

وَقُلْ رَبِّ زِدْنِي عِلْمًا



RESPIRATORY SYSTEM

HAYAT BATCH



SUBJECT : Pharmacology _____

LEC NO. : 1/copd _____

DONE BY : Anas zakarneh /johainah Taya _____



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

Respiratory system

Second year

Medical school

Hashemite University

2nd semester 23/24

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ملاحظة كلامي و ملاحظاتي را ح تكون باللون الأزرق





Facts & numbers

- Estimated cost of COPD 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

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

384 MILLION
people suffer from Chronic Obstructive Pulmonary Disease (COPD) in the world

3 MILLION
people die each year of COPD

COPD is currently the **3RD** leading cause of death globally

COPD is highly prevalent in low resource countries

EARLY DIAGNOSIS - SYMPTOMS INCLUDE

- Shortness of breath
- A repetitive cough
- Increased phlegm or mucus production
- Feeling tired
- More frequent chest infections
- Longer to recover from a cold/chest infection

BIGGEST RISK FACTORS

- Smoking
- Indoor and outdoor pollution
- Occupational dusts and chemicals

LEAVE NO ONE BEHIND. ON WORLD LUNG DAY CALL FOR **HEALTHY LUNGS FOR ALL**

firsnet.org

WORLD LUNG DAY
25 september

#WorldLungDay

• **SMOKING** (irreversible)

مهمة [**It is NOT curable but treatable**]

- Approximately 15-20% of the cases occur in nonsmokers.

بالدباية هاي السلايد مجرد مقدمة لنعرف بشكل عام عن شو حنحكي؛ مهم تعرفوا ال management تبعت ال COPD عالية، و المقصود بكلمة management هي تكلفة الدواء، و الرعاية الصحية، و المواصلات...الخ
 ثانيًا السبب الرئيسي لل COPD هو التدخين زي ما اخدنا بالباثو
 ثالثًا ال COPD ما له علاج يا للأسف، انا بستعمل الأدوية فقط لأخفف الأعراض
 لهيك بنحكي **COPD is not curable but treatable**

Definition & sub-types

Defining "Chronic Obstructive Pulmonary Disease (COPD)"

Systemic disease, largely manifesting as an **airflow-obstructing** respiratory disorder; can manifest in the form of any of the following disorders:

Emphysema
Lung tissue destruction & abnormal, permanent enlargement of lung acini: airspaces distal to terminal bronchioles

Chronic Bronchitis
Chronic, productive cough for a total duration of 3 months per year, over 2 continuous years

~~Asthma~~
Asthma that does not remit completely with treatment (thus, chronic airflow obstruction) is defined as asthma-COPD overlap syndrome (ACOS)

Bronchiectasis
Destruction and widening of large airways, resulting in mucus hyper-secretion and recurrent infections

Cystic Fibrosis
Multisystem disease due to CFTR gene mutation, that presents in the lungs as bronchiectasis

Most common COPD manifestations (most patients suffer from a combination of emphysema and chronic bronchitis)

Emphysema

Chronic Bronchitis

Bronchiectasis, Cystic Fibrosis, etc

Chronic Obstructive Pulmonary Disease (COPD)

Emphysema

Chronic Bronchitis

Bronchiectasis, Cystic Fibrosis, etc

Asthma

Clinically, COPD is seen as:

- Progressive, partially reversible **airflow obstruction** and lung hyperinflation (causing respiratory symptoms like cough, sputum production, and dyspnea)
- Post-bronchodilator spirometry results: FEV1/FVC ratio <0.7 (FEV1 is not a defining feature of COPD, but a marker of severity)
- ↑ frequency & severity of acute exacerbations
- Systemic manifestations such as deconditioning and muscle weakness

Legend: Pathophysiology Mechanism Sign/Symptom/Lab Finding Complications

Published January 7, 2013, updated October 5, 2021 on www.thecaligaryguide.com

The Lungs on COPD
Learn what damage from COPD looks like and why it becomes so hard to breathe.

Branchial tubes are clear and inflammation-free.
Alveoli (air sacs) expand and collapse with each breath.
Oxygen moves through the air-sac walls into the blood.
Carbon dioxide moves into the air sacs to be exhaled.

Alveoli lose their elasticity and shape making it hard to exhale.
Air gets trapped in the lungs.
Branchial tubes become inflamed and narrowed.
Thick mucus forms causing a chronic cough.

Chronic Bronchitis

Healthy: Inflammation & excess mucus

Emphysema

Healthy: Alveolar membranes break down

هسا هاي السلايد باثو؛ اقرأوا الي عليه هايلايت ،حأترككم 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 حكي 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 usually begins 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

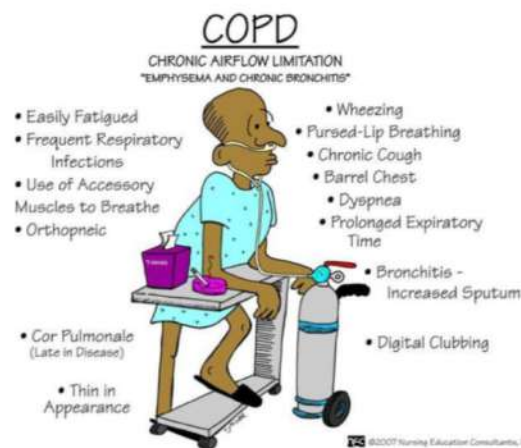
*Drug therapy for COPD is aimed at **relief** of symptoms and **prevention** of disease progression.(Not curable)

*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.**

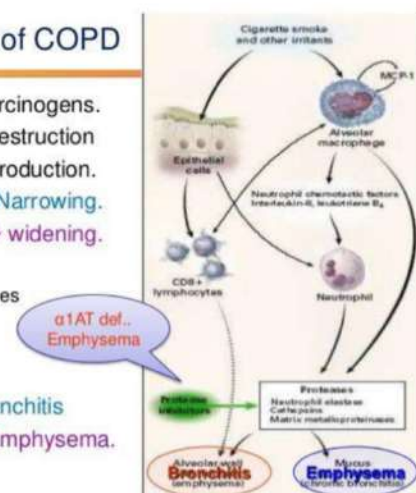


Pathogenesis

- **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.

Pathogenesis of COPD

1. Smoke, irritants, carcinogens.
 2. Tissue irritation & destruction
 3. Inflammation → Mucous production.
 4. Airway damage → Narrowing.
 5. Alveolar damage → widening.
- Increase in
 - Alveolar macrophages
 - CD8 Lymphocytes
 - Neutrophils
 - Proteases.
 - Airway inflammation → Bronchitis
 - Alveoli damage → Emphysema.
 - Both → COPD.



These are one of the most important differences 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.

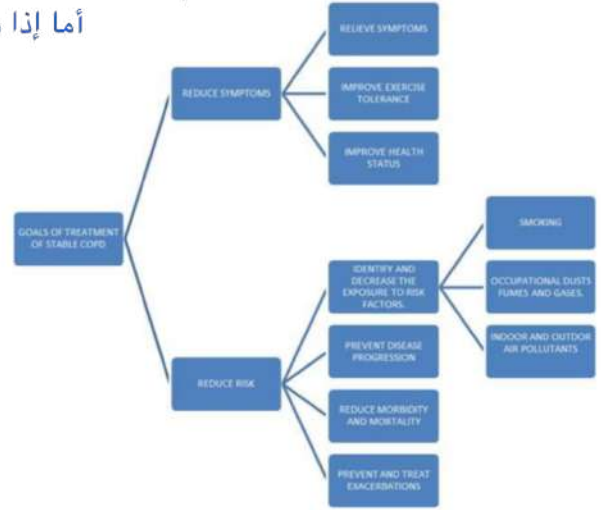
+ it is reversible

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** quit smoking **المسبب الرئيسي بس مش** pharmacological cause **بدنه يكون** pharmacological cause **بدنه يكون دواء** أما إذا طلب
- **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

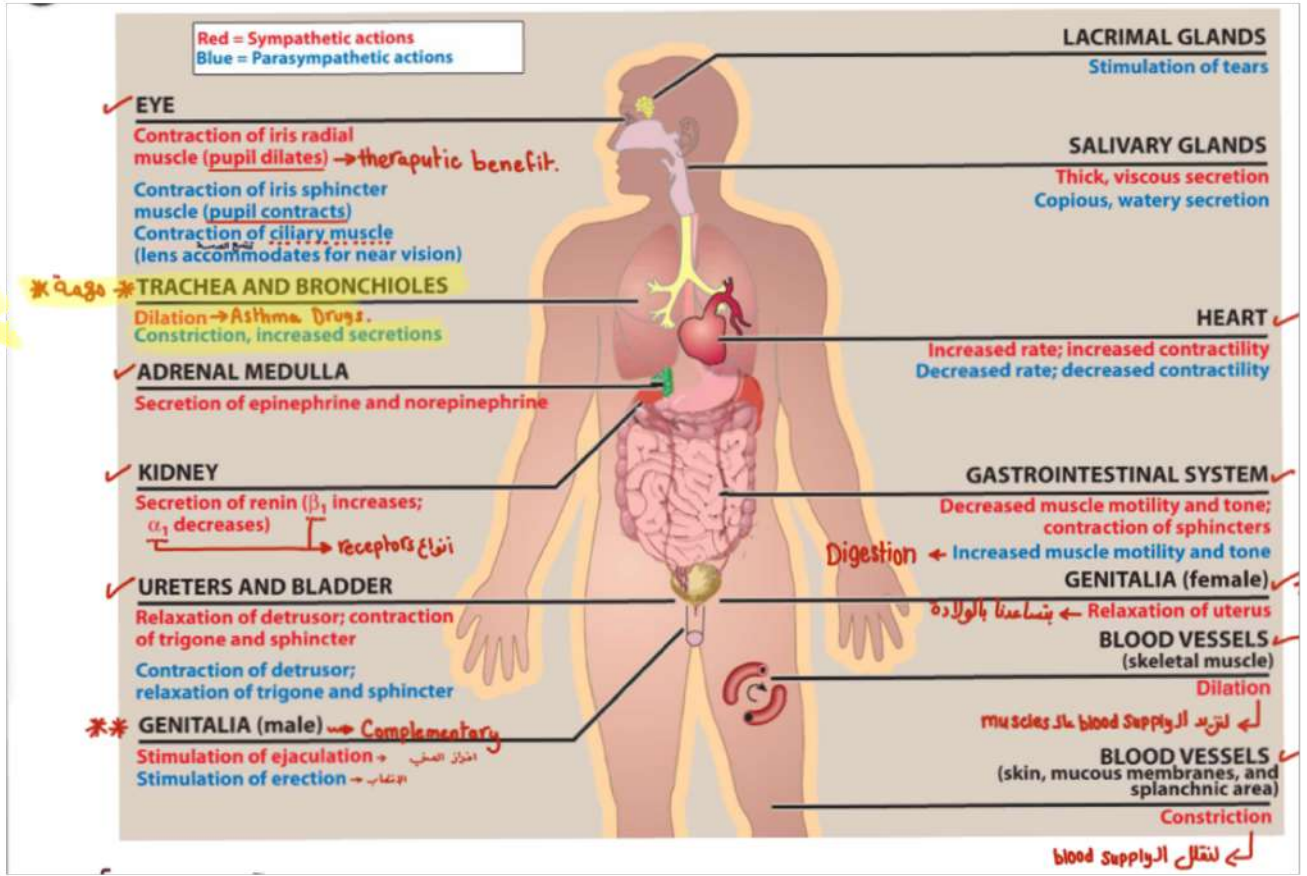
ثالثاً بعطيه vaccine ، خصوصاً الvaccines تبعت الفايروسات الي بتصيب و بتستهدف

الجهاز التنفسي لحتى أحميهم من أي sever complication

رابعاً بدي اهتم بغذائهم و وزنهم، حكينا بالباتو انه الاشخاص هذول غالباً بصاحبهم

obesity و السبب طبعا غير معروف لآن ، المهم لازم يلتزم بالغذاء الhealthy

كل الي اخدناه لآن مقدمات، و هسا بدنا نبداً بالجد، بس قبل بدي أشرح الكم و أذكركم بشغلات أخذناها 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 بيسيستم ال RS 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 ال receptors لحتى يصير مجرى التنفس أوسع

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

لهيك حلو نعمل دواء يثبط عمل هدول ال receptors 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
+ the main

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

و أول 4 مثل ما بنلاحظ يستهدفوا ال receptors الي حكيتمك 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.

دخنف

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

*The long-acting bronchodilators, 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.**

We must know them

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

Pharmacological agents

MEDICATION	IND	LONG-ACTING β_2 ADRENERGIC AGONIST/CORTICOSTEROID COMBINATION
SHORT-ACTING β_2 ADRENERGIC AGONISTS (SABAs)		
<i>Albuterol</i> PROAIR, PROVENTIL, VENTOLIN <i>Levalbuterol</i> XOPENEX	Asthma, COPD Asthma, COPD	<i>Formoterol/budesonide</i> SYMBICORT <i>Formoterol/mometasone</i> DULERA <i>Salmeterol/fluticasone</i> ADVAIR <i>Vilanterol/fluticasone</i> BREO ELLIPTA
LONG-ACTING β_2 ADRENERGIC AGONISTS (LABAs)		
<i>Arformoterol</i> BROVANA <i>Formoterol</i> FORADIL, PERFORMIST <i>Indacaterol</i> ARCAPTA <i>Olodaterol</i> STRIVERDI RESPIMAT <i>Salmeterol</i> SEREVENT	COPD Asthma, COPD COPD COPD Asthma, COPD	SHORT-ACTING ANTICHOLINERGIC <i>Ipratropium</i> ATROVENT
INHALED CORTICOSTEROIDS		
<i>Beclomethasone</i> BECNASSE AQ*, QVAR <i>Budesonide</i> PULMICORT, RHINOCORT* <i>Ciclesonide</i> ALVESCO, OMNARIS*, ZETONNA* <i>Fluticasone</i> FLOINASE*, FLOVENT <i>Mometasone</i> ASMANEX, NASONEX* <i>Triamcinolone</i> NASACORT*	Allergic rhinitis, Asthma, COPD Allergic rhinitis, Asthma, COPD Allergic rhinitis, Asthma Allergic rhinitis, Asthma, COPD Allergic rhinitis, Asthma	SHORT-ACTING β_2 AGONIST/SHORT-ACTING ANTICHOLINERGIC COMBINATION <i>Albuterol/ipratropium</i> COMBIVENT RESPIMAT, DUONEB
LONG-ACTING ANTICHOLINERGIC (LAMA)		
		<i>Aclidinium</i> TUDORZA PRESSAIR <i>Glycopyrrolate</i> SEEBRI NECHALER <i>Tiotropium</i> SPIRIVA <i>Umeclidinium</i> INCRUSE ELLIPTA
LABA/LAMA COMBINATION		
		<i>Formoterol/glycopyrrolate</i> BEVESPI AEROSPHERE <i>Indacaterol/glycopyrrolate</i> UTIBRON NECHALER <i>Vilanterol/umeclidinium</i> ANORO ELLIPTA <i>Olodaterol/tiotropium</i> STIOLTO RESPIMAT
OTHER AGENTS		
<i>Roflumilast</i> DALIRESP <i>Theophylline</i> ELIXOPHYLLIN, THEO-24		COPD Asthma, COPD

اللي عليهم highlight يكونو لل COPD
الباقى لل COPD + asthma

Just ignore it

Pharmacological agents

و هاد مراجعة للي حنكي
عنه بالمحاضرة ارجعوله بالآخر

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
<ul style="list-style-type: none"> • <i>Metaproterenol, terbutaline</i>: Similar to albuterol; terbutaline available as an oral drug • <i>Formoterol</i>: 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
• <i>Beclomethasone, budesonide, flunisolide, others</i> : Similar to fluticasone				
CORTICOSTEROIDS, SYSTEMIC				
• Prednisone	Like fluticasone	Like fluticasone	Asthma • adjunct in COPD	Oral • duration 12–24 hours • Toxicity: Multiple • see Chapter 39
• <i>Methylprednisolone</i> : 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

MEDICATION	IND	LONG-ACTING β_2 ADRENERGIC AGONIST/CORTICOSTEROID COMBINATION
SHORT-ACTING β_2 ADRENERGIC AGONISTS (SABAs)		
<i>Albuterol</i> PROAIR, PROVENTIL, VENTOLIN <i>Levalbuterol</i> XOPENEX	Asthma, COPD Asthma, COPD	<i>Formoterol/budesonide</i> SYMBICORT <i>Formoterol/mometasone</i> DULERA <i>Salmeterol/fluticasone</i> ADVAIR <i>Vilanterol/fluticasone</i> BREO ELLIPTA
LONG-ACTING β_2 ADRENERGIC AGONISTS (LABAs)		
<i>Arformoterol</i> BROVANA <i>Formoterol</i> FORADIL, PERFORMIST <i>Indacaterol</i> ARCAPTA <i>Olodaterol</i> STRIVERDI RESPIMAT <i>Salmeterol</i> SEREVENT	Asthma, COPD COPD Asthma, COPD COPD Asthma, COPD	SHORT-ACTING ANTICHOLINERGIC <i>Ipratropium</i> ATROVENT
INHALED CORTICOSTEROIDS		
<i>Beclomethasone</i> BECNASSE AQ*, QVAR <i>Budesonide</i> PULMICORT, RHINOCORT* <i>Ciclesonide</i> ALVESCO, OMNARIS*, ZETONNA* <i>Fluticasone</i> FLOINASE*, FLOVENT <i>Mometasone</i> ASMANEX, NASONEX* <i>Triamcinolone</i> NASACORT*	Allergic rhinitis, Asthma, COPD Allergic rhinitis, Asthma, COPD Allergic rhinitis, Asthma Allergic rhinitis, Asthma, COPD Allergic rhinitis, Asthma	SHORT-ACTING β_2 AGONIST/SHORT-ACTING ANTICHOLINERGIC COMBINATION <i>Albuterol/ipratropium</i> COMBIVENT RESPIMAT, DUONEB
LONG-ACTING ANTICHOLINERGIC (LAMA)		
		<i>Aclidinium</i> TUDORZA PRESSAIR <i>Glycopyrrolate</i> SEEBRI NECHALER <i>Tiotropium</i> SPIRIVA <i>Umeclidinium</i> INCRUSE ELLIPTA
LABA/LAMA COMBINATION		
		<i>Formoterol/glycopyrrolate</i> BEVESPI AEROSPHERE <i>Indacaterol/glycopyrrolate</i> UTIBRON NECHALER <i>Vilanterol/umeclidinium</i> ANORO ELLIPTA <i>Olodaterol/tiotropium</i> STIOLTO RESPIMAT
OTHER AGENTS		
<i>Roflumilast</i> DALIRESP <i>Theophylline</i> ELIXOPHYLLIN, THEO-24		COPD Asthma, COPD

كلهم لل asthma + copd
الا اللي عليهم تحبوا لل copd بس

هاي من سلايداتنا

كأنو الدكتور مقل عدد الأدوية



لازم تعرف ال short / long



SABAs (Short-Acting Beta Agonists)	LABAs (Long-Acting Beta Agonists)	ICS (Inhaled Corticosteroids)	LABAs+ICS	SAMA (Short-Acting Muscarinic Antagonist)	SABA/SAMA	LAMA (Long-Acting Muscarinic Antagonists)	LABA/LAMA	others
Albuterol	Salmeterol	Fluticasone	Salmeterol/Fluticasone	Ipratropium	Albuterol/Ipratropium	Glycopyrrolate	Formoterol/Glycopyrrolate	Roflumilast
Levalbuterol	Formoterol	Budesonide	Formoterol/Budesonide			Tiotropium	Olodaterol/Tiotropium	Theophylline
	Olodaterol	Mometasone	Formoterol/Mometasone					

Pharmacological agents:

β₂-adrenergic agonists

COPD pharmacological treatment include

1. Short-acting β₂ agonists (SABAs)
2. Long-acting β₂ agonists (LABAs): indacaterol, olodaterol and vilanterol (once-daily). Arformoterol, formoterol, and salmeterol (twice-daily)

MEDICATION	INDICATION
SHORT-ACTING β₂ ADRENERGIC AGONISTS (SABAs)	
Albuterol PROAIR, PROVENTIL, VENTOLIN	Asthma, COPD
Levalbuterol XOPENEX	Asthma, COPD
LONG-ACTING β₂ ADRENERGIC AGONISTS (LABAs)	
Arformoterol BROVANA	COPD
Formoterol FORADIL, PERFORMIST	Asthma, COPD
Indacaterol ARCAPTA	COPD
Olodaterol STRIVERDI RESPIMAT	COPD
Salmeterol SEREVENT	Asthma, COPD

+ vilanterol

الجدول حفظ طبعاً
كلهم بنتهوا ب terol

Pharmacological agents:

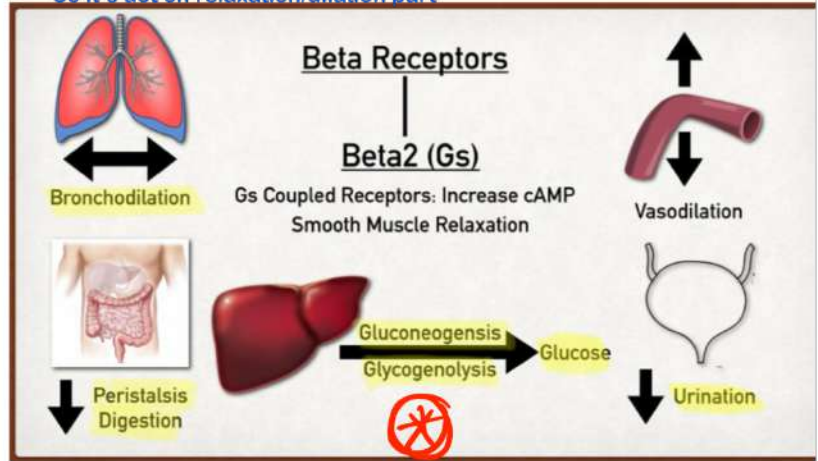
β₂-adrenergic agonists (adrenergic β₂ receptor agonists):

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.

They will go to the beta 2 receptor and then will bind with the receptor and they will do what the receptor can do
شو يعمل ال receptor أصلاً؟

Beta 2 receptor : vasodilation/ bronchodilation / release glucose / release of insulin / relaxation
So it's act on relaxation/dilation part



❖ 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**

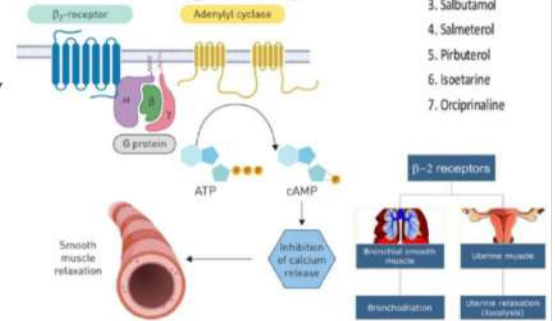
Pharmacological agents:

β 2-adrenergic agonists

➤ **MOA:** You need to know the steps بالترتيب

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

Selective agonists of beta adrenergic receptors 2



➤ Anti-inflammatory effects?

reducing intercellular adhesion molecule-1 (ICAM-1)

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

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

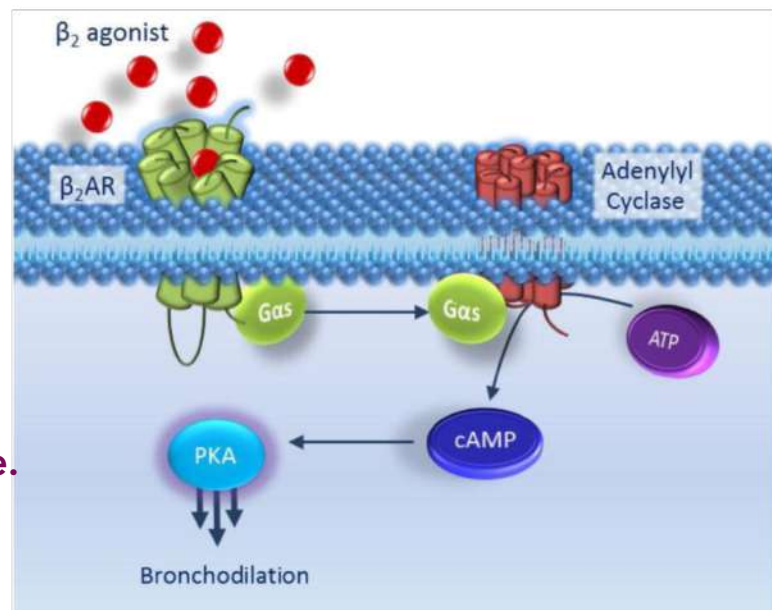
*Binding of β 2-agonist to β 2AR induces a conformational change allowing the α -subunit of the G-protein to dissociate and bind to adenylyl cyclase.

*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 subunits from each other.

هسا ال PKA بروج 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.



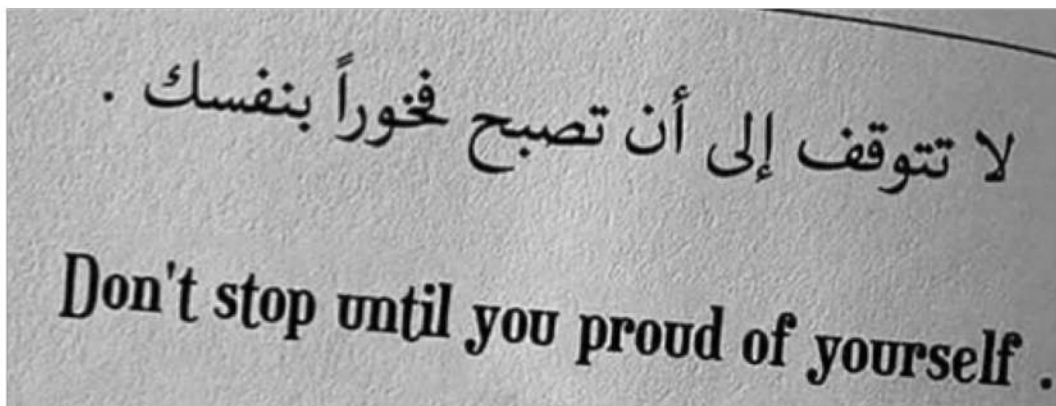
العلماء وجدوا انه هاي الأدوية الها effect آخر كمان و هو anti-inflammatory بس قبل ما نحكي عن شو بتعمل خرينا نراجع كم مصطلح اخدناهم بالجينييرال

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 adrenergic agonists بيحوا ليققلوا من ICAM1 على سطح الخلايا و بالتالي
بنقل الinflammation

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

لهيك B2 adrenergic agonists بيحوا ليققلوا من هدول الfactors و بالتالي بنقل
الinflammation



الدكتور رعب يسأل عنكم

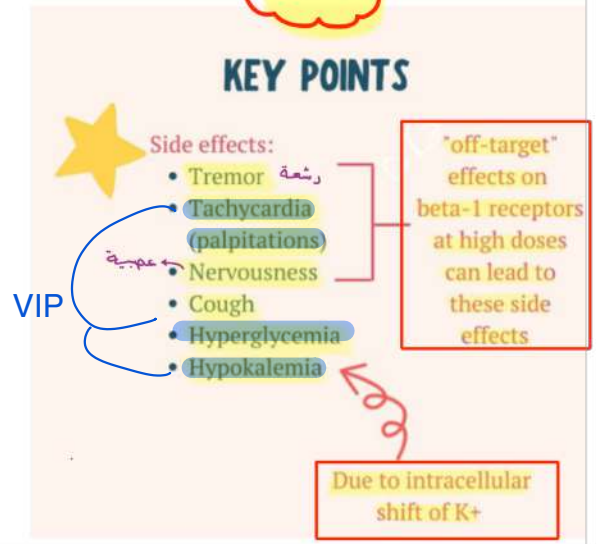
مغيبين

Pharmacological agents: β₂-adrenergic agonists

β₂-adrenergic agonists (adrenergic β₂ receptor agonists):

❖ Side effects:  See the figure

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



*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 يرتبط ب beta 1

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

*Hypokalemia -> Insulin and epinephrine 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
• 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*

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): Acclidinium, tiotropium, glycopyrrolate and umeclidinium

الجدول
حفظ

SHORT-ACTING ANTICHOLINERGIC	
<i>Ipratropium</i> ATROVENT	Allergic rhinitis, Asthma, COPD
SHORT-ACTING β_2 AGONIST/SHORT-ACTING ANTICHOLINERGIC COMBINATION	
<i>Albuterol/ipratropium</i> COMBIVENT RESPIMAT, DUONEB	COPD
LONG-ACTING ANTICHOLINERGIC (LAMA)	
<i>Acclidinium</i> TUDORZA PRESSAIR	COPD
<i>Glycopyrrolate</i> SEEBRI NEOHALER	COPD
<i>Tiotropium</i> SPIRIVA	Asthma, COPD
<i>Umeclidinium</i> 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): All drugs here will try to dayloid the bronchi

✓ Muscarinic receptors are predominately present on glandular cells, smooth muscle cells, and cardiac muscle cells.

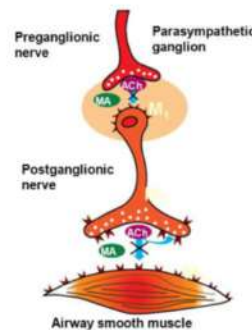
✓ Competitively inhibit the effect of **acetylcholine (ACh)** at muscarinic receptors (M1 and M3)

✓ M1: CNS

✓ M3: smooth muscle GI, UT, airway, and blood vessels
مهم تعرف انو ال m3 موجود بال GI/UT/airways

✓ Side effects: dry mouth, constipation and urinary retention

Mechanism of action of muscarinic antagonists



• Muscarinic antagonists block M₁ and M₃ receptors, thus preventing binding of acetylcholine and inhibiting airway smooth muscle contraction

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

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

These drugs will block the (M3) to prevent airway smooth muscle contraction

*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)

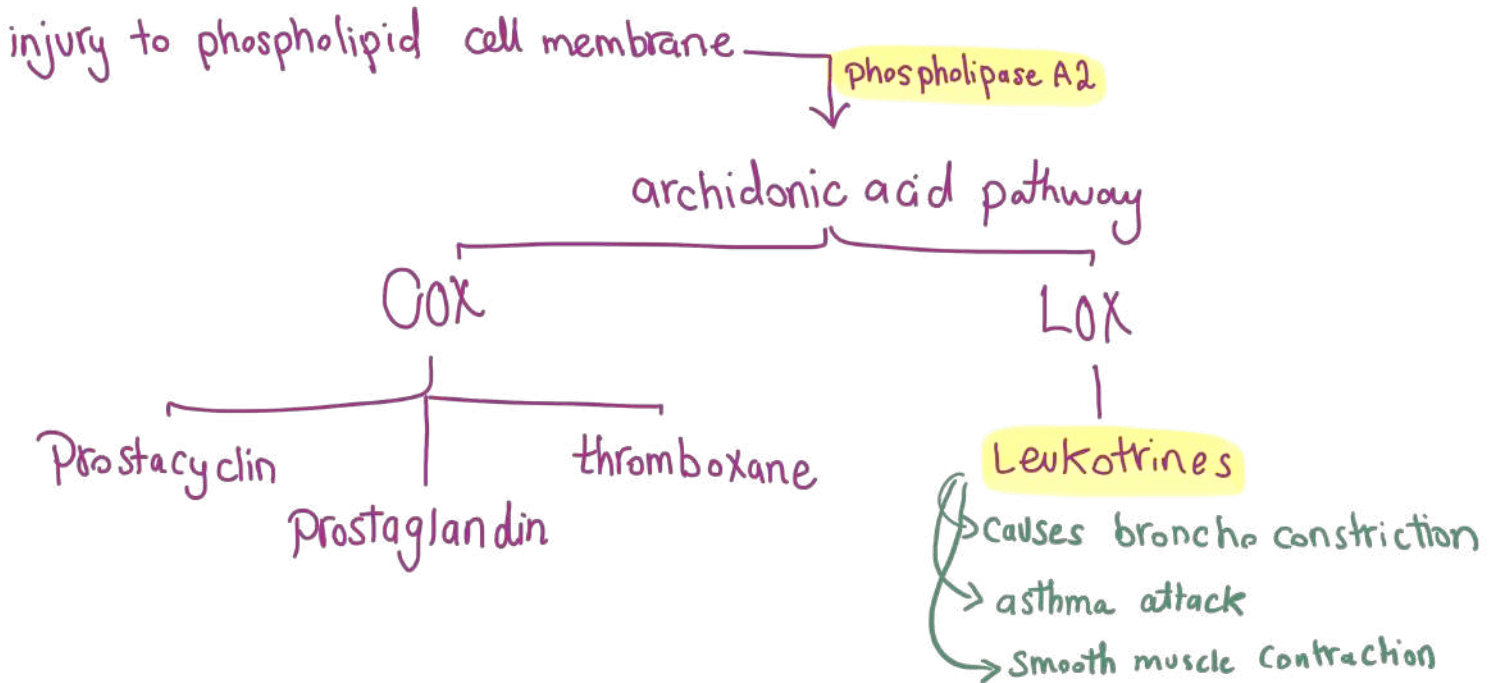
COPD pharmacological treatment include

5. Inhaled corticosteroids (ICS)

INHALED CORTICOSTEROIDS		*Combinations	
Beclomethasone BECONASE AQ*, QVAR	Allergic rhinitis, Asthma, COPD	LONG-ACTING β_2 ADRENERGIC AGONIST/CORTICOSTEROID COMBINATION	
Budesonide PULMICORT, RHINOCORT*	Allergic rhinitis, Asthma, COPD	Formoterol/budesonide SYMBICORT	Asthma, COPD
Ciclesonide ALVESCO, OMNARIS*, ZETONNA*	Allergic rhinitis, Asthma	Formoterol/mometasone DULERA	Asthma, COPD
Fluticasone FLOINASE*, FLOVENT	Allergic rhinitis, Asthma, COPD	Salmeterol/fluticasone ADVAIR	Asthma, COPD
Mometasone ASMANEX, NASONEX*	Allergic rhinitis, Asthma	Vilanterol/fluticasone BREO ELLIPTA	COPD
Triamcinolone NASACORT*	Allergic rhinitis, Asthma		

له نيم one

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



Pharmacological agents:

Inhaled corticosteroids (ICS)

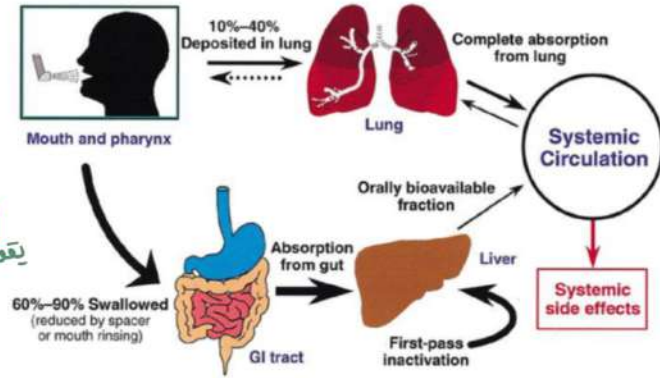
They are used in all diseases and symptoms

oral ما تحطهم يشتغلو بس هون راح نركز على اللي يكونو بخاخات مش ال
systemic لأثر التأثير العكسي تبعهم

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

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

• Main effect: **inhibition of the infiltration of lymphocytes, eosinophils, and mast cells.** 3

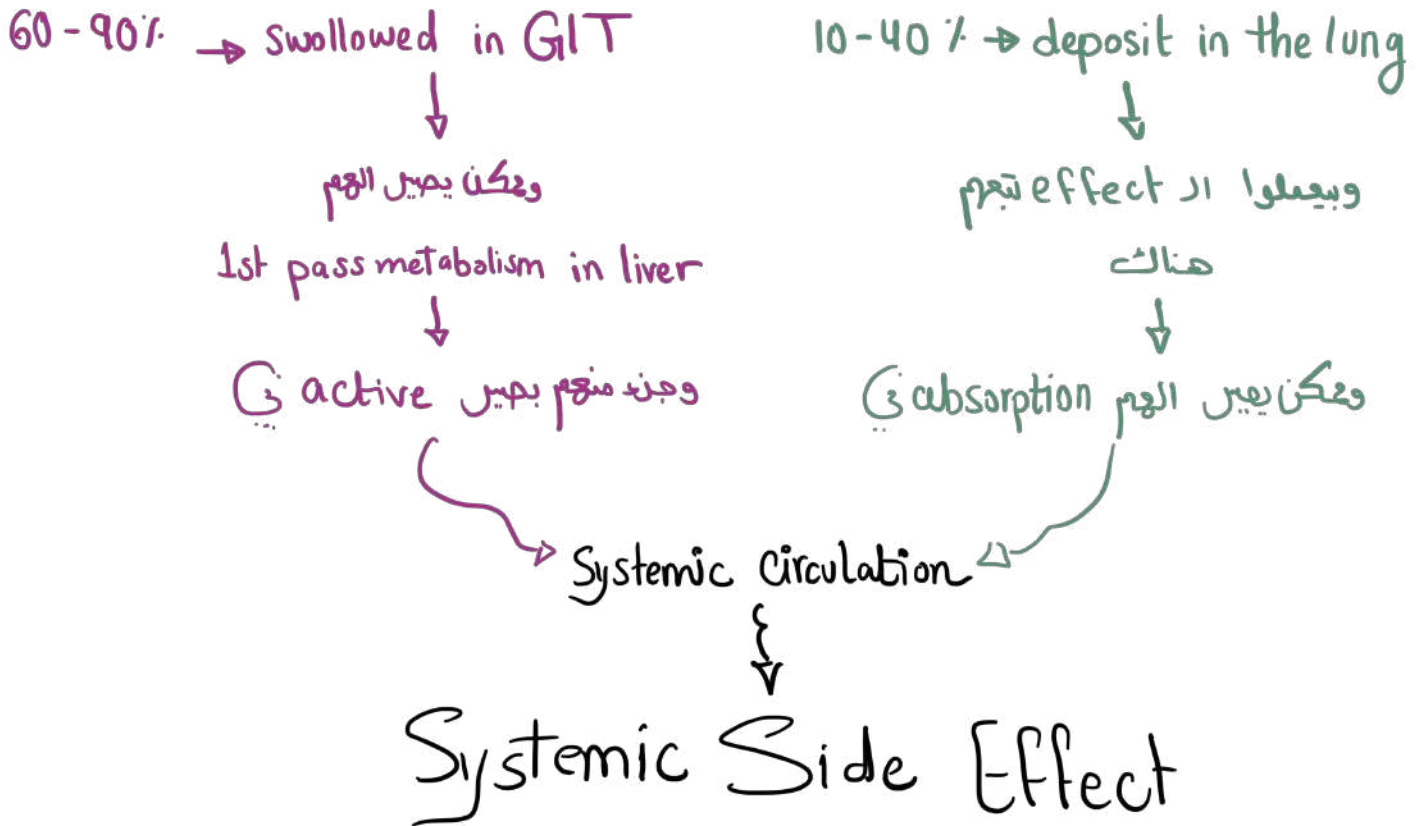


بالعادة ما ينعطى لحالو يكون معو دواء ثاني و إذا كان لحاله يكون عشان inflammatory process تاغته

*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 : (حاكتبهم 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 ← لانهم بيجلوا

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

?combination متى بعطي هاد ال



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 β_2 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

اللي تحت هو اللي حفظ
اللي تحت من سلايداتنا



Pharmacological agents: Drug combinations

COPD pharmacological treatment include
6. Combinations of different drug classes



لايم تعرف ال short / long

SABAs (Short-Acting Beta Agonists)	LABAs (Long-Acting Beta Agonists)	ICS (Inhaled Corticosteroids)	LABAs+ICS	SAMA (Short-Acting Muscarinic Antagonist)	SABA/SAMA	LAMA (Long-Acting Muscarinic Antagonists)	LABA/LAMA	others
Albuterol	Salmeterol	Fluticasone	Salmeterol/Fluticasone	Ipratropium	Albuterol/ipratropium	Glycopyrrolate	Formoterol/Glycopyrrolate	Roflumilast
Levalbuterol	Formoterol	Budesonide	Formoterol/Budesonide			Tiotropium	Olodaterol/Tiotropium	Theophylline
	Olodaterol	Mometasone	Formoterol/Mometasone					



إذا حفظت الجدول بتحل كل اسئلة الدكتور

LABA+ corticosteroids

LONG-ACTING β_2 ADRENERGIC AGONIST/CORTICOSTEROID COMBINATION	
<i>Formoterol/budesonide</i> SYMBICORT	Asthma, COPD
<i>Formoterol/mometasone</i> DULERA	Asthma, COPD
<i>Salmeterol/fluticasone</i> ADVAIR	Asthma, COPD
SHORT-ACTING β_2 AGONIST/SHORT-ACTING ANTICHOLINERGIC COMBINATION	
<i>Albuterol/ipratropium</i> COMBIVENT RESPIMAT, DUONEB	COPD
LONG-ACTING ANTICHOLINERGIC (LAMA)	
LABA/LAMA COMBINATION	
<i>Formoterol/glycopyrrolate</i> BEVESPI AEROSPHERE	COPD
<i>Olodaterol/tiotropium</i> STIOLTO RESPIMAT	COPD

SABA+
SAMA for
COPD
only

LABA+ LAMA for COPD

Pharmacological agents:

Other agents

7. Vaccines, antibiotics and other agents

• **Roflumilast**

* Oral phosphodiesterase-4 (PDE4) inhibitor
← كان بيكس CAMP

* Reduces exacerbations in patients with severe chronic bronchitis (Not emphysema)

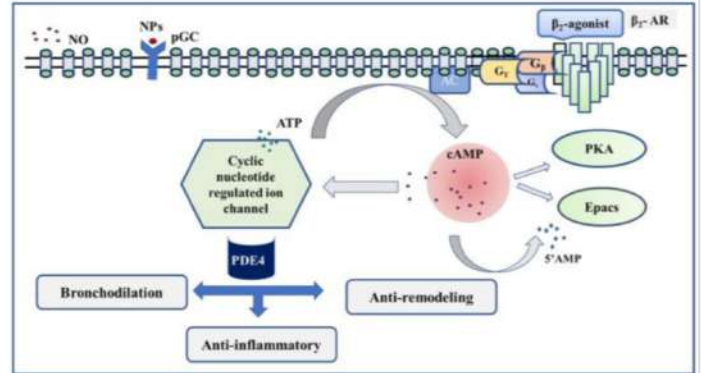
* Reduce inflammation by increasing levels of intracellular cAMP in lung cells.

PDE4: (inhibit broncho dilation)

اهو إنزيم يوقف كل اشئ بالرسمه

فأنا بس اعمله inhibiting بزيده فعالية كل اشئ

هيك بده الدكتور



* 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-inflammatory 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

VIP

Or mental issue

* 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 لأنني بخاف من ال side effects و resistance

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 narrow therapeutic index و adverse effect

- 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 ال Beta blockers يفضل ما اعطيهم الا بحالة وحدة و هي انه يكون المريض معاه cardiovascular disease

patients when you can't fix the COPD they've had for 30 years in one visit





Pharmacological agents: Other agents

هاض السلايد و اللي وراه من سلايداتنا
اللي فوق سلايدات وريد

- **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



Pharmacological agents: Other agents

موجود بالشاي

- **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.

- 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 الفقرة بالامتحان



CAT & mMRC scales



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

مش مطالبين بالاسلايد لامتحان
بس حلو تقراهم

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) (1) (2) (3) (4) (5) I am very sad

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

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



Treatment plans

اللي محدد هو المهم

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

New diagnosis of COPD*

- Recommended general and preventative care for all patients:
- Avoidance of smoking and other risk factors
 - Influenza, pneumococcal, and COVID-19 vaccinations
 - Regular physical activity
 - Short-acting bronchodilator as needed for acute dyspnea (refer to below for selection)
 - Regular review of correct inhaler technique
 - Assessment of hypoxemia and hypercarbia for long-term oxygen and/or noninvasive ventilation

Has the patient had 2 or more moderate exacerbations OR at least 1 hospitalization for COPD exacerbation in the past year?

إذا ما عنده فهو قروب AB

Quantify dyspnea and symptoms using the mMRC dyspnea scale (refer to Table 1) and CAT. Does the patient have mMRC ≥ 2 or CAT ≥ 10 ?

مهم تعرف أسم الفحصين و قيمتهم

GOLD Group A

GOLD Group B

GOLD Group E

Does the patient have high peripheral eosinophil levels ($\geq 300/\text{microL}$) OR Hospitalization for COPD exacerbation?

بنا corticosteroids

LAMA plus as-needed SABA (preferred) OR LABA plus SAMA/SABA or SABA OR As-needed SAMA-SABA or SABA

مع بعض

LAMA-LABA dual bronchodilator therapy AND SABA as needed for acute dyspnea

هون بصير زي B

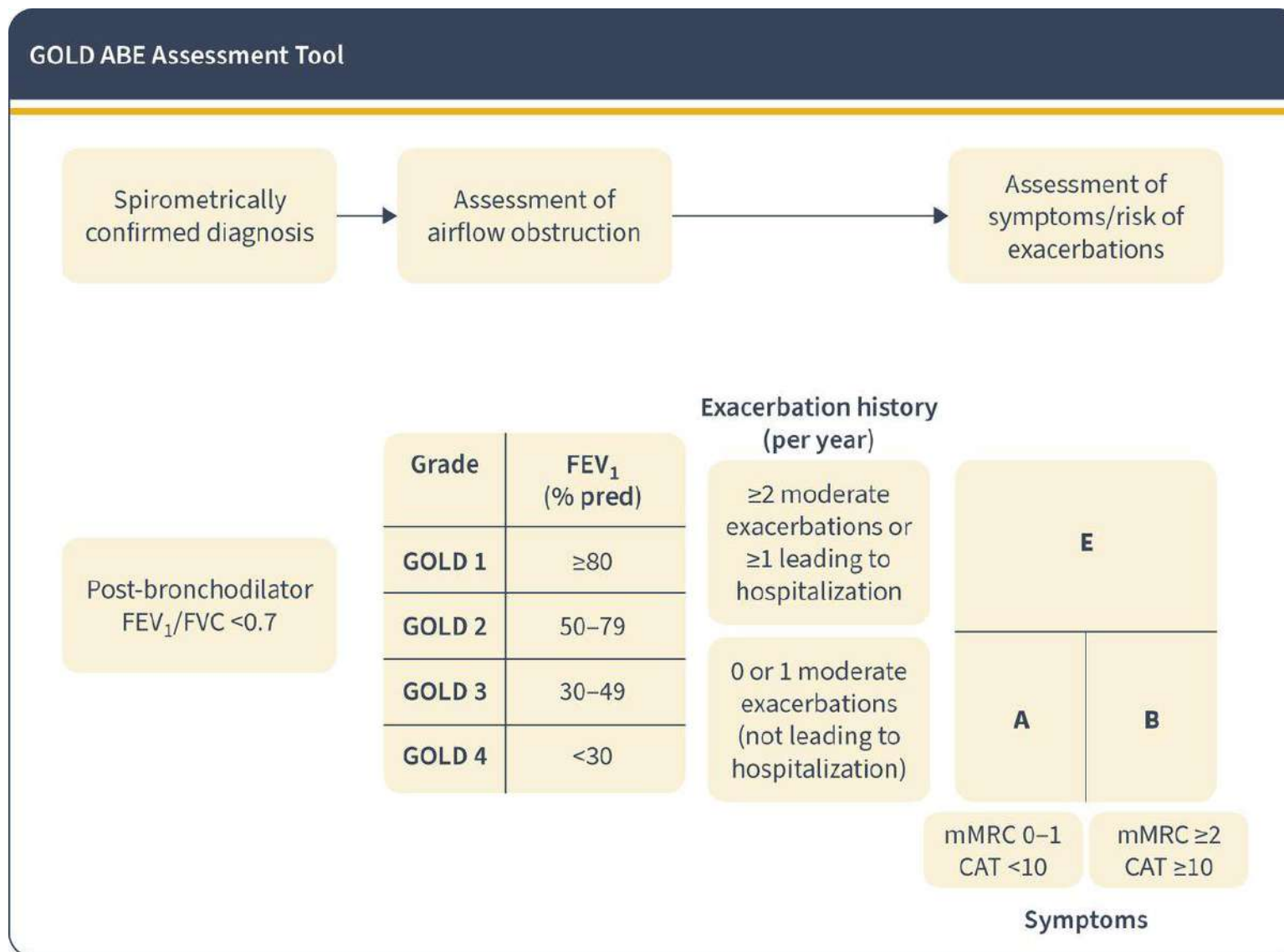
LAMA-LABA dual bronchodilator therapy AND SABA as needed for acute dyspnea

ICS-LAMA-LABA therapy AND SABA as needed for acute dyspnea



GOLD ABE assessment tool.

السلامة اللي فوق بهم الدكتور(اللي حددناه)

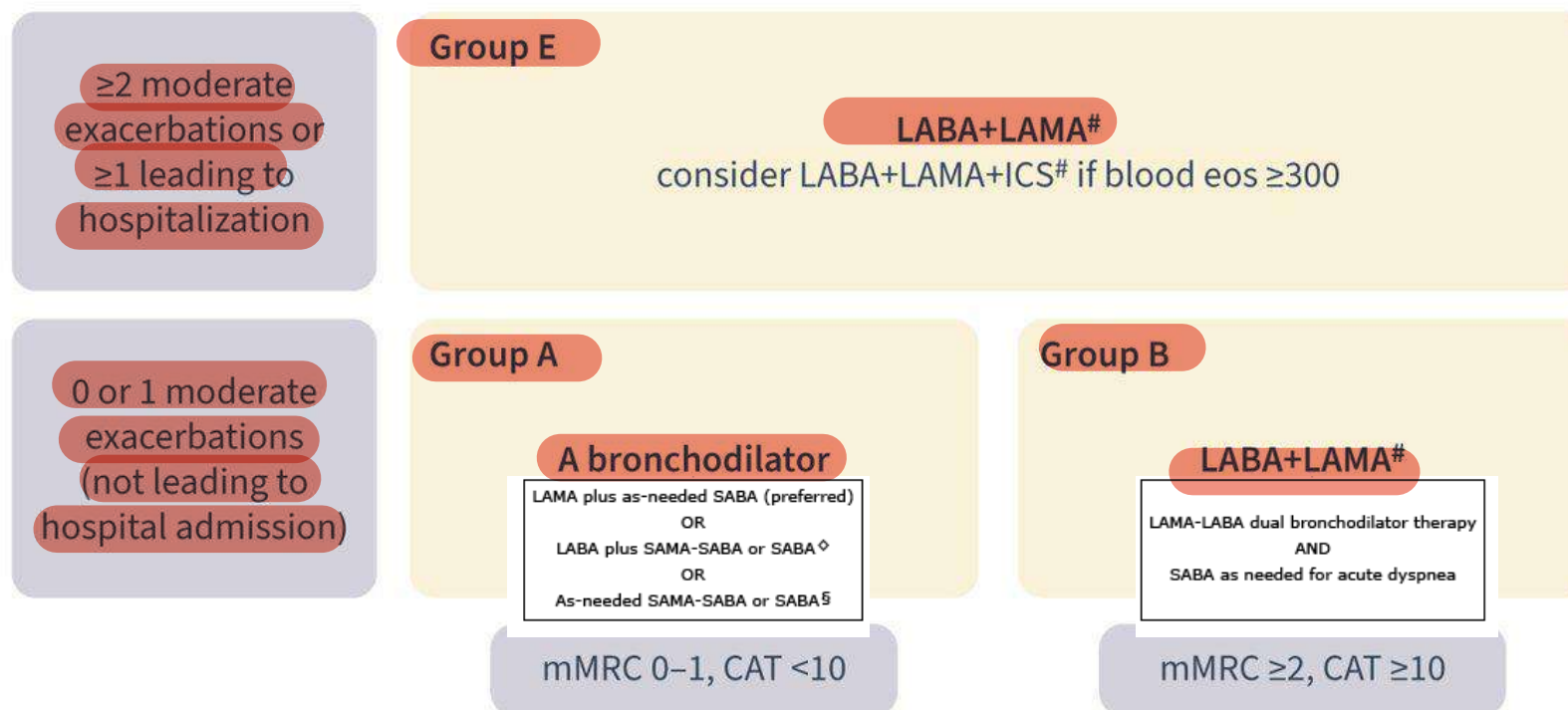




Initial pharmacological treatment

الأصفر قرابية

Initial pharmacological treatment



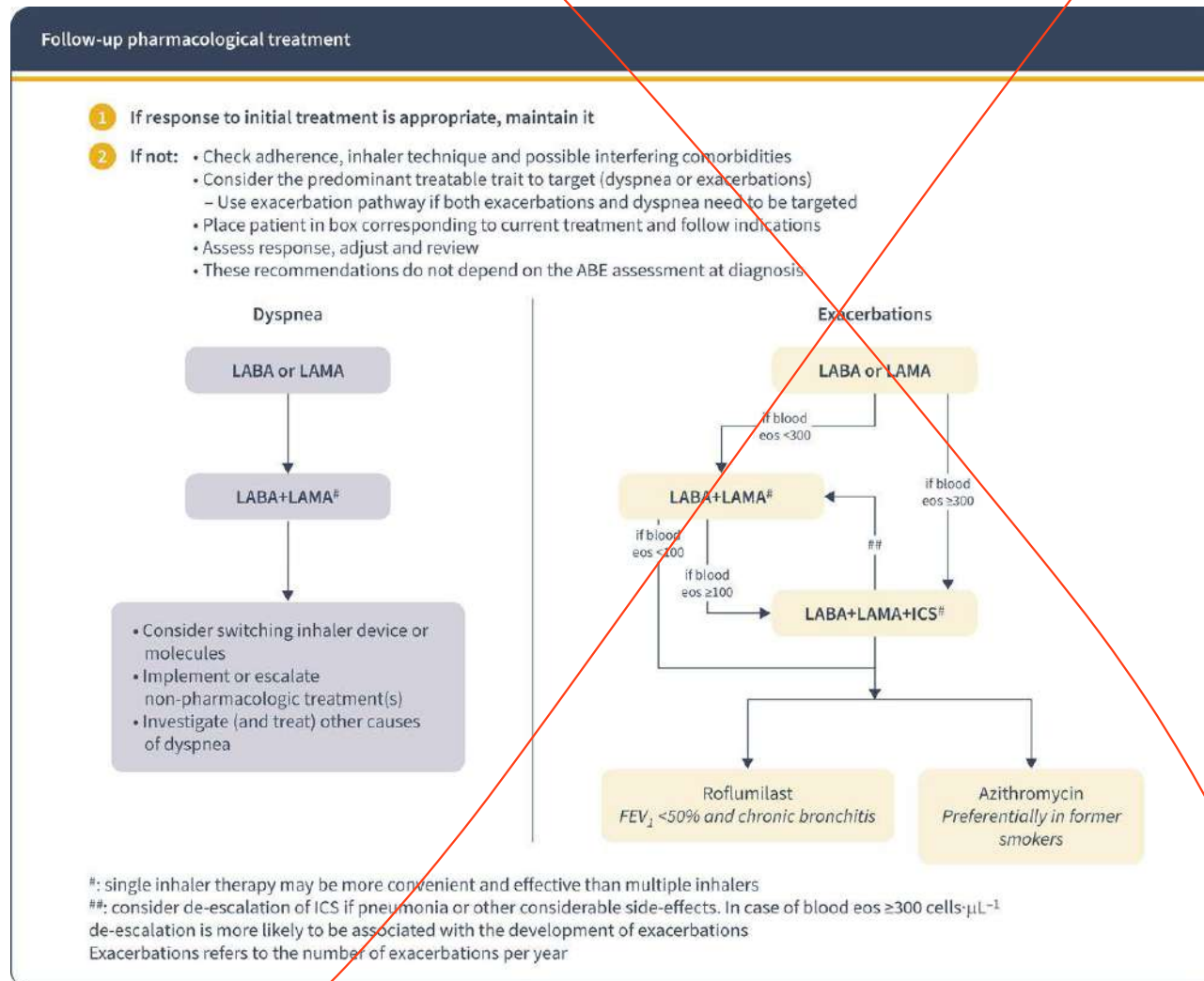
#: single inhaler therapy may be more convenient and effective than multiple inhalers
Exacerbations refers to the number of exacerbations per year

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.



Follow-up pharmacological treatment.



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.

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

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

4- How many stages of COPD disease there are? A- 1 stage

- B- 2 stages
- C- 3 stages
- D- 4 stages

5-What is the first line treatment option for COPD?

- A-Bronchodilator
- B- Muscarinic agent
- C- Corticosteroids
- D- None of the above

6-Roflumilast is a medication that belongs to class of: A- Anticholinergics

- B- Methylxanthines
- C- Phosphodiesterase inhibitors
- D- Long-acting beta agonist

Answers

- 1. C
- 2. C
- 3. D
- 4. D
- 5. A
- 6. C