وقل رب زدني علماً

النادي الطبي

RESPIRATORY SYSTEM

HAYAT BATCH

SUBJECT : Pharmacology

LEC NO. : 3/asthma

DONE BY : Anas zakarneh

تفاريغ المادة

RS-Pharmacology notes

YouTube Videos

اضغط على الكلام المكتوب باللون الأزرق لتنتقل مباشرة الى المحاضرة

ملاحظة: يوجد تقاطع كبير بين ادوية الربو و ادوية COPD

و اغلب المصادر بتشرح الربو اول لهيك رح احط فيديوهات من شرح الربو تستفيدو منها دراستكم لل COPD

الموضوع	الفيديوهات المطلوبة 1	الفيديوهات المطلوبة 2	الفيديوهات المطلوبة 3
Treatment of COPD lec 1	احضر هذا الفيديو كامل رح يشرح موضوع الربو و الCOPD الفيديو رهيبيب	للي بحب شرح فودة احضروا هذا الفيديو من الدقيقة 36 الى الساعة و 13 دقيقة اما اذا بتحضره كامل بتكون خلصت الربو يعني درست محاضرتين	

شرح عبدالمتعال فودة

FOUDA

هسا الdrugs اللي كنا نستعملهم بين الasthma و الCOPd بتقاطعوا كثير
بس اللي بفرق هو الrank مثلا بالasthma كنا نركز على steroid
و الCOPD كنا نركز على SABA
طب ليش؟
لانو الasthma بتميل إنها تكون inflammatory disease صح انو الasthma فيها allergy و الcopd لا
بس هي بتميل اكثر تكون inflammation

طبعا هدول الclass بتقاطعوا بس اللي بدنا نحكي فيهم اليوم بتقاطعوا بشكل بسيط مع COPD

يلا بسم الله الرحمن الرحيم

هسا احنا حكينا انو بنستعمل الsteroid مع inflammatory
طب شو بعملو الsteroid ؟
هسا الeffect تاعهم immunosuppression
طب في molecules بتأثر فيهم مثل phospholipase
طب كيف بشتغل أصلا

شرح خارجي للفهم

Steroids work by binding to specific receptors inside or on the surface of cells. This binding triggers various cellular responses, including changes in gene expression, activation of signaling pathways, and modulation of physiological processes. Different types of steroids have different effects, such as reducing inflammation and suppressing the immune system (e.g., glucocorticoids), or influencing growth, development, and reproduction (e.g., sex hormones). Overall, steroids exert their effects by interacting with cellular receptors and regulating biological pathways.

