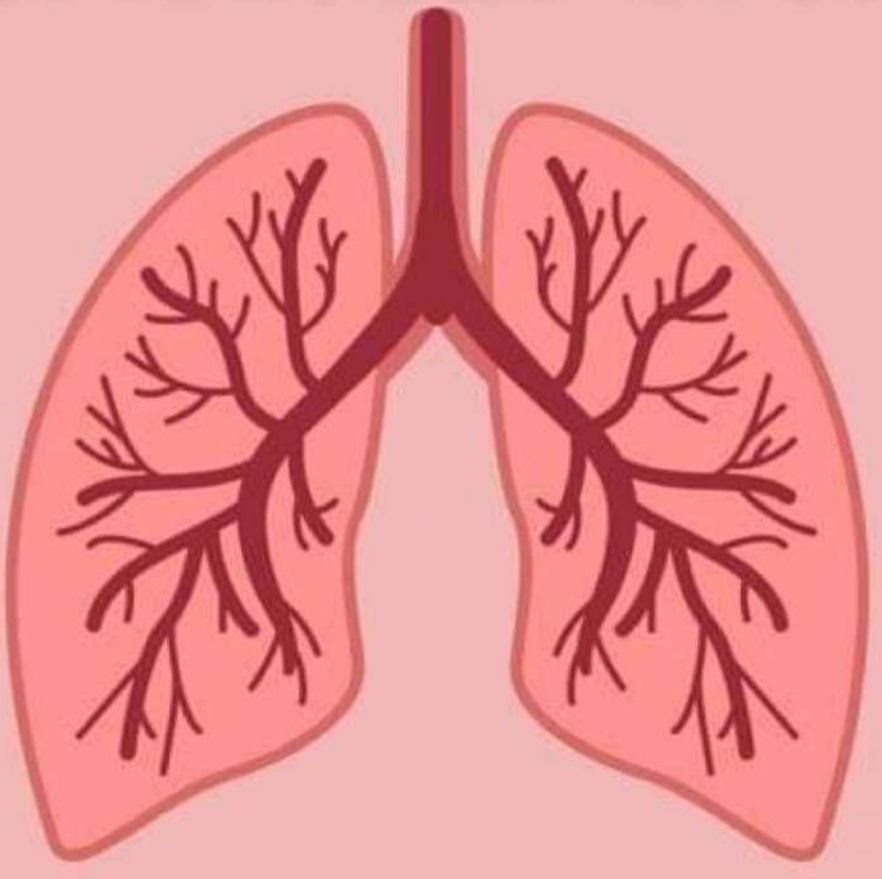
النادي الطبي

RESPIRATORY SYSTEM



SUBJECT : Pharmacology

LECTURE : 1

DONE BY : Johainah Taha

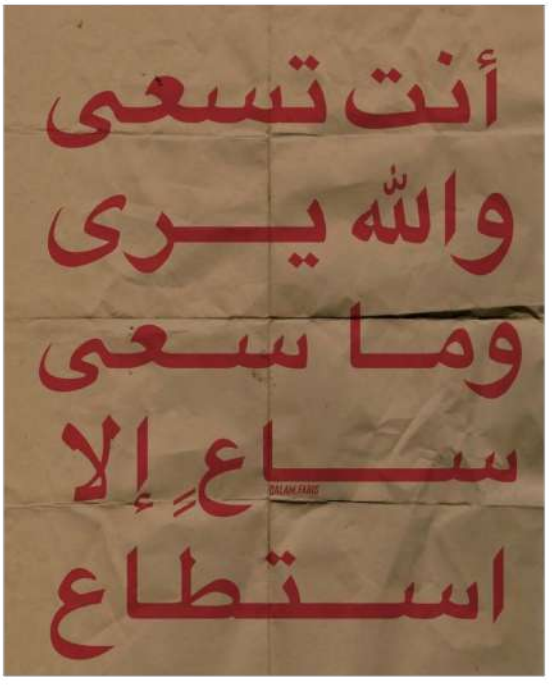
Lecture 1: Treatment of Chronic Obstructive Pulmonary Disease (COPD)

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

بسم الله نبدأ بسيستم الRS، هاد الفصل حأكون معكم بتفريغ مادة الفارما انا و زميلاتي سلسبيل و سارة

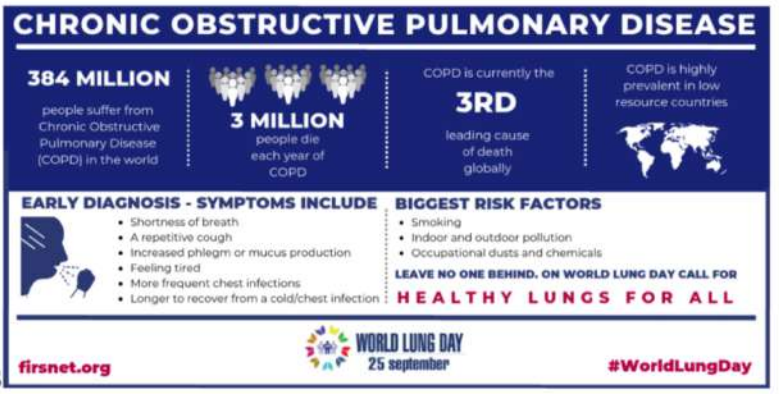
التفريغ يشمل : كلام و ملاحظات الدكتور، الكتاب المعتمد، شروحات و توضيحات لأي شي بيحتاج توضيح، كويز بنهاية المحاضرة لنختبر دراستنا 🫶🫶

تنبيه : ضروري تكونوا دارسين محاضرة 2 باثو قبل هاي المحاضرة 🙏 عشان تعرفوا شو هو المرض الي حنعالجه



Facts & numbers

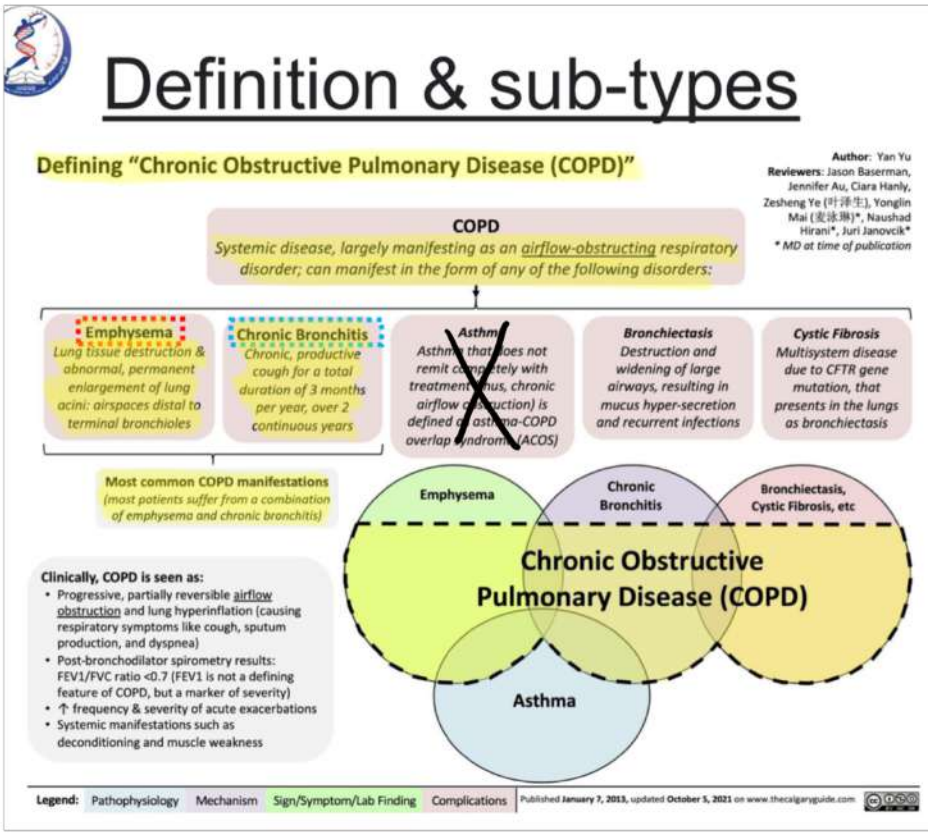
- Estimated cost of CODP management ~$50 billion!
- Nearly half COPD patients say it limit their work and social activity
- Known as disease of old age but can occur as young as 35 years
- SMOKING (irreversible)
- Approximately 15-20% of the cases occur in nonsmokers.

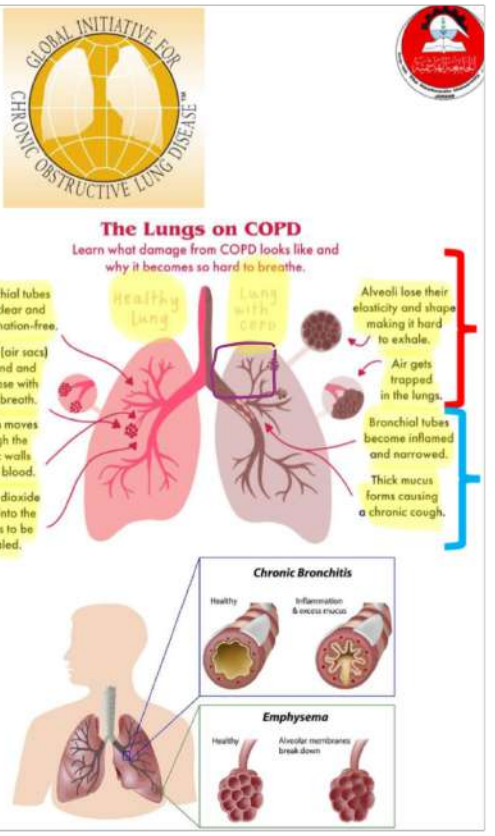


يعني [**It is NOT curable but treatable**

بالبداية هاي السلايد مجرد مقدمة لنعرف بشكل عام عن شو حنحكي؛ مهم تعرفوا
الmanagement تبعت الCOPD عالية، و المقصود بكلمة management هي تكلفة الدواء،
و الرعاية الصحية، و المواصلات...الخ
ثانياً السبب الرئيسي للCOPD هو التدخين زي ما اخدنا بالباثو
ثالثاً الCOPD ما اله علاج يا للأسف، انا بستعمل الأدوية فقط لأخفف الأعراض
لهيك بنحكي COPD is not curable but treatable .

