SUMMARY
Respiratory block

Important

In male and female slides

Only in male slides

Only in female slides

Extra information

Editing file

ANTICHOLINERGIC DRUGS
Antimuscarinic Drugs

MOA	Reversible competitive blockade of muscarinic Receptors.
Adverse Effects	**-** Confusion, agitation, delirium. **-** Dry mouth, hot flushed skin. **-** Palpitation. **-** Skin flushing. **-** Mydriasis, blurred vision. **-** Tachycardia. **-** Constipation, urinary retention. **-** hyperthermia.
Contra-indications	- Glaucoma. - Constipation. - Prostate hypertrophy. - Paralytic ileus. - Children in case of atropine. - Tachycardia.

Name of drug	Source	Structure	Selectivity	Pharmacokinetics	Uses
Atropine (Hyoscyamine)	Natural	Tertiary amines (Lipid soluble)	Non-selective	- Lipid soluble. - Good oral absorption. - Good distribution. - Cross blood brain barrier (have CNS actions).	**CNS:** - Pre-anesthetic medication. - Antispasmodic. - Reverses muscarinic effects of cholinergic poisoning. **CVS:** Sinus bradycardia.
Hyoscine (scopolamine)					**CNS:** - Pre-anesthetic medication. - Motion sickness. - antispasmodic.
Homatropine	semisynthetic	-	-	Passive mydriasis due to paralysis of circular muscle.	**Eye: Ophthalmic examination of Retina (**Fundus examination)
Benztropine	Synthetic	-	-	-	**CNS:** Parkinson's disease.
Tropicamide		-	-	Passive mydriasis due to paralysis of circular muscle.	**Eye:** Ophthalmic examination of Retina (Fundus examination.)
Ipratropium		Quaternary ammonium	Non-selective	- inhalation. - Can not cross BBB.	**Respiratory system:** - asthma. - COPD. - inhalation.
Pirenzepine		-	Selective (M_1)	↓ Gastric acid secretion	**Stomach:** Peptic ulcer.
Glycopyrrolate		Quaternary ammonium	-	↓ GIT Motility → Antispasmolytic effect	**GI:** Antispasmodics in hypermotility ,Biliary and renal colics
Oxybutynin		-	Selective (M_3)	Relaxation of urinary bladder and sphincter contraction	**UT:** - Urinary urgency - Urinary incontinence. Contraindicated in old men (+60 y.o) with prostatic hypertrophy
Darifenacin		-	Selective (M_3)	-	

Adrenergic agonists

Drug	Receptor	Administration Route/ Contraindications	Uses
Direct/ Catecholamines/ Non-selective			
Adrenaline	**α1, α2, β1, β2, β3**	**Route**: I.V, S.C, inhalation. **Contra**: -CHD - Ischemic heart disease (angina) -Hyperthyroidism -glaucoma	- Combined with local anesthetic - Haemostatic (Stops bleeding) - In acute asthma - Anaphylactic shock - Cardiac arrest
Noradrenaline	**α1, α2, β1, weak β2**	**Route**: I.V Only	-Locally: as a local haemostatic with local anesthetic - Systemically: hypotensive states
Isoprenaline	**β1, β2, β3**	**Route**: Parenteral, Inhalation. **Contra**: -CHD -Hyperthyroidism	- cardiac arrest (preferred) - Rarely in acute attack of asthma
Dopamine	**D1 > β1 > α1 (in order)**	**Route**: Parenterally.	-Treatment of shocks: septic, Hypovolemic (after fluid replacement), cardiogenic (I.V)
Direct/ Catecholamines/ selective			
Dobutamine	**β1**	**Route**: I.V	-Short term management of Cardiac decompensation. - Acute myocardial infarction (AMI) & heart failure. -specifically indicated for cardiogenic shock