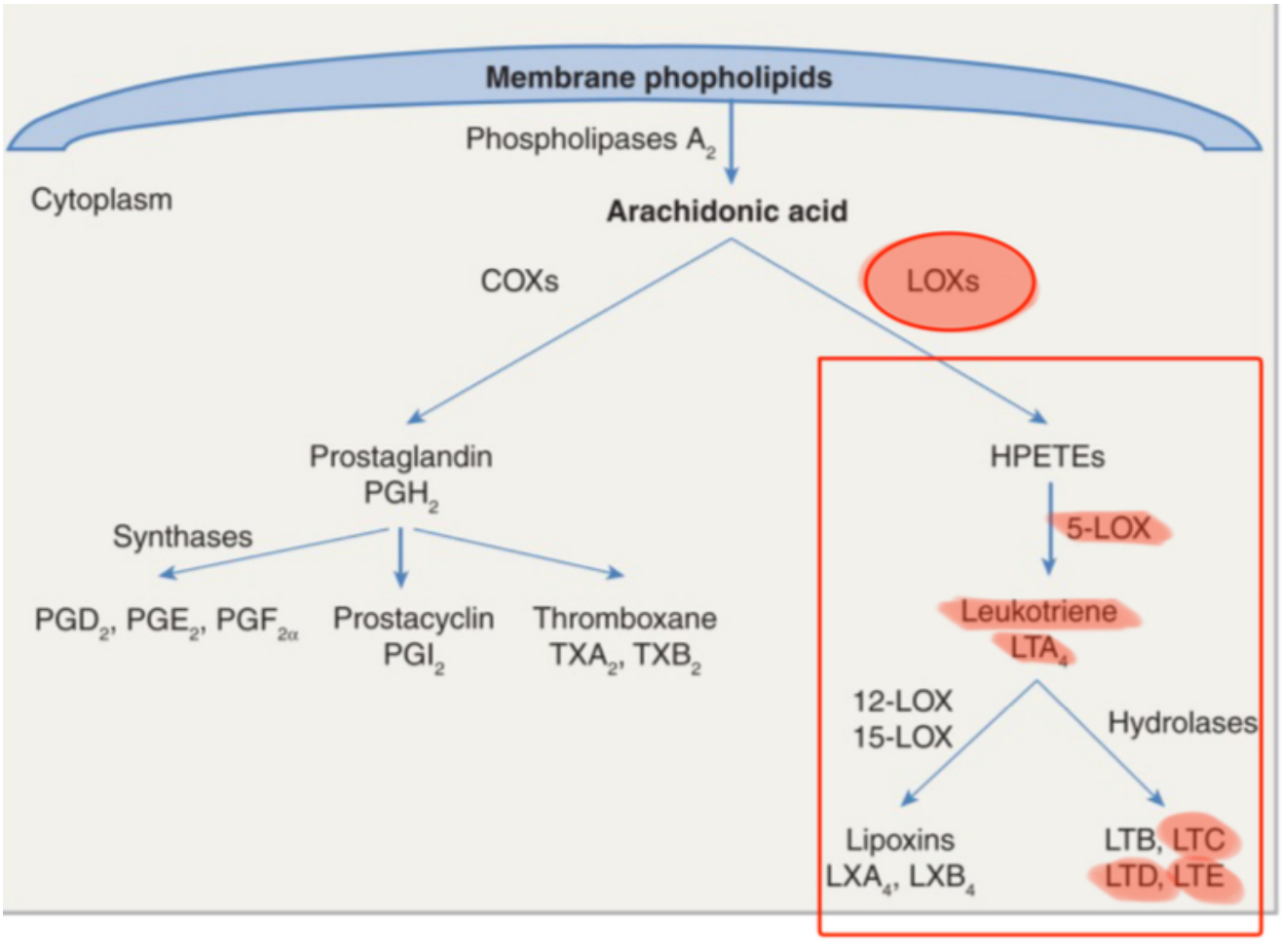
Revision
😁منـي

**Leukotrienes are chemicals your body releases when you come into contact with something you're allergic to. They can cause:

1-Coughing.
2-Extra mucus and fluid in your chest and throat.
3-Inflammation or swelling in your airway. 4-Tight muscles in your airway. 5-Tightness in your chest.
6-Wheezing or difficulty breathing.

**Leukotriene modifiers, also called leukotriene receptor antagonists or leukotriene synthesis inhibitors, are medications that block the effect of leukotrienes or stop your body from producing them.
**Names of specific leukotriene modifiers include:
1-Montelukast
2-Zafirlukast
3-Zileuton

Leukotrienes (LT) 4 and the cysteinyl leukotrienes, LTC4 , LTD4 , and LTE4 , are products of the 5-lipoxygenase pathway of arachidonic acid metabolism and part of the inflammatory cascade.



Agents used for Asthma: Alternative drugs

هسا الها تأثير inflammatory cells بتشتغل على steroidهسا ال
بس بسيط inflammation process على
بس بدنا drugs بتشتغل ع العملية نفسها أصلا
مثل leikotriene modifiers
تأثير الsteroid عادة بكون down stream بنهايات الcascade
وين ما في inflammatory cells بوقفها
وين ما في cytokines بوقفهم بس ما بوقف العملية من فوق زي الleukotriene modifiers

- Useful for treatment of asthma in patients who are poorly controlled by conventional therapy or experience adverse effects secondary to corticosteroid treatment.
- Should be used in conjunction with ICS therapy for most patients.

A. **Leukotriene ((LT) modifiers** (Zileuton, Zafirlukast, montelukast
B. **Cromolyn**
C. **Cholinergic antagonists** (ipratropium and Tiotropium)
D. **Theophylline**
E. **Monoclonal antibodies** (Omalizumab, mepolizumab, benralizumab and reslizumab)

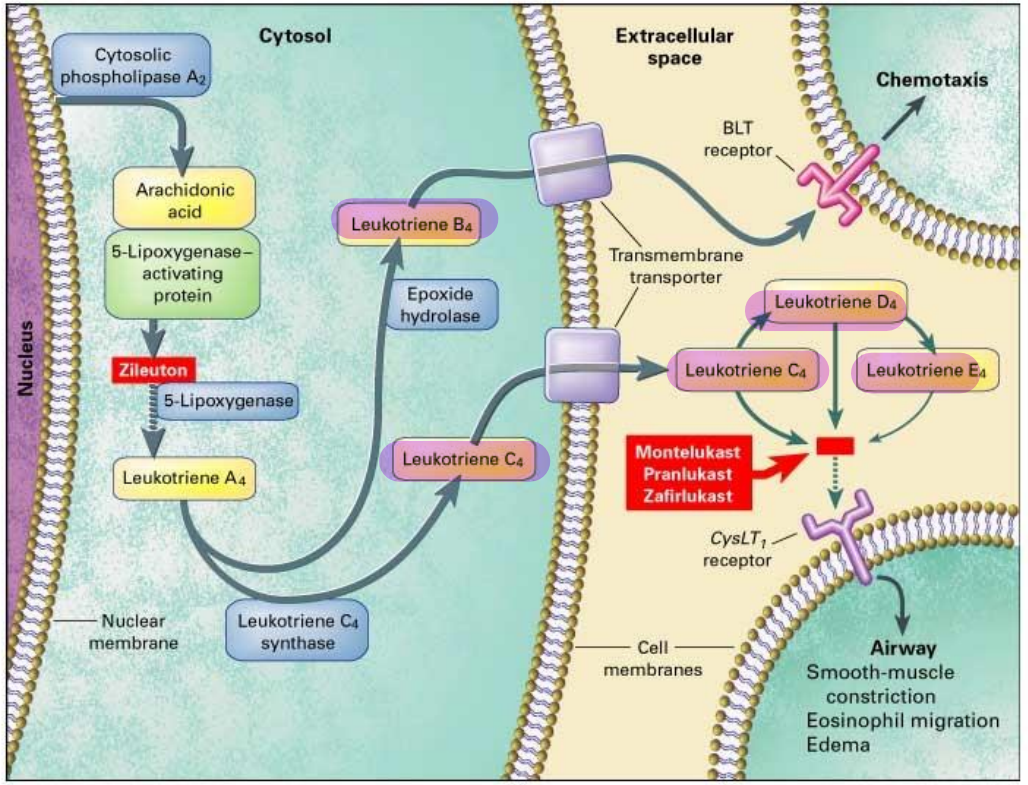
Agents used for Asthma: Leukotriene modifiers

- LTB4 and the cysteinyl leukotrienes (LTC4, LTD4, and LTE4) are **products of the 5-lipoxygenase pathway** of arachidonic acid metabolism and part of the inflammatory cascade.

