PHARMACOLOGY

Lecture: drugs for asthma & COPD

OBJECTIVES:

The students should be able to

1. Different types of drugs used for treatment of asthma
2. Differentiate between treatment and prophylactic therapy for asthma
3. Recognize the different types of bronchodilators regarding pharmacokinetics, pharmacodynamics, uses and side effects.
4. Identify the different anti-inflammatory drugs for asthma in respect to kinetics, dynamics, uses and side effects.

Bronchial asthma VS COPD

Obstructive diseases	Bronchial Asthma	COPD (chronic obstructive pulmonary disease)
Definition	Asthma is a chronic (often reversible) inflammatory disorder of bronchial airways that result in airway obstruction in response to external stimuli or triggers (as pollen grains, cold air and tobacco smoke, animal fur). Inflammation causes bronchospasm and mucus blockade of airways. • occurs in adults below 35 years old, common in children.	COPD is a chronic irreversible airflow obstruction, caused by lung damage and inflammation of the air sacs (alveoli). Damage of the air way and the alveoli reduces Surface area, which reduces the ability of respiration. Bronchioles lose their shape and become clogged with mucus. • Includes emphysema + chronic bronchitis • occurs in adults above 35 years old, never in children.
Causes	Exogenous chemicals or irritants, Chest infection, Stress, cold air is the trigger during exercise, Pets, Seasonal changes, Emotional conditions, Some drugs as **aspirin and β- blockers.**	**high risk factor:** Smoking **Other factors can contribute:** air pollution & genetic factors
Treatment	**Anti asthmatic drugs:** **1- Bronchodilators (Quick relief medications= Rescue medication)** "علاج نوبات الربو الحادة" **used to** relieve acute episodic attacks of asthma. • Short acting β2-agonists • Anti-muscarinics • Xanthine preparations **2- Anti-inflammatory Agents (Prophylactic therapy) "وقاية" (Control therapy)** Drug therapy for long-term control of asthma is designed to reverse and prevent airway inflammation. **used to** reduce the frequency of attacks, and nocturnal awakenings. • Corticosteroids • Mast cell stabilizer • Leukotrienes antagonists • Anti-IgE monoclonal antibody • Long acting ß2-agonists YouTube asthma	**Drugs for COPD:** ❖ Inhaled bronchodilators: **1. Inhaled anti-muscarinics** ➢ In COPD -unlike asthma- Ipratropium & tiotropium are superior to β2 agonists **2. β_2 agonists** ➢ These drugs can be used either alone or combined with anti-muscarinics: – salbutamol + ipratropium (short acting) – salmeterol + Tiotropium (both are long acting, thus less dose frequency is required). ❖ Inhaled glucocorticoids (for inflammation) ❖ Oxygen therapy (for COPD's hypoxia) ❖ **Antibiotics** specifically macrolides such as **azithromycin** to reduce the number of exacerbations by inhibiting bacterial infection causing COPD exacerbations ❖ Lung transplantation in very severe cases YouTube COPD

Bronchial asthma

Airways Innervations

Afferent nerves (sensory)

- Irritant receptors in upper airways.
- C-fiber receptors in lower airways.

Afferent nerves (sensory) stimulated by :

- Exogenous chemicals or irritants
- Physical stimuli (cold air)
- Endogenous inflammatory mediators e.g.: histamine (causing airway hyper-reactivity)

In treatment of asthma, bronchodilation is acquired by using M3 antagonists or B2 agonists .

Efferent nerves (motor)

Parasympathetic supply: M3 receptors in smooth muscles and glands.

stimulation of M3receptors by the vagus nerve causes Bronchoconstriction & Increases mucus secretion

No sympathetic supply but scattered B_2 receptors in smooth muscles and glands.

Stimulation of B2 causes Bronchodilation & Decreases mucus secretion

Characters of airways in asthmatic patients :

- **Airway hyper-reactivity:** abnormal sensitivity of the airways to any external stimuli.
- Inflammation: ↑ edema, swelling + ↑ Thick mucus production.
- Bronchospasm (constriction of the bronchial smooth muscles).

Symptoms of asthma:

Asthma produces recurrent episodic attack of : Acute bronchoconstriction, Shortness of breath, Chest tightness, Wheezing, Rapid respiration, Cough.

Symptoms can happen each time the airways are irritated by inhaled irritants or allergens.

Anti-asthmatic drugs:

1st: Bronchodilators (quick relief medication)

- Short acting β2-agonists: first and only choice for acute asthma attacks
- Anti-muscarinics: COPD: first choice. Asthma: adjunctive to B2-agonists
- Xanthine preparations

1. β- adrenoceptor agonists (Sympathomimetics)

Mechanism of Action:

- **Direct β2 stimulation → stimulate adenyl cyclase → ↑ cAMP → bronchodilation.**
- **Increase mucus clearance by increasing ciliary activity.**
- **Stabilization of mast cell membrane** (release of histamine will decrease).

