

وَقُلْ رَبِّ زِدْنِي عِلْمًا



# RESPIRATORY SYSTEM

## HAYAT BATCH



SUBJECT : Pharmacology

LEC NO. : 2

DONE BY : Mahmoud Al Qusairi / Juhainah Taha


# Lectures 2-3: Treatment of Asthma

Respiratory system  
Second year  
Medical school  
Hashemite University  
2<sup>nd</sup> semester 22/23  
Sofian Al Shboul, MD, PhD.

فيديوهات استفدت منها :

www.youtube.com › watch ▾

Respiratory Pharmacology (Ar) - Therapy of bronchial asthma



Chapter 07: Respiratory Pharmacology  
Google Play link to Android App: <https://play.google.com/store/apps/details?...>  
YouTube · Clinical Pharmacology Lectures · Feb 14, 2017

رهييب ♥ ↗



بسمة صائم 6 || طلاب الطب شاركونا فرحة 80 يتيم  
Medical Club · 1.8K views · 1 day ago

↗ احضروه كـ Break ☺ واعمولنا like

incurable ← COPD → irreversible  
 Asthma → reversible.

# Overview & definition

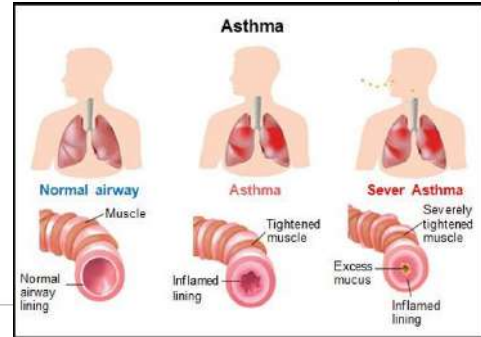
❖ A chronic inflammatory disease characterized by variable and reversible airflow obstruction, and easily triggered bronchospasms by hyperresponsive airways inhaled stimuli.

الفرق بينه وبين COPD انه reversible و لكن بسبب انه chronic فما اله curable treatment

❖ Incurable, but most people can control their symptoms.

❖ Majority of kids with asthma eventually grow out of it.

\* الحياة مع Asthma ايجي بكتير من COPD



لو كان في طفل معاه asthma بستناه ليكبر و يصير بال teen-age لأنه ممكن تختفي ال asthma منه

Asthma is characterized by episodes of acute bronchoconstriction that cause shortness of breath, cough, chest tightness, wheezing, and rapid respiration.

ما راح يجي عليهم ائمة ولكن بيت هم فكلور

السبب الرئيسي ل COPD ← Smoking  
 السبب الرئيسي ل Asthma ← inflammation

## Risk factors & triggers

trigger risk factor  
 risk factor (trigger)  
 asthma ليست وراثية ولكن genetic background بتكبر دور فيها  
 فودة ركز عليها



ال family history كمان شي بيميز ال asthma عن COPD  
 ال smoking ما بسبب asthma بس بعمل asthma attack



Asthma تون على مستوي bronchi  
ke wsi alveoli من emphysema

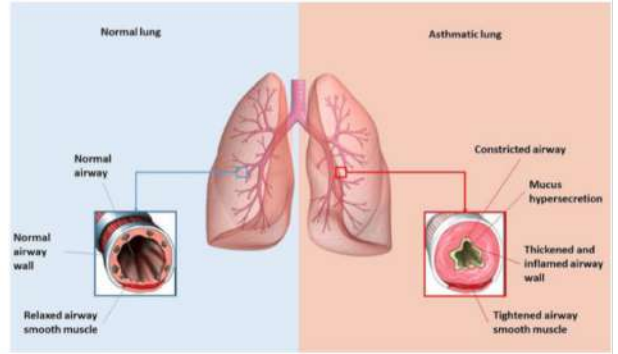
# Pathophysiology

Contraction of bronchial smooth muscle  
bronchial wall inflammation  
increased secretion of mucus

bronchoconstriction and  
airflow obstruction.

Asthma is usually not a progressive disease. However, if untreated, asthma may cause airway remodeling, resulting in increased severity and incidence of asthma exacerbations and/or death.

↻ COPD is progressive



without treatment  
exacerbation ⇐ exposure to risk factors

The underlying inflammation of the airways contributes to airway hyper-responsiveness, airflow limitation, respiratory symptoms, and disease chronicity.

Asthma attacks may be triggered by exposure to allergens, exercise, stress, and respiratory infections.

Unlike COPD, cystic fibrosis, and bronchiectasis, asthma is usually not a progressive disease.