Direct/ Non-Catecholamines/ selective			
Phenylephrine	**α1**	**Route**: Oral **Contra**: -Hypertension	- Vasopressor (anti-hypotensive) Topically: - Haemostatic with Local anesthesia. - Mydriatic - Nasal decongestant
Salbutamol	**β2**	**Route**: Oral, Inhalation, Parenteral.	Bronchodilator for acute attacks of asthma & COPD
Ritodrine	**β2**	**Route**: Oral, Parenteral.	-Tocolytic
Terbutaline	**β2**	-	-Bronchodilator -Tocolytic
Direct / Imidazoline / Selective			
Clonidine	**α2(presynaptic)**	**Route**: Oral, Patch.	-Anti-Hypertensive
Brimonidine	**α2**	-.	-Glaucoma
Indirect / Non-catecholamine / Non-selective			
Amphetamine	**α & β** similar to epinephrine but has CNS stimulant effects	**Route**: Oral	Not used therapeutically anymore ADR: Tachyphylaxis & psychosis
Mixed / Non-catecholamine / Non-selective			
Ephedrine	**α & β** CNS stimulant effects (less than amphetamine)	**Route**: Oral	Not used therapeutically anymore ADR: Tachyphylaxis
Pseudoephedrine	**α & β**	-	-has less pressor effects compared to ephedrine. -Used as nasal & ocular decongestant & in flu remedies

Treatment of rhinitis

Drugs for treating rhinitis can be divided into :
1- Anti-histamines
2- Anti-allergics
3- Corticosteroids
4- Decongestants
5- Anti-cholinergics
6- Antibiotics

Antihistamines (HI–receptor antagonists)

more effective in preventing symptoms than reversing them

	First generation	Second generation	Third generation
Drug	• Chlorpheniramine • Dimenhydrinate • Diphenhydramine • Antazoline • Promethazine • Cyclizine • Azatidine • Ketotifen • Cyproheptadine • Meclizine	• Cetirizine • Loratadine	• Levocetirizine • Desloratadine • Fexofenadine
overview	- Short duration - Inexpensive - Dimenhydrinate and meclizine are both useful for preventing the symptoms of motion sickness. - Meclizine is useful for the treatment of vertigo associated with vestibular disorders.	Longer duration = better control . specific for H1 receptors, so they don't block other receptors	Longer duration = better control, specific for H1 receptors
Parmaco - kinetics	- Interactions; with enzyme inhibitors (macrolides, antifungals, calcium antagonists). - Cross BBB (so causes sedation) - Metabolized by the hepatic cytochrome P450 - Excretion occurs via kidney except fexofenadine in feces	- No drug interactions - They are polar groups (so do not penetrate the BBB) - Metabolized by the hepatic cytochrome P450 - Excretion occur via kidney except fexofenadine in feces	No drug interactions, Metabolized by the hepatic cytochrome P450 , , Excretion occur via kidney except fexofenadine in feces
uses	Allergic rhinitis, common cold,Motion sickness , Allergic dermatoses (control itching associated with insect bites), Nausea and vomiting		
ADRs	- interact with other receptors, producing a variety of unwanted adverse effects. They can block cholinergic, Adrenergic,or serotonin receptors. - Cyproheptadine has significant serotonin antagonism and is known to increase appetite.	Minimal ADRs,	Minimal ADRs

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	Anti-allergics		Corticosteroids	Decongestants		Anti-cholinergics
Drug	**Cromolyn & nedocromil**	**Montelukast**	**Beclomethasone & fluticasone**	**Pseudo-ephedrine**	**Phenylephrine Methoxamine Naphazoline Oxymetazoline Xylometazoline**	**Ipratropium**
overview	mast cell stabilizer that reduces histamine release and leukotrienes. Used in prophylaxis only. No effect once the acute setting has occurred	Block leukotriene actions (leukotriene receptor antagonist)	Anti-inflammatory,that blocks phospholipase A2 .So arachidonic acid synthesis decreases. Which leads to decreased level of prostaglandins & leukotrienes	Indirect sympathomimetic. Stimulates release of NE from sympathetic neurons	a1-agonist	Anti-muscarinic
uses	- in perennial allergic rhinitis in children - prophylaxis in asthma or allergic conjunctivitis	Used for:- - prophylaxis from perennial allergen. - Exercise . - Aspirin-induced asthma. - chronic maintenance therapy in asthma (not in acute attacks) -chronic rhinosinusitis	- Allergic rhinitis - Asthma Given in severe intermittent or moderate persistent symptoms	Nasal decongestant	Nasal decongestant	Given as nasal drops to control rhinorrhea. very effective in watery hyper-secretion. Indicated as a bronchodilator in COPD (first-line therapy) and in asthma (second-line therapy)
ADRs	Should never be stopped abruptly.		- Nasal irritation - fungal infection - hoarseness of voice	nervousness, insomnia, tremors, cardiac arrhythmias, hypertension.	can cause Rebound nasal stuffiness (if repeated administration is >10 days -2 weeks)	