	Non-selective β_2 agonist	Selective β_2 agonist (preferable)	
Examples	-Epinephrine -Isoprenaline	Short acting: -Salbutamol (albuterol) -Terbutaline	Long acting: - Salmeterol - Formoterol
Advantages	• Potent bronchodilator . • Given subcutaneously , (any drug that can affect the heart is given s.c not I.V to reduce the side effects on the CVS) • Rapid action (maximum effect within 15 min) • Has short duration of action (60-90 min) • Adrenaline is the drug of choice for acute anaphylaxis (hypersensitivity reaction**), can be used for asthma BUT selective B2 are better**	• Mainly given by inhalation • Can be given orally, parenterally. • Minimal CVS side effects. • Suitable for asthmatic patients with CV disorders as hypertension or heart failure.	
Dis-advantages	- Not effective orally . - Hyperglycemia. - Skeletal muscle tremor. - CVS side effects (β_1 actions): tachycardia, arrhythmia, hypertension. - Contraindications: CVS patients (hypertension, heart failure) ,diabetic patients	-Skeletal muscle tremors . - Nervousness. - Tolerance (β-receptors down regulation (due to repeated use, resulting in decrease in response) - Overdose may produce tachycardia due to β_1 stimulation.	

Selective β2 -agonists

Selective β2 –agonists:

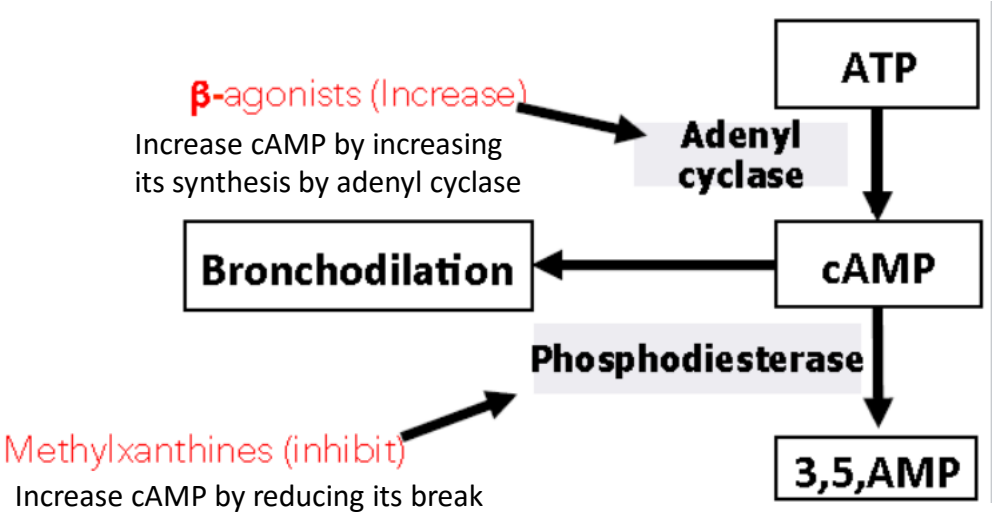
- Are mainly given by inhalation by (metered dose inhaler or nebulizer)

- Can be given orally, parenterally.

	Short acting selective ß$_2$ agonists	Long acting selective ß$_2$ agonists
Examples	-Salbutamol (albuterol): given by inhalation, orally , I.V(only in status asthmaticus) -Terbutaline: given by inhalation, orally, s.c.	- Salmeterol -Formoterol Are given by inhalation.
Pharmaco-kinetics & dynamics	- Have rapid onset of action (15-30 min) - Short duration of action (4-6 hr.) - Used for acute episodic attack of asthma (drugs of choice)	- Long acting bronchodilators (12 hours) due to high lipid solubility (creates depot effect). depot= storage - Are not used to relieve acute episodes of asthma. - Used for nocturnal asthma. «الربو الليلي» - combined with inhaled corticosteroids to control asthma as prophylactic therapy (to decreases the number and severity of asthma attacks)

Inhaler

Nebulizer



* Team 434

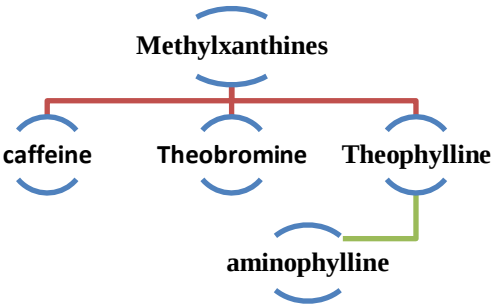
2. Muscarinic antagonists

	Ipratropium short duration of action (3-5 h)	**Tiotropium** longer duration of action (24 h).
Mechanism of action:	– Act by blocking muscarinic receptors . – Have delayed onset of action. – Have minimal systemic side effects, because: – given by aerosol inhalation (local effect). – Quaternary derivatives of atropine (polar). Thus don't diffuse into the blood neither enter CNS.	
Pharmaco-dynamics	– Inhibit bronchoconstriction and mucus secretion – Less effective than β_2-agonists. – No anti-inflammatory action only bronchodilator	
Uses	♣ Main choice in chronic obstructive pulmonary diseases (**COPD**). The main supply of Respiratory system is from Autonomic nervous system and the predominant is the parasympathetic >> main line treatment affect on parasympathetic ♣ In acute severe asthma combined with β_2 agonists & corticosteroids. Response in patients is variable, in some severe cases, β_2 agonists can't relief the bronchoconstriction, so we have to add other medications (either Antimuscarinics or corticosteroids) ♣ Never use as a rescue medication. Since it has delayed response and it is less effective than β_2-agonists	
Side effect	- dryness of mouth (parasympathomimetic Antimuscarinic side effects) Antimuscarinics have other side effects, but since it is given by inhalation the only prominent ADR is dryness of the mouth.	