- 5-Lipoxygenase is found in cells of **myeloid** origin, such as mast cells, basophils, eosinophils, and neutrophils.

we want to stop the process from the start
هسا بستعمل هدول الdrugs في حالة الattack ؟ لا
لانو أصلا بهمني انو الbronchospasm اللي عندي أوسعه
بهمنيش هسا أوقفها من فوق

- **LTB4** is a potent chemoattractant for **neutrophils** and **monocytes**, stimulates production of proinflammatory cytokines.
- **cysteinyl leukotrienes constrict** bronchiolar smooth muscle, **increase** endothelial permeability, **promote** mucus secretion, eosinophil recruitment and airway remodeling in chronic asthma



هسا إذا اجا سؤال بالامتحان و كان فيه صيغة attack ما بتستخدم هدول (leukotrine modifiers)
إذا فيه bronchodilator مثل saba
لازم تفكر بالbronchodilator ما دام عندك attack
بهم أتعامل مع الattack بعدين مع الmaintenance

Agents used for Asthma: Leukotriene modifiers

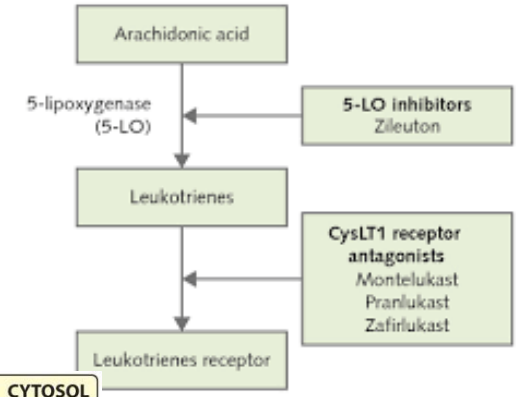
First drug

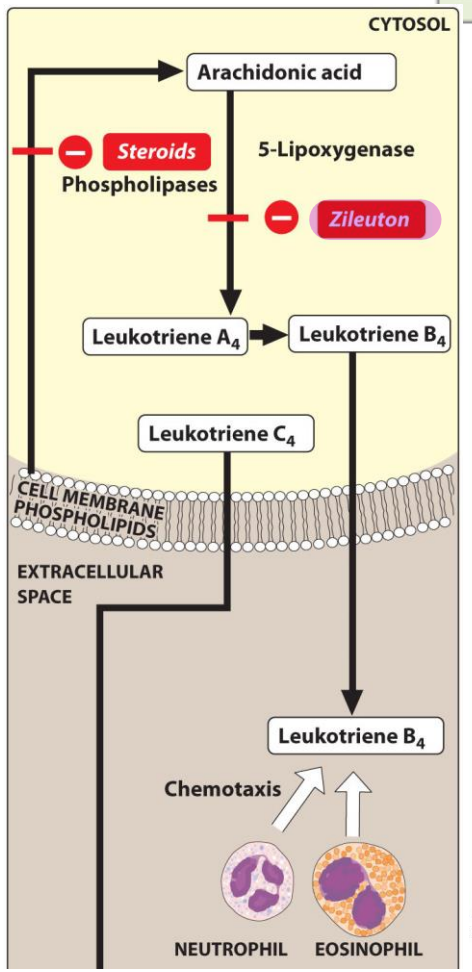
- ✓Zileuton is a selective and specific inhibitor of 5-lipoxygenase, preventing the formation of **both** LTB4 and the cysteinyl leukotrienes.
- ✓Zafirlukast and montelukast are selective antagonists of the cysteinyl leukotriene-1 receptor (CysLT1), and they block the effects of cysteinyl leukotrienes. (Approved for the prevention of asthma symptoms).

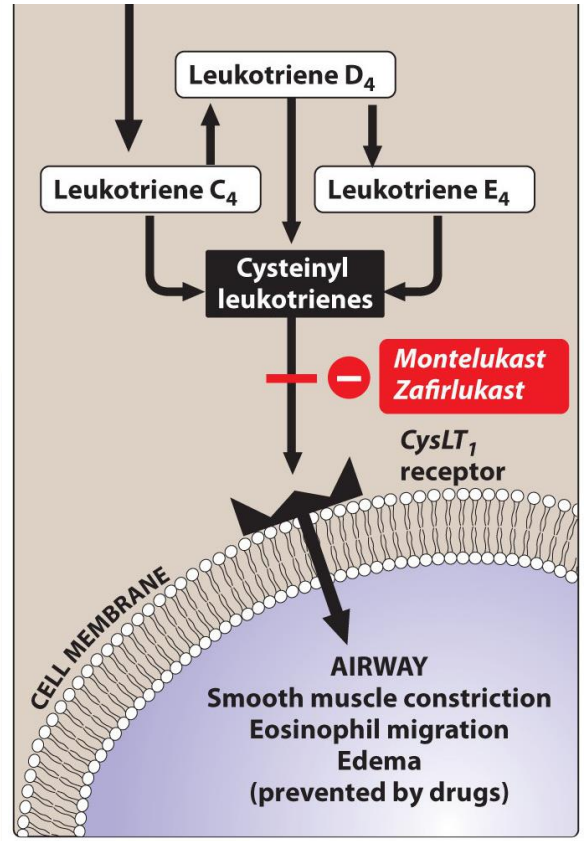
كتبت فوق ليش بالأحمر

- ✓Should not be used in situations where immediate bronchodilation is required.
- ✓Leukotriene receptor antagonists have also shown efficacy for the prevention of exercise-induced bronchospasm.