COPD is progressive, which means it gets worse over time. Asthma is a reversible condition when the right treatment is received at the right time.

This makes early treatment important, especially when ACOS occurs.

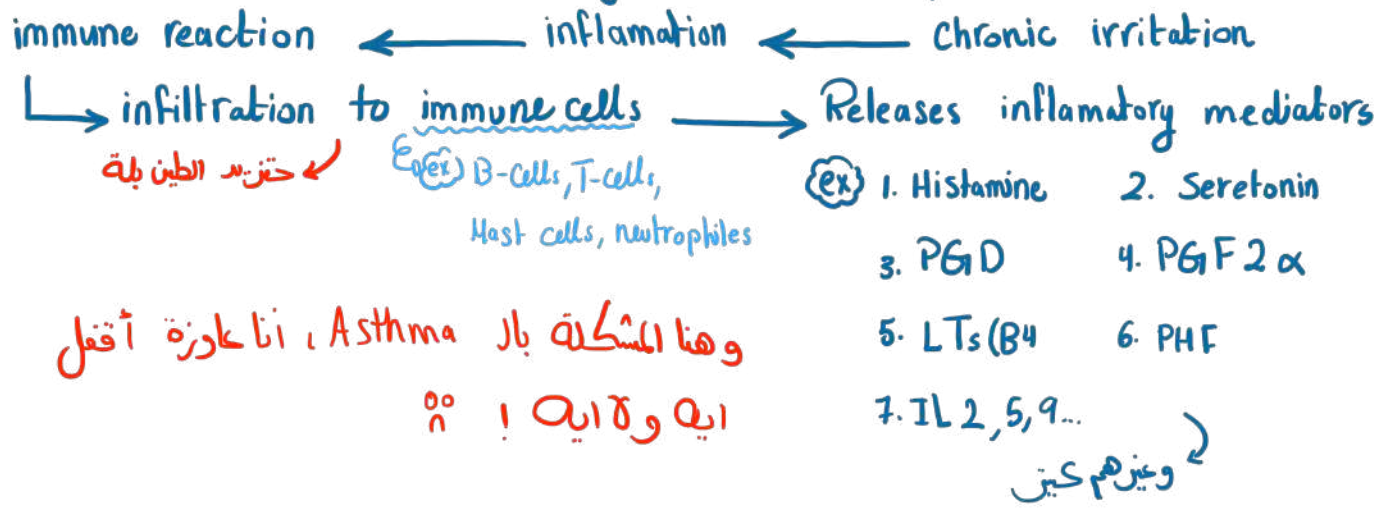
↪ Asthma COPD  
overlap syndrom

↪ حنجري عنه كمان شوي

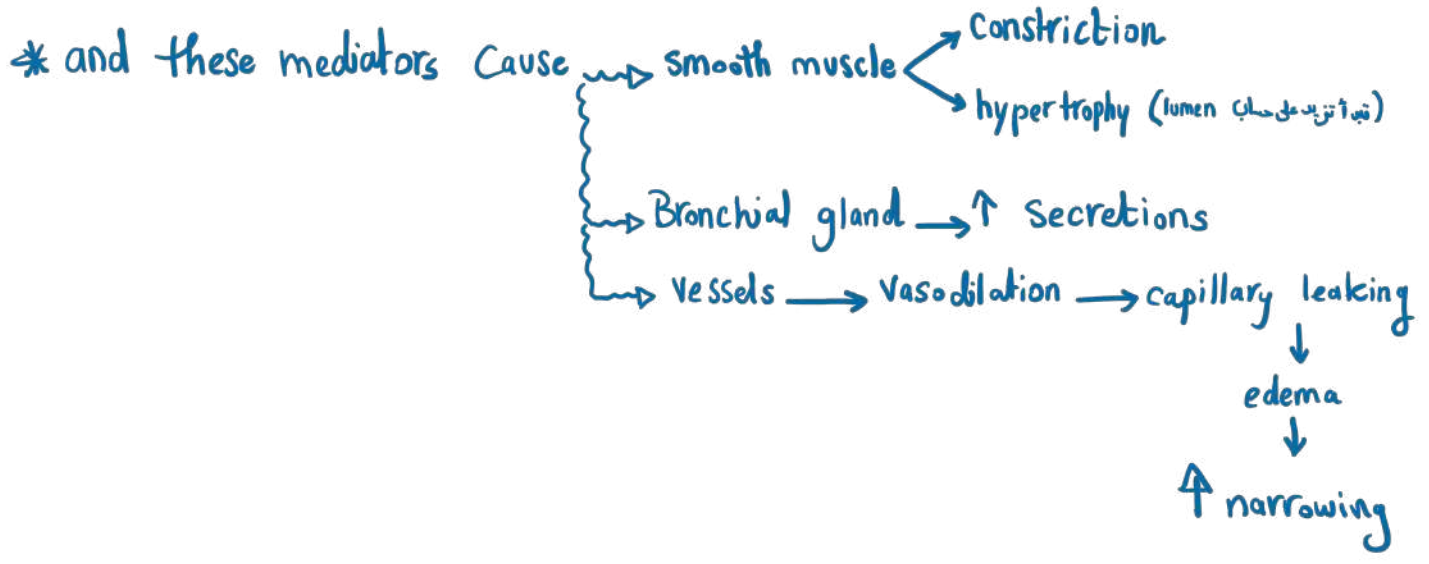
بداية  
المرض  
المرحلة  
الاولى

منا فودة

\* factors التي حكيانم فوق (dust, smoking, cold air) يعطوا



وهنا المشكلة بار Asthma ، انا عارزة أقفل ايه وة ايه ! °°



بالطرح لازم أعطي اول شي non-specific anti-inflammatory drug ← ليقدر يغطي كل mediators

\* وافضل مثال :- Cortisol

ثانياً : بدي أعطي شي بيخلصني من Spasm ويعمل dilation

# Pathophysiology & pathogenesis

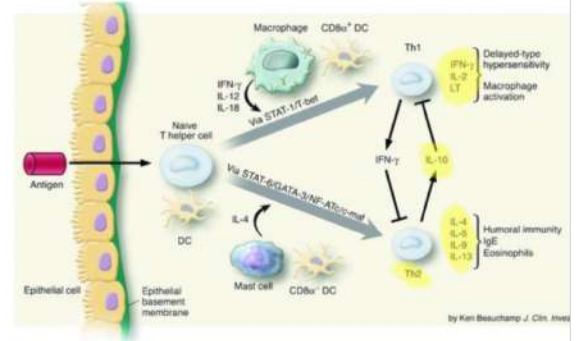
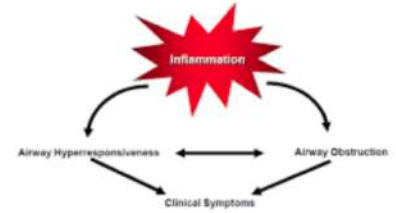
## Asthma pathophysiology components:

1. Airway inflammation
2. Intermittent airflow obstruction
3. hyperplasia of the cells of all structural elements of the airway wall.