Treatment for cough

Drugs for cough management can be divided into 3 classes :
1- Antitussives
2- Mucolytics
3- Expectorants

Antitussives (Used for dry cough)

	Central Antitussives		Peripheral Antitussives			
Drug	**Opioids :-** E.g: - Codeine - Pholcodine	**Non-opioids** E.g: dextromethorphan	**1- steam** (mixed with menthol زيت النعناع, eucalyptus شجرة الكينا or benzoin compounds , Tincture)	**2- Lozenges** (strepsils), Or **Gargles** (الغرغرة)	**3-Benzonatate**	**4- Lidocaine, Benzocaine, Tetracaine**
overview	Act on **μ (mu)** receptors on CNS, its effect is similar to morphine	Antihistaminics	Forms a protective coat. and acts as Emollients (ملطف) since glands get stimulated to secrete mucous	Forms a protective coat. and acts as Demulcent (ملطف) since glands get stimulated to secrete mucous	Local anesthetic. It inhibits stretch receptors in alveoli	Local anesthetic aerosols
uses	-	-	Relieves respiratory airways	Relieves pharynx	reduces cough	In bronchography في حالات تصوير القصبات الهوائية بالمنظار
ADRs	- Physical dependence - respiratory depression - constipation	No analgesic or addictive properties, so it's prefered over opioids	-	-	Nausea, vomiting, dizziness, rash and pruritus	-

Treatment for cough

Drugs for cough management can be divided into 3 classes :
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2- Mucolytics
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	Mucolytics			Expectorants		
	Reduce the viscosity of mucous. Used for productive cough			Increase the amount of mucous, so that sputum can be coughed up easily. Used for productive cough		
Drug	**N-Acetyl cysteine**	**Bromhexine & Ambroxol**	**Pulmozyme (Dornase Alpha)**	**Potassium iodide**	**Ammonium chloride, Ipecacuanha**	**Guaifenesin**
overview	Sputum is a glycoproteins that is bounded by disulfide bonds.**Acetyl cysteine** breaks the S-S bonds in glycoprotein, so the viscosity decreases	They increase the immune defense, and decrease acute sore throat pain	Cleavage of extracellular bacterial DNA, that contributes to viscosity of sputum in case of infection. It is a recombinant human deoxyribo-nuclease-1 enzyme that is neubilized	-	-	-
uses	used in acetaminophen (paracetamol) overdose as well	-	-	Common cold, Bronchitis, Pharyngitis ,Chronic paranasal sinusitis		
ADRs	-	-	-	**metallic taste, hypersensitivity, hypothyroidism, swollen salivary glands (overstimulation of salivary secretion).** Since K iodide is a metal, ADRs can be memorized through the word MITAL (instead of metal) M: **M**etallic taste I: **I**rritation of glands (overstimulation) T: **T**hyroid hormones undersecretion (hypo**T**hyroidism) AL: **Al**lergy (hypersensitivity)	-	Dry mouth, chapped lips, risk of kidney stones (increase in uric a. excretion)