They are Second time of drugs







Agents used for Asthma: Leukotriene modifiers

بتهمنا الأشياء المميزه
depression مثل
common ما بدنا أشياء

Pharmacokinetics

بدك تعرف أنهم oral

- These agents are orally active
- Undergo extensive **hepatic** metabolism (zileuton and zafirlukast reported with liver toxicity).
- Montelukast is the most prescribed (taken without regard to meals+ once-daily treatment).

Adverse effects

- Elevations in serum hepatic enzymes>> requiring periodic monitoring and discontinuation when enzymes exceed three to five times the upper limit of normal.
- Headache and dyspepsia.

Agents used for Asthma:
Cromolyn

هسا راح نشبك شوي مع المحاضرة اللي جاي يعني في أدوية عنا هسا شابكين مع المحاضرة اللي جاي

- ✓a prophylactic anti-inflammatory agent that inhibits mast cell degranulation and release of histamine.

Usually Used as inhaler or oral inhaler بس ركزو على

- ✓An alternative (prophylaxis) therapy for mild persistent asthma and is available as a nebulized solution.

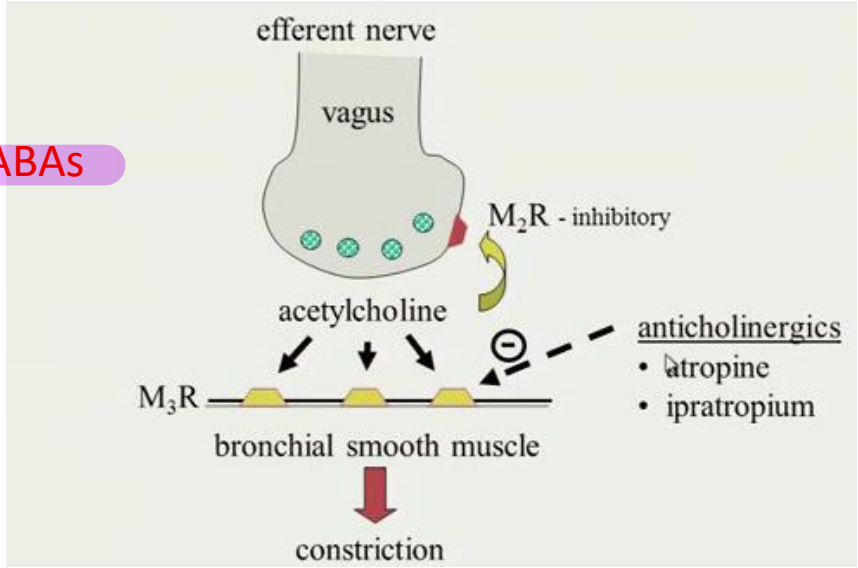
VIP

- ✓NOT a bronchodilator>> NOT useful in managing an acute asthma attack.
- ✓Short duration of action>>dosing three or four times daily
- ✓Adverse effects are minor and include cough, irritation, diarrhea, and unpleasant taste.

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. (LABA مثل)
- Adverse effects:

xerostomia and bitter taste are related to local anticholinergic effects.

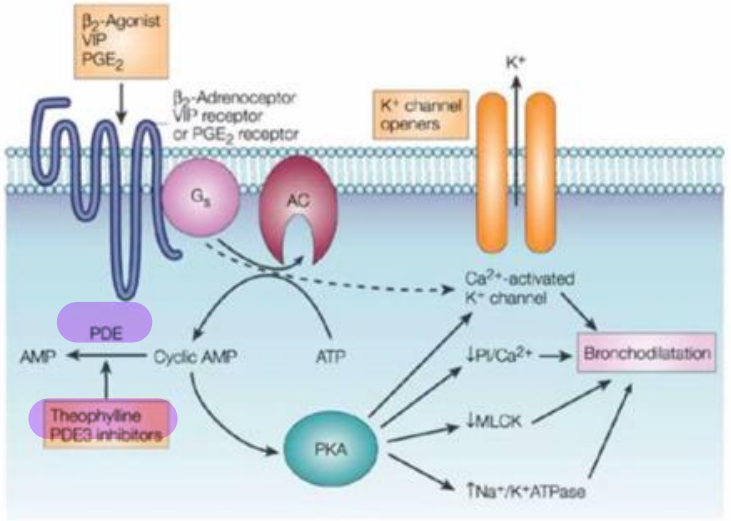


Agents used for Asthma:
Theophylline

ما بتهمني لأنها مش واضحة processال

- bronchodilator that relieves airflow obstruction in chronic asthma and decreases asthma symptoms.
- It may also possess anti-inflammatory activity, although the mechanism of action is unclear.
- Overdose may cause seizures or potentially fatal arrhythmias.
- Theophylline is metabolized in the liver and is a CYP1A2 and 3A4 substrate.

Theophylline



PDE=Phosphodiesterase
PKA=Protein Kinase A

Drug that inhibit PDE 4
Reflumilast
Roflumilast: Used to treat severe COPD and reduce the risk of exacerbations.

