Pharmacology most important RS

Lec 1

inhibit the release of arachidonic acid through inhibition of phospholipase A2

Pharmacological agents:
Inhaled corticosteroids (ICS)

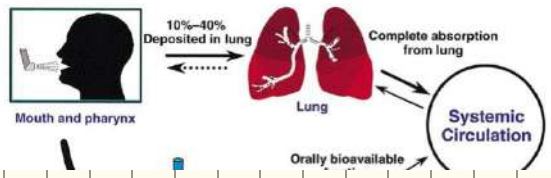
- Anti-inflammatory agents that should be reserved for patients with frequent or severe exacerbations and high blood eosinophils (~10% of the COPD population), or those with concomitant asthma

They are used in all diseases and symptoms

oral وبين ما تحطهم بشتغلو بس هون راح نركز على اللي بكونو بخاخات مش ال

systemic لأثر التأثير العكسي تبعهم

Oral glucocorticoids can be effective in treating an acute exacerbation **BUT** generally they are not recommended



بالعادة ما ينعطى لحالو يكون معو دواء ثاني و إذا كان لحاله بكون عشان تاعته **inflammatory process**

Attention: if an option says that ICS is first line maintenance therapy in COPD NO!!

Pharmacological agents:
Other agents

- **Roflumilast**
- **NOT** a bronchodilator and is **NOT** indicated for the relief of acute bronchospasm, it decreases inflammation in lungs
- Used in treating those with chronic bronchitis and a history of exacerbations.
- Use is limited by common adverse effects including weight loss, nausea, diarrhea, and headache. used with caution in those suffering from depression.

Or mental issue

VIP

- Cough medicines are not recommended. Beta blockers are not contraindicated for those with COPD and should only be used where there is concomitant cardiovascular disease

احتمال كبير تيجي هاي الفقره بالامتحان

CVD + COPD → β blocker

not routinely used

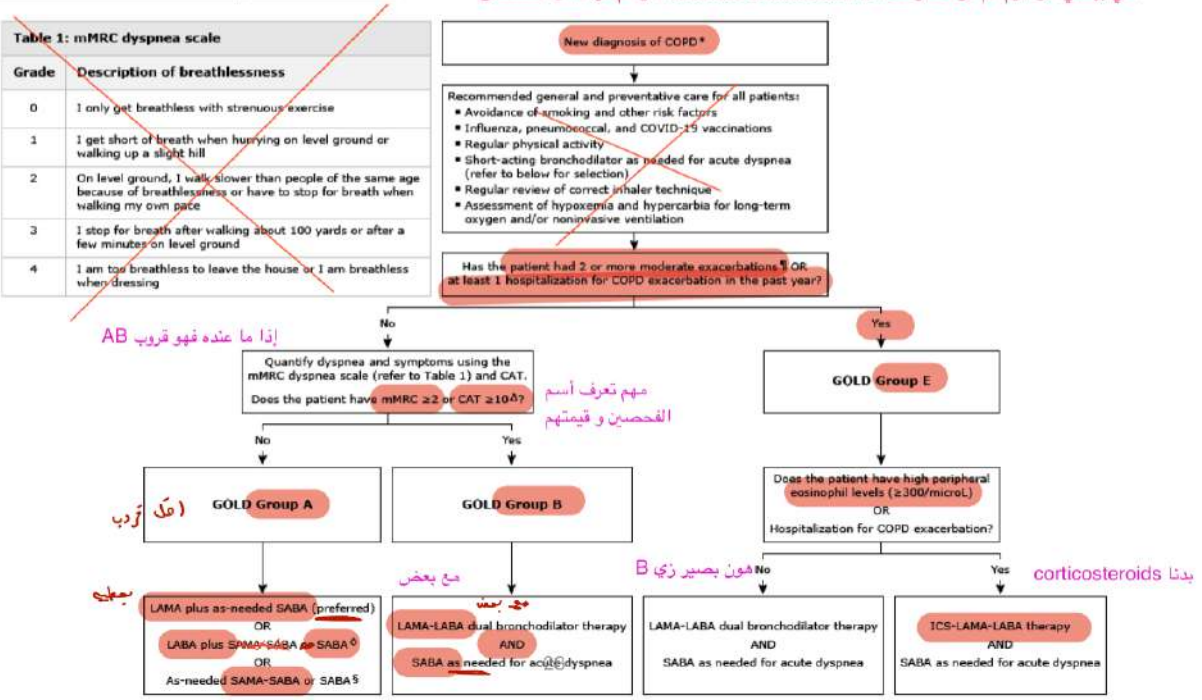
اللي محدد هو المهم

Treatment plans

هون مريض معه COPD

اللي بهمني انو أقيم كم مره صار عنده moderate exacerbations او كم مره دخل المستشفى

Table 1: mMRC dyspnea scale	
Grade	Description of breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness or have to stop for breath when walking my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing



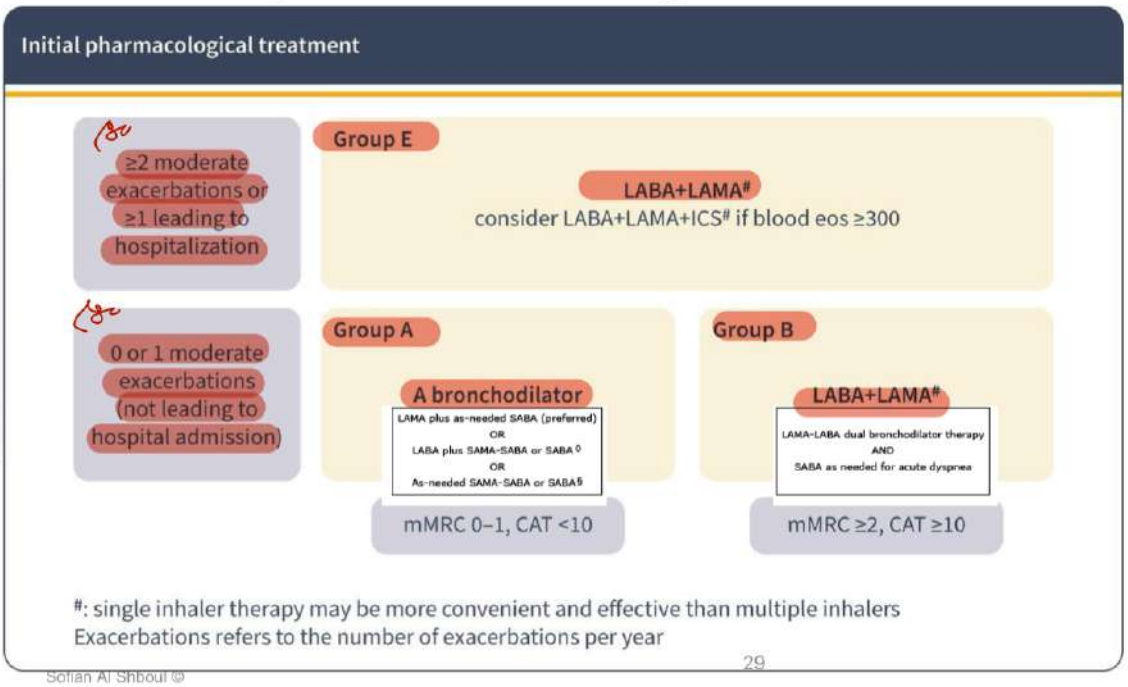
إذا ما عنده فهو قروب AB

مهم تعرف أسم الفحصين و قيمتهم

هون بصير زي B

بدنا corticosteroids

Initial pharmacological treatment



الأصفر قراية

If there is an indication for an ICS, then LABA+LAMA+ICS has been shown to be superior to LABA+ICS and is therefore the preferred choice

The use of LABA+ICS in COPD is no longer encouraged.

Alvar Agustí et al. Eur Respir J 2023;61:2300239

Lec 2

	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 variable	Persistent

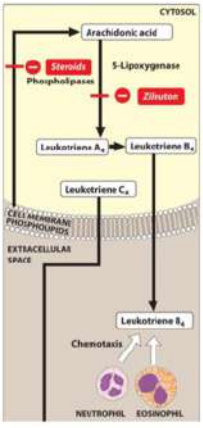
Agents used for Asthma:
β2-adrenergic agonists

- 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).

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**

Agents used for Asthma:
Inhaled corticosteroids (ICS)

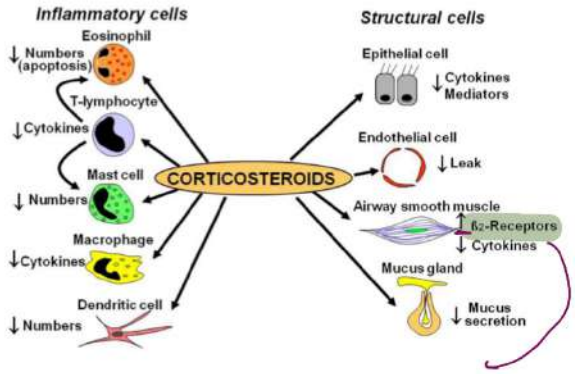
- Do NOT relax airway smooth muscle directly but **reduce bronchial reactivity** and reduce the frequency of asthma exacerbations if taken regularly
- They inhibit the release of arachidonic acid through inhibition of phospholipase A2, thereby producing **direct anti-inflammatory** properties in the airways



Agents used for Asthma:
Inhaled corticosteroids (ICS)

- 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.