Bronchial asthma

Bronchodilators

	Non selective β2 agonists	Selective β2 agonists		Muscarinic Antagonist	Methylxanthines
		Short acting	Long acting		
Drug	1- **EPINEPHRINE (ADRENALINE)** 2- **ISOPRENALINE**	1- **SALBUTAMOL (ALBUTEROL).** 2- **TERBUTALINE**	1- **SALMETROL** 2- **FORMETROL**	1- **Ipratropium** 2- **Tiotropium**	1- **Theophylline** 2- **Aminophylline**
MOA	* Direct B2 stimulation ^ stimulate adenyl cyclase ^ cAMP^ bronchodilation * Increase mucus clearance * Mast cell stabilization			Act by blocking muscarinic receptor,, (non-selective)	* They are phosphodiestrase inhibitors: ↑ cAMP → bronchodilation. * Adenosine receptors antagonists(A1). * Increase diaphragmatic contraction. *Mast cell stabilization.
P.K	Onset within (15 min) Duration of action (60-90 min)	Onset (15-30 min) Duration of action (4-6 h)	Bronchodilator for (12 h)	Delayed onset	T1/2 = 8 h Metabolized by Cyt P450 enzyme in liver
Administration	Subcutaneous **NOT** orally	inhalation, orally, salbutamol can be given I.V	Inhalation	Aerosol inhalation	Theophylline > orally Aminophylline> slow infusion
P.D	–	–	–	* Inhibit bronchoconstriction & mucus secretion. * Less effective than B2 agonist. * Not anti-inflammatory & don't enter CNS	* Bronchial muscle relaxation. * Increase: contraction of diaphragm,heart rate & force of contraction,Gastric acid secretion, renal blood flow. * CNS stimulation: respiratory center,decrease fatigue, elevate mood.
Uses	1- Bronchodilator 2- acute anaphylaxis	acute attack of asthma	For nocturnal asthma **not** for acute attack of asthma	1- COPD 2- Acute severe asthma used with B2 agonist & corticosteroids	Theophylline >second line in asthma. Aminophylline> status asthmaticus
ADRs	* Hyperglycemia * Skeletal muscle tremor * CVS side effects: tachycardia, Arrhythmia, hypertension	* Skeletal muscle tremors * Nervousness. * Tolerance (B-receptor down regulation). * Overdose may produce tachycardia		Minimal systemic side effects	GIT: Nausea,Vomiting CVS: hypotension,arrhythmia CNS: tremor, nervousness, insomnia,convulsion.
Others	**CONTRA-INDICATIONS:** 1- CVS patient 2- Diabetic patients 3- Asthmatic patients with hypertension or heart failure.	**Advantage:** 1- Minimal CVS side effect 2- Suitable for asthmatic patients with CVS disorders as hypertension & heart failure		**Characteristic:** Quaternary derivative of Atropine (polar)	**Drug interactions:** 1- Cyt P450 inducers (phenobarbitone,rifampicin) ^ metabolism of theophylline > decrease T1/2 2- Cyt P450 inhibitors (erythromycin)> decrease metabolism ^ T1/2

