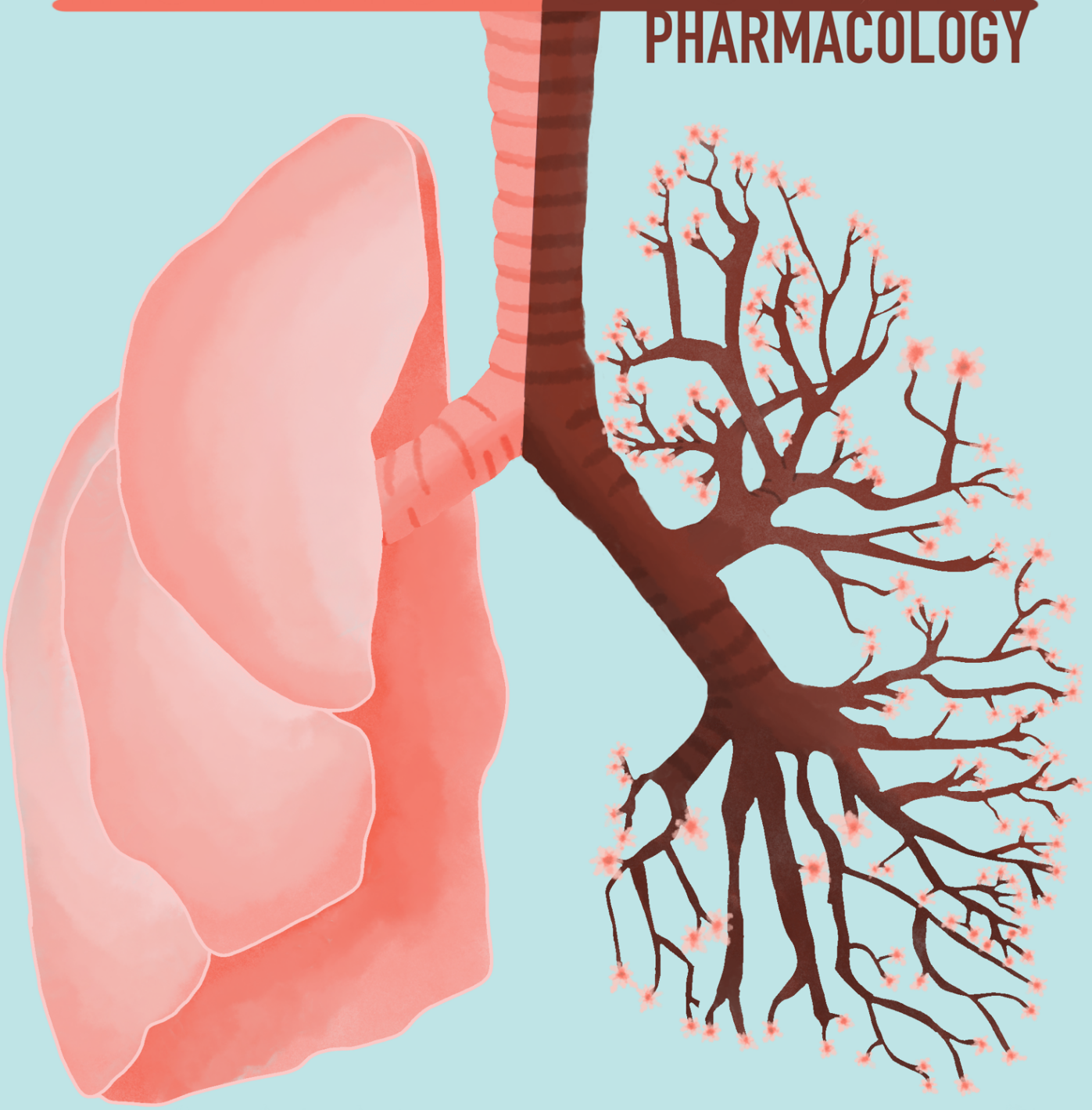
RESPIRATORY SYSTEM
PHARMACOLOGY



Title: Pharmacology sheet 5

Writer: Reham badayneh

Science: Obada Froukh

Final: Lina abdelhadi

Doctor: Manar zraikat

Treatment of Bronchial asthma :-

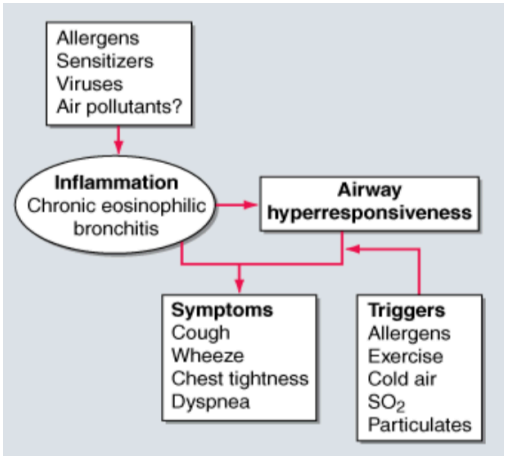
-Definition of Asthma :

Chronic inflammatory disorder with intermittent narrowing of the airways.

Or a condition characterized by wide variations, over short periods of time, in the resistance to flow in the intrapulmonary airways.

-Pathogenesis

1- Early Asthmatic Response:



Allergens (such as stress and others shown in the figure on the right) can provoke IgE production. (The tendency to produce IgE is genetically determined) -> Re-exposure to the allergen causes antigen- antibody interaction on the surface of the mast cells leading to:-

A-Release of already stored mediators.

B-Synthesis of other mediators.

C- Also, activation of neural pathways

Prevented by bronchodilators (which causes bronchodilation of the airways and prevent the early phase of the reaction)

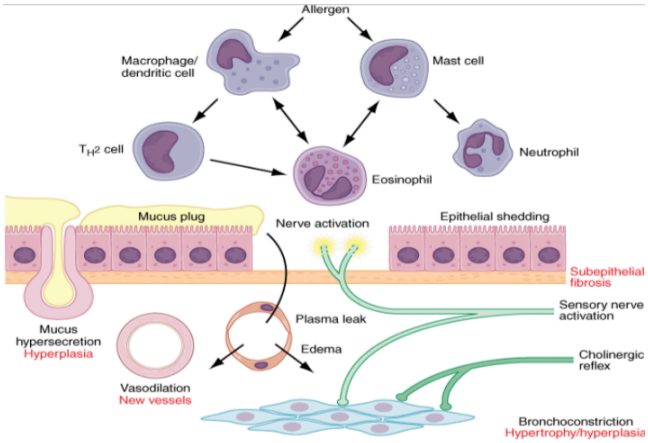
2- Late Asthmatic Response:

4-5 hours later. More sustained phase of bronchoconstriction.

Influx of inflammatory cells and an increase in bronchial responsiveness.

The mediators here are cytokines produced by TH2 lymphocytes, especially interleukins 5, 9, and 13 —> These will stimulate IgE production by B lymphocytes, and directly stimulate mucus production.

Prevented by corticosteroids (in this stage we can't depend only on bronchodilators, instead, we need also corticosteroids to be added).



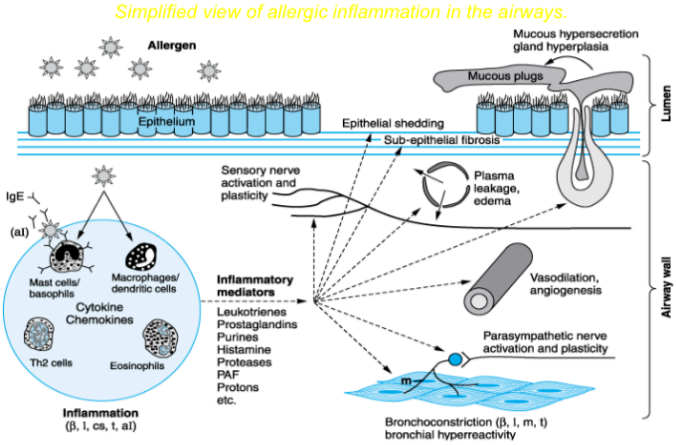
This figure shows the mechanism of the early phase in which the most important thing is the changes that occur in this stage , which are :-

1-increased mucus production

2-Vasodilation

3-Bronchoconstriction