## Several immune cells are implicated:

1. Eosinophils and CD4+
2. Mast cells *not CD8+*
3. Th2 lymphocytes
4. Basophils

- Foreign materials (allergens) >> ↑ IgE (genetically determined) >> IgE antibodies bind to mast cells in the airway mucosa



*losing weight*  
*discoloration* } in COPD

# Signs & symptoms

- Wheezing (could be absent during most severe episode)
- Shortness of breath
- Chest tightness *usually genetic background ← Asthma فيه ما بتقدر تتخلص منه (يعني تبعد عن triggers)*
- Coughing *موت صغير*
- Symptoms are usually worse at night and in the early morning or in response to exercise or cold air.

مهمين لل case لتعرف عن اي مرض عم نحكي





# خلي ببالكم انه ال attack من ال asthma اقل من COPD

## Asthma vs COPD

لن يأتي عليهم امثلة ولكنها مهمة  
حتى نفهم mechanism of drugs

ACOS: Asthma COPD overlap syndrome

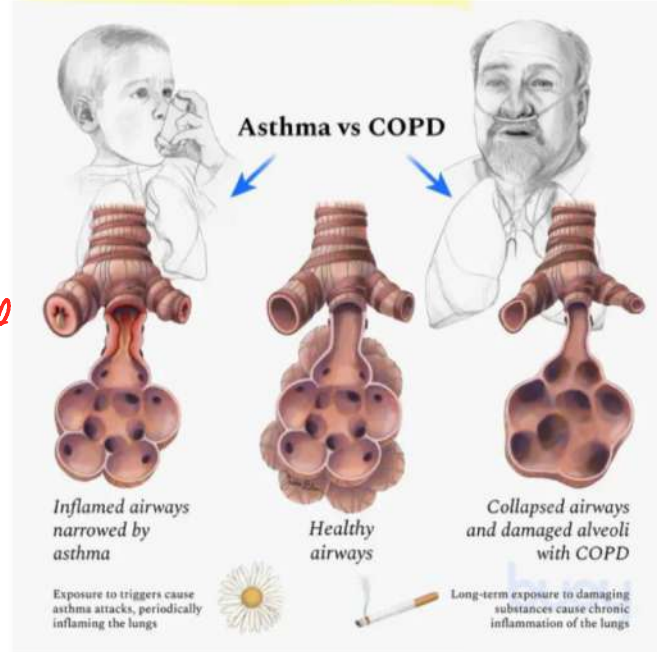
Asthma is not considered as a part of COPD because:

1. Airway obstruction in asthma is usually **reversible** (if left untreated, it can become irreversible)
2. Asthma affects the **bronchi** (emphysema effect the alveoli)

Asthma + component of irreversible airways obstruction = the asthma-chronic obstructive disease (COPD) overlap syndrome (ACOS).

people with ACOS exhibit **increased morbidity, mortality and possibly more comorbidities**

One component of COPD.



Compared to asthma, **COPD** occurs in **older** patients, is associated with **neutrophilic** rather than eosinophilic inflammation, is **poorly responsive** even to high-dose inhaled corticosteroid therapy, and is associated with **progressive, inexorable loss of pulmonary function** over time, especially with continued cigarette smoking.

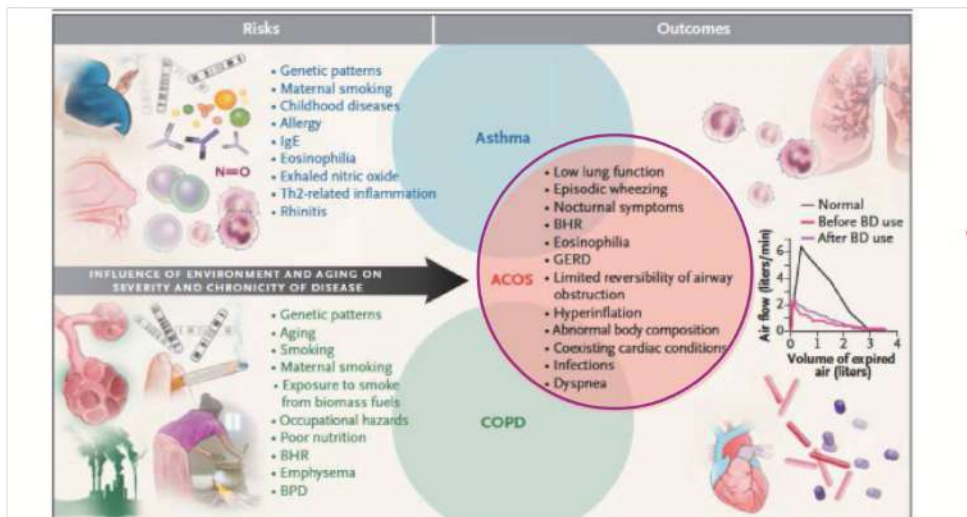
	Asthma	COPD
Age of onset	Usually < 40 years	Usually > 40 years
Smoking history	Not causal	Usually > 10 pack-years
Sputum production	Infrequent	Often
Allergies	Often	Infrequent
Disease course	Stable (with exacerbations)	Progressive worsening (with exacerbations)
Spirometry	Often normalizes	Never normalizes
Clinical symptoms	Intermittent and <b>variable</b>	<b>Persistent</b>

ذلك يكون عند الكبار

لم يمكن توريده فقط

ممكن توريده أو تتحسن

**Asthma-COPD overlap syndrome (ACOS)** is diagnosed when you have symptoms of both asthma and COPD. ACOS is not a separate disease, but rather a way for doctors to recognize the mix of symptoms and select a treatment plan that is most appropriate for you.



صورة من النت  
بتوضيح تداخل المرضين

أكثره بتختلف عن COPD

# Asthma management → first step in treatment → avoid triggers

- Identifying triggers and **eliminating exposure** to them is considered the most effective treatment

محفزات

مثلا لو كان ال trigger هو بسة لازم نعمل elimination لها

## Aims of asthma therapy:

- Decrease the intensity and frequency of asthma symptoms
  - Prevent future exacerbations
  - Minimize limitations in activity related to asthma symptoms
- كل مرضى ال asthma بتضايقوا من الدخان لهيك ما بصيروا يقربوا من اي مكان فيه تدخين
- Medications for asthma are broadly classified into fast-short-acting and long-acting categories