3. Methylxanthines (Theophylline - aminophylline)

Mechanism of action:

1. Phosphodiesterase inhibition → ↑ cAMP → bronchodilation
2. Adenosine receptors antagonists (A1) → bronchial smooth muscle relaxation
3. Increase diaphragmatic contraction
4. Stabilization of mast cell membrane



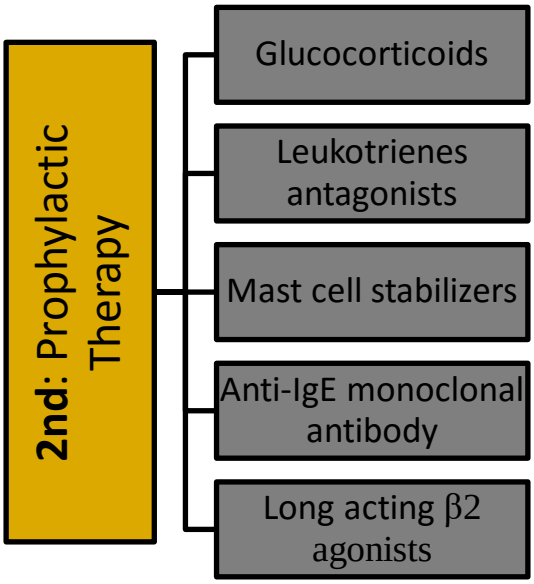
	Pharmacological effects :	Side Effects :
Respiratory system	– Bronchial muscle relaxation – ↑contraction of diaphragm → improve ventilation	Low therapeutic index: **(narrow safety margin),** therefore, monitoring of theophylline blood level is necessary.
Kidney	↑renal blood flow, weak diuretic action	
GIT	↑ gastric acid secretions #peptic ulcer	nausea & vomiting
CVS	↑ heart rate (tachycardia), ↑ force of contraction	hypotension, arrhythmia.
CNS	• stimulant effect on respiratory center. • decrease fatigue & elevate mood. All effects are similar to caffeine's	Overdose = increased concentration in blood: tremors, nervousness, insomnia, convulsion

Pharmacokinetics :

- **metabolized by Cytochrome P450 enzymes in liver, thus has many drug interactions.**
- T ½= 8 hours, this half-life may change depending on drug interaction:
  - ✓ **Enzyme inducers:** e.g. :Alcohol & Nicotine
    - as phenobarbitone hypnotic drug (helps sleeping) & rifampicin (for TB) ↑ metabolism of theophylline → ↓ T ½.
  - ✓ **Enzyme inhibitors:**
    - as erythromycin (antibiotic) : ↓ metabolism of theophylline → ↑ T ½.

Methylxanthines	
Theophylline	**Aminophylline**
given orally	Salt derivative of theophylline, given as slow infusion
Second line drug in asthma	Used for status asthmatics (severe form of asthma)

Prophylactic Therapy: 1. Glucocorticoids



(control medications/prophylactic therapy/ Anti-inflammatory drugs) effects:

- ↓ bronchial hyper-reactivity.
- ↓ reduce inflammation of airways
- ↓ reduce the spasm of airways

Glucocorticoids Mechanism of action:

Inhibition of phospholipase A2 (inhibiting arachidonic acid degradation pathway)

- ↓ prostaglandin and leukotrienes
- ↓ Number of inflammatory cells in airways.
- Mast cell stabilization →↓ histamine release.
- ↓ capillary permeability and mucosal edema.
  Note: when capillary permeability decreases, it leads to fluids staying in the circulation which will prevent edema but will cause hypertension and weight gain
- Inhibition of antigen-antibody reaction. Thus decrease immune response
- Upregulate β2 receptors (have additive effect to β2 agonists).

Glucocorticoids in asthma

- Are not bronchodilators
- Reduce bronchial inflammation
- Reduce bronchial hyper-reactivity to stimuli
- Have delayed onset of action (effect usually attained after 2-4 weeks).
- Maximum action at 9-12 months.
- Given as prophylactic medications, used alone or combined with β2 agonists.