Definition & sub-types





هسا هاي السلايد باثو؛ اقرأوا الي عليه هايلايت ،حأتركلكم جزئية شرح الكتاب
مع بعض التوضيحات

*COPD is a chronic, irreversible obstruction of airflow that is usually progressive and characterized by persistent symptoms.

Progressive : بضل يسوء مع العمر و خصوصاً مع عدوم وجود علاج

*These may include cough, excess mucus production, chest tightness, breathlessness, difficulty sleeping, and fatigue.

مهيمن لأسئلة الكيسات ، الدكتور حكى انه بجيب الاعراض بالكيس و بسألنا عن اسم المرض و العلاج تبعه و لتحت حنضيف عليهم شغلات من السلايدات

*Although symptoms are similar to asthma, the characteristic irreversible airflow obstruction of COPD is one of the most significant differences between the diseases.

*Smoking is the greatest risk factor for COPD and is directly linked to the progressive decline of lung function, as demonstrated by forced expiratory volume in one second (FEV1) .

forced expiratory volume in 1 second (FEV1) is the maximum amount of air that the subject can forcibly expel during the first second following maximal inhalation هون بتكون اقل من 0.7

80-90% of COPD patients are smokers.It is usually begin after 20 pack year smoker.

*Smoking cessation (stopage) should be recommended regardless of stage and severity of COPD, or the age of patient.

وقف التدخين شي أساسي بمرحلة العلاج 🙏🏻

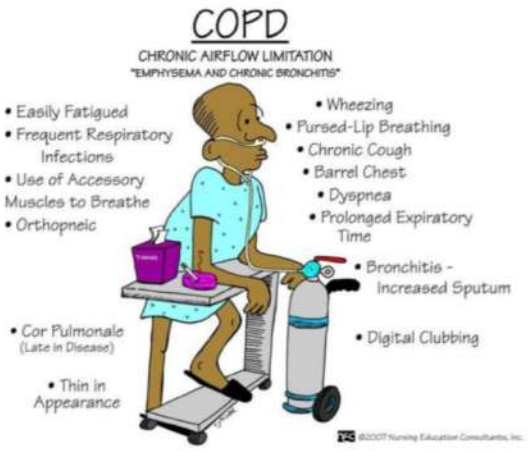
*Drug therapy for COPD is aimed at relief of symptoms and prevention of disease progression.(Not curable)

*Unfortunately, with currently available care, many patients still experience a decline in lung function over time.

Signs & symptoms

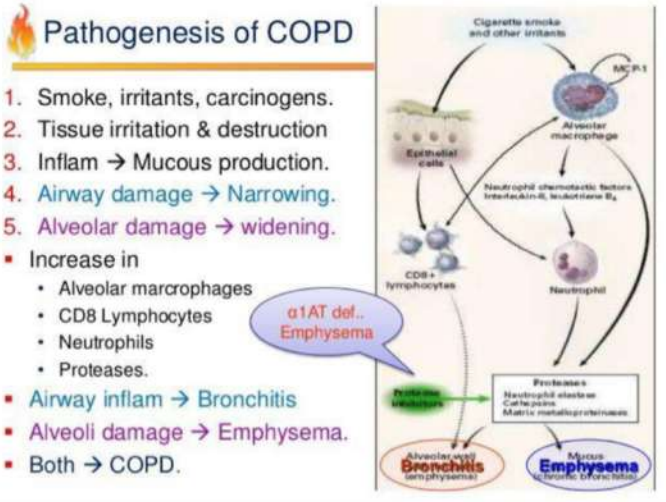
important

- Dyspnea
- Chronic cough
- Sputum production
- Wheezing and chest tightness
- Breathlessness
- Difficulty sleeping
- Fatigue.



Pathogenesis

- Chronic bronchitis and emphysema: CD8+ T-lymphocytes, neutrophils, and CD68+ monocytes/macrophages in the airways.
- the bronchial inflammation of asthma: presence of CD4+ T-lymphocytes, eosinophils, and increased interleukin (IL)-4 and IL-5.



These are one of the most important differances between COPD and Asthma:

***The evidence shows that patients with COPD have increased numbers of CD8 + T lymphocyte in the lung, neutrophils and CD68+ monocytes in the airways.**
+ it is irreversible

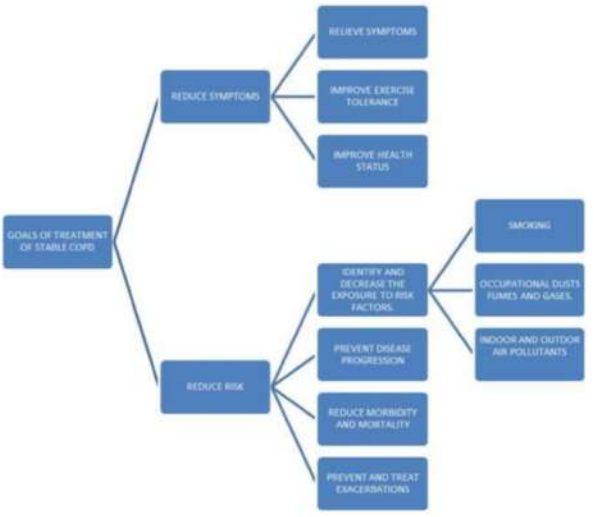
allergic

***In Asthma, there is an increase in CD4+ T Lymphocyte, eosinophils and IL4 + IL5.**
+ it is reversible

Revision :
CD4 T cells are MHC-II restricted and pre-programmed for helper functions, whereas CD8 T cells are MHC I-restricted and pre-programmed for cytotoxic functions

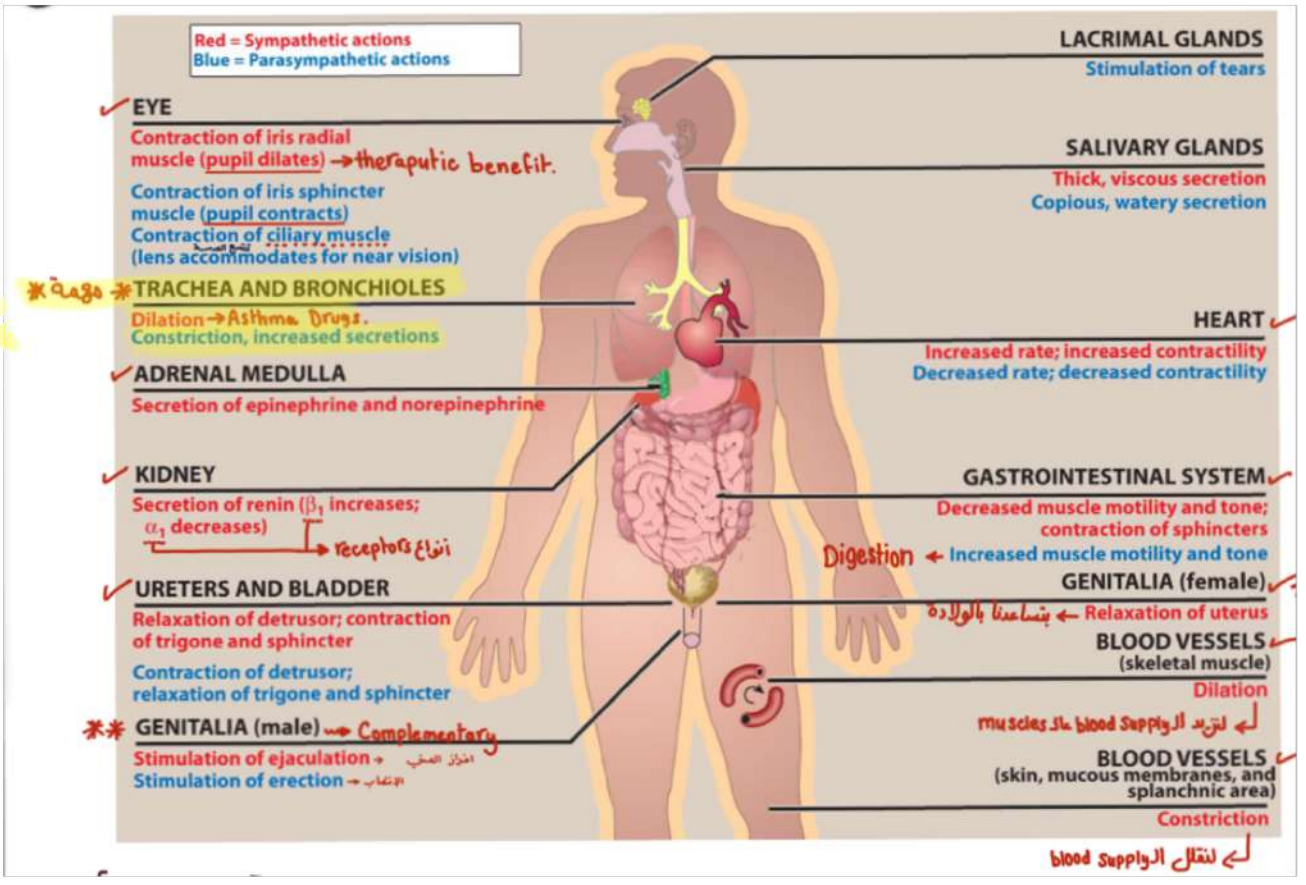
Treatment & management

- Quit smoking
- education and counselling (about COPD and inhaler techniques).
- Seasonal influenza and COVID-19 vaccinations.
- Diet: no ideal COPD diet but excess weight can contribute to dyspnea >>> normal body mass index (BMI).