Agents used for Asthma:
Inhaled corticosteroids (ICS)

Adverse effects

- ICS, particularly if used with a spacer, have few systemic effects.
- Deposition on the oral and laryngeal mucosa can cause **oropharyngeal candidiasis** (due to local immune suppression) and **hoarseness.**
- Patients should be instructed to 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.

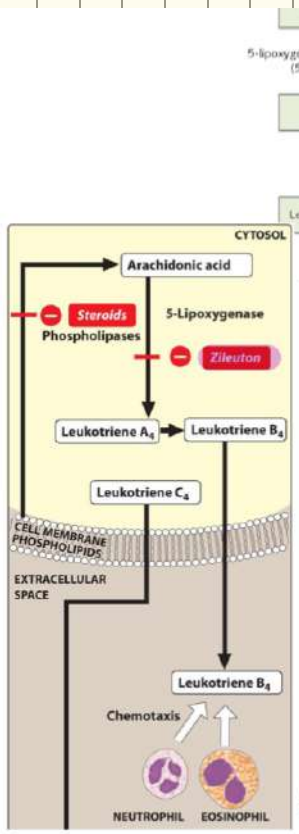
Lec 3

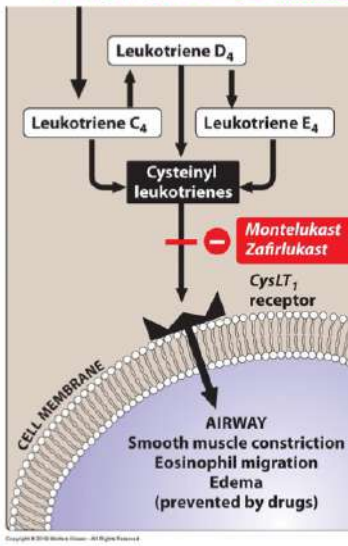
Agents used for Asthma: Leukotriene modifiers

First drug

- ✓Zileuton is a selective and specific inhibitor of 5-lipoxygenase, preventing the formation of **both** LTB4 and the cysteinyl leukotrienes.
- ✓Zafirlukast and montelukast are selective antagonists of the cysteinyl leukotriene-1 receptor (CysLT1), and they block the effects of cysteinyl leukotrienes. (Approved for the prevention of asthma symptoms).
- ✓Should not be used in situations where immediate bronchodilation is required. attack
- ✓Leukotriene receptor antagonists have also shown efficacy for the prevention of exercise-induced bronchospasm.

They are Second time of drugs

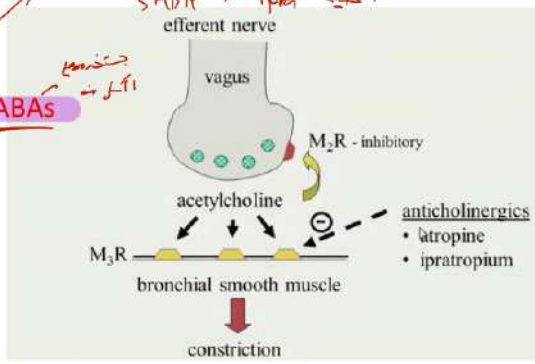




Agents used for Asthma: muscarinic antagonist

- ➢Inhaled ipratropium is **NOT** recommended for the **routine** treatment of **acute** bronchospasm in asthma, why? its onset is much slower than that of inhaled SABAs
- ➢Tiotropium (only FDA approved) can be used **as an add-on** treatment in adult patients with severe asthma and a history of exacerbations.
- ➢Adverse effects:

xerostomia and bitter taste are related to local anticholinergic effects.



Asthma classification

Guidelines for asthma
مهم نعرف شو الstep و شو الأدوية لكل step
مهم الجدول (كله مهم)

Asthma symptoms/lung function	Therapy*
لازم كلهم يكونو موجودات عشان نسميهم step 1 — **Step 1**	
All of the following: ▪ Daytime symptoms ≤2 days/week ▪ Nocturnal awakenings ≤2/month ▪ Normal FEV_1 ▪ Exacerbations ≤1/year	▪ SABA, as needed **or** ▪ Low-dose ICS-formoterol as needed (preferred)Δ
هون لازم وحده تكون موجوده — **Step 2**	
Any of the following: ▪ Daytime symptoms >2 but <7 days/week ▪ Nocturnal awakenings up to 3 to 4 nights/month ▪ Minor interference with activities ▪ Exacerbations ≥2/year	▪ Low-dose ICS daily **and** SABA as needed **or** ▪ Low-dose ICS-formoterol as needed (preferred) **Alternative option(s)** ▪ Daily LTRA **and** SABA as needed
Step 3	
Any of the following: ▪ Daily symptoms ▪ Nocturnal awakenings ≥1/week ▪ Daily need for reliever ▪ Some activity limitation ▪ FEV_1 60 to 80% predicted ▪ Exacerbations ≥2/year	▪ Low-dose ICS-formoterol as maintenance and reliever therapy◊ (preferred) **or** ▪ Low-dose ICS-LABA combination daily **and** SABA as needed **Alternative option(s)** ▪ Medium-dose ICS daily **and** SABA as needed
Step 4	
Any of the following: ▪ Symptoms all day ▪ Nocturnal awakenings nightly ▪ Need for SABA several times/day ▪ Extreme limitation in activity ▪ FEV_1 <60% predicted ▪ Exacerbations ≥2/year ▪ An acute exacerbation	▪ Medium-dose ICS-formoterol as maintenance and reliever therapy◊ (preferred) **or** ▪ Medium dose ICS-LABA daily **and** SABA **Alternative option(s)** Medium-dose ICS daily **plus** anti-leukotriene **and** SABA as needed"