Bronchial asthma

Anti-inflammatory drugs

	Glucocorticoids	Mast cell stabilizer	Anti-IgE monoclonal antibody	Leukotrienes antagonists
Drug	Budesonide, Fluticasone, beclometasone, Prednisone, methylprednisolone, Hydrocortisone, dexamethasone.	1-Cromoglycate (cromolyn) 2- Nedocromil	Omalizumab	1- Zafirlukast 2- Montelukast 3- Pranlukast
MOA	Anti-inflammatory action due to: 1- Inhibition of phospholipase A2 >> ↓ prostaglandin & leukotrienes >>↓ Number of inflammatory cells in airways. 2- Mast cell stabilization →↓ histamine release >> ↓ capillary permeability & mucosal edema. 3- Inhibition of antigen-antibody reaction. 4- Upregulate β2 receptors.	stabilization of mast cell membrane.	A monoclonal antibody directed against human IgE: 1- prevents IgE binding with its receptors on mast cells & basophils. 2- Decrease the release of allergic mediators.(IgE)	selective, reversible antagonists of cysteinyl leukotriene receptors (CysLT1 receptors).
P.K	Delayed onset (2-4) weeks. Maximum action at 9-12 months.	–	–	have delayed onset of action
Administration	Inhalation: Budesonide, Fluticasone, beclometasone Orally: Prednisone, methylprednisolone Injection: Hydrocortisone, dexamethasone.	inhalation (aerosol, nebulizer poor oral absorption (10%).).	given by injection (s.c.)	orally
Uses	Reduce bronchial inflammation & hyperreactivity to stimuli	Reduce bronchial hyperreactivity	–	Have anti-inflammatory action less effective than inhaled corticosteroids. * Have glucocorticoids sparing effect.
	* Effective in allergic, exercise, antigen and irritant induced asthma. * Given as prophylactic medications, * inflammatory disorders (asthma, rheumatoid arthritis). * autoimmune disorders (ulcerative colitis, psoriasi) & after organ transplantation * Antiemetics in cancer chemotherapy.	1- Prophylactic therapy in asthma especially in children. 2- Allergic rhinitis . 3- Conjunctivitis.	moderate to severe allergic asthma which does not respond to high doses of corticosteroids.	Prophylaxis of mild to moderate asthma (e.g. aspirin-induced asthma, antigen & exercise induced asthma) ● Not effective in acute attack of asthma.
ADRs	Immunosuppressant effects * Metabolic effects: Hyperglycemia, ↑ protein catabolism,↓ protein anabolism, Stimulate lipolysis. * Mineralocorticoid effects: sodium/fluid retention, hypokalemia, hypertension. * Behavioral changes: depression * osteoporosis due to: Inhibit bone formation, ↓ calcium absorption from GIT. * Oropharyngeal candidiasis * Dysphonia	* Bitter taste * minor upper respiratory tract irritation (burning sensation,nasal congestion)	–	Elevation of liver enzymes, headache, dyspepsia
Others	–	not effective in acute attack of asthma Children respond better than adults.	Disadvantages: Expensive-not first line therapy.	Target: Leukotrienes examples: ● Leukotriene B4: chemotaxis of neutrophils. ● Cysteinyl leukotrienes C4, D4 & E4

Treatment of COPD

1- Antibiotic (macrolides e.g : azithromycin)
2- **Inhaled bronchodilators**
3- Lung transplantation
4- Inhaled glucocorticosteroids
5- oxygen therapy

Inhaled bronchodilators in COPD

	β2 Agonists	Inhaled antimuscarinics
Drugs	**These drugs can be used alone or combined :** • Salbutamol + ipratropium(short acting) • Salmeterol + tiotropium. (Long acting-less dose frequency)	• Ipratropium & tiotropium • Are superior to **β2** agonists in COPD

"واعلموا أن مهمتكم ليست في ورقة تنالونها.. ولكن أمة تحيونها"
علي الطنطاوي

Take a break ...:

Treatment of respiratory tract infection

	Penicillins Beta-lactam antibiotics			Cephalosporins Beta-lactam antibiotics		
Drug	**Amoxicillin** Clavulanic acid	**Ampicillin** Sulbactam	**Piperacillin** Tazobactam	**First generation** **Cephalexin**	**Second generation** **Cefuroxime** **(Cefuroxime axetil)** **Cefaclor**	**Third generation** **Ceftriaxone** **Cefixime** **Cefotaxime**
Route of administration	-Given orally or parenterally			Orally	well absorbed Orally	-Mainly IV
Spectrum	Act on both gram +ve & gram -ve microorganisms			Gram +ve Bacteria	-Mainly Gram -ve Bacteria -active against β-lactamase-producing bacteria.	More effective against Gram -ve bacilli
MAO	Bactericidal. Inhibit bacterial cell wall synthesis through inhibition of peptidoglycan layer on the cell wall			Bactericidal Inhibit bacterial cell wall synthesis (similar mechanism to Penicillins)		
Parmaco-kinetics	- Not metabolized in human. - Relatively lipid insoluble. - Excreted mostly unchanged in urine - Half-life: 30-60 min (increased in renal failure). - Probenecid (uricosuric) **slows** their elimination and prolongs their half life			-Given parenterally & orally. -Relatively lipid insoluble -Do not penetrate cells or the CNS except for 3rd generation. -Mostly excreted unchanged by the kidney -Probenecid slows their elimination & prolongs their half lives -Half-life: 30-90 min , long half-life-> ceftriaxone (4-7 hr).		
ADRs	-Hypersensitivity reactions - Diarrhea. - Superinfections - Nephritis. - Convulsions (after high I.V dose or in renal failure)			-Hypersensitivity reactions. -Thrombophlebitis -Superinfections. -Diarrhea.		
Uses	- URTIs - LRTIs			URTIs	-URTIs -LRTIs	In treatment of pneumonia