اجاك شخص معه COPD كيف لازم تتعامل معه؟؟
أولاً خليه يقلع عن التدخين
ثانياً اشرحله شو يعني COPD و مدى خطورة هاد المرض لحتى يلتزم بالعلاج و علمه كيف يستخدم البخاخات صح لحتى يستفيد من العلاج
ثالثاً بعطيه vaccine ، خصوصاً الvaccines تبعت الفايروسات الي بتصيب و بتستهدف الجهاز التنفسي لحتى أحميهم من أي sever complication
رابعاً بدي اهتم بغذاءهم و وزنهم، حكينا بالباثو انه الاشخاص هدول غالباً بصاحبهم obesity و السبب طبعاً غير معروف للآن ، المهم لازم يلتزم بالغذاء الhealthy

كل الي اخدناه للآن مقدمات، و هسا بدنا نبدأ بالجد، بس قبل بدي أشرح الكم و أذكركم بشغلات أخدناها بالجينيرال مع دكتورة أروى مهمة و بتفيدنا بهاي المحاضرة 👏🏻



The sympathetic nervous system prepares the body for the "fight or flight" response during any potential danger.

The parasympathetic nervous system inhibits the body from overworking and restores the body to a calm and composed state.

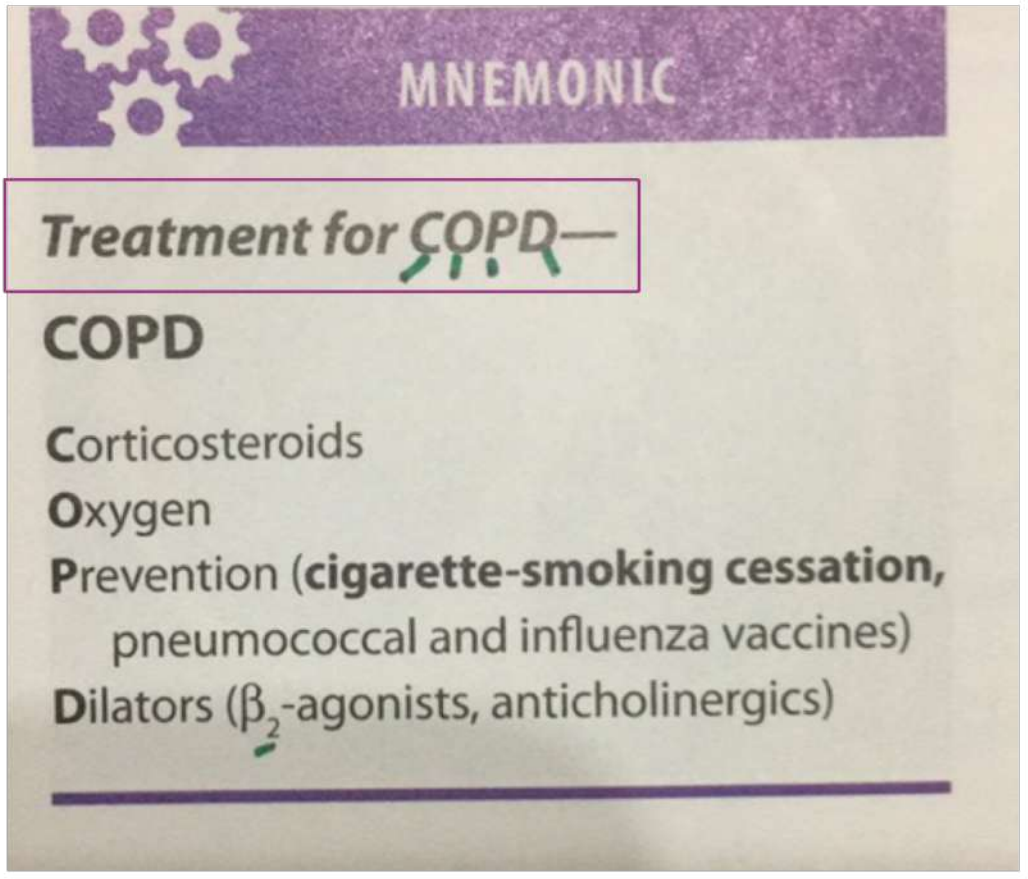
و بما انه احنا بسيستم الRS ركزولي على عمل كل واحد فيها عالجهاز التنفسي

The Sympathetic nervous system causes trachea and brochioles dilation by the activation of Beta adrenergic agonist that relaxes muscles of the air way, causing widening of the airway and resulting in easier breathing.

لهيك حلو نعمل دواء يحفز عمل هدول الreceptors لحتى يصير مجرى التنفس أوسع

The parasympathetic nervous system causes trachea and brochioles constriction because the muscarinic receptors increses the bronchoconstriction and mucus secretion that limit the air flow.

لهيك حلو نعمل دواء يثبط عمل هدول الreceptors لحتى يصير مجرى التنفس أوسع


MNEMONIC
Treatment for COPD—
COPD
Corticosteroids
Oxygen
Prevention (cigarette-smoking cessation, pneumococcal and influenza vaccines)
Dilators (β_2-agonists, anticholinergics)

Pharmacological agents

COPD pharmacological treatment include

1. Short-acting β_2 agonists (SABAs)
2. Long-acting β_2 agonists (LABAs)
3. Short-acting muscarinic antagonist (SAMA)
4. Long-acting muscarinic antagonist (LAMA)
5. Inhaled corticosteroids (ICS)
6. Combinations of these classes
7. Vaccines, antibiotics and other agents

→ Inhaled bronchodilators

هدول هم الtretments الي بنستعملهم، أول 4 بنطلق عليهم مسمى inhaled bronchodilators

و أول 4 مثل ما بنلاحظ بستهدفوا الreceptors الي حكيتلكم عنهم فوق، يا إما بتحفيز عملهم أو تثبيطه

Revision:

*An agonist is a drug that binds to the receptor, producing a similar response to the intended chemical and receptor.

*An antagonist is a drug that binds to the receptor either on the primary site, or on another site, which all together stops the receptor from producing a response

From the book :

*Inhaled bronchodilators, including the B2-adrenergic agonists and anticholinergic agents (muscarinic antagonists), are the foundation of therapy for COPD.

*These drugs increase airflow, alleviate symptoms, and decrease exacerbations.

*The long-acting bronchodllators, LABAs and long-acting muscarinic antagonists (LAMAs), are preferred as first-line treatment of COPD for all patients except those who are at low risk with less symptoms.

هاي السلايد بتحكي عن الادوية الي حنحكي عنها خلال 3 محاضرات الجايين

Pharmacological agents

MEDICATION	IND
SHORT-ACTING β_2 ADRENERGIC AGONISTS (SABAs)	
Albuterol PROAIR, PROVENTIL, VENTOLIN	Asthma, COPD
Levalbuterol XOPENEX	Asthma, COPD
LONG-ACTING β_2 ADRENERGIC AGONISTS (LABAs)	
Arformoterol BROVANA	COPD
Formoterol FORADIL, PERFOROMIST	Asthma, COPD
Indacaterol ARCAPTA	COPD
Olodaterol STRIVERDI RESPIMAT	COPD
Salmeterol SEREVENT	Asthma, COPD
INHALED CORTICOSTEROIDS	
Beclomethasone BECONASE AQ*, QVAR	Allergic rhinitis, Asthma, COPD
Budesonide PULMICORT, RHINOCORT*	Allergic rhinitis, Asthma, COPD
Ciclesonide ALVESCO, OMNARIS*, ZETONNA*	Allergic rhinitis, Asthma
Fluticasone FLONASE*, FLOVENT	Allergic rhinitis, Asthma, COPD
Mometasone ASMANEX, NASONEX*	Allergic rhinitis, Asthma
Triamcinolone NASACORT*	Allergic rhinitis, Asthma

LONG-ACTING β_2 ADRENERGIC AGONIST/CORTICOSTEROID COMBINATION	
Formoterol/budesonide SYMBICORT	Asthma, COPD
Formoterol/mometasone DULERA	Asthma, COPD
Salmeterol/fluticasone ADVAIR	Asthma, COPD
Vilanterol/fluticasone BREO ELLIPTA	COPD
SHORT-ACTING ANTICHOLINERGIC	
Ipratropium ATROVENT	Allergic rhinitis, Asthma, COPD
SHORT-ACTING β2 AGONIST/SHORT-ACTING ANTICHOLINERGIC COMBINATION	
Albuterol/ipratropium COMBIVENT RESPIMAT, DUONEB	COPD
LONG-ACTING ANTICHOLINERGIC (LAMA)	
Aclidinium TUDORZA PRESSAIR	COPD
Glycopyrrolate SEEBRI NEOHALER	COPD
Tiotropium SPIRIVA	Asthma, COPD
Umeclidinium INCRUSE ELLIPTA	COPD
LABA/LAMA COMBINATION	
Formoterol/glycopyrrolate BEVESPI AEROSPHERE	COPD
Indacaterol/glycopyrrolate UTIBRON NEOHALER	COPD
Vilanterol/umeclidinium ANORO ELLIPTA	COPD
Olodaterol/tiotropium STIOLTO RESPIMAT	COPD

OTHER AGENTS	
Roflumilast DALIRESP	COPD
Theophylline ELIXOPHYLLIN, THEO-24	Asthma, COPD