البريفيرد لكل واحد ومتى بستخدمه

اعرف التارغيت لكل واحد

Agents used for Asthma:
Monoclonal antibodies

produced by, being, or composed of cells derived from a single cell. and specific for this target

- Omalizumab Bind to IgE
- Mepolizumab
- Benralizumab
- Reslizumab)

Bind to IL-5

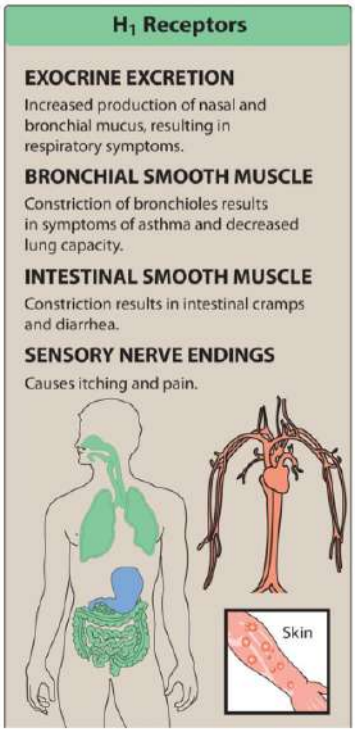
- **Omalizumab**: selectively binds to human **immunoglobulin E (IgE)>> decreased** binding of IgE to its receptor on the surface of mast cells and basophils>>**limits the release of mediators** of the allergic response.
- Mepolizumab, benralizumab and reslizumab: interleukin-5 **(IL-5) (antagonists).**
- IL-5 is the major cytokine involved in recruitment, activation, and survival of eosinophils in eosinophilic asthma.
- These agents are indicated for the treatment of **severe persistent asthma in patients who are poorly** controlled with conventional therapy.
- Their use is limited by the high cost, route of administration (IV for reslizumab and subcutaneous for others), and adverse effect profile.
- Adverse effects include serious anaphylactic reactions (rare), arthralgias, fever, rash, and increased risk of infections.
- New malignancies have been reported.

واحد ما بستحيب لاشي بعطيه

Lec 4

Histamine effects

- Histamine is present in all tissues
- Higher concentrations in mast cells and basophils
- Functions as a neurotransmitter in the brain
- **Released** by allergies, anaphylaxis and as a result of destruction of cells (cold, toxins from organisms, venoms from insects and spiders, and trauma)
- H1 receptor: **smooth muscle contraction** and **increasing capillary permeability**
- Can **enhance** the secretion of **proinflammatory** cytokines



Pharmacological treatments

Mild or episodic symptoms:

1. **Oral antihistamine** (cetirizine (≥6 months), fexofenadine or loratadine): regularly or as needed (two to eight hours before exposure)
2. **nasal spray antihistamine:** azelastine >6 years of age
3. **nasal spray glucocorticoid (more effective than antihistamines):** regularly or as needed (initiating therapy two days before, continuing through, and for two days after the end of exposure): Mometasone, fluticasone or triamcinolone
4. **nasal spray Cromolyn** → most use

Pharmacological treatments: Other agents

Intranasal

- **Cromolyn:** Prevented
  - regularly or as needed (ideally 30 minutes before an exposure).
  - helpful for brief exposures (minutes to hours).
  - For prolonged exposures: begin four to seven days in advance
  - Has very excellent safety profile
- **Leukotriene receptor antagonists may be a reasonable option in patients who also have asthma.**

Pharmacological treatments: Antihistamines

- Oral antihistamines (H1 receptor antagonists) have a **fast onset of action** and are useful for the **management of symptoms** of allergic rhinitis caused by **histamine release**, such as sneezing, watery rhinorrhea, and itchy eyes/nose.

Codeine

- ✓Decreases the sensitivity of cough centers in CNS to peripheral stimuli **and** decreases mucosal secretion.
- ✓Doses to get these effects are lower than those required for analgesia.
- ✓Adverse effects: constipation, dysphoria, and fatigue.
- ✓**Codeine has addictive potential**