(because of the additive effects, dose of glucocorticoids could be reduced)

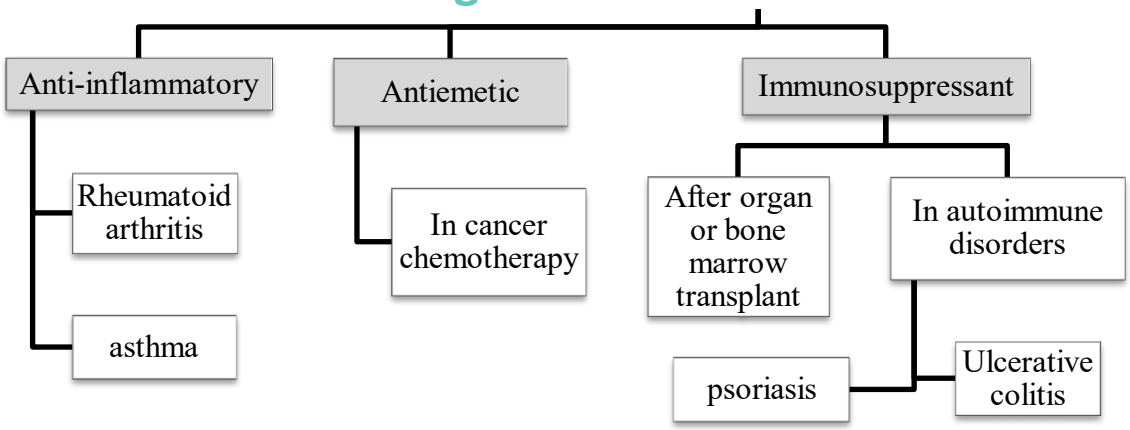
- Effective in controlling allergic, exercise, antigen and irritant-induced asthma.

YouTube Introduction to glucocorticoids

Systemic VS inhaled Glucocorticoids

	Systemic Glucocorticoids	Inhaled Glucocorticoids
Adminis-tration	**Orally:** • Prednisone • Methyl prednisolone **Injection:** • Hydrocortisone • Dexamethasone	-Budesonide -Fluticasone -Beclometasone Given by inhalation (metered-dose inhaler).
Used in	Status asthmaticus (i.v.) *Because unlike inhaled corticosteroids, systemic corticosteroids will show most of the side effects so it is only reserved for status asthmaticus where using corticosteroids is extremely important.	**Should be considered when asthma is not maintained, for adults/children with the following:** • using inhaled β2 agonists three times/week (inflammatory changes cause attacks where β2 agonists are insufficient and need to be used repeatedly) • symptomatic three times/ week or more • waking one night/week.
Side effects	**Remember: pharmacological effects of a drug other than the desired ones, are regarded as "side effects":** •Adrenal suppression • Susceptibility to infections, because it has immunosuppressant effect. • Bone loss (osteoporosis), due to Inhibited bone formation and ↓calcium absorption from GIT. This causes Growth retardation in children • Behavioral changes: depression & Psychosis ❖ Mineralocorticoid effects: • sodium/fluid retention → weight gain, •↑ blood volume (hypertension) •(because of the decreased capillary permeability) •↑potassium excretion (hypokalemia). ❖ Metabolic effects: • Hyperglycemia •Stimulation of lipolysis, which leads to Fat redistribution •↑protein catabolism & ↓protein anabolism. protein causes Cataract when deposited on the eye. **Withdrawal:** corticosteroids cause adrenal suppression. With prolonged suppression, the adrenal glands atrophy, and can take months to recover full function. Thus, abrupt(sudden) stop of corticosteroids should be avoided and dose should be tapered in order to avoid adrenal insufficiency syndrome.	They have first pass metabolism, which would be helpful to prevent systemic effects if any inhaled particles reach the liver. They are the best choice to control asthma, due to less side effects: • Oropharyngeal candidiasis (thrush). Which is an infection of the mouth and throat by a yeastlike fungus, causing whitish patches • Dysphonia (voice hoarseness). These effects could be avoided by gargling with water after using the inhaler to washout the deposits.

Clinical uses of glucocorticoids



2. Mast cell stabilizers:

e.g. Cromoglycate – Nedocromil

- act by stabilization of mast cell membrane (reduce histamine release)
- given by inhalation (aerosol, nebulizer).
- Have poor oral absorption (10%)

Pharmacodynamics

- **Not** effective in acute attack of asthma, because they are **Not** bronchodilators
- Prophylactic anti-inflammatory drugs
- Reduce bronchial hyper-reactivity.
- Effective in controlling exercise, antigen and irritant-induced asthma.
- Children respond better than adults

Uses

- Prophylactic therapy in asthma especially in children.
- Allergic rhinitis.
- Conjunctivitis.

Side effects

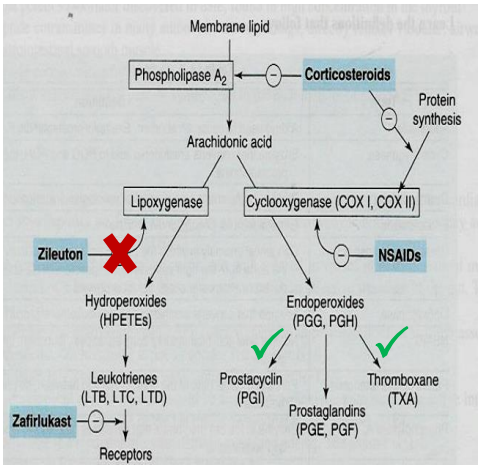
- Bitter taste طعمه مُر
- minor upper respiratory tract irritation (burning sensation, nasal congestion)