Pharmacological agents

و هاد مراجعة للي حنحكي عنه بالمحاضرة ارجعوله بالاخر

Subclass	Mechanism of Action	Effects	Clinical Applications	Pharmacokinetics, Toxicities
BETA AGONISTS				
• Albuterol	Selective β_2 agonist	Prompt, efficacious bronchodilation	Asthma, chronic obstructive pulmonary disease (COPD) • drug of choice in acute asthmatic bronchospasm	Aerosol inhalation • duration several hours • also available for nebulizer and parenteral use • *Toxicity:* Tremor, tachycardia • overdose: arrhythmias
• Salmeterol	Selective β_2 agonist	Slow onset, primarily preventive action; potentiates corticosteroid effects	Asthma prophylaxis	Aerosol inhalation • duration 12–24 h • *Toxicity:* Tremor, tachycardia • overdose: arrhythmias
• *Metaproterenol, terbutaline: Similar to albuterol; terbutaline available as an oral drug*				
• *Formoterol: Similar to salmeterol*				
CORTICOSTEROIDS, INHALED				
• Fluticasone	Alters gene expression	Reduces mediators of inflammation • powerful prophylaxis of exacerbations	Asthma • adjunct in COPD • hay fever (nasal)	Aerosol • duration hours • *Toxicity:* Limited by aerosol application • candidal infection, vocal cord changes
• *Beclomethasone, budesonide, flunisolide, others: Similar to fluticasone*				
CORTICOSTEROIDS, SYSTEMIC				
• Prednisone	Like fluticasone	Like fluticasone	Asthma • adjunct in COPD	Oral • duration 12–24 hours • *Toxicity:* Multiple • see Chapter 39
• *Methylprednisolone: Parenteral agent like prednisone*				
METHYLXANTHINES				
• Theophylline	Uncertain • phosphodiesterase inhibition • adenosine receptor antagonist	Bronchodilation, cardiac stimulation, increased skeletal muscle strength (diaphragm)	Asthma, COPD	Oral • duration 8–12 h but extended-release preparations often used • *Toxicity:* Multiple (see text)

Pharmacological agents:

1 β2-adrenergic agonists

COPD pharmacological treatment include

1. Short-acting β_2 agonists (SABAs)
2. Long-acting β_2 agonists (LABAs): indacaterol, olodaterol and vilanterol (once-daily). Arformoterol, formoterol, and salmeterol (twice-daily)

MEDICATION	INDICATION
SHORT-ACTING β_2 ADRENERGIC AGONISTS (SABAs)	
Albuterol PROAIR, PROVENTIL, VENTOLIN	Asthma, COPD
Levalbuterol XOPENEX	Asthma, COPD
LONG-ACTING β_2 ADRENERGIC AGONISTS (LABAs)	
Arformoterol BROVANA	COPD
Formoterol FORADIL, PERFOROMIST	Asthma, COPD
Indacaterol ARCAPTA	COPD
Olodaterol STRIVERDI RESPIMAT	COPD
Salmeterol SEREVENT	Asthma, COPD

+ Vilanterol

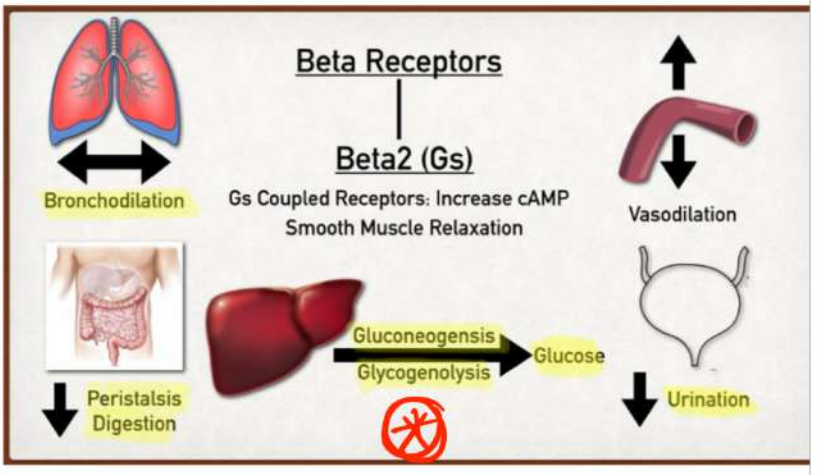
الجدول حفظ طبعاً
كلهم بنتهوا بterol

Pharmacological agents:

β2-adrenergic agonists (adrenergic β2 receptor agonists):

act on the β2 adrenergic receptor:

- smooth muscle relaxation
- dilation of bronchial passages
- vasodilation in muscle and liver
- relaxation of uterine muscle
- release of insulin.



❖**Primarily used to treat asthma and COPD.**

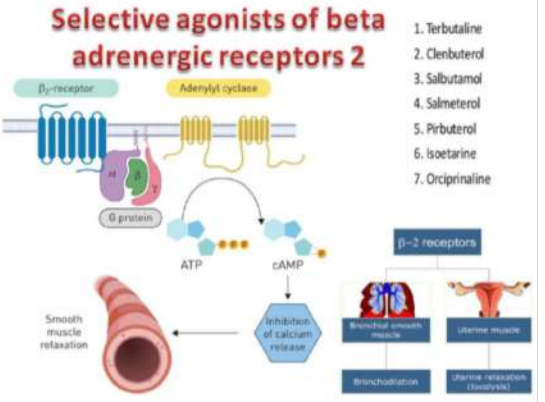
تعليق على نقطة 3
بصير عندي vasodilation لل liver فبطلع glucose اكثر
بصير عندي vasodilation لل muscle لأقدر أوصل الها ال glucose
بصير عندي release لل insulin ليسمح لل glucose يدخل جوا الخلايا، بس طبعاً بكون بكميات قليلة
أهم شي و الدكتور ركز عليه، هو انه هاي الأدوية بتعمل Hyperglycemia

Pharmacological agents:

β2-adrenergic agonists

➢**MOA**:

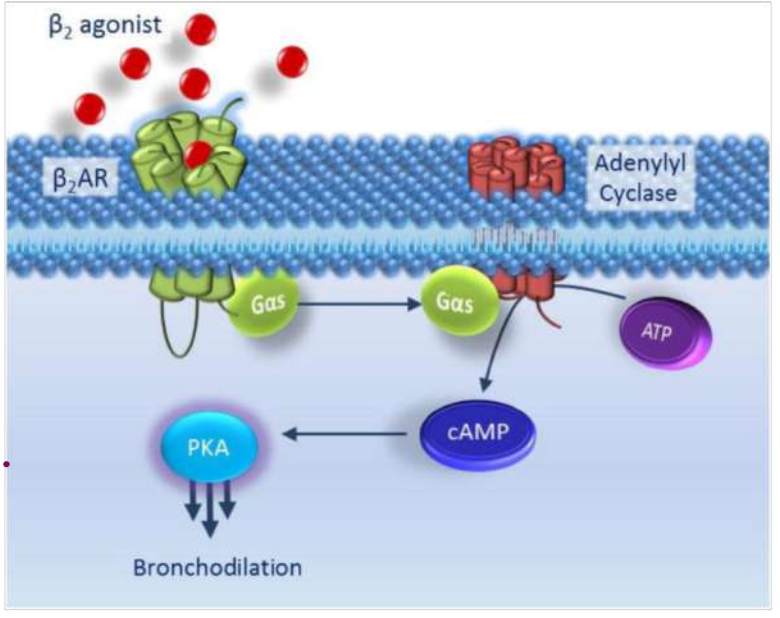
Receptor activation (G protein (Gs) + adenylyl cyclase) >> **increases intracellular cAMP >> activate protein kinase A (PKA)** >> phosphorylate Gq-coupled receptors >> **reduce intracellular Ca2+ or decrease the sensitivity of Ca2+ >> inhibition of myosin light chain phosphorylation (MLCK)** >> preventing airway smooth muscle contraction. ⬇️شرح خارجي



➢Anti-inflammatory effects?

reducing intercellular adhesion molecule-1 (ICAM-1)

reducing granulocyte-macrophage colony-stimulating factors (GM-CSF) release الشرح عالصفحة التالية



*β2AR(beta 2 adrenergic recetor) is a member of the G-protein coupled receptor (GPCR) family.

*Binding of β2-agonist to β2AR induces a conformational change allowing the α-subunit of the G-protein to dissociate and bind to adenyl cyclase.

*Adenylyl cyclase is thus activated and catalyses the formation of cyclic AMP (cAMP) from ATP.

*cAMP molecules bind to PKA (protein kinase A) which induces the dissociation of the catalytic and regulatory subunitsfrom each other.

هسا الPKA بروح يعمل فسفرة في Gq coupled receptor فبالتالي بقلل من الكالسيوم المهم بانقباض العضلات

*Once released, the PKA catalytic subunits phosphorylate and hence activate myriad cellular targets which results in airway smooth muscle relaxation and hence bronchodilation.

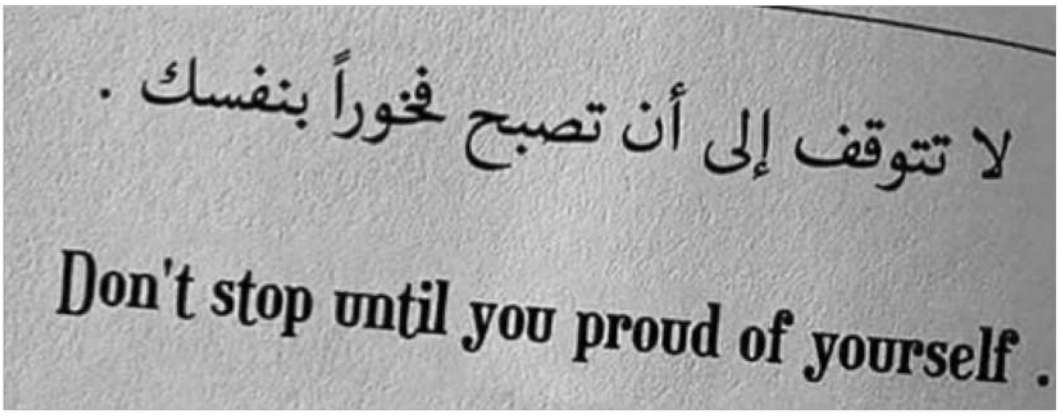
العلماء وجدوا انه هاي الأدوية الها effect آخر كمان و هو anti-inflamatory
بس قبل ما نحكي عن شو بتعمل خلينا نراجع كم مصطلح اخدناهم بالجينيرال

Intercellular adhesion molecule 1 (ICAM-1) is a cell surface glycoprotein which is on endothelial cells and an adhesion receptor that is best known for regulating leukocyte recruitment from circulation to sites of inflammation
It is highly expressed on the surface of respiratory epithelial cells in allergic patients.