Treatment of respiratory tract infection

	Macrolides Prototype: Erythromycin		Fluoroquinolones		
Drug	**Clarithromycin**	**Azithromycin**	**Ciprofloxacin** (prototype)	**Moxifloxacin**	**Gatifloxacin**
Spectrum	More effective on G+ve bacteria	More effective on G-ve bacteria	Mainly against Gram -ve	-G-ve & G+ve bacteria -Highly active against pseudomonas species.	
Half life	6-8 hours	3 days	Relatively long half-life		
Dose	-	Once daily dosing	Twice daily	Once daily	
metabolism	Metabolized in liver to active metabolite	Undergo some hepatic metabolism (inactive metabolite)	-		
CYT P450	Inhibits cytochrome P450 system	No effect on cytochrome P450	-		
MAO	-Bacteriostatic. -Bactericidal at high concentrations. -Inhibit bacterial protein synthesis by binding to 50S ribosomal subunit of the bacterial ribosome.		-block bacterial DNA synthesis by Inhibiting DNA gyrase enzyme (an enzyme involved in DNA supercoiling)		
ADRs	-GI disturbances -Hypersensitivity reactions		Nausea , vomiting , diarrhea. -CNS effects (confusion, insomnia, headache, anxiety). -Damage of growing cartilage (arthropathy). -Phototoxicity (avoid excessive sunlight).		
Uses	-Chlamydial pneumonia -Legionella pneumonia		-Acute exacerbation of COPD. -Community acquired pneumonia -Legionella pneumonia.		
Pk	-Major route of elimination: biliary route. -Stable at gastric acidity -clarithromycin & azithromycin-> only 10-15% excreted unchanged in urine.		-oral or parenteral -Concentrates in many tissues (kidney, prostate, lung, and bones/joints) -Excreted mainly through kidney		
CI	-		-Not recommended for patients under 18 years -Pregnancy. -Breastfeeding women.		

Treatment of respiratory tract infection

	Tetracyclines Chlortetracycline, Doxycycline, Minocycline	Aminoglycosides
Drug	**Doxycycline (a long acting tetracycline)**	**Streptomycin, Neomycin, Gentamicin**
MAO	-bacteriostatic antibiotics. -Broad-spectrum-> Active against many G+ and G- bacteria (anaerobes, rickettsiae, chlamydiae, and mycoplasmas). -Inhibit protein synthesis by binding reversibly to 30S ribosomal subunit of the bacterial ribosome.	-Bactericidal antibiotics -only active against Gram -ve aerobic organisms. -Inhibits bacterial protein synthesis by binding to 30S subunit of the bacterial ribosome.
Pk	-Usually given orally. -Absorption is 90-100% -Absorbed in the upper s. intestine & best in absence of food. -Food & di & tri-valent cations (Ca, Mg, Fe, AL) impair absorption by reducing absorption) -Protein binding 40-80 %. -Distributed well, including CSF. -Cross placenta and excreted in milk. -Largely metabolized in the liver.	-Poorly absorbed orally (highly charged). -Given parenterally IM , IV -Half-life=2-3 hours and increased to 24-48 in renal impairment -Cross placenta (so, contraindicated in pregnancy) -Excreted unchanged in urine
Uses	Treatment of URTIs caused by S.pyogenes, S.pneumonia & H. influenza.	Severe infections caused by Gram -ve organisms.
ADRs	-Nausea, vomiting ,diarrhea & epigastric pain -Thrombophlebitis – i.v -Hepatic toxicity (prolonged therapy with high dose). -Brown discolouration of teeth – children -Deformity or growth inhibition of bones – children. -Phototoxicity. -Vertigo. -Superinfections.	-Ototoxicity -Nephrotoxicity. -In very high doses:neuromuscular blockade that results in respiratory paralysis
CI	-Children (below 10 yrs). -Pregnancy. -Breast feeding.	