3. Leukotrienes antagonists

Leukotrienes:

- synthesized by inflammatory cells found in the airways (eosinophils, macrophages, mast cells).
- produced by the action of 5-lipoxygenase on arachidonic acid.
- **Leukotriene B4:** chemotaxis of neutrophils
- **Cysteinyl leukotrienes (C4, D4 & E4):**
  - bronchoconstriction
  - increase bronchial hyper-reactivity
  - ↑ mucosal edema, ↑ mucus secretion

Arachidonic acid degradation pathway:



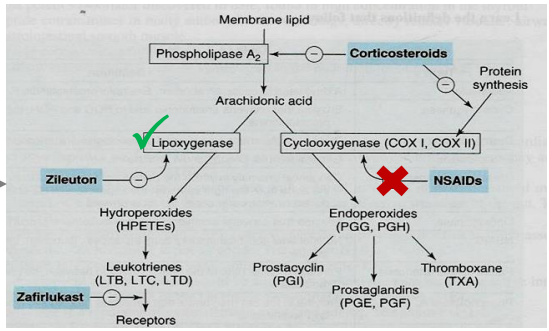
Leukotriene receptor antagonists:

e.g. zafirlukast, montelukast, pranlukast (to memorize: luk = lock leukotriene)

- are selective, reversible antagonists of cysteinyl leukotriene receptors **($CysLT_1$receptors).**
- Taken orally.
- Bronchodilators.
- Have anti-inflammatory action, but less effective than inhaled corticosteroids

Uses:

- **Not** effective in acute attack of asthma.
- **Used for Prophylaxis** of mild to moderate asthma.
- Aspirin-induced asthma. **WHY?**
- Antigen and exercise-induced asthma
- Can be combined with glucocorticoids , because they have glucocorticoids' sparing effect (additive), they potentiate corticosteroid actions, thus lower dose of glucocorticoids can be used.



Because aspirin block Cyclooxygenase so it will shift to Lipoxygenase which produce a lot of leukotrienes then more bronchoconstriction

Adverse effects:

Elevation of liver enzymes, headache, dyspepsia

4. Anti-IgE monoclonal antibody

- **Anti-IgE monoclonal antibody** E.g. Omalizumab , is a monoclonal antibody directed against human IgE
- given by injection (subcutaneous)

Suffix mab= antibody drug, always given by injection (not orally) because it is a protein

- prevents IgE binding with its receptors on mast cells & basophiles, thus ↓ release of allergic mediators.
- Expensive, therefore it is not first line therapy.
- used for treatment of moderate to severe allergic asthma which does not respond to high doses of corticosteroids.