لهيك B2 adrenegic agonists بيجوا ليقللوا من ICAM1 على سطح الخلايا و بالتالي بنقلل الinflamation

Granulocyte-macrophage-colony-stimulating-factors are substances that helps make more white blood cells, especially granulocytes, macrophages, and cells that become platelets.

لهيك B2 adrenegic agonists بيجوا ليقللوا من هدول الfactors و بالتالي بنقلل الinflamation



Pharmacological agents:

β2-adrenergic agonists

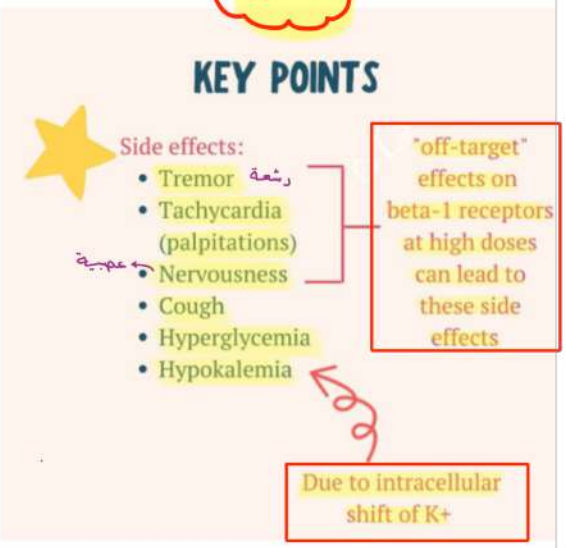
β2-adrenergic agonists (adrenergic β_2 receptor agonists):

❖Side effects: See the figure

❖All β2 agonists are available in inhaler form: metered-dose inhalers (MDI) or dry powder inhalers (DPI)

الدكتور رغب يسأل عنهم

مهمين



*Off target effect: Describes the effects that can occur when a drug binds to targets (proteins or other molecules in the body) other than those for which the drug was meant to bind

بدل ما يرتبط ب beta 2 بصير كمان يربط ب beta 1

Beta-1-adrenergic receptors regulate heart rate and myocardial contractility

*Hypokalemia -> Insulin and epinphrine activate Na+/K+ pump, and that leads to Efflux of K+ extracellularly

Subclass	Mechanism of Action	Effects	Clinical Applications	Pharmacokinetics, Toxicities
BETA AGONISTS				
• Albuterol	Selective β_2 agonist	Prompt, efficacious bronchodilation	Asthma, chronic obstructive pulmonary disease (COPD) • drug of choice in acute asthmatic bronchospasm	Aerosol inhalation • duration several hours • also available for nebulizer and parenteral use • *Toxicity:* Tremor, tachycardia • overdose: arrhythmias
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• *Metaproterenol, terbutaline:* Similar to albuterol; terbutaline available as an oral drug • *Formoterol:* Similar to salmeterol				

هاد مقطع من الجدول الملخص

Pharmacological agents:

muscarinic antagonist

These inhibit the parasympathetic nervous system and leads to bronchodilation

COPD pharmacological treatment include

3. Short-acting muscarinic antagonist (SAMA)

4. Long-acting muscarinic antagonist (LAMA): Aclidinium, tiotropium, glycopyrrolate and umeclidinium

الجدول حفظ

SHORT-ACTING ANTICHOLINERGIC	
Ipratropium ATROVENT	Allergic rhinitis, Asthma, COPD
SHORT-ACTING β2 AGONIST/SHORT-ACTING ANTICHOLINERGIC COMBINATION	
Albuterol/ipratropium COMBIVENT RESPIMAT, DUONEB	COPD
LONG-ACTING ANTICHOLINERGIC (LAMA)	
Aclidinium TUDORZA PRESSAIR	COPD
Glycopyrrolate SEEBRI NEOHALER	COPD
Tiotropium SPIRIVA	Asthma, COPD
Umeclidinium INCRUSE ELLIPTA	COPD

The combination of an anticholinergic and a Beta 2 agonist may be helpful in patients who have inadequate response to a single inhaled bronchodilator and are at risk of exacerbations.

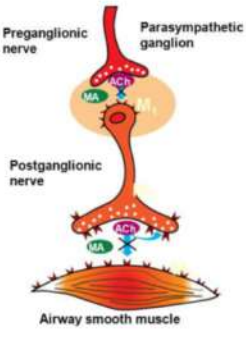
Pharmacological agents:

muscarinic antagonist (muscarinic receptor antagonist (MRA):

- ✓Muscarinic receptors are predominately present on glandular cells, smooth muscle cells, and cardiac muscle cells.
- ✓Competitively inhibit the effect of **acetylcholine (ACh)** at muscarinic receptors (M1 and M3)
- ✓M1: CNS
- ✓M3: smooth muscle GI, UT, airway, and blood vessels
- ✓Side effects: dry mouth, constipation and urinary retention

مهمين

Mechanism of action of muscarinic antagonists



- Muscarinic antagonists block M_1 and M_3 receptors, thus preventing binding of acetylcholine and inhibiting airway smooth muscle contraction

ACh, acetylcholine; M_x, muscarinic receptor; MA, muscarinic antagonist

Tashkin DP, Fabbri LM. *Respir Res.* 2010;11:149.

***The molecule acetylcholine activates muscarinic receptors, allowing for a parasympathetic reaction**

بعد ما خلصنا الأربع مجموعات من bronchodilators صار دور نحكي عن أدوية جديدة كمان بنستخدمها لمرضى COPD

Pharmacological agents:

Inhaled corticosteroids (ICS)

COPD pharmacological treatment include

5. Inhaled corticosteroids (ICS)

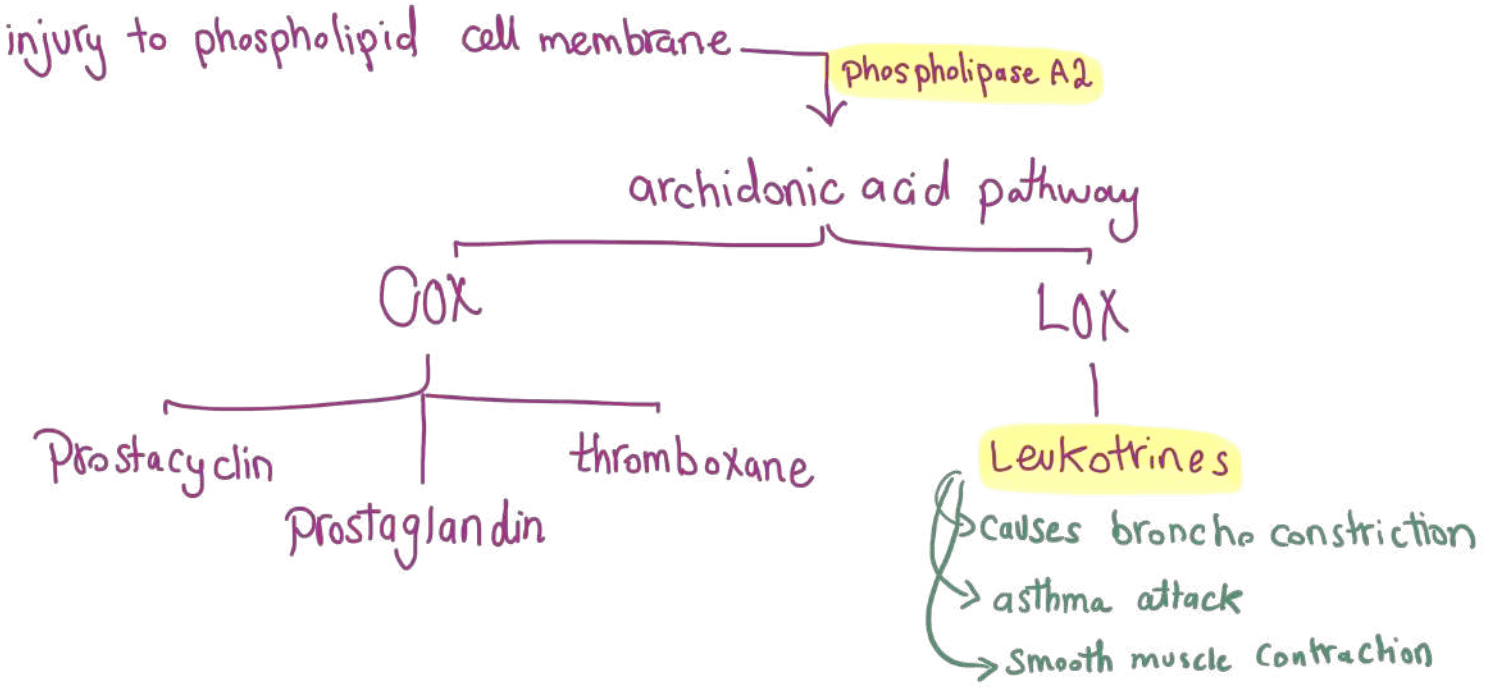
INHALED CORTICOSTEROIDS	
Beclomethasone BECONASE AQ*, QVAR	Allergic rhinitis, Asthma, COPD
Budesonide PULMICORT, RHINOCORT*	Allergic rhinitis, Asthma, COPD
Ciclesonide ALVESCO, OMNARIS*, ZETONNA*	Allergic rhinitis, Asthma
Fluticasone FLONASE*, FLOVENT	Allergic rhinitis, Asthma, COPD
Mometasone ASMANEX, NASONEX*	Allergic rhinitis, Asthma
Triamcinolone NASACORT*	Allergic rhinitis, Asthma