Antimycobacterial Drugs (TB)

1st line treatment

Drug	Isoniazid (INH)	Rifampin (RIF)	Ethambutol	Pyrazinamide (PZA)	Streptomycin
Duration	6-9 months	6-9 months	First 2 months	First 2 months	USED IN LIFE THREATENING SITUATION
Site of action	Is effective against intracellular and extracellular bacilli			Active against Intracellular Bacilli	Active mainly on extracellular bacilli
MAO	-Bacteriostatic for resting bacilli. -Bactericidal for rapidly growing bacilli. -Inhibits the synthesis of mycobacterial cell wall (inhibit the synthesis of mycolic acid)	-Bactericidal -Inhibits RNA synthesis by binding to DNA dependent RNA polymerase enzyme.	-Bacteriostatic -Inhibitor of mycobacterial arabinosyl transferase (alters the cell barrier) disrupts the assembly of mycobacterial cell wall.	-Bacteriostatic -Mechanism of action is **unknown** converted to pyrazinoic acid—the active form which disrupts mycobacterial cell membrane metabolism & transport functions	-Bactericidal -Inhibitors of protein synthesis by binding to 30 S ribosomal subunits.
Adverse effects	-Peripheral neuritis -Optic neuritis and atrophy. -Hepatitis (toxic metabolites)	-Harmless red-orange discoloration of body secretions (saliva, sweat, tears .....) -Hepatitis less common compared to INH -Flu-like syndrome -Hemolytic anemia	-Impaired visual acuity -Red-green color blindness. -Ethambutol is contraindicated in children under 5 years.	-Hepatotoxicity (common) same as INH -Hyperuricemia (gouty arthritis) -Drug fever & skin rash	-Ototoxicity -Nephrotoxicity -Neuromuscular block
Uses	-Treatment of TB -Treatment of Latent TB in patients with positive tuberculin skin test -Prophylaxis against active TB in individuals who are in great risk .	-Treatment of TB -Prophylaxis Against other bacterial infection such as meningococcal & staphylococcal infections.	Treatment of tuberculosis in combination with other drugs.	-Mycobacterial infections mainly in multidrug resistance cases. -It is important in short –course (6 months) regimen. -Prophylaxis of TB.	**Severe** , life-threating form of T.B. as meningitis, disseminated disease.
Drug Interaction	-Enzyme inhibitor -Slow and fast acetylators.	-Enzyme inducer -Clinically significant drug interactions such as warfarin, methadone will be metabolized faster	-	-	-

Antimycobacterial Drugs (TB)

2nd line treatment
(more toxic than the first line)

Drug	Ethionamide	Fluoroquinolones (ciprofloxacin)	Rifabutin	**Para Aminosalicylic acid (PAS)** There is no info. about this drug in the males slides (ONLY IN FEMALE SLIDES)
MAO	Inhibits the synthesis of mycolic acid Same MAO as INH	-	-RNA inhibitor Same MAO as Rifampin -Cross –resistance with rifampin is complete.	-Bacteriostatic -Inhibits folic acid synthesis thus slows bacterial cell growth & multiplication
Adverse effects	-Teratogenic -Poorly tolerated Because of : Severe gastric irritation and Neurological manifestations	-	-GIT intolerance -Orange-red discoloration of body secretions. (Same as Rifampin)	-GIT upset -peptic ulceration & hemorrhage -Crystalluria (cloudy urine)
Clinical Uses	As a secondary line agent ,treatment of TB.	Effective against multidrug-resistant tuberculosis.	-Effective in prevention and treatment of T.B. -In prevention & treatment of atypical TB.	-As a 2nd line agent in the Treatment of chronic pulmonary & other forms of TB -Help to slow development of resistance to other drugs especially INH and streptomycin
Drug Interaction	-	-	Enzyme inducer	-