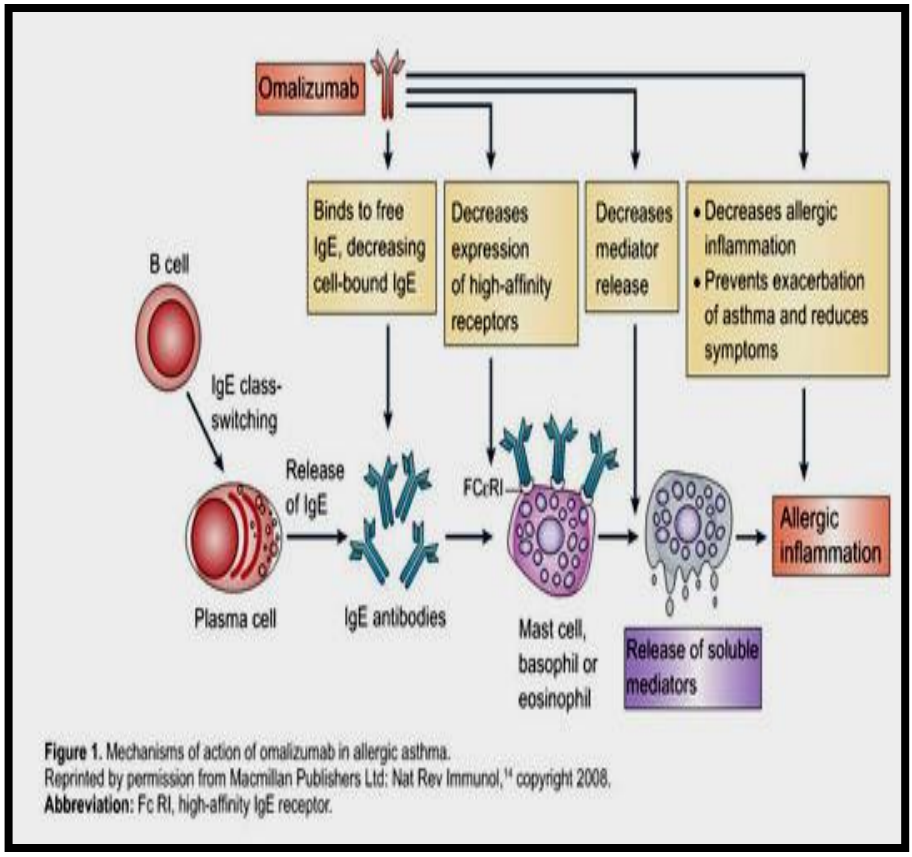


Figure 1. Mechanisms of action of omalizumab in allergic asthma.
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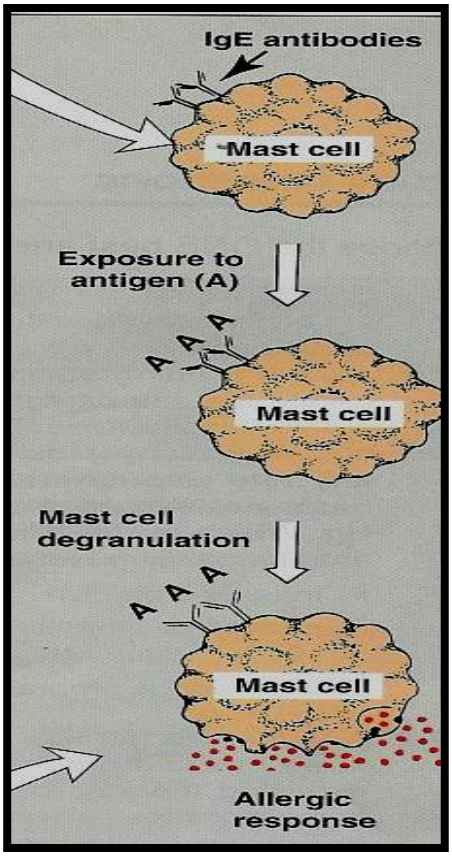
Abbreviation: Fc RI, high-affinity IgE receptor.



Bronchodilators (relievers for bronchospasm)

Drugs	Important notes
Selective Short acting B2 agonists: **Salbutamol, terbutaline**	• Stimulate Adenyl cyclase. ↑ cAMP • given by **Inhalation** • It is the **main choice** in acute attack of asthma
Antimuscarinics: **Ipratropium (Short)** **Tiotropium (long)**	Block M receptors **Main drugs For COPD** Given by **Inhalation**
Xanthine derivatives:	Inhibits phosphodiesterase . ↑ cAMP
Theophylline	**(orally)** 2nd line drug in asthma
Aminophylline	**(parenterally)** for status asthmatics
Non-selective β2 agonist: Epinephrine - Isoprenaline	• **Only adrenaline is the choice for Anaphylaxis (hypersensitivity reaction), can be used for asthma but not selective**

Anti-inflammatory drugs (prophylactic)

Corticosteroids:	(Inhibit phospholipase A2)	
Fluticasone, budesonide, Beclometasone	**Inhalation,** First choice in control of asthma	
Prednisolone, Methyl prednisolone	**Orally**	**for** Status asthmaticus (i.v.)
Dexamethasone, Hydrocortisone	**Parenterally**	
Mast stabilizers: **Cromoglycate (Cromolyn), Nedocromil**	**Inhalation, used for prophylaxis in children**	
Cysteinyl antagonists (CyLT1 antagoist) **Zafirlukast, montelukast, pranlukast**	**Orally. Used for Prophylaxis** of mild to moderate asthma.	
Omalizumab (Anti IgE antibody)	**Injection, SC** used for treatment of allergic asthma which does not respond to high doses of corticosteroids.	
Selective Long acting B2 agonists: **Salmeterol, formoterol**	• **Stimulate Adenyl cyclase. ↑ cAMP** • **given by Inhalation** • **used for Prophylaxis & Nocturnal asthma**	

SAQ

A 47 year old diabetic female presents to the ER with dyspnea, cough and audible wheezing, she has been taking aspirin for prophylactic purpose. A pulmonary function test (spirometer) was performed, the results showed decreased FEV1 and decreased FEV1/VC ratio. The doctor gave her a drug that relived her symptoms and then prescribed an inhaler to her.

1- What is the best diagnoses in her case?
Intrinsic asthma induced by aspirin.

2- describe the pathogenesis of her condition.
video: https://www.youtube.com/watch?v=NNfx27io8-k

3- What drug did the doctor use to relive her symptoms? explain how it works?
Salbutamol. Fast onset of time so rescue medication
direct β_2 stimulation –→ stimulate adenyl cyclase –→ ↑ cAMP → bronchodilation.

4- What inhaler will you prescribe in her case?
Budesonide and formoterol combined preparation for prophylactic therapy.

5- Is epinephrine fine in her case? and why?
No, because she has diabetes and one of the side effects of epinephrine is hyperglycemia.

6- Mention 3 inflammatory mediators that can be seen in her case. Explain briefly the function of one of them.
Histamine, IL4,5 and 13.
IL4 :
1. Regulates isotype switching in B cells to IgE.
2. Induces MHC II on antigen-presenting cells.
3. Induces adhesion molecule expression.
4. Activate mast cells and eosinophils.

