MED438
KING SAUD UNIVERSITY

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pharmacology

Team 438

SUMMARY

Editing File

Anticholinergic Drugs

Muscarinic Antagonists	Drug	Organ	Clinical uses
Natural alkaloids	Atropine	CNS	Pre-anesthetic medication, Antispasmodic
		CVS	Sinus bradycardia
		GIT	Used for treatment of Traveler's diarrhea with opioid
	Hyoscine	CNS	Pre-anesthetic medication, Antispasmodic,Vomiting (Motion sickness).
Synthetic atropine substitute	Benztropine AND Benzhexol	CNS	Parkinson's disease
	Homatropine AND Tropicamide	Eye	Fundus examination of eye
	Ipratropium	Respiratory System	Bronchial Asthma, COPD, (By inhalation to reduce side effects)
	Pirenzepine	GIT	Peptic ulcer
	Glycopyrrolate		Antispasmodics In hypermotility
	diphenoxylate		Used for treatment of Traveler's diarrhea with opioid
	Oxybutynin and Darifenacin	GUT	Urinary urgency, Urinary incontinence

Contraindications:

- Tachycardia
- Glaucoma
- Prostate Hypertrophy
- Constipation
- Paralytic ileus
- Children in case of Atropine.

Adverse Effects:

- **CNS**: 1-confusion 2-agitation 3 -delirium
- **Urinary tract**: Urinary retention
- **CVS**: 1-Tachycardia 2-Hot flushed skin
- **GIT**: Constipation
- **Eyes**: 1-Blurred vision 2-Mydriasis
- **Secretions**: 1-Dryness of mouth 2-Sandy eyes 3-Hyperthermia

Drugs for Bronchial asthma

1) **Bronchodilators** (Quick relief medications): to relieve acute episodic attacks of asthma.

Short acting β2 agonists	Non-selective	epinephrine	**MOA:** • Stimulates adenyl cyclase • ↑ mucus clearance. • Stabilize Mast cell.	**Uses**: acute anaphylaxis. Not effective orally	**ADR:** CVS effects, hyperglycemia, skeletal muscle tremor **Contra:** CVS pts, diabetes, asthmatic pts with hypertension
		isoprenaline			
	selective	Salbutamol (albuterol)		**Uses**: acute attack of asthma	**Advantages:** Minimal CVS side effects, suitable for pts with CV disorders. **ADRS:** Tremors, nervousness, tolerance, Tachycardia (Overdose)
		Terbutaline			
Muscarinic antagonists Less effective than β2-agonists		Ipratropium	**Uses:** Main choice in COPD + In asthma combined with β2 agonists & corticosteroids. - Never use as a rescue medication. - Have minimal side effects		
		Tiotropium			
Methylxanthines		Theophylline Second line drug in asthma	**MOA:** Phosphodiestrase inhibitors. • Block adenosine receptors. • Stabilize Mast cell membrane. • ↑ diaphragmatic contraction.	**Pharmacologic effects:** bronchial muscle relaxation, ↑ contraction of diaphragm, ↑ COP , ↑ Gastric acid secretion, ↑ renal blood flow, stimulates the respiratory center, ↑ mood ↓ fatigue. **Overdose:** insomnia, nervousness, tremors, convulsion. تذكر تأثير شرب الكافيين و استنتج الجواب	**P.K:** Metabolized by Cyt P450 enzymes in liver. **drug interactions:** Enzyme inducers (Phenobarbitone & rifampicin): ↑ Metabolism of theophylline + ↓T ½. Enzyme inhibitors (Erythromycin): ↓ Metabolism of theophylline + ↑ T ½.
		aminophylline used in Status asthmaticus			

2) **Prophylactic therapy** (Anti-inflammatory Agents): reduces the frequency of attacks