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. infection /malignancy لعده أسباب منها
- التكلفة بتكون انو الشركات بدها تربح
- 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. + malignancy
- New malignancies have been reported.

Asthma classification

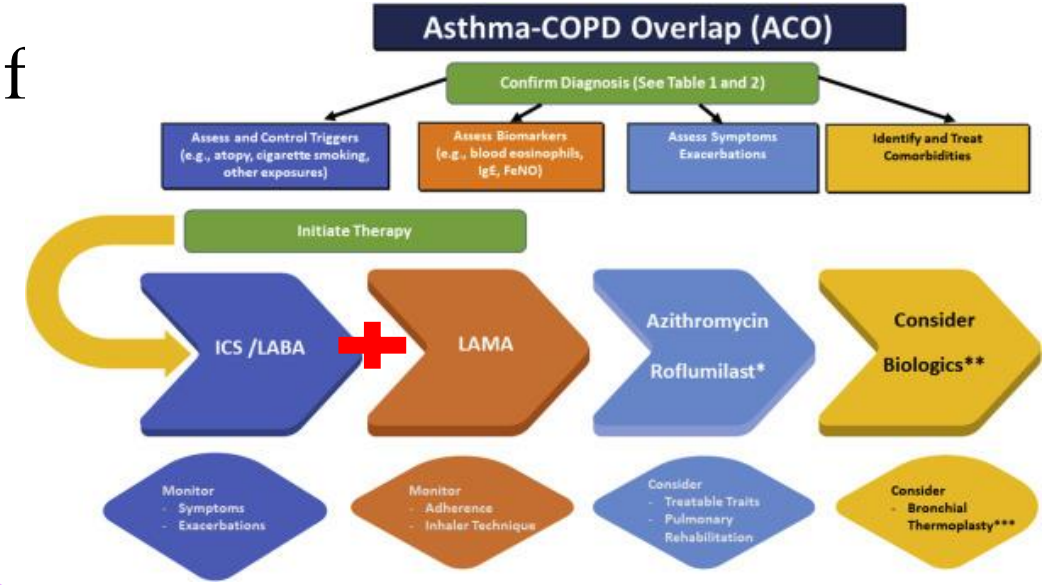
Guidelines for asthma
مهم نعرف شو الstep و شو الأدوية لكل step
مهم الجدول (كله مهم)

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*

Asthma-COPD overlap syndrome (ACOS)

Start with corticosteroid with LABA
و عادة منزيد معهم LAMA و ممكن مبلش فيهم كلهم
someways complicated لانو هون الحالة

- Approach similar asthma: ICS
- Inhaled bronchodilator with rapid onset of action (SABA, SAMA combination) for as-needed symptom relief.
- Regular therapy ICS (low to moderate doses) + LABA and/or LAMA may be necessary to control symptoms.
- **LABA monotherapy should be avoided, as in asthma.**



Diego Jose Maselli, Nicola Alexander Hanania, Management of asthma COPD overlap, Annals of Allergy, Asthma & Immunology, Volume 123, Issue 4, 2019, Pages 335-344, ISSN 1081-1206, https://doi.org/10.1016/j.anai.2019.07.021.

Agents under investigation

- Astegolimab: human IgG2 mAb, selectively inhibits the IL-33 receptor, ST2.

https://pubmed.ncbi.nlm.nih.gov/33872652/.

- Tozorakimab: mAb with a dual pharmacological profile that can inhibit IL-33 activities through the ST2 and RAGE/EGFR signalling pathways. To reduce excess inflammation and epithelial remodelling in IL-33-driven disease.
- https://www.atsjournals.org/doi/abs/10.1164/ajrccm-conference.2022.205.1_MeetingAbstracts.A2397

مش راح تسأل عن الinhaler
اقرأه إذا حاب تعرف

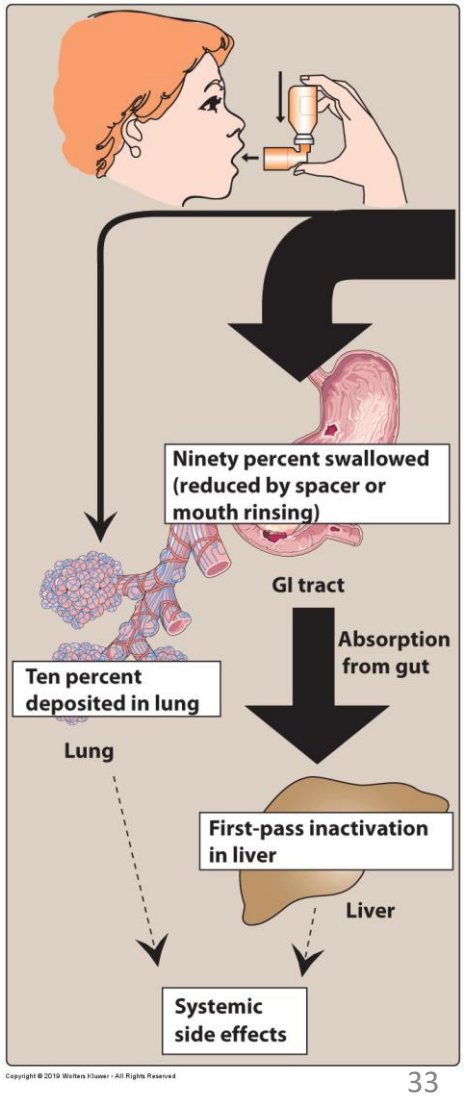
Inhaler Techniques:
Metered-dose inhalers (MDIs) & dry powder inhalers (DPIs)

Exhale before using the inhaler, and then begin to inhale slowly as they press the canister and continue inhaling slowly and deeply throughout actuation.