Q- How can we increase cAMP concentration in the body ?
1- using β agonists to stimulate Adenyl cyclase enzyme which convert ATP to cAMP .
2- using Methylxanthines to block Phosphodiesterase enzyme which convert cAMP to 3,5,AMP

Mind map for asthma, made by Monerah AlOmary

Asthma Drugs summary

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

b2-agonists

b2-agonists Mechanism of action:

- direct β_2 stimulation → stimulate **adenyl cyclase** → ↑ cAMP → **bronchodilation**.
- Increase mucus clearance by (increasing ciliary activity).
- Stabilization of mast cell membrane.

Non-selective

epinephrine

Potent Bronchodilator/given by **S.C.**(subcutaneously) /**rapid action** (max effect within 15min) & **short duration** (60-90min)
Uses: *acute anaphylaxis.* **(hypersensitivity reactions)** (Drug of choice)
ADRS: • Not effective orally. / Hyperglycemia. / Skeletal muscle tremor.
• **CVS side effects:** tachycardia, arrhythmia, hypertension.
Contraindications: asthmatic patients with hypertension or heart failure (CVS patients), diabetic patients.

isoprenaline

Same as Epinephrine

Selective

Short action	Salbutamol (albuterol)	**inhalation**, orally, **i.v.**	**Rapid onset of action** (15-30min). **Short duration of action** (4-6 hr). **Used for:** *acute attack of asthma* (**Drugs of choice**).	**Advantages:** Minimal CVS side effects, suitable for patients with CV disorders. **ADRS:** Skeletal muscle tremors. Nervousness Tolerance (β-receptors down regulation). **Overdose** may produce tachycardia due to β1 stimulation.
Short action	Terbutaline	**inhalation**, orally, **s.c.**		
Long action	Salmeterol	by **inhalation**	**Long acting** bronchodilators (12 hr) due to high lipid solubility (creates **depot effect**). Not used to relieve acute episodes of asthma. **Used for:** **nocturnal asthma**. **Combined with:** inhaled corticosteroids (↓ number and severity of asthma attacks)	
Long action	Formoterol			

Muscarinic antagonists

Less effective than β_2-agonists

Ipratropium	Short duration (3-5hr).	Given by aerosol **inhalation**, delayed onset of action. Quaternary derivatives of atropine (polar). Doesn't diffuse into blood nor enter CNS / minimal systemic side effects. **Pharmacodynamics:** Inhibit bronchoconstriction and mucus secretion. No anti-inflammatory action only bronchodilator. **Uses:** Main choice in **COPD** / Never use as a rescue medication. In acute severe asthma combined with β2 agonists & corticosteroids.
Tiotropium	Longer duration (24 h).	

Methylxanthines

Theophylline	Given orally	**Mechanism:** Phosphodiestrase inhibitors = ↑ cAMP = **bronchodilation** • Block adenosine receptors (A1). • Stabilize Mast cell membrane. • ↑ diaphragmatic contraction.	**Pharmacokinetic:** Metabolized by **Cyt P450** enzymes in liver. T ½= 8 hr. **drug interactions:** (with theophylline) **Enzyme inducers:** Phenobarbitone & rifampicin Metabolism/↓T ½. **Enzyme inhibitors:** Erythromycin ↓ Metabolism/↑T ½.	**Uses:** •Second line drug in asthma (theophylline). •Status asthmatics (aminophylline). **ADRS:** Low therapeutic index. **GIT:** nausea & vomiting **CVS:** hypotension, arrhythmia. **CNS:** tremors, nervousness, insomnia, convulsion.
aminophylline	slow infusion			

Pharmacologic effects:
Bronchial muscle relaxation, ↑ diaphragm contraction/improve ventilation.
CVS: ↑ heart rate & contraction force / **GIT:** ↑ secretions.
Kidney: ↑renal blood flow, weak diuretic action
CNS: Stimulant effect on respiratory center / Decrease fatigue & elevate mood /**overdose** (tremors, nervousness, insomnia, convulsion)

Asthma Drugs summary

2) Prophylactic therapy: (Anti-inflammatory Agents) to reduce frequency of attacks, & nocturnal awakenings.