Glucocorticoids (Immunosuppressant effects)	**MOA:** Anti-inflammatory action by Inhibiting phospholipase A2 + Upregulate β2 receptors. - they're NOT bronchodilators they reduce bronchial inflammation.	**P.K:** Inhalation Best choice: Budesonide & Fluticasone, beclomethasone. Orally: Prednisone, methyl prednisolone. Injection: Hydrocortisone, dexamethasone.	**Uses:** -Inflammatory & autoimmune disorders, Antiemetics, prophylactic medications. -Systemic corticosteroids for Status asthmaticus (IV)	**Metabolic effects:** Hyperglycemia, Stimulation of lipolysis. ↑protein catabolism, ↓protein anabolism. **Mineralocorticoid effects:** hypertension, hypokalemia, sodium-fluid retention. Depression, Osteoporosis.
Leukotrienes antagonists	zafirlukast montelukast pranlukast	**MOA:** Selective, reversible antagonists of CysLT1 receptors, bronchodilators, have anti-inflammatory action. **Uses:** Prophylaxis of mild to moderate asthma, Aspirin-induced asthma , Antigen and exercise-induced asthma. NOT effective in acute asthma. **ADR:** Elevation of liver enzymes, headache, dyspepsia.		
Mast cell stabilizers	Cromoglycate Nedocromil	-Children respond to them better than adults - has bitter taste, can cause irritation of the URT.		
Anti-IgE monoclonal antibody	Omalizumab	**MOA**: monoclonal antibody directed against human IgE → prevents IgE binding with its receptors on mast cells & basophiles → ↓ release of allergic mediators. Expensive-not first line therapy. **Uses**: moderate to severe allergic asthma which doesn't respond to corticosteroids.		
Long acting 2-agonists (Selective)	Salmeterol Formoterol	**P.K**: Long acting **bronchodilators** but NOT used for acute asthma. **Uses**: nocturnal asthma. Combined with inhaled corticosteroids.	**Advantages & ADRS:** same as short acting selective β2 agonists	

Drugs used in chronic obstructive pulmonary disease (COPD)

Treatment: Supportive therapy only

Inhaled bronchodilators in COPD:

Unlike in asthma ; antimuscarinic are superior to β2 agonists in COPD.

Inhaled antimuscarinics	β2 agonists these drugs can be used either alone or combined : **Short acting**	**Long Acting-less dose frequency**
Ipratropium & Tiotropium.	Salbutamol + Ipratropium	Salmeterol+Tiotropium

Other treatment:

- Inhaled glucocorticoids
- Oxygen therapy
- Antibiotics

(specifically macrolides such as azithromycin to reduce the number of exacerbations.)

- Lung transplantation

Drugs for rhinitis

	Gen	drug	duration	Actions	Uses	ADRs
Anti-histamines generations	1st	**Alkylamine:** Chlorpheniramine (Chlorphenamine) **Ethanolamine:** Dimenhydrinate Diphenhydramine **Ethylenediamine:** Antazoline **Phenothiazine:** Promethazine **Piperazine:** Cyclizine **Piperidine:** Azatidine, Ketotifen **Miscellaneous:** Cyproheptadine	short duration Can cross BBB and cause sedation	1.action of all the H1 receptor blocker is similar. 2.much more effective in preventing symptoms than reversing them. 3.have additional effects **(especially 1st generation)** unrelated to their blocking H1 receptors which reflect binding of H1 antagonists to: -Cholinergic -Adrenergic -Serotonin receptors	•Allergic rhinitis •Motion sickness •Nausea and vomiting •Common cold •Allergic dermatoses	• Sedation • tinnitus • fatigue • dizziness • blurred vision • dry mouth. these reactions were more evident in 1st generation **Drug interaction:** • CNS depressants • cholinesterase inhibitors **Over-dose:** acute poisoning are those on CNS; including hallucinations, excitement, ataxia and convulsions Ataxia:abnormal gait.
	2nd	**Cetirizine Loratadine**	long duration (better control) Can't cross BBB → no sedation			
	3rd ★	**Levocetirizine Fexofenadine** (least sedating) **Desoloratadine**				
Anti-allergics		**Mast cell stabilizers:** Cromolyn and Nedocromyl	★ M.O.A decrease Histamine release (mast cell stabilizers by inhibiting Cl channels), i.e. can act only as a prophylactic; **it doesn't antagonize released histamine**		**children** for prophylaxis of perennial allergic rhinitis	Can induce cough, wheezes, headache, rash
		Leukotriene receptor antagonists: Montelukast	Block leukotriene action		prophylaxis of lower respiratory tract allergies	As in asthma
Decongestants		Systemic: **Pseudoephedrine**	α-adrenergic agonists vasoconstrictor of blood vessels in nasal mucosa & reduce the rhinorrhea.		Treatment of nasal stuffiness	nervous , insomnia, tremors, palpitations, and hypertension. **Contra:** hypertension, heart failure, angina pectoris, hyperthyroidism. glaucoma.
		Topical: **1-Phenylethylamines:** • Phenylephrine • Methoxamine **2-Imidazoline:** • Naphazoline • Oxymetazoline HCL • Xylometazoline HCL				Can cause Rebound nasal stuffiness (repeated administration)
Corticosteroid		**Beclomethasone,** budesonide and **fluticasone**	Anti-inflammatory → block phospholipase A2 → ↓ arachidonic acid synthesis → ↓ prostaglandins & leukotrienes		For severe cases **Administration:** inhaled	Nasal irritation, fungal infection, hoarseness of voice
Anticholinergics		Ipratropium	———		★ **Very effective in Vasomotor rhinitis**	Minimal systemic side effects.