محفزات

## Asthma classification

		Persistent Asthma		
	Intermittent	Mild	Moderate	Severe
<b>1</b> Symptoms	≤2 days/week	≤2 days/week but not daily	Daily	Throughout the day
<b>2</b> Night Awakenings	≤2 days/month	3-4 times/month	>1 time/week but not nightly	Often 7 times/week
<b>3</b> Use of SABAs (not for EIB)	≤2 days/week	>2 days/week but not daily	Daily	Several times per day
<b>4</b> Interference w/ Normal activity	None	Minor limitation	Some limitation	Extremely limited
<b>5</b> Lung Function	FEV <sub>1</sub> >80% predicted FEV <sub>1</sub> /FVC normal	FEV <sub>1</sub> ≥80% predicted FEV <sub>1</sub> /FVC normal	FEV <sub>1</sub> =60-80% predicted FEV <sub>1</sub> /FVC reduced 5%	FEV <sub>1</sub> <60% predicted FEV <sub>1</sub> /FVC reduced >5%
<b>Recommend Step for Initiating Treatment</b>	Step 1	Step 2	Step 3	Steps 4 - 6

→ Severity of Symptoms →

EIB: Exercise induced bronchoconstriction

FEV1: forced expiratory volume in one second

FVC: forced vital capacity

SABA: short-acting beta-2 agonists.



\* نفس drugs بيسم استعمال في Asthma و COPD ولكن الؤوق فيه الترتيب في الؤؤؤؤؤ drugs

# Agents used for Asthma: Adrenergic agonists

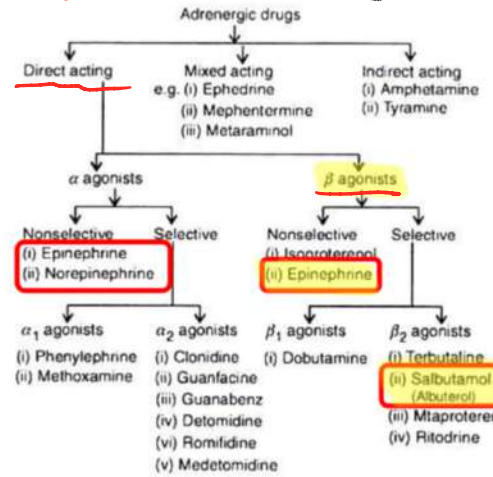
MEDICATION	
<b>SHORT-ACTING <math>\beta_2</math> ADRENERGIC AGONISTS (SABAs)</b>	
Albuterol PROAIR, PROVENTIL, VENTOLIN	Asthma, COPD
Levalbuterol XOPENEX	Asthma, COPD
<b>LONG-ACTING <math>\beta_2</math> ADRENERGIC AGONISTS (LABAs)</b>	
Arformoterol BROVANA	COPD
Formoterol FORADIL, PERFORMIST	Asthma, COPD
Indacaterol ARCAPTA	COPD
Olodaterol STRIVERDI RESPIMAT	COPD
Salmeterol SEREVENT	Asthma, COPD



❖ pharmacological asthma related actions:

1. Relax airway smooth muscle
2. Inhibit release of bronchoconstricting mediators from mast cells
3. Inhibit microvascular leakage (no edema)

Epinephrin → **Adrenergic receptors ( $\alpha, \beta$ )**   
 الي بيهيمنه لانّه موجود في لؤؤؤؤ



❖ **Epinephrine, albuterol, levalbuterol**

↪ bronchodilation  
 ↪ secretion

Why is epinephrine preferred over norepinephrine for asthma?

epinephrine has a **greater effect on beta receptors** compared with norepinephrine, norepinephrine binds very poorly to  $\beta_2$  receptors.

# Agents used for Asthma: Adrenergic agonists (Epinephrine)

- Best delivered by inhalation (greatest effect on airway + least systemic toxicity)

• Effective, rapidly acting bronchodilator when injected or inhaled as from a pressurized canister.

عابو ↪ مضموط ↪

• International asthma guidelines recommend **against** epinephrine (adrenaline) administration in acute asthma unless associated with **anaphylaxis or angio-oedema**

مؤؤؤؤؤ

**severe** \* \* انا ما بستخدم ال epinephrine الا بحالات الي بتكون و بستخدم مكانه selective beta 2 agonists

Epinephrine بستخدم في Asthma (لان allergic reaction هو جزء من pathophysiology) لانه لا بستخدم في COPD لانّه مايفيد allergic reaction

# Agents used for Asthma: Adrenergic agonists (Epinephrine)

given as life saving drug

Maximal bronchodilation is achieved 15 minutes after inhalation and lasts 60–90 minutes.

tachycardia, arrhythmias, and worsening of angina pectoris are troublesome adverse effects.