A large fraction (typically 80% to 90%) of inhaled medication (for example, corticosteroids) is either deposited in the mouth and pharynx or swallowed. The remaining 10% to 20% of a dose of inhaled glucocorticoids that is not swallowed reaches the site of action in the airway.

اهم اشي تعرفه و هي معلومة عامة

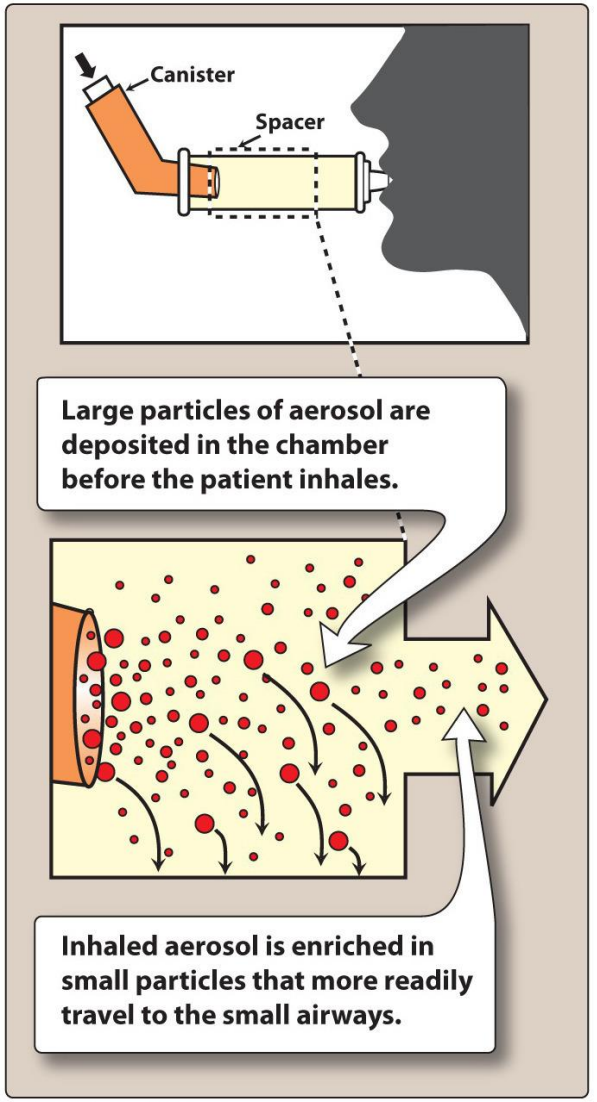
DPIs require a different inhaler technique. Patients should be instructed to inhale quickly and deeply to optimize drug delivery to the lungs. Patients using any type of inhaled corticosteroid device should be instructed to rinse the mouth after use to prevent the development of oral candidiasis.