Drugs for cough

For reproductive cough

★ Expectorants	MOA	ADRs
Reflex stimulation (Guaifenesin)	Irritate GIT ↓ stimulate gastropulmonary vagal reflex ↓ loosening and thinning of secretions	Dry mouth, chapped lips, risk of kidney stones (uric acid excretion).
Direct stimulation Chronic paranasal sinusitis. e.g. Iodinated glycerol, Na or K iodide/ acetate , Ammonium chloride, Ipecacuahna.	Stimulate secretory glands ↓ ↑ respiratory fluids production	Unpleasant metallic taste, hypersensitivity, hypothyroidism, swollen salivary glands & flare of old TB.

Mucolytics	MOA	Overview
Hypertonic saline & NaHCO3	↓ Viscoelasticity by ↑ water content	-
Steam inhalation	↓ Adhesiveness	
N-Acetyl Cysteine	Breakdown S-S bonds → less viscid mucous	A free radical scavenger used in acetaminophen overdose
Bromhexine and its metabolite (ambroxol)	Synthesize serous mucus + activate ciliary clearance and increases the immune defence	↑immune defence → ↓antibiotics usage + ↓pain in acute sore throat
Pulmozyme (Dornase Alpha or rhDNAase)	Cleavage of extracellular bacterial DNA, that contributes to viscosity of sputum in case of bacterial infection only	A recombinant human (deoxyribonuclease 1) enzyme genetically engineered that is neubilized

For dry cough: Antitussive agents

Peripherally	Drug	Target
Inhibitors of Airway stretch receptor	Demulcents (protective coat): Lozenges & gargles	Pharynx
	Emollients (protective coat): Menthol & eucalyptus	Larynx
	aerosols or inhalation of hot steam: Eucalyptol & tincture benzoin compound	Tracheobronchial
	local anesthetic aerosols: Lidocaine, benzocaine & tetracaine	Bronchoscopy or bronchography
Inhibitors of pulmonary stretch receptor in Alveoli	Benzonatate	**MOA:** reduces sensitivity (numbing) of receptors by local anesthetic action.

Centrally	MOA	ADRs
Opioids: Codeine & pholcodine	activating μ opioid receptors	
Non-opioids: AntiHistamine & **Dextromethorphan**	↑ **Threshold at cough center.** It has benefits over opioids in being: 1. As potent as codeine 2- Less constipating 3- No respiratory depression. 4- No inhibition of mucociliary clearance 5- No addiction.	In normal doses: Nausea Vomiting Dizziness Rash Pruritus OVERDOSE: Opiate-like ADRs on RT & GIT + Hallucination