Class	Glucocorticoids	Mast cell stabilizers	Leukotrienes antagonists	Anti-IgE monoclonal antibody
Drugs		Cromoglycate	zafirlukast	
			montelukast	Omalizumab
		Nedocromil	pranlukast	
Mechanism	**Anti-inflammatory action due to:** • Inhibition of **phospholipase A2.** • ↓ prostaglandin and leukotrienes. • ↓ Number of inflammatory cells. • Mast cell stabilization (↓histamine) • ↓ capillary permeability and mucosal edema. • Inhibition of antigen-antibody reaction. **Upregulate β2 receptors** (have additive effect to B2 agonists).	Stabilization of mast cell membrane.	synthesized by inflammatory cells found in the airways (eosinophils, macrophages, mast cells). produced by the action of 5-lipoxygenase on arachidonic acid. **Leukotriene B4:** chemotaxis of neutrophils Cysteinyl leukotrienes C4, D4 & E4: bronchoconstriction increase bronchial hyper-reactivity ↑ mucosal edema, ↑ mucus secretion	Any drug ends with suffix (-mab) means that it deals with antibodies. So it's a protein, and will be broken by stomach.
Pharmacological actions	**Anti-inflammatory actions.** **Reduce bronchial hyper-reactivity to stimuli** **Immunosuppressant effects.** **Metabolic effects:** • Hyperglycemia. • ↑ protein catabolism, ↓ protein anabolism. • Stimulation of lipolysis - fat redistribution. **Mineralocorticoid effects:** • sodium/fluid retention • Increase potassium excretion **(hypokalemia).** • Increase blood volume **(hypertension).** Behavioral changes: **depression**. Bone loss **(osteoporosis)** due to • Inhibit bone formation • ↓ calcium absorption from GIT.	• **Are <u>Not</u> bronchodilators.** • **<u>Not effective</u> in acute attack of asthma.** Prophylactic anti-inflammatory drug Reduce bronchial hyper-reactivity Effective in exercise, antigen and irritant-induced asthma. Children respond better than adults.	are selective, reversible antagonists of cysteinyl leukotriene receptors **($CysLT_1$receptors)** Are bronchodilators Have anti-inflammatory action Less effective than inhaled corticosteroids Have glucocorticoids sparing effect (potentiate corticosteroid actions).	a monoclonal antibody directed against human IgE ▪prevents IgE binding with its receptors on mast cells & basophiles. ▪↓ release of allergic mediators.
Duration	• Delayed onset of action (effect usually attained after **2-4 weeks**). • Maximum action at 9-12 months.			
administration	**Inhalation: Budesonide** & **Fluticasone**, **beclometasone** Have first pass metabolism Best choice in asthma, less side effects. **Orally:** Prednisone, methyl prednisolone **Injection:** Hydrocortisone, dexamethasone.	Given by inhalation (aerosol, nebulizer). Have poor oral absorption (10%)	Taken orally.	Given by injection (s.c.)

Asthma Drugs summary

2) Prophylactic therapy: (Anti-inflammatory Agents) to reduce frequency of attacks, & nocturnal awakenings.

	Glucocorticoids	Mast cell stabilizers	Leukotrienes antagonists	Anti-IgE monoclonal antibody
Drugs		Cromoglycate Nedocromil	zafirlukast montelukast pranlukast	Omalizumab
Clinical use	• Inflammatory disorders (**asthma, rheumatoid arthritis**). • Autoimmune disorders (**ulcerative colitis, psoriasis**) and after organ or bone marrow transplantation as **immunosuppressants**. • Antiemetics in cancer **chemotherapy**. • Given as **prophylactic medications**, used alone or combined with β2 agonists. • Effective in **allergic, exercise, antigen and irritant-induced asthma**. Using **Systemic corticosteroids** for **Status asthmaticus (i.v.).** Inhaled steroids should be considered for adults, children with any of the following features: • **using inhaled β2 agonists three times/week** • **symptomatic three times/ week or more;** • **or waking one night/week.**	• **Prophylactic therapy** in asthma especially in children. • **Allergic rhinitis**. • **Conjunctivitis**.	**Uses of leukotriene receptor antagonists** Not effective in acute attack of asthma. Prophylaxis of mild to moderate asthma. Aspirin-induced asthma Antigen and exercise-induced asthma Can be combined with **glucocorticoids** (additive effects, low dose of glucocorticoids can be used).	(Expensive-not first line therapy) treatment of **moderate to severe allergic asthma** which does not respond to high doses of corticosteroids
Side effects	**With systemic corticosteroids:** 1. Adrenal suppression. 2. Growth retardation in children. 3. Susceptibility to infections. 4. Osteoporosis. 5. Fluid retention, weight gain, hypertension. 6. Hyperglycemia. 8. Cataract. 7. Fat distribution. 9. Psychosis. **Inhalation has very less side effects:** • Oropharyngeal candidiasis (thrush). • Dysphonia (voice hoarseness). **Withdrawal of systemic corticosteroids** Abrupt stop of corticosteroids should be avoided and dose should be tapered (adrenal insufficiency syndrome).	• **Bitter taste** • minor upper respiratory tract **irritation** (burning sensation, nasal congestion)	Elevation of liver enzymes, headache, dyspepsia	

Drugs used in chronic obstructive pulmonary disease (COPD)

What is it:
a chronic irreversible airflow obstruction, lung damage and inflammation of the air sacs (alveoli).

Risk factor:
Smoking + pollution & genetic factors.

Treatment:
- Inhaled bronchodilators
- Inhaled glucocorticoids
- Oxygen therapy
- **Antibiotics** specifically macrolides such as **azithromycin** to reduce the number of exacerbations.
- Lung transplantation.

Inhaled bronchodilators in COPD:

Inhaled antimuscarinics
- Ipratropium & tiotropium.
- are superior to β2 agonists in COPD

β2 agonists
- these drugs can be used either alone or combined

Salbutamol + Ipratropium
Salmeterol + Tiotropium (long acting-less dose frequency).

QUIZ

THANK YOU FOR CHECKING OUR WORK

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Thanks for sarah alhussain for all her great work for the drug summaries

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