-one نيم

*Combinations

LONG-ACTING β_2 ADRENERGIC AGONIST/CORTICOSTEROID COMBINATION	
Formoterol/budesonide SYMBICORT	Asthma, COPD
Formoterol/mometasone DULERA	Asthma, COPD
Salmeterol/fluticasone ADVAIR	Asthma, COPD
Vilanterol/fluticasone BREO ELLIPTA	COPD

نفس الشي قبل ما نبدأ نشرح عن هدول الأدوية بدنا نتذكر كم شغلة من الجينيرال



inhibit the release of arachidonic acid through inhibition of phospholipase A2 ①

Pharmacological agents:

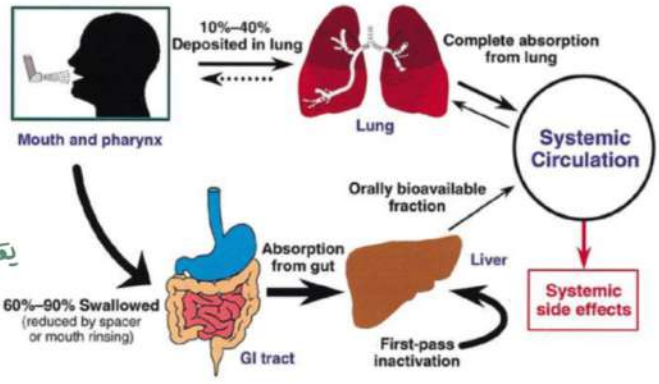
Inhaled corticosteroids (ICS)

- Anti-inflammatory agents that are recommended by GOLD as a first-line maintenance treatment in COPD cases with repeated exacerbations تفاقم

- Do not relax airway smooth muscle directly but reduce bronchial reactivity and potentiate the effects of β-receptor agonists ② يعزي

③

- Main effect: inhibition of the infiltration of lymphocytes, eosinophils, and mast cells.



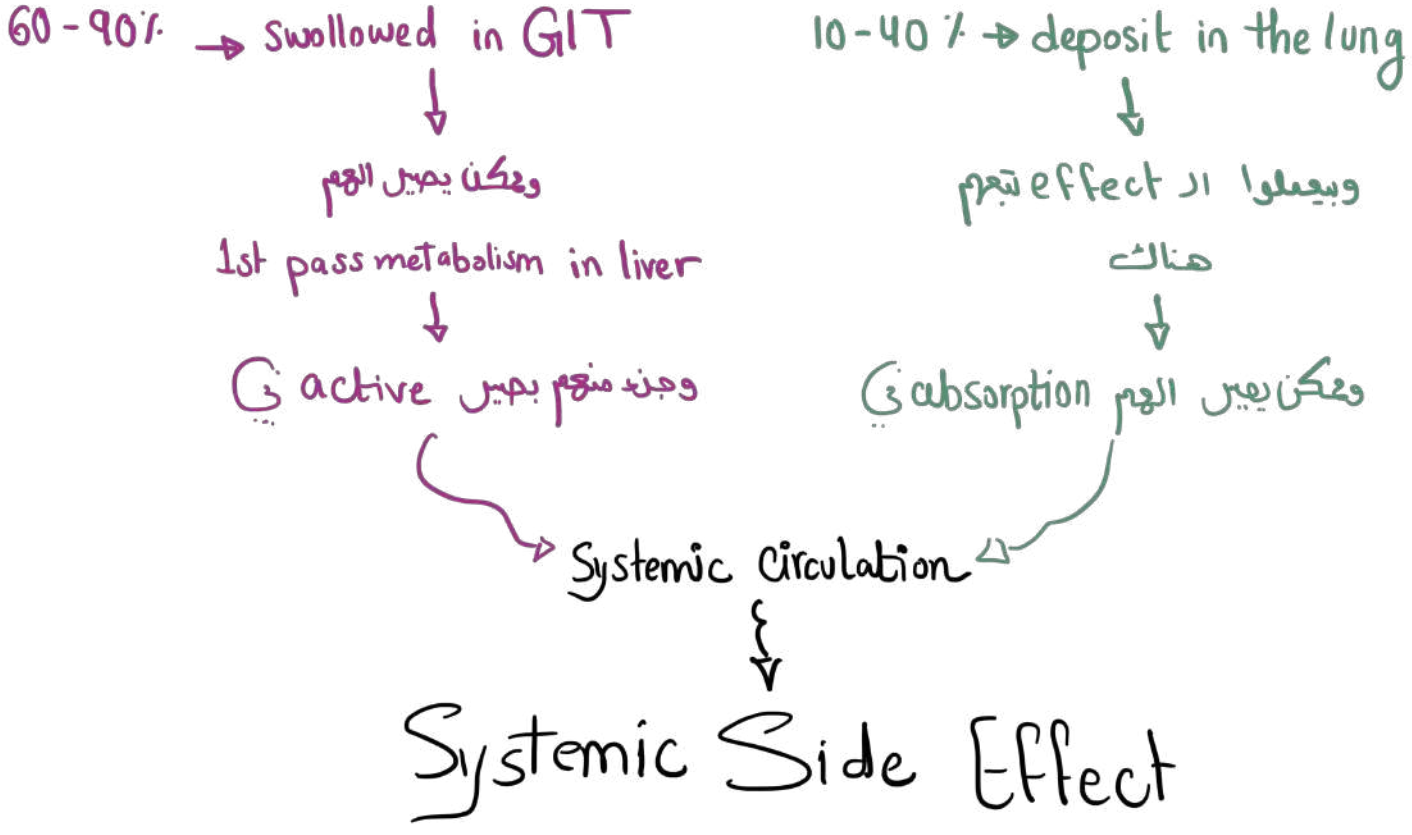
***Inhaled corticosteroids MOA:**

1- inhibit phospholipase A2.

2- Potentiate the effect of Beta receptor agonists .

3- Inhibit the infiltration of lymphocyte, mast cells and eosinophils.

***Side effects : (حأكتبهم بخط ايدي عشكل مايند ماب)**



Pharmacological agents:
Inhaled corticosteroids (ICS)

- Combining ICS with long-acting bronchodilator may improve symptoms, lung function, and quality of life in **COPD patients with FEV1 of less than 60%** predicted or **patients with symptoms of both asthma and COPD**.

- ICS treatment in COPD should be restricted to **the above** patients, since use is associated with an increased risk of pneumonia.

drop in immunity لـ بتزيد بجلوا

Oral glucocorticoids can be effective in treating an acute exacerbation **BUT** not recommended for **long-term** treatment???!!!

متى بعطي هاد الcombination?

Although often used for acute exacerbations, oral corticosteroids are not recommended for long-term treatment of COPD.

Pharmacological agents:
Drug combinations

COPD pharmacological treatment include

6. Combinations of different drug classes

حفظ

LONG-ACTING β_2 ADRENERGIC AGONIST/CORTICOSTEROID COMBINATION	
Formoterol/budesonide SYMBICORT	Asthma, COPD
Formoterol/mometasone DULERA	Asthma, COPD
Salmeterol/fluticasone ADVAIR	Asthma, COPD
Vilanterol/fluticasone BREO ELLIPTA	COPD
SHORT-ACTING β2 AGONIST/SHORT-ACTING ANTICHOLINERGIC COMBINATION	
Albuterol/ipratropium COMBIVENT RESPIMAT, DUONEB	COPD
LABA/LAMA COMBINATION	
Formoterol/glycopyrrolate BEVESPI AEROSPHERE	COPD
Indacaterol/glycopyrrolate UTIBRON NEOHALER	COPD
Vilanterol/umeclidinium ANORO ELLIPTA	COPD
Olodaterol/tiotropium STIOLTO RESPIMAT	COPD

Pharmacological agents:

Other agents

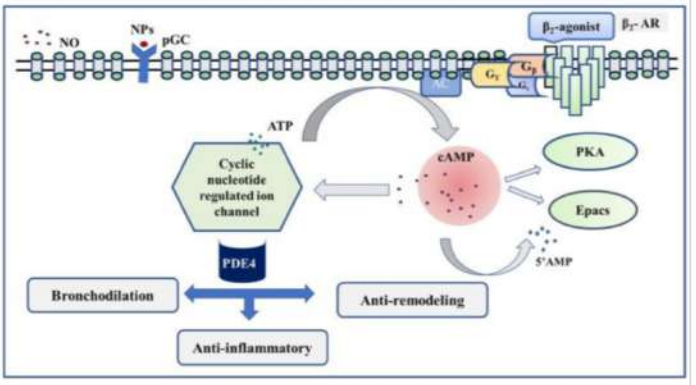
7. Vaccines, antibiotics and other agents

- **Roflumilast**

* Oral phosphodiesterase-4 (PDE4) inhibitor cAMP لـ كان يكسر

* Reduces exacerbations in patients with severe chronic bronchitis.

* Reduce inflammation by increasing levels of intracellular cAMP in lung cells.



*Although its activity is not well defined in COPD, it is theorized to reduce inflammation by increasing levels of intracellular cAMP in lung cells by inhibiting PDE4 work (break down cAMP).
So it has an anti-inflamatory effect.

- **Roflumilast**
- **NOT** a bronchodilator and is **NOT** indicated for the relief of acute bronchospasm. It is essentially used in treating those with chronic bronchitis along with systemic corticosteroids

* Use is limited by common adverse effects including weight loss, nausea, diarrhea, and headache. used with caution in those suffering from depression.

- Antibiotics such as erythromycin used to reduce the frequency of exacerbations in those who have two or more a year. But could potentially lead to antibiotic resistance, and side effects including hearing loss, tinnitus, and changes to the heart rhythm known as long QT syndrome.

نادر ما استعمله لأني بخاف من ال resistance و side effects
طيب متى بفكر فيه ؟ لما يكون عندي frequency exacerbations لسنتين اول اكثر

*Long QT syndrome (LQTS) is a heart signaling disorder that can cause fast, chaotic heartbeats (arrhythmias)

- Methylxanthines such as theophylline which has mild bronchodilatory effect in stable COPD. Theophylline is seen to improve breathlessness when used as an add-on to salmeterol. Methylxanthines are not recommended for use in exacerbations due to adverse effects.

بطلنا نستعمله بسبب ال adverse effect و narrow theraputic index

- 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.
- Annual influenza vaccinations and pneumococcal vaccination

الشخص الي معاه COPD ما بعطيه cough medicine و السبب انه cough بتهمني لانها بتطلع mucous و بتمنع تراكمه

و الBeta blockers يفضل ما اعطيهم الا بحالة وحدة و هي انه يكون المريض معه cardiovascular disease

حنبدأ هسا نحكى عن تصنيفات (كيف نصنف و نحدد مدى خطورة COPD الي مع المريض، ففي عنا اكثر من مقياس و Scale معتمدين

CAT & mMRC scales

Range of CAT scores from 0–40. Higher scores denote a more severe impact of COPD on a patient's life.

Scale ال 0 من 40 الى

How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy 0 X 2 3 4 5 I am very sad

		SCORE
I never cough	0 1 2 3 4 5 I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5 My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5 My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5 When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5 I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5 I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5 I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5 I have no energy at all	
		TOTAL SCORE

بسأله مجموعة اسألة وبترجم على شكل علامات

COPD Assessment Test and the CAT logo are trademarks of the GlaxoSmithKline group of companies. © 2009 GlaxoSmithKline. All rights reserved.

Modified Medical Research Council (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 at 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

Scale ال 0 من 4 الى

26

CAT score

بسأل المريض 8 أسئلة و بطلب منه يعطيني عكل سؤال علامة من 5، مثلا هل بتكح؟ ولو اه قيم الكحة من 5، و بالنهاية بجمع العلامات و بتطلع العلامة من 40، كل ما قربنا عال40 كل ما كانت حالة المريض اخطر

mMRC score

الscale ببدأ من 0 الى 5 ، شوف حالة المريض و حدد هو من أي Grade
شوفوا الجدول و اعرفوا كل حالة اي grade بتمثل

Treatment plans

قبل ما ابدأ بالعلاج بدي احدد خطورة المرض، و حأستخدم الscales الي حكينا عنهم

GOLD: Severity of airflow limitation (based on postbronchodilator FEV_1)		
Stage	**Severity**	**FEV_1 (percent predicted)**
In patients with FEV_1/FVC <0.7:Δ		
GOLD 1	Mild	≥80
GOLD 2	Moderate	50 to 79
GOLD 3	Severe	30 to 49
GOLD 4	Very severe	<30

في عنا كمان هاد الscale ، اسمه GOLD و بيعتمد على FEV1 الي عرفناها ببداية المحاضرة ، شوفوا الجدول و اعرفوا كل رقم بعطيه اي gold

Combined multidimensional assessment of COPD

GOLD "ABCD" groups: Assessment of symptoms and risk of exacerbations for initiation of COPD therapy		
Assess exacerbation risk: Exacerbations/Hospitalizations	**Assess symptoms**	
	mMRC* 0 to 1; CAT <10¶	**mMRC ≥2; CAT ≥10**
0 or 1 exacerbations without hospitalization	A	B
≥2 exacerbations or ≥1 hospitalization	C	D

الاول mMRC و CAT الي حيقيموا الSymptoms

و الثاني risk Exacerbation و hospitalization يعني كم مرة دخل المستشفى بسبب الاعراض، و هدول حيقيموا الRisk

According to these, we have 4 groups

A: Low symptoms / Low Risk

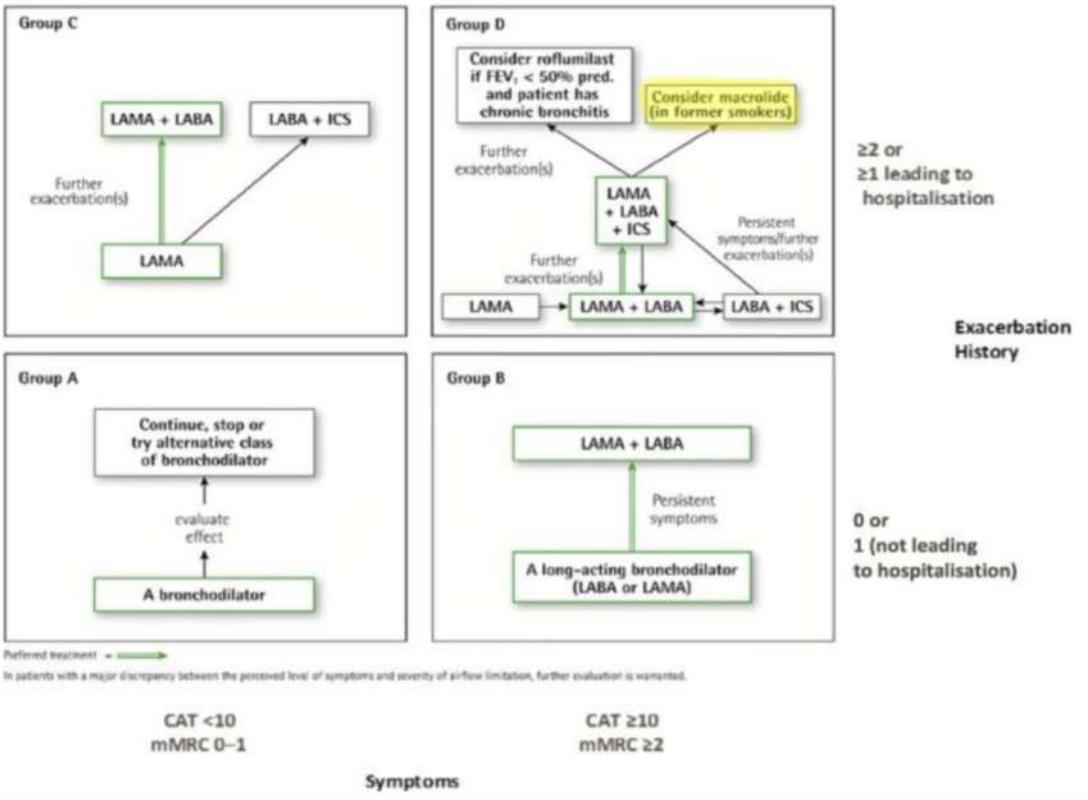
B: High symptoms / Low Risk

C: Low symptoms / High Risk

D: High symptoms / High Risk

Treatment plans

هسا بدنا نحكي عن
طريقة العلاج



اللي حَتّ نفسها بس العفّ

PATIENT GROUP	RECOMMENDED FIRST CHOICE	RECOMMENDED ESCALATION
A Low risk Fewer symptoms	**Bronchodilator:** SABA or LABA or Short-acting anticholinergic or LAMA	Try alternative class
B Low risk More symptoms	**Long acting bronchodilator:** LABA or LAMA	LAMA + LABA (Combination)
C High risk Fewer symptoms	LAMA	LAMA + LABA or LABA + ICS
D High risk More symptoms	LAMA + LABA	LAMA + LABA + ICS (May consider *roflumilast* if FEV_1 < 50% predicted and chronic bronchitis)

شو بعني بالأول

لو ما زبط بعطي هدول

"لَا أَبْرَحُ حَتَّى أَبْلُغَ".

Treatment plans

Management of stable COPD: Initiation of therapy based on the GOLD ABCD assessment of symptoms and risk of exacerbation*

Groups	Symptoms	Risk	Suggested treatment
All			• Avoidance of risk factor(s), such as smoking • Annual influenza vaccination • Pneumococcal vaccination • Regular physical activity • Regular review/correction of inhaler technique • Long-term oxygen therapy if chronic hypoxemia • Pulmonary rehabilitation
A	**Less symptomatic** Mild or infrequent symptoms (ie, breathless with strenuous exercise or when hurrying on level ground or walking up a slight hill)¶ or CAT <10Δ	**Low risk** 0 or 1 exacerbations in the past year without associated hospitalization	Short-acting bronchodilator (SABA, SAMA, or combination of SABA-SAMA), as needed.
B	**More symptomatic** Moderate to severe symptoms (ie, patient has to walk more slowly than others of same age due to breathlessness, has to stop to catch breath when walking on level ground at own pace, or has more severe breathlessness)¶ or CAT ≥10Δ	**Low risk** 0 or 1 exacerbations in the past year without associated hospitalization	Regular treatment with a long-acting bronchodilator, either LAMA or LABA, based on patient preference. Short-acting bronchodilator (usually SABA) for symptom relief as needed.
C	**Less symptomatic** Mild or infrequent symptoms (ie, breathless with strenuous exercise or when hurrying on level ground or walking up a slight hill)¶ or CAT <10Δ	**High risk** ≥2 exacerbations per year with one or more leading to hospitalization	Regular treatment with a LAMA; SABA available for symptom relief as needed.
D	**More symptomatic** Moderate to severe symptoms (ie, patient has to walk slower than others of same age due to breathlessness, has to stop to catch breath when walking on level ground at own pace, or has more severe breathlessness)¶ or CAT ≥10Δ	**High risk** ≥2 exacerbations per year with one or more leading to hospitalization	Regular treatment with LAMA **or**, if severe breathlessness (eg, CAT >20), combination LABA plus LAMA. Combination glucocorticoid-LABA inhaler may be preferred, if features of asthma/COPD overlap. SABA available for symptom relief as needed.

تكرار

SABA: Albuterol and Levalbuterol
SAMA: Ipratropium

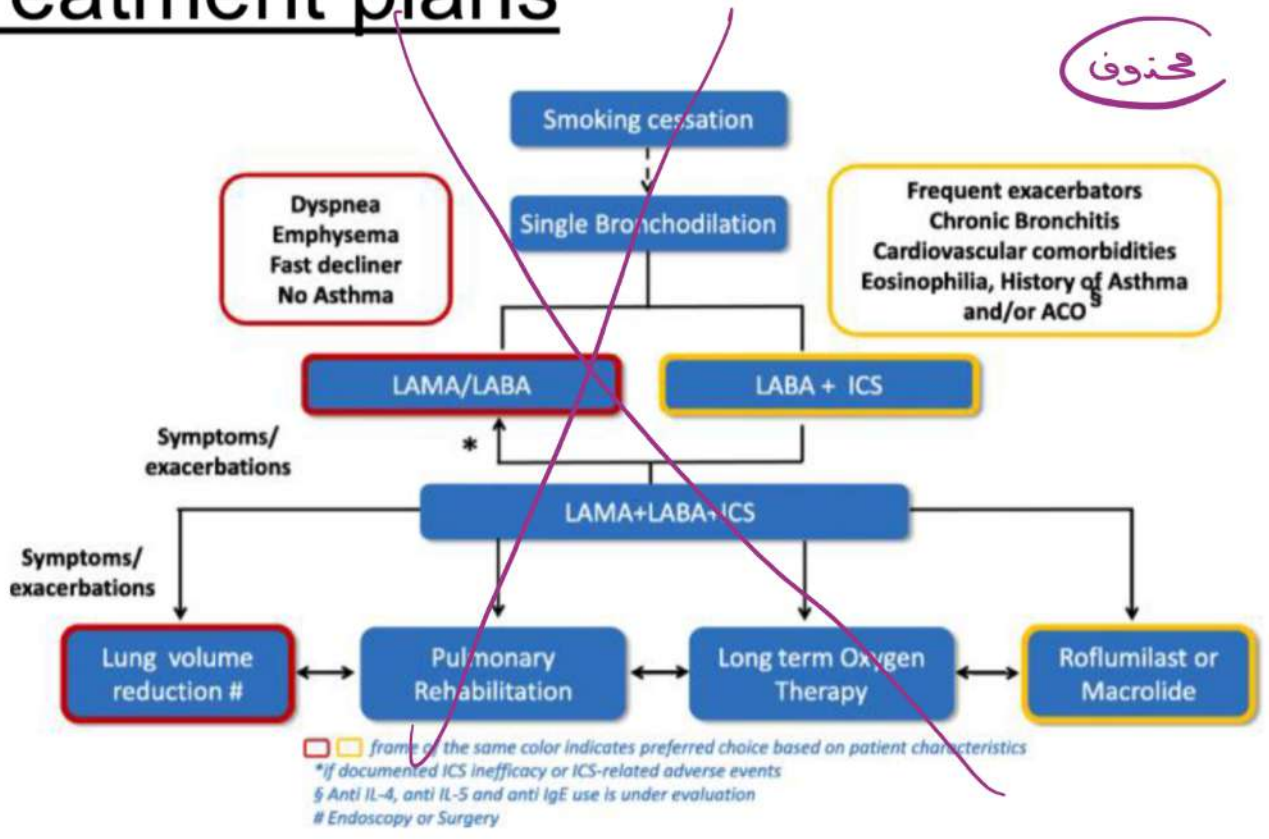
* Long-acting bronchodilators have been shown to be superior to short-acting bronchodilators taken on a regular basis.
* LAMA + SABA (rescue use).
* LABA+ SABA or a combination SAMA—SABA
* Both LAMAs and LABAs reduce exacerbations, but LAMAs have a greater effect

If at high risk of an exacerbation due to their history of exacerbations in the past year (ie, ≥2 exacerbations per year with one or more leading to hospitalization)>> LAMA+LABA or LAMA+ICS

LAMA+LABA; further exacerbations>> add ICS, further exacerbations>> consider Roflumilast or antibiotics in former smokers

Treatment plans

محذوف



Latest clinical guidelines

- A) COPD and dyspnea or exercise intolerance: use of LABA/LAMA combination therapy over LABA or LAMA monotherapy in patients
- A)+ experienced one or more exacerbations in the past year requiring antibiotics or oral steroids or hospitalization : use of triple therapy with inhaled corticosteroids (ICS)/LABA/LAMA
- IF NO exacerbations occurred over past year: ICS withdrawal
- NO maintenance oral corticosteroids in patients with COPD and a history of severe and frequent exacerbations

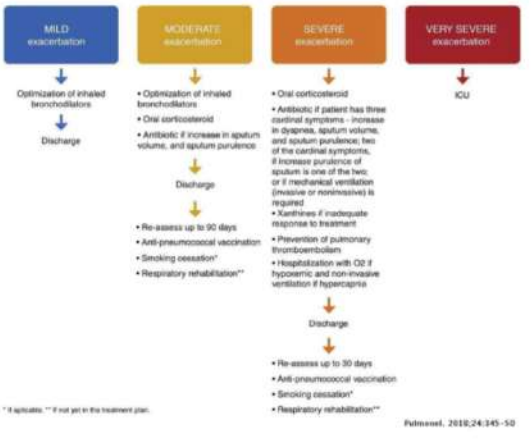
Treatment plans

- Theophylline may have a particular place in the treatment of COPD, as it may improve contractile function of the diaphragm, thus improving ventilatory capacity.

- The use of antibiotics in this context is routine in COPD, because such exacerbations involve bacterial infection of the lower airways far more often in COPD than in asthma.

Exacerbations management

- A sudden worsening of signs and symptoms that lasts for several days.
- The key symptom is increased breathlessness (excessive mucus, increased cough and wheeze)
- The usual cause of an exacerbation is a viral infection (common cold), bacterial infection (Haemophilus influenzae), exposure to tobacco smoke and environmental pollutants
- Acute exacerbations in COPD are often unexplained, could be a pulmonary embolism



Quiz Time ⏳

1- A 58-year-old woman with COPD has been hospitalized three times in the past year for COPD exacerbations. She reports only mild symptoms between exacerbations. Her regimen for the past year has included inhaled salmeterol twice daily and inhaled tiotropium once daily. Her current FEV1 is below 60%. Which is an appropriate change in her drug therapy?
A. Discontinue the tiotropium.
B. Discontinue the salmeterol.
c. Change the salmeterol to a combination product that
includes both a LABA and an inhaled corticosteroid(for example, salmeteroVfluticasone DPI).
D. Add theophylline.
Answer : C

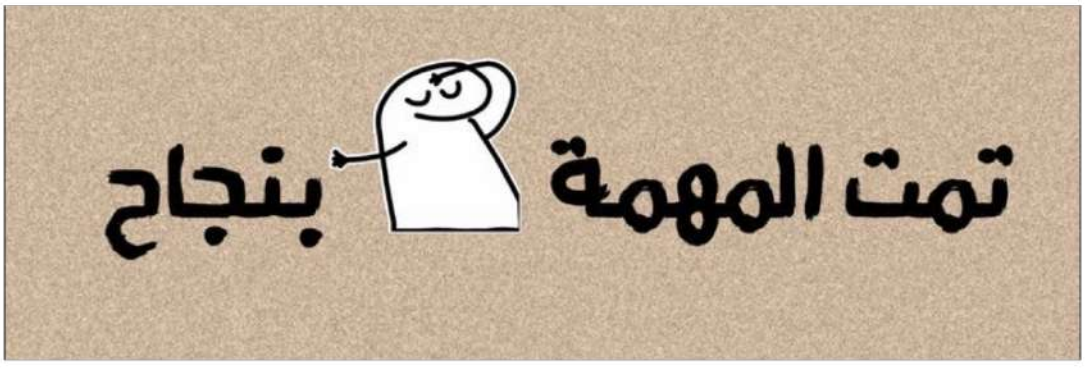
2- A 68-year old man has COPD with moderate airway obstruction. Despite using salmeterol twice daily, he reports continued symptoms of shortness of breath with mild exertion. Which agent is an appropriate addition to his currant therapy?
A. Systemic corticosteroids
B. Albuterol
C. Tiotropium
D. Roflumilast
Answer : C

3- A 58-year-old man who is a smoker with chronic obstructive pulmonary disease (COPD) presents to the emergency department (ED) with shortness of breath and a productive cough. This is the fourth time this year he has come to the ED because of COPD exacerbation. After this hospital stay, his primary care physician prescribes roflumilast in hopes of decreasing his ED visits for COPD exacerbation. What is roflumilast's mechanism of action?
(A) Blocks arachidonic acid production
(B) Bronchodilation
(C) Inhibition of leukocyte chemotaxis by interfering with microtubules
(D) PDE4 inhibitor
(E) Thins and loosens mucus
Answer : D

4- How many stages of COPD disease there are?
A- 1 stage
B- 2 stages
C- 3 stages
D- 4 stages
Answer : D

5-What is the first line treatment option for COPD?
A- Bronchodilator
B- Muscarinic agent
C- Corticosteroids
D- None of the above
Answer: A

6-Roflumilast is a medication that belongs to class of:
A- Anticholinergics
B- Methylxanthines
C- Phosphodiesterase inhibitors
D- Long-acting beta agonist
Answer: C



دعواتكم 🙏