Treatment of Anaphylaxis

1st line therapy

Adrenaline (epinephrine) Sympathomimetic

Mechanism	A nonselective adrenergic agonist [a1, a2, b1, b2]
Indication	**Drug of choice for anaphylactic shock**
Actions	1-As an α-Adrenergic agonist :vasoconstriction,decrease edema. 2-As a β-Adrenergic β1:↑ force of myocardial contraction. β2:Dilates bronchial airways +↓ histamine & leukotriene release from mast cells . 3-As histamine antagonist : Adrenaline is the physiological antagonist of histamine
ADRs	**Causes dysrhythmias if given IV.**
Contraindications	-Not given for cardiac patient who are older than 40 years -Patients taking β-blockers
Administration	-**IM**: why? -Easily accessible by using Auto-injectors Kits,safety,No need to wait for IV line -Repeat every 5 -10 min as needed -Patient should be observed for 4-6 hours (fear of biphasic anaphylaxis)

2nd line therapy

Corticosteroids(anti- inflammatory)

Mechanism	**Non-genomic action:** ● Immediate actions on **Membrane-bound receptors**,which leads to modulating 2nd messengers levels. ● Rapid onset of action (seconds or minutes) **genomic action:** ● Takes hours to days to be activated.
Action	● Reverse hypotension & bronchoconstriction. ● ↓ release of inflammatory and allergic mediators ● ↓ mucosal swelling and skin reaction. ● May help to limit biphasic reactions by **decreasing allergic mediators.**

Treatment of Anaphylaxis

Corticosteroids(Cont.)

Administration	• Given slowly IV or IM. • Not used alone (not life saving).

H1 Blockers

Drug	Pheniramine (first generation antihistamine)
Action	• Though mast cells have already de-granulated, yet these drugs can still help to counteract (prevent) histamine-mediated vasodilation and bronchoconstriction. • May help to limit biphasic reactions by blocking histamine receptors.
Administration	• Given slowly I.V or I.M • It can not be used alone (not life saving).

Adjuvant to 2nd line therapy

H2 Blockers AND Proton pump inhibitors

Drugs	**Ranitidine,Cimetidine**(H2 blockers) **Pantoprazole** (proton pump inhibitors)
Action	• The significance of H2 blockers is not established, these drugs are associated with serious adverse drug interactions. -**Pantoprazole is a Proton pump inhibitor it is safer and given once.**
Contraindications	**Cimetidine** shouldn't be given to elderly, renal/ hepatic failure, or if on b-blockers. Why? Because it inhibits cytochrome P450 (CYP450) which controls drug-drug interactions So when given it may increase the toxicity of other drugs , therefore it's replaced by ranitidine.

Treatment of Anaphylaxis

Bronchodilators

Drugs	Salbutamol nebulizer	Ipratropium nebulizer	Aminophylline IV
Administration	Inhalation		Parenteral IV
action	**β2 agonist** ●(Bronchodilation) ● ↓mediators action released from mast cell and basophils ● inhibit airway microvascular leakage	**Anticholinergic** Decrease secretion of mucus ● Bronchodilator ●Decreases cGMP, therefore decreases the contractility of smooth muscles.	● treatment of anaphylaxis when,inhaled bronchodilators are not effective bronchospasm is persistent. ● Given in hospital setting as levels of drug should be therapeutically monitored because it has narrow therapeutic index.
P.K	● Short acting. ● Rapid onset of acting.	● Longer acting ● Less rapid in action	

Glucagon

Mechanism	act on glucagon receptors in the heart.
Action	● Has both positive inotropic & chronotropic effect on heart→ increase cardiac cyclic AMP. ● This effect is completely **independent of Adrenergic Receptors,** That is why effective in spite of β-adrenergic blockade. ● Efficacy of acting on bronchi is less prominent than that of the heart → no evident bronchodilation
Clinical Use	Drug of choice for severe anaphylaxis in patients taking Clinical uses β-blockers.

GOOD LUCK!

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