وعدم انتظام نبضات القلب

الذبحة الصدرية

مزيجين

diverse side effects receptors لأنه يعمل على كل receptors لذلك قل استخدامه ولكن

asthmatic patient + allergic attack Epinephrin is drug of choice.

its use in asthma has been displaced by other, more  $\beta_2$ -selective agents.

# Agents used for Asthma: $\beta_2$ -adrenergic agonists

Used for quick relief of asthma symptoms, and as adjunctive therapy for long-term control of the disease

short acting

SABAs have a rapid onset of action (5 to 30 minutes) and provide relief for 4 to 6 hours.

Used for symptomatic treatment of bronchospasm

anti-inflammatory effects? mild asthma

Can be used as monotherapy for patients with persistent asthma?

patient كى يلقى تاثير على حياة

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releaver treatment → attacks يستخدم عند حدوث  
maintenance treatment → long term treatment  
حتى لو ما عنده attack  
(ما عنده attack بي حاسى حارة تلبان) يسهل الدواء

\*Inhaled Beta 2-adrenergic agonists directly relax airway smooth muscle.

\*All patients with asthma should receive a SABA inhaler for use as needed.

\*Beta 2 agonists have no anti-inflammatory effects, and they should not be used as monotherapy for patients with persistent asthma.

However, monotherapy with SABAs may be appropriate for patients with mild, intermittent asthma or exercise-induced bronchospasm.

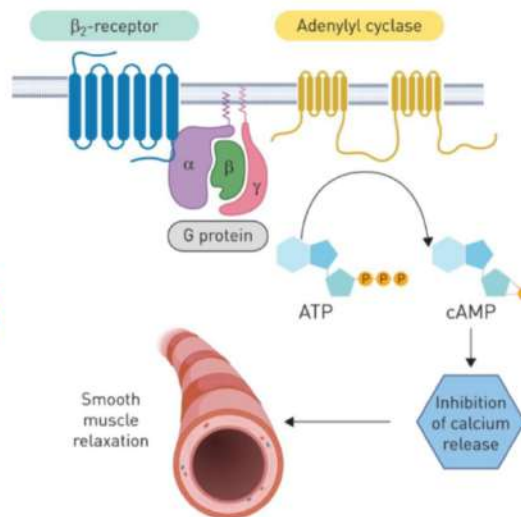
\*Direct-acting Beta 2-selective agonists include a/buterol and levalbuterol.



# Agents used for Asthma: β2-adrenergic agonists

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<i>Levalbuterol</i> XOPENEX	Asthma, COPD
<b>LONG-ACTING β<sub>2</sub> ADRENERGIC AGONISTS (LABAs)</b>	
<i>Arformoterol</i> BROVANA	COPD
<i>Formoterol</i> FORADIL, PERFORMIST	Asthma, COPD
<i>Indacaterol</i> ARCAPTA	COPD
<i>Olodaterol</i> STRIVERDI RESPIMAT	COPD
<i>Salmeterol</i> SEREVENT	Asthma, COPD

- SABAs monotherapy may be appropriate for patients with mild, intermittent asthma or exercise-induced bronchospasm.
- Can be diluted in saline for administration from a hand-held nebulizer but are no more effective.
- Nebulized therapy should thus be reserved for patients unable to coordinate inhalation from a metered-dose inhaler

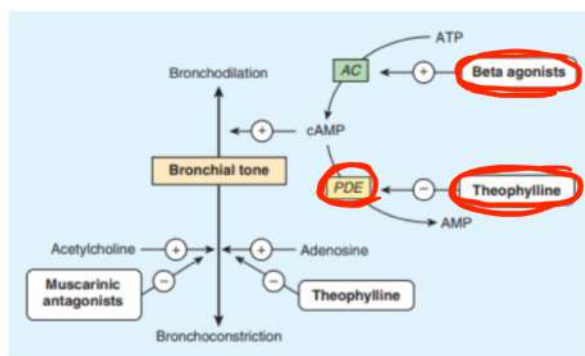


# Agents used for Asthma: β2-adrenergic agonists

- MOA: COPD lecture

Receptor activation (G protein (Gs) + adenylyl cyclase) >> increases intracellular cAMP >> activate protein kinase A (PKA) >> phosphorylate Gq-coupled receptors >> reduce intracellular Ca<sup>2+</sup> or decrease the sensitivity of Ca<sup>2+</sup> >> inhibition of myosin light chain phosphorylation (MLCK) >> preventing airway smooth muscle contraction.