adrenergic drugs

drug	receptor	P.K \ contra..	uses
Direct / Catecholamine / Non-selective			
Adrenaline	α1 α2 β1 β2	**P.K:** I.V, S.C, inhalation **contra:** • CHD, Ischemic heart disease (angina) •Hyperthyroidism •glaucoma	1-locally : .Haemostatic or combined with local anesthetic 2-systematically: •In acute asthma (status asthma) .Anaphylactic shock .Cardiac arrest (i.v.)
Noradrenaline	α > β1	IV	1-Locally: as a local haemostatic with local anesthetic 2-Systemically: hypotensive states
Isoprenaline	β	**P.K:** . Parenteral ,inhalation **contra:** •CHD •Hyperthyroidism	. cardiac arrest (Parenteral). . acute attack of asthma (inhalation).
Dopamine	D1 >β1 >α1	Given parenterally by infusion	. Drug of choice in treatment of shocks. . acute heart failure (HF) but Dobutamine is better.
Direct / catecholamine / Selective			
Dobutamine	β1	IV	. short term management of cardiac decompensation after cardiac surgery . in acute myocardial infarction & heart failure
Direct / Non-catecholamine / Selective			
Midodrine & Phenylephrine	α1	**P.K:** Orally **contra:** hypertension	. Systemically: Vasopressor (anti-hypotensive) . Topically: Haemostatic, Mydriatic and Nasal decongestant
Salbutamol	β2	Orally, by inhalation or parenteral	Bronchodilator for acute attacks of asthma & COPD

Terbutaline	β2	___	Bronchodilator & Tocolytic
Ritodrine	β2	Orally or injection	Tocolytic
Direct / Imidazoline / Selective			
Clonidine	Presynaptic α2	Orally or patch	Antihypertensive drug
Brimonidine	α2 agonist	___	glaucoma
Indirect / Non-catecholamine / Non-selective			
Amphetamine	α & β similar to epinephrine but has CNS stimulant effects	orally	Not used therapeutically anymore **ADR**: Tachyphylaxis & psychosis
Dual / Non-catecholamine / Non-selective			
Ephedrine	α & β CNS stimulant effects (less than amphetamine)	orally	Not used therapeutically anymore **ADR**: Tachyphylaxis
Pseudo-ephedrine	α & β	___	. has less pressor effects compared to ephedrine. . Used as nasal & ocular decongestant & in flu remedies

drugs of Anaphylaxis

1st line therapy

Adrenaline
(A Sympathomimetic)

MOA: nonselective (α1, α2, β1, β2, β3) agonist.
Uses: Drug of choice for anaphylactic shock.
Contra: cardiac patient> 40 years ,Patients taking β-blockers
ADRS: Dysrhythmias. if given IV
P.K: IM? easy -safety-Repeat as needed

2nd line therapy

Corticosteroids
(anti- inflammatory)

MOA:
Non-genomic action in anaphylactic shock:
●Reverse hypotension & bronchoconstriction by ↓ release of inflammatory mediators.(help to limit biphasic reactions)
● ↓ mucosal swelling and skin reaction.
Corticosteroids are not used alone in anaphylaxis

H1 Blockers

pheniramine

MOA: can help to **counteract histamine-mediated vasodilation & bronchoconstriction** after mast cells are de-granulated, May help to **limit biphasic reactions** by **blocking histamine** receptors
P.K: IM or IV (can't be used alone, not lifesaving)

Adjuvant to 2nd line therapy

H2 Blockers

Ranitidine , Cimetidine, Pantoprazole

MOA: these drugs are associated with serious adverse drug interactions.
Pantoprazole is a Proton pump inhibitor it is safer and given once. " to decrease GIT acidity, it's safer than H2 blockers "
Contra: Cimetidine shouldn't be given to elderly, renal/hepatic failure, or if on b-blockers.
Why? Because it inhibits cytochrome P450 which controls drug-drug interactions. So when given it may increase the toxicity of other drugs , therefore it's replaced by ranitidine

Bronchodilators
(used for asthma as well)

Salbutamol
(inhalation)

β2 agonist:●short acting,●Rapid onset of acting ●↓ mediators released from mast cell and basophils. ●inhibit airway microvascular leakage● (Bronchodilation)*Not effective in Patients taking β blockers,

Ipratropium
(inhalation)

Anticholinergic: ●longer acting ●Less rapid in action●↓**secretion**
● ↓ cGMP,therefore decreases the contractility of smooth muscles.