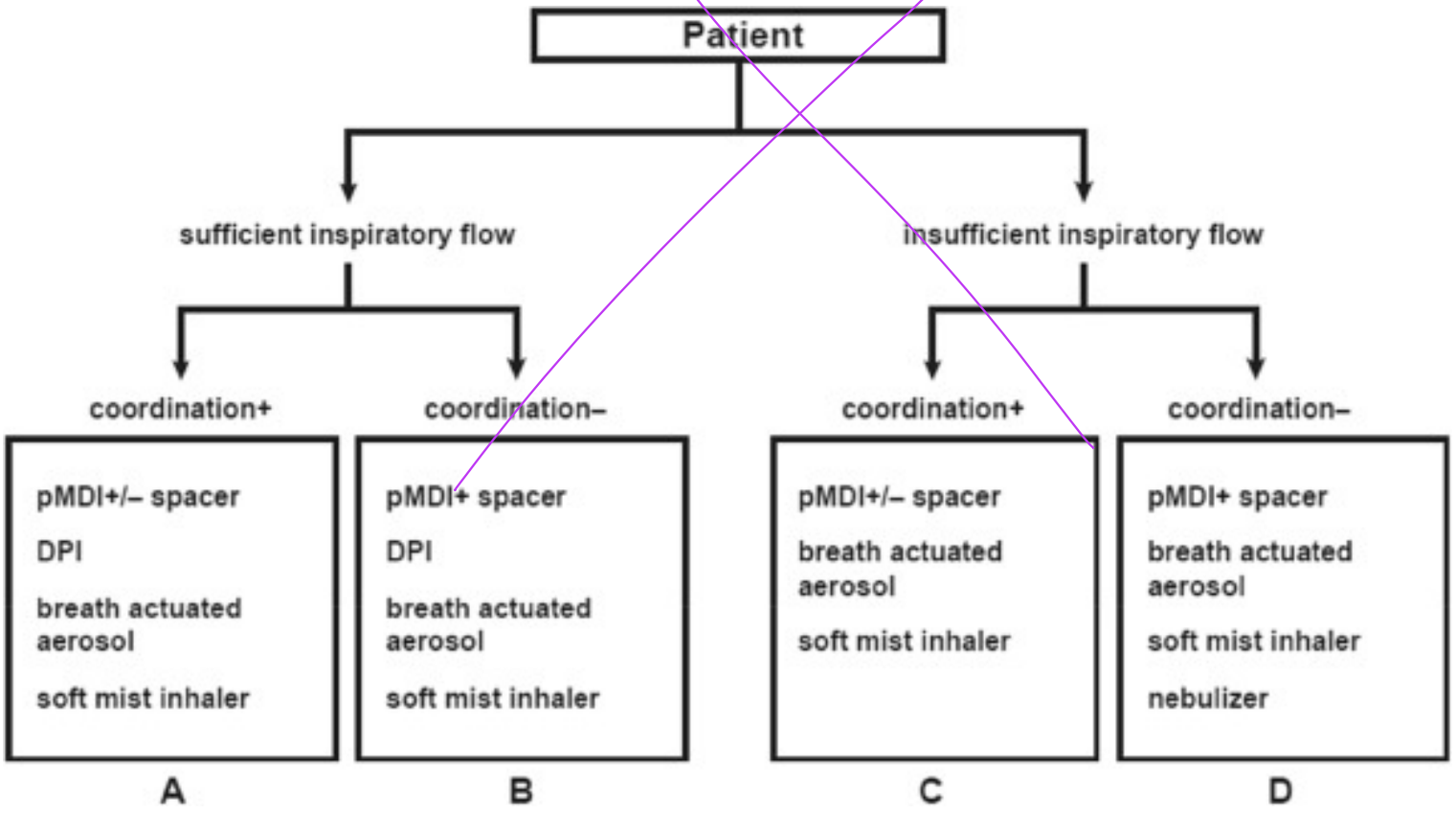
Inhaler Techniques: Spacers

A spacer is a large-volume chamber attached to an MDI. The chamber reduces the velocity of the aerosol before entering the mouth, allowing large drug particles to be deposited in the device. The smaller, higher-velocity drug particles are less likely to be deposited in the mouth and more likely to reach the target airway tissue.

Patients should be advised to wash and/or rinse spacers to reduce the risk of bacterial or fungal growth that may induce an asthma attack.



Inhaler Techniques:
Metered-dose inhalers (MDIs) & dry powder inhalers (DPIs)



Quiz time 🕰️

Test bank 😎😎

1)A 31-year-old man is brought to the emergency department complaining of dyspnea. He has a history of asthma and has had multiple asthma attacks requiring intubation for airway maintenance. He is noncompliant with his medications prescribed for this condition.Physical examination reveals a young man in acute distress. His room air oxygen saturation is 87%. In addition to administration of oxygen, immediate drug administration of albuterol should be administered by which of the following routes?
(A) Inhalation
(B) Intranasal puff metered dose
(C) Subcutaneous
(D) Sublingual
(E) Topical
Answer = A
2)A 7-year-old boy is brought to the emergency department by his parents after being stung by a bee. The parents say he is allergic to bee stings, and the patient is having great difficulty breathing. Epinephrine is administered immediately. His symptoms improve as molecules of epinephrine bind to beta 2- receptors in bronchiolar smooth muscle. Which of the following drugs also stimulates these receptors?
(A) Acebutolol (B) Phenylephrine (C) Prazosin
(D) Salmeterol
(E) Timolol

Answer = D
3)A 23-year-old male college graduate student with a history of asthma presents to the ambulatory care clinic for follow-up. He uses a beta 2-agonist via inhaler when he has an attack. The treating physician should be alert to which of the following possible findings on examination and laboratory studies?
(A) Bradycardia
(B) Hyperglycemia
(C) Hyperkalemia
(D) Hypermagnesemia (E) Hypertension
Answer = B

4)A 47-year-old man presents to the ambulatory care center with symptoms of hypoglycemia and is found to have an insulinoma. His medical history is significant for occasional asthma to which he treats using an albuterol inhaler, and an MI for which he takes daily low-dose aspirin. Because he takes aspirin, he is not able to immediately undergo surgery. The physician prescribes diazoxide for therapy until the tumor can be removed. Diazoxide stimulates potassium channels leading to inhibition of insulin release. Which of the following is most likely to occur in this patient as a result of diazoxide therapy? (A) Bronchoconstriction
(B) Hypertension (C) Hypoglycemia (D) Hypotension (E) Seizures
D
5)A 42-year-old woman with a history of asthma has an attack and is brought to the emergency department for evaluation and treatment. She is wheezing and is short of breath. What is the most likely pathophysiology of this condition?
(A) Bronchodilation
(B) Increased secretion of mucus
(C) Inflammation of the bronchial serosa
(D) Relaxation of bronchial smooth muscle
Answer = B

6)A 5-year-old boy is brought to the clinic by his parents who say that he often has trouble catching his breath when he has been playing hard outside. He is allergic to peanuts. At the moment, he is breathing fine. Which of the following drugs would dilate his bronchioles in an acute asthma attack?
(A) Albuterol
(B) Methacholine (C) Neostigmine (D) Nicotine
(E) Pilocarpine

Answer = A

7)Five patients undergo surgery for various reasons. Each patient has a particular prior medical history. Which of the following patients would be most problematic to the anesthesiologist if thiopental is used during the surgery?
(A) A 5-year-old boy with recurrent otitis media
(B) A 7-year-old boy with recurrent sinusitis
(C) A 9-year-old boy with asthma
(D) A 12-year-old boy with anemia of chronic disease
(E) A 15-year-old boy who has never received anesthesia