- Adverse effects: tachycardia, hyperglycemia, hypokalemia, hypomagnesemia, and skeletal muscle tremors



مهمين  
عليهم سؤال

له رجفة





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# Agents used for Asthma: $\beta_2$ -adrenergic agonists

LABAs إلى بيك استخدام في Asthma  
Olodaterol ← استخدام قليل

- LABAs used in Asthma: salmeterol and formoterol (both are chemical analogs of albuterol).
- longer duration of action, providing bronchodilation for at least 12 hours (because of their high lipid solubility).
- Use of LABA monotherapy is **contraindicated**, and LABAs should be used **only in combination with an asthma controller medication**, such as an inhaled corticosteroid (ICS).

monotherapy ← LABA في الأشمان وأحد الخيارات ← كإحدى

موانع الاستخدام

Salmeterol Multicenter Asthma Research Trial (SMART) randomized trial comparing salmeterol (MDI) VS placebo. An interim analysis in 26,355 patients found an **increase in respiratory-related deaths and asthma-related deaths**.

بسبب استخدام salmeterol لمدة

drug that has no therapeutic effect.

\*ICS remain the long-term controllers of choice in asthma, and LABAs are considered to be useful adjunctive therapy for attaining control in moderate to severe asthma.

\*Although both LABAs are usually used on a scheduled basis to control asthma, adults and adolescents with moderate persistent asthma can use the ICS/formoterol combination for relief of acute symptoms.

\*Adverse effects of LABAs are similar to quick-acting Beta 2 agonists.



# Agents used for Asthma:

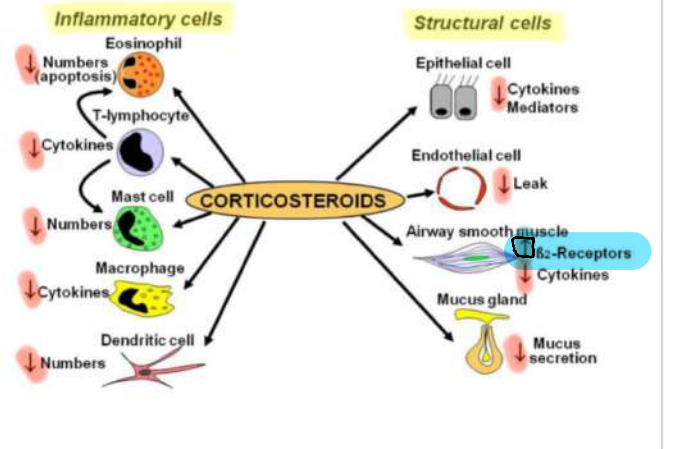
## Inhaled corticosteroids (ICS)

### Actions on lung:

- These drugs directly targets underlying airway inflammation:

1. Decreasing the inflammatory cascade (eosinophils, macrophages, and T lymphocytes)
2. Reversing mucosal edema
3. Decreasing the permeability of capillaries
4. Inhibiting the release of leukotrienes.

INHALED CORTICOSTEROIDS	
Beclomethasone BECONASE AQ <sup>®</sup> , QVAR	Allergic rhinitis, Asthma, COPD
Budesonide PULMICORT, RHINOCORT <sup>®</sup>	Allergic rhinitis, Asthma, COPD
Ciclesonide ALVESCO, OMNARIS <sup>®</sup> , ZETONNA <sup>®</sup>	Allergic rhinitis, Asthma, COPD
Fluticasone FLOINASE <sup>®</sup> , FLOVENT	Allergic rhinitis, Asthma, COPD
Mometasone ASMANEX, NASONEX <sup>®</sup>	Allergic rhinitis, Asthma
Triamcinolone NASACORT <sup>®</sup>	Allergic rhinitis, Asthma



← موهين عليهم سؤال

They decrease everything except beta 2 receptors.  
They are used in Asthma more than COPD.

حمل معلومات  
هذا السلايد مهمة

# Agents used for Asthma:

## Inhaled corticosteroids (ICS)

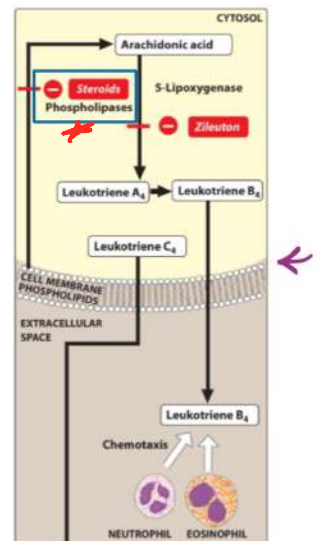
- Do NOT relax airway smooth muscle directly but **reduce bronchial reactivity** and reduce the frequency of asthma exacerbations if taken regularly

→ indirect effect

- They inhibit the release of arachidonic acid through inhibition of phospholipase A2, thereby producing **direct anti-inflammatory** properties in the airways

↳ B2-agonists يعكس

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To be effective in controlling inflammation, these agents must be used regularly.