Aminophylline
(Parenteral IV)

●May be useful in Treatment of anaphylaxis **when inhaled** Bronchodilators are not effective & bronchospasm is persistent. ●Given in hospital setting as levels of drug should be Therapeutically Monitored (has narrow therapeutic index)
● Increase cAMP ● Smooth muscle relaxation

Glucagon

Glucagon

MOA:
● act on glucagon receptors in the heart
Action:
● increase cardiac cyclic AMP.
● This effect is completely independent of Adrenergic Receptors, **Therefore effective in spite of β-adrenergic blockade.** ●no evident bronchodilation

Uses:
severe anaphylaxis in patients taking b-blockers

TB Drugs

Drug	Uses	MOA	ADRs
First-line treatment			
Isoniazid	Treatment of: -TB, latent TB in patients with Positive tuberculin skin test, Prophylaxis against TB. **Drug interaction:** (enzyme inhibitor) cytochrome P450 2C19 isoform	- Bacteriostatic & Bactericidal. -Inhibit synthesis of cell wall (Mycolic acid)	Peripheral neuritis, optic neuritis & hepatitis. Hepatitis with INH, is age dependent; it is rare in persons younger than 20years, risk **increases with age & alcohol use.**
Rifampin	Treatment & Prophylaxis for TB. - **Drug interaction:** (enzyme inducer) **strongly induces** most cytochrome P450 isoforms 2C19,2C9,3A4. .	-Bactericidal. -inhibit RNA synthesis.(Binds to bacterial **DNA-dependent RNA polymerase enzyme**)	-Harmless red-orange decolorized secretions. - Hepatitis. - Flu-like syndrome. - Hemolytic anemia .
Ethambutol	Combined with other drugs to treatment TB.	Inhibit mycobacterial **arabinosyl transferase** disrupts the assembly of mycobacterial cell wall. .	- Impaired visual acuity.(Optic neuritis). -Red-green color blindness. **Contraindicated: Children under 5 years .**
Pyrazinamide (PZA)	-Mycobacterial infections mainly in multidrug resistance cases. -It is important in short course (6 months) regimen. -Prophylaxis of TB .	**converted to pyrazinoic acid (the active form)** which disrupts mycobacterial cell membrane metabolism & transport functions. converted to its active form by the bacteria	-Hepatotoxicity(common) - Hyperuricemia. -Drug fever & Skin rash.
Streptomycin	-Severe Life-threatening form of TB a meningitis, disseminated disease (never used as a first option)	-Bactericidal. -Inhibit of protein synthesis by binding to 30S ribosomal subunits .	-Ototoxicity. -Nephrotoxicity. -Neuromuscular blac **Reminder: it can cross the placenta >contraindicated in pregnancy**
Second- line treatment			
Ethionamide	**2nd line treatment of TB (po).** po = orally	**Inhibit mycolic acid synthesis** **same MOA as INH**	-Teratogenic. - Poorly tolerated due to severe **Gastric irritation & neurological manifestation.**
Rifabutin	**Prevention & treatment of TB & atypical TB.**	**-RNA inhibitor.** **-Cross-resistance with Rifampin is completed .** **-Enzyme inducer**	**-GIT intolerance.** **-Orange-red discoloration of body secretions.**
Fluoroquinolones (ciprofloxacin)	effective against MRTB **(multidrug- resistant tuberculosis.)**	*Fluoroquinolones are a class of antibiotics that includes Ciprofloxacin	-