Answer = C
8)A 4-year-old boy is hospitalized on the pediatric service with cough, runny nose, and chest pressure. Concern for respiratory syncytial virus is brought up by the treating physician. Treatment with zanamivir is undertaken. Which of the following underlying conditions can worsen bronchospasm in this patient?
(A) Adenoiditis
(B) Asthma
(C) Floppy tongue syndrome
(D) Pharyngitis
(E) Tracheitis
Answer = B
9) 6-year-old boy presents to his pediatrician for follow-up of recurrent hay fever and asthma. He usually has two to three attacks per week. For symptom control, he uses an albuterol inhaler, but his parents would like to try something more. They would like him to take something that would lessen the amount of attacks he has. Although corticosteroids would probably work best for prophylaxis, they are contraindicated in children. Which of the following drugs would decrease the amount of asthma attacks by preventing an arachidonic acid derivative from binding to its receptor? (A) Aspirin
(B) Celecoxib (C) Ipratropium (D) Montelukast (E) Zileuton

Answer = D

10) A 27-year-old man with recurrent asthma attacks is being considered for preventative therapy with cromolyn sodium. This agent is not effective as an acute treatment of an asthma attack because of the lack of which of the following properties?
(A) Anti-inflammatory
(B) Bronchodilator
(C) Immune modulator
(D) Mast cell stabilizer
(E) Neutrophil inhibitor
Answer = B

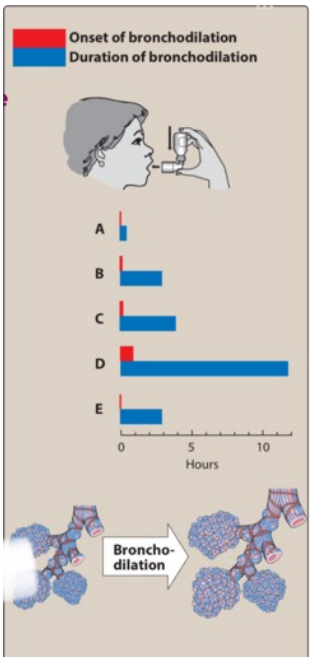
11) A 48-year-old man with a known history of asthma takes daily theophylline. He is found unconscious in his bathroom with an open bottle of theophylline that is now empty nearby. He is found by EMS to be apneic and pulseless. What is the most likely cause of death in this patient?
(A) Apnea
(B) Cardiac arrhythmia (C) Pulmonary embolism (D) Seizures
(E) Tetany
Answer = B
12) A 52-year-old man with asthma treated with a beta 2-agonist via inhaler has been having difficulty with therapy because of persistent changes in blood pressure, nausea, vomiting, and hypomagnesemia. Which of the following medications would be best for this patient? (A) beta 2-Agonist via inhaler every other day
(B) beta 2-Agonist via inhaler every third day
(C) beta 2-Agonist via inhaler twice daily
(D) Change to ipratropium
(E) Change to epinephrine
Answer = D

13) A 13-year-old male has begun having spells of wheezing and difficulty breathing while playing outside. He is diagnosed with asthma and given an inhaler to treat acute attacks. His medication is working well, but he would also like something to prevent attacks from happening. Which of the following drugs would be best to add to his regimen?
(A) Albuterol
(B) Epinephrine (C) Ipratropium (D) Isoproterenol (E) Salmeterol
Answer = E
14) A 13-year-old boy with moderate asthma presents to the clinic for follow-up. His symptoms appear to be better controlled since adding salmeterol to his regimen. He has had to use his rescue inhaler once over the past 2 weeks during exertion. His breathing at night has improved as well. How does salmeterol exhibit its beneficial effects for asthma?
(A) Long-acting beta1-agonist
(B) Long-acting beta1-antagonist
(C) Long-acting beta1- and %2-agonist (D) Long-acting beta2-agonist
(E) Long-acting beta 2-antagonist

Answer = D
15) A 24-year-old man presents to the primary care clinic for follow-up of his asthma. He has had asthma since he was 8 years old and requires daily treatment for his symptoms. He often has nighttime awakenings with coughing spells. On physical exam, diffuse wheezing is heard bilaterally. He is willing to try anything to improve his symptoms. The physician decides to add cromolyn to his regimen. What is the mechanism of action of cromolyn?
(A) Blocks leukotriene receptors (B) Inhibits endothelin-1 receptors (C) Mast cell stabilizer
(D) Muscarinic antagonist
(E) Phosphodiesterase inhibitor

Answer = C

16) A 34-year-old man with exercised-induced asthma is searching for a bronchodilator that will allow him to run in a marathon. The event will take him approximately
6 h and 30 min to complete. The following
diagram shows five bronchodilators. Which of the following agents will provide him with the most efficacious therapy during his run? (A) Letter A
(B) Letter B
(C) Letter C
(D) Letter D (E) Letter E



Answer = D

17) A 6-year-old boy is brought to his primary care
physician with a history of hay fever and asthma.
He usually has two to three attacks per week.
For symptom control, he uses an albuterol inhaler,
but his parents would like to try something more. They would like him to take something that would lessen the amount of attacks he has. Although corticosteroids would probably work best for prophylaxis, they are contraindicated in children. He is instead give montelukast.
How does montelukast works?
(A) Blocks leukotriene receptors
(B) Blocks muscarinic acetylcholine receptors (C) Inhibits COX-1 and COX-2
(D) Inhibits COX-2 only
(E) Inhibits lipoxygenase
Answer = A