After several months of regular use, ICS reduce the hyperresponsiveness of the airway smooth muscle to a variety of



# Agents used for Asthma:

## Inhaled corticosteroids (ICS)

- 1- reduce inflammation in the airways
- 2- decrease the frequency and severity of asthma symptoms
- 3- improve overall lung function



INHALED CORTICOSTEROIDS	
<b>Beclomethasone</b> BECONASE AQ <sup>®</sup> , QVAR	Allergic rhinitis, Asthma, COPD
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<b>Triamcinolone</b> NASACORT <sup>®</sup>	Allergic rhinitis, Asthma

- ICS are the **drugs of choice for long-term control in patients with persistent asthma**
- **Potentiatio**n of the effects of  $\beta$ -receptor agonists
- Treatment of exacerbations or severe persistent asthma may require the addition of a short course of oral or intravenous corticosteroids.

مهمة

severe persistent asthma  
↓  
systemic corticosteroids (يعطى في المستشفى)

→ Keep in mind that ICS are highly effective for long-term management, but they are not used to treat acute asthma exacerbations.

SABA

ضروري نعرف انه Oral CS او IV CS ممنوع استخدمهم ب كورسات طويلة و فترات طويلة و السبب هو انه side effect تبعتهم خطيرة و ممكن تعمل disregulation في الهرمونات

# Agents used for Asthma:

## Inhaled corticosteroids (ICS)

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### Routes of administration

I. Inhalation → long term use, ↓ side effects.

This formula has markedly reduced the need for systemic corticosteroid (less side effects) but appropriate inhalation technique is critical to the success of therapy

II. Oral/systemic → Short term use, Severe

Patients with a severe exacerbation of asthma may require IV methylprednisolone or oral prednisone to reduce airway inflammation.

In most cases, suppression of the hypothalamic-pituitary-adrenal cortex axis does not occur during the oral prednisone "burst" (short course) typically prescribed for an asthma exacerbation. Thus, a dose taper is unnecessary prior to discontinuation.

### Inhaled vs. Oral Corticosteroids



#### Inhaled

- Treatment for persistent asthma
- Intended for long-term use
- Fewer and less severe effects such as headache, sore throat, common cold or flu, and muscle aches



#### Oral

- Treatment for severe asthma and/or attacks
- Intended for short-term usage
- More severe, diverse side effects such as nausea, acne, weight gain, and irregular heartbeat

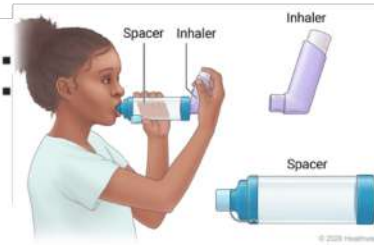


الانذار حكى لوجبت سؤال، و العلاج حيكونى بشرى، هل بنختار Oral او inhaled؟  
أجيب inhaled.



# Agents used for Asthma:

## Inhaled corticosteroids (ICS)



لهيئت استعماله  
لائظفالك

### Adverse effects

- ICS, particularly if used with a spacer, have few systemic effects.
- <sup>توسيع</sup> Deposition on the oral and laryngeal mucosa can cause oropharyngeal candidiasis (due to local immune suppression) and hoarseness.
- Patients should be instructed to <sup>تعليمات</sup> rinse the mouth in a “**swish-and-spit**” method with water following use of the inhaler to decrease the chance of these adverse events.
- Chronic maintenance with oral corticosteroids should be reserved for patients who are not controlled on an ICS.

\*Oral or parenteral corticosteroids have a variety of potentially serious adverse effects, whereas Inhaled CS, particularly if used with a spacer, have few systemic effects.



← oropharyngeal candidiasis



Swish and spit method ←

مِنَّا جِبِّ  
ذَانِكُمْ  
لَا تَقَعْدُ  
الْأُمَّلُ

انتهى التفريغ الحمد لله 🙏

ما تنسوني بدعوة بهاي الأيام الفضيلة 🙏

بالتوفيق ❤️❤️

النادي\_الطبي ❤️#