Respiratory Tract Infection

Drug	Pharmacokinetics	Uses	ADRs
Cell wall synthesis inhibitors (through inhibition of peptidoglycan layer of the cell wall.)			
β-lactam antibiotics Penicillins (Bactericidal)			
Amoxicillin (Broad spectrum)	Clavulanic acid	**URTI's, LRTI's.**	Hypersensitivity Diarrhea . Nephritis. Superinfections. Convulsions (after high IV dose or in renal failure).
Ampicillin (Broad spectrum)	Sulbactam		
Piperacillin (Broad spectrum)	Tazobactam		
	Drug interaction: Probenecid Slows their excretion.		
β-lactam antibiotics Cephalosporins (Bactericidal)			
Cephalexin-PO	1st Generation Mainly against gram + bacteria.	URTI ' s	•Hypersensitivity reactions. •Thrombophlebitis. •Superinfections. • Diarrhea.
Cefuroxime-PO Cefaclor-PO	2nd Generation Mainly against Gram - bacteria. (Active against β-lactamase –producing bacteria.)	• URTI's • LRTI's	
Ceftriaxone-IV Cefotaxime-IV Cefixime-PO	3rd Generation - Mainly against Gram - bacilli. -Penetration into CNS -Half-life(4-7h) **(Ceftriaxone only)** -Excreted mostly in urine "All generations" **Drug interaction: Probenecid** Slows their excretion."All generations"	Pneumonia	
Protein synthesis inhibitors (by binding to 50S subunit of the bacterial ribosomes)			
Macrolides (Bacteriostatic) (Bactericidal at high concentration)			
Erythromycin	-	-Chlamydial pneumonia -Legionella pneumonia	Hypersensitivity Reactions GIT disturbances. Erythromycin can cause hepatic failure.
Azithromycin	Mainly against Gram – bacteria -Inactive metabolite -No effect on cytochrome P450 system. -Undergo Biliary excretion		
Clarithromycin	Mainly against gram + bacteria -Active metabolite -Inhibits cytochrome P450 system. -Undergo Biliary excretion		

Respiratory Tract Infection (Cont.)

DNA synthesis inhibitors (Inhibit DNA Gyrase enzyme (an enzyme involved in DNA supercoiling)

Drug	Pharmacokinetics	Uses	ADRs
Fluoroquinolones			
Ciprofloxacin Moxifloxacin Gatifloxacin	-Given orally or parenterally. -Excreted mainly by kidney -Concentrates in many tissue (kidney, prostate, lung, bones) Relatively. -given once daily (moxifloxacin & Gatifloxacin) & twice-daily (Ciprofloxacin). **Antibacterial spectrum:** Ciprofloxacin mainly effective Gram - bacteria, Moxifloxacin & Gatifloxacin G – & G + (highly active against Pseudomonas species) **Contraindications**: < 18 years, Pregnancy, Breast feeding.	-Acute exacerbation of COPD. -Community acquired pneumonia. -Legionella pneumonia.	Nausea, vomiting, diarrhea. **CNS effects:** (Confusion, insomnia, headache, anxiety). Arthropathy. Phototoxicity.
Protein synthesis inhibitors (by binding to 30-S subunit of the bacterial ribosome.)			
Aminoglycosides			
Gentamicin	●Given parenterally (IM, IV) poorly absorbed orally (highly charged). ● Cross placenta **Contraindication: pregnancy and breastfeeding** ● Excreted unchanged in urine ● Half-life: 2-3 h & increased to 24-48 h in renal impairment	-Severe infection caused by **gram -ve organisms**	-Ototoxicity -Nephrotoxicity -In very high doses → neuromuscular blockade that results in respiratory paralysis
Tetracyclines "Contraindication: pregnancy and lactation"			
Doxycycline	- Food & di & tri-valent cations **(Ca, Mg, Fe, AL) impair absorption.** it bind With Ca ,so patient should avoid dairy products - Distributed well, including CSF -Cross placenta and excreted in milk **Contraindication: pregnancy, breastfeeding and children below 10 years** - Largely metabolized in the live	-Active against Gram+ and-. -Treatment of URTIs caused by S.pyogenes, S.pneumonia & H.influenza.	-nausea, vomiting ,diarrhea & epigastric pain -Thrombophlebitis – I.V -Hepatic toxicity - Brown discolouration of teeth in children - Deformity or growth inhibition of bones in children -Phototoxicity -Vertigo -Superinfections.

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Team 438

GOOD LUCK

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PHARMACOLOGY
435

**A very special thanks to our AMAZING team members,
your hardworking efforts are truly appreciated.
YOU GUYS ROCK !**

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