration of skin
- Children with <8 years with tetracycline (dose)
 cause tooth discolouration
- Doxycycline, Tigecycline, Minocycline can be used in patients with renal failure because of fecal elimination.





- Do not take tetracyclines with milk (Ca 2+), antacids (Ca 2+ or Mg 2+), or iron-containing preparations because divalent cations inhibit drugs' absorption in the gut.
- Effective against intracellular organisms like Rickettsia and Chlamydia
- Tetracyclines are used for prophylaxis of Cholera & Leptospirosis





Macrolides

- Binds to 50S ribosome and block the translocation of peptide chain
- Erythromycin is excreted by biliary root.
- Erythromycin can cause diarrhea by the stimulation of motilin receptors
- DOC for

Chancroid by Haemophilus ducreyi, Corynebacterium, Campylobacter, Legionella infection, Atypical pneumonia,

Whopping cough



- Erythromycin estolate can cause pyloric stenosis,
 cholestatic jaundice, QT prolongation
- Azithromycin is DOC for Mycoplasma pneumoniae
 and genitalium, Campylobacter, Legionella and Chancroid



- Azithromycin is DOC for treatment of cholera and chlamydia in pregnancy
- Macrolides decrease inflammatory mediators and have anti-inflammatory and immunomodulatory effect.





Chloramphenicol

- Bacteriostatic and blocks peptidyltransferase
 at 50S ribosomal subunit.
- It can cause dose independent aplastic anemia and gray baby syndrome (in premature infants because they lack liver UDP-glucuronosyltransferase)

Clindamycin

Clindamycin treats anaerobic infections above
 the diaphragm and metronidazole treats anaerobic infections
 below diaphragm.



- Cause Pseudomembranous colitis (C difficile overgrowth)
- DOC for treatment of Toxic Shock Syndrome (TSS)





Linezolid

- Active against MRSA, VRSA & VRE
- MAO inhibitory activity can cause Serotonin syndrome
- It is associated with bone marrow suppression, optic neuritis and lactic acidosis

Sulfonamides

- Bacteriostatic, inhibit folate synthase competitively
- Not effective in the presence of pus because it contains large amount of PABA

Drugs undergo hepatic metabolism by Acetylation

- Sulfisoxazole is most soluble and has minimum risk of causing crystalluria
- Sulfadoxine is longest acting and Sulfacytine is shortest acting
- Sulfadoxine along with pyrimithamine and Artesunate is used for the treatment of chloroquine resistant malaria
- Sulfadiazine along with pyrimithamine is the treatment of choice of Toxoplasmosis





- Spiramycin is the DOC for toxoplasmosis in pregnancy
- Side effects Aplastic anemia, Bilirubin displacement (kernicterus), Crystalluria, Rash, Acetylation, SLE,
 Hemolysis in G-6-PD deficiency

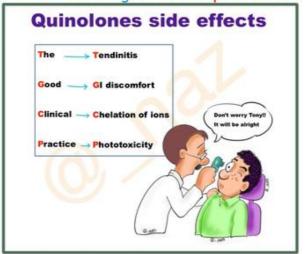






Fluoroquinolones

- Inhibit DNA gyrase and topoisomerase IV
- Sparfloxacin has longest half life
- Gatifloxacin has maximum bioavailability
- Ciprofloxacin is the DOC for prophylaxis and treatment of anthrax and for prophylaxis of meningococcal meningitis
- In case of Acute diarrhea Ciprofloxacin is DOC and used only if patient is febrile
- NSAIDs increase CNS toxicity of fluoroquinolones



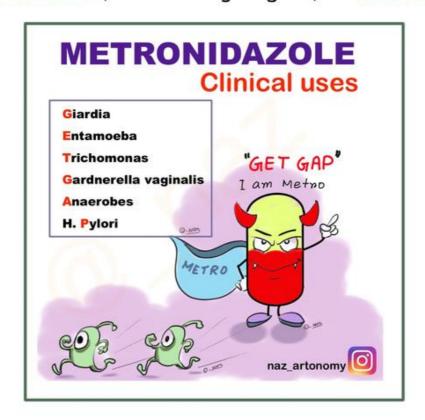
- Pefloxacin is the most lipid soluble fluoroquinolone and cross BBB maximum
- Ozenoxacin is a topical fluoroquinolone recently approved for treatment of Impetigo
- Contraindicated in pregnant women, nursing mothers, and children < 18 years old due to possible damage to cartilage. Some may prolong QT interval
- QT prolongation is maximum with sparfloxacin May cause tendonitis or tendon rupture in people
 - > 60 years old and in patients taking prednisone





Metronidazole

- Forms toxic free radical metabolites in the bacterial cell that damage DNA. Bactericidal, antiprotozoal
- Disulfiram-like reaction (severe flushing, tachycardia, hypotension) with alcohol
- Treats anaerobic infection below the diaphragm
- DOC for the treatment of pseudomembranous colitis, bacteroides, symptomatic intestinal amebiasis, extra intestinal amebiasis, bacterial vaginosis, trichomoniasis (strawberry vagina) & tetanus







- Dapsone cause Hemolysis in G6PD deficient patients, methemoglobinemia
- Trimethoprim can cause Megaloblastic anemia, leukopenia, granulocytopenia, which may be avoided with coadministration of folinic acid.



- Antitubercular drugs - Rifampin, Isoniazid, Pyrazinamide, Ethambutol

Rifampin
Isoniazid
Pyrazinamide
Ethambutol

"RIPE"





Refampicin

- Bactericidal and acts by inhibiting DNA dependent RNA polymerase
- It undergoes enterohepatic circulation and can be used safely in renal failure patient
- It can penetrate BBB and placental barrier
- Only bactericidal drug active against dormant bacteria and solid caseous lesions
- It is the most effective and fastest acting drug in leprosy
- It is the least toxic drug for TB and is also the safest drug in pregnancy

Rifampin's 4 R's:

RNA polymerase inhibitor

Ramps up microsomal cytochrome P-450

Red/orange body fluids

Rapid resistance if used alone



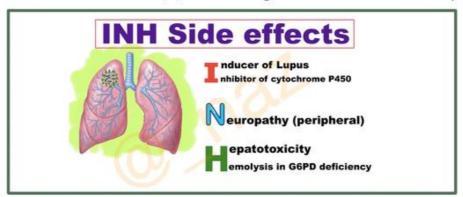






Isoniazid

- Isoniazid is a prodrug activated by catalase-peroxidase
- Bacteriostatic against resting and bactericidal against rapidly dividing organisms
- Metabolized by Acetylation which is genetically controlled
- Kat G gene mutation is the most common mechanism of resistance
- DOC for prophylaxis of TB
- Isoniazid causes B 6 deficiency (peripheral neuropathy, sideroblastic anemia) (Mn. INH Injures Neurons and Hepatocytes)



- Peripheral neuritis can be prevented and treated by pyridoxine
- Can cause hemolysis in G6PD deficient patients
- Side effects of INH



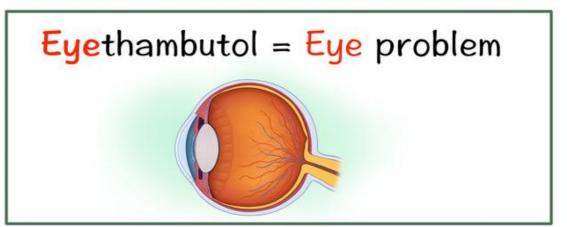


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Ethambutol

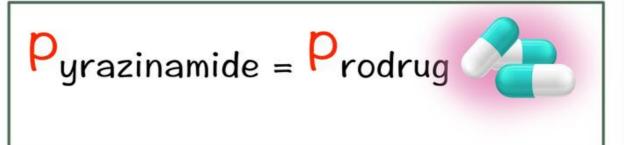
- Bacteriostatic and inhibit arabinosyl transferase
- Contraindicated in Children
- Ethambutol cause Optic neuropathy



Pyrazinamide

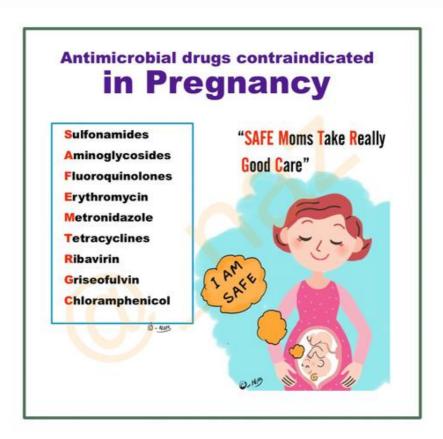
 Weakly bactericidal and works best at acidic pH (eg, in host phagolysosomes)

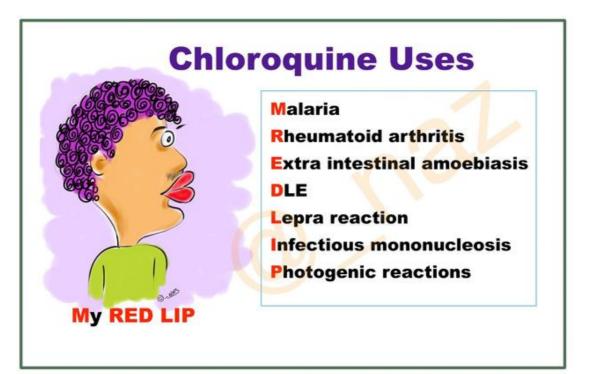
Pyrazinamide is a prodrug that is converted to the active compound pyrazinoic acid















Miscellaneous

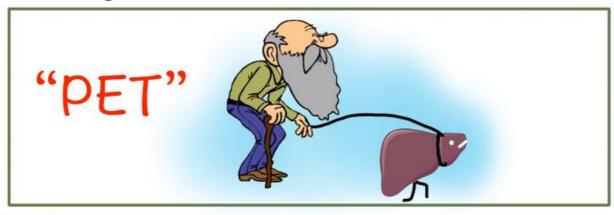
Antibiotics contraindicated in Renal failure

- Cephalothin
- · Cephaloridine
- · Nitrofurantoin
- · Nalidixic acid
- Tetracyclines (except Doxycycline)



Antibiotics contraindicated in Liver disease

- · Pyrazinamide, Pefloxacin
- Erythromycin estolate
- Tetracycline







Antibiotics causing important syndromes

Gray baby syndrome — Chloramphenicol

Pseudocholecystitis — Ceftriaxone

Fanconi syndrome — Outdated Tetracycline

Red man / Red neck syndrome — Vancomycin

Sicca syndrome — Sulfonamides

Sicca syndrome – Sulfonamides

Antimicrobial prophylaxis

- High risk for endocarditis and undergoing surgical or dental procedures - Amoxicillin
- Exposure to gonorrhea Ceftriaxone
- Rheumatic fever Benzathine penicillin
- Meningococcal meningitis Rifampicin / Ciprofloxacin / Ceftriaxone
- Rickettsial infection Tetracyclines
- Malaria Chloroquine / Mefloquine / Doxycycline
- Otitis media Amoxicillin
- History of recurrent UTIs TMP-SMX





- Exposure to meningococcal infection Ceftriaxone, ciprofloxacin, or rifampin
- Petrussis Azithromycin
- Plague Tetracyclines
- Toxoplasmosis Clotrimoxazole
- Pregnant woman carrying group B strep Intrapartum penicillin G or ampicillin
- Prevention of gonococcal conjunctivitis in newborn
- = Erythromycin ointment on eyes
- Prevention of postsurgical infection due to S aureus
- = Cefazolin
- Prophylaxis of strep pharyngitis in child with prior
 rheumatic fever Benzathine penicillin G or oral penicillin V
- Exposure to syphilis Benzathine penicillin G





ONE LINERS

- MIC (Minimum Inhibitory Concentration) is the lowest possible concentration of the drug that inhibits visible growth after 24 hours of incubation. Lesser MIC = more Potent
- Optimal dose is the dose of antimicrobial drug that inhibits
 growth of 90% organisms at the site of infection
- Mutation cause resistance to one drug whereas plasmid can cause multidrug resistance
- Ambler's classification of beta lactamase is based on structure of enzyme and Bush's classification is based on substrate of enzymes and it's inhibitors
- Long post antibiotic effect has been noted with Fluoroquinolones,
 aminoglycosides, Beta-lactam antibiotics
- Bactericidal drugs are must in immunocompromised patients
- DOC for syphilis in pregnancy Penicillin
- Longest acting fluoroquinolone Sparfloxacin (20 hrs)
- Methicillin resistance occurs due to altered PBP (Penicillin Binding Proteins)
- DOC for chlamydial infection Doxycycline
- Demeclocycline > Doxycycline cause photosensitivity
- Isoniazid maximum crosses BBB & is associated with neuropsychiatric symptoms like memory loss, euphoria & hallucinations
- Multi Drug Resistance (MDR) TB is resistance to both
 Isoniazid & Rifampicin





ONE LINERS

- Extremely Drug Resistance (XDR) TB is a case of MDR with additional resistance to Fluoroquinolone and to at least one of the injectable second line drugs like Amikacin, Kanamycin or Caperomycin.
- Bedaquiline & Delamanid are recent drugs for the treatment of MDR TB
- DOC for chlamydial infection in pregnancy Macrolides
 (eg. Erythromycin)
- Sulfonamides can cause Acute intermittent porphyria
- Brinzolamide is contraindicated in patient with sulfonamide allergy because of structural similarity
- Sulfasalazine is used orally for the treatment of Ulcerative colitis
- Sparfloxacin and Astemizole can cause Ventricular arrhythmia
- Multiple drug resistance is transferred through Conjugation
- Most common mechanism of transfer of resistance in Staphylococcus aureus is Transduction
- Sutezolid is currently under trial for treatment of TB
- Chloramphenicol is responsible for Bone marrow suppression
- Mupirocin is a topical antibiotic of choice for staphylococcal nasal carriage





Anti-tumor Antibiotics

Dactinomycin

Doxorubicin (Adriamycin)

Daunorubicin

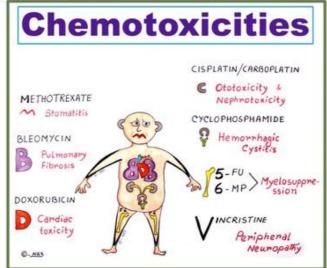
Bleomycin

Mitomycin C

Mitoxantrone

"mycin & bicin"

- Substances derived from microorganisms that have inhibitory effect on tumor cells
- Bind to DNA inhibit Topoisomerase II and generate free radicals due to electron transfer
- They cause DNA damage in all phases, but the cell cycle arrest is seen particularly in G2 and S phase
- Toxicities mostly caused by free radicals that can cause
 Cardiomyopathy and Pulmonary fibrosis





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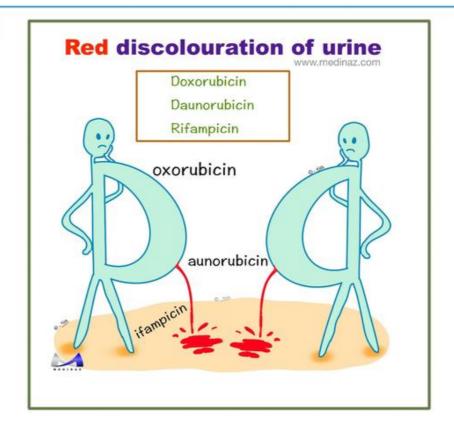


Anthracycline Group

- Derived from a fungus Streptomyces peucetius
- Free radical production requires Fe atoms for electron transport
- Fe chelating agent Dexrazoxane is the antidote of choice for anthracycline toxicity
- Doxorubicin is used for the treatment of Ovarian cancer, Sarcoma (Osteosarcoma), Lymphoma, Multiple myeloma
- Daunorubicin/ Idarubicin along with cytarabine (Ara-c) is the treatment of choice for Acute Myelogenous Leukemia (AML)
- Doxorubicin & Daunorubicin are the DOC for Kaposi sarcoma
- Epirubicin is used for Breast cancer
- Valrubicin is used for Bladder cancer
- Mitoxantrone is a doxorubicin derivative with less cardiotoxicity (cause secondary leukemia)
- Cardiotoxicity is maximum with Doxorubicin & Daunorubicin
- Acute toxicity presents as Pericarditis-myocarditis syndrome followed by Arrhythmia
- Long term use can cause Congestive heart failure due to Dilated cardiomyopathy
- Vacuolar myofibril degeneration is seen under electron microscopy
- Doxorubicin is a powerful vesicant (Given by rapid flowing IV line)
- Doxorubicin & Daunorubicin cause Red discoloration of urine
- Doxorubicin, Daunorubicin & Actinomycin D Cause Radiation recall syndrome







(Radiation recall syndrome: Radiotherapy cause local changes like desquamation, erythema etc, which subsides with time. After this if chemotherapy is started and the same local changes reappear, which is called as Radiation recall)

Mitomycin-C

- Potent radiosensitizer and has an alkylating agent like activity
- It is used along with 5-FU for the treatment of anal cancer
- It is used for the prevention of laryngotracheal, esophageal stenosis & post nasal surgery synechiae formation
- It can cause Haemolytic Uremic Syndrome (HUS), TTP & Pulmonary fibrosis





Dactinomycin (actinomycin D)

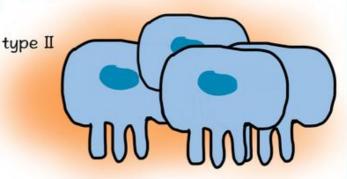
- Intercalates into DNA, prevent RNA synthesis.
- Wilms tumor, Ewing sarcoma, rhabdomyosarcoma. Used for childhood tumors.
- It can cause early myelosuppression, radiation recall syndrome.

Bleomycin

- Induces free radical formation which breaks in DNA strands
- Used for the treatment of Testicular cancer in BEP regimen, Hodgkin lymphoma in ABVD regimen.
- It can cause Pulmonary fibrosis, flagellate dermatitis (skin hyperpigmentation). Minimal myelosuppression & Raynaud's phenomenon
- Free radicals damage type I pneumocytes which leads to type II pneumocytes hyperplasia

type I









- Cell wall synthesis inhibitors like penicillin and vancomycin increase uptake of aminoglycosides.
- Drugs blocking enzymes sequentially like DHPS with sulfamethoxazole and DHFR with trimethoprim gives a synergistic effect in the form of bactericidal effect.
- Combination of Cilastatin & Imipenem inhibits metabolism of Imipenem and increases it's effect



- Bacteriostatic drugs like Tetracycline and Macrolides can inhibit the effect of Bactericidal drugs like penicillin
- Antibiotics like ampicillin, cefoxitin and imipenem can induce beta lactamase production and increase degradation of other beta lactamase drugs
- Penicillin can inactivate aminoglycosides in solutions
- DOC for gonococcal plus non-gonococcal mucopurulent cervicitis Azithromycin 2 gm oral single dose





- Biofilm mechanism of resistance to antibiotics includes -

Mechanical barrier (exopolysaccharide matrix)

Growth rate decreased

Persisters: Bacteria undergoes

phenotypic modification into dormant,

spore like structures and survive antibiotic insult

Efflux pump which pump the drug out of the biofilm

Enzymatic inactivation



- Empirical drug of choice for treatment of meningococcal meningitis —
 Ceftriaxone
- DOC for prophylaxis and treatment of pneumocystis infection in both immunocompetent as well as immunocompromised is cotrimoxazole
- Treatment of choice for Burkholderia Cepacia Carbepenams & 3rd generation cephalosporin
- Auditory toxicity is caused by Kanamycin, Amikacin, Neomycin

Kanamycin Amikacin Neomycin







- H. influenza has a plasmid for activity against beta lactamase, hence Cefotaxime is preferred over ampicillin
- Silver sulfadiazine can be applied topically for the treatment of keratomycosis
- ESBL production is detected by the ability of the microorganism to hydrolyze 3 rd generation cephalosporin
- Cefoperazone is safe in renal failure
- Cephalosporins like Ceftriaxone and Cephamandole can cause drug induced thrombocytopenia

DOC for typhoid -

Outpatients — Cefixime 20mg/kg/day for 14 days or Azithromycin 500 mg BD for 7 days

Inpatients — Ceftriaxone 2gm IV BD for 2 weeks +/- Azithromycin 500mg BD for 7 days

- Empirical treatment for meningitis
- 0-3 months Ampicillin + Cefotaxime
- 3 months 55 years Vancomycin + Cefotaxime / Ceftriaxone / Cefepime
- > 55 years Vancomycin + cefotaxime / ceftriaxone / cefepime + Ampicillin Most effective antibiotic for acne - Minocycline





- Ceftriaxone is the best drug for the treatment of diplococci like streptococcus and gonococcus
- Antibiotic of choice in Campylobacter gastroenteritis Erythromycin
- Daptomycin depolarizes the cell membrane and bacteria dies due to potassium efflux
- Daptomycin can cause myopathy
- Jarisch-Herxheimer reaction is seen in syphilis with Penicillin
- DOC for Nocardiosis Trimethoprim + SMX
- Streptomycin is a glycoside
- Streptomycin can enhance the toxicity of depolarizing skeletal muscle relaxant
- Rifabutin is more effective against Mycobacterium avium complex

(MAC) as compared to Rifampicin

Second line antitubercular drugs

Two = Thioacetazone

P = PAS

E = Ethionamide

A = Amikacin

C = Caperomycin, Calithromycin

0 = Ofloxacin

C = Ciprofloxacin, Cycloserine

K = Kanamycin

S = Streptomycin

Making = Moxifloxacin

Blind = Bedaquilline

Love = Linezolid

On

Date = Delamanid







- Rifampicin being an enzyme inducer can decrease efficacy of anti-HIV drugs like Nevirapine and Protease inhibitors which are metabolized by microsomal enzymes should be avoided in HIV +ve patients
- Gene responsible for Rifampicin resistance rpoB

Rifampicin resistance - rpoB

- Fidaxomicin the new FDA approved drug for Clostridium difficile infection
- Antitubercular drug associated with hypothyroidism —
 Ethionamide
- Cross resistance of Isoniazid is seen with Ehionamide
- Most common drug used in leprosy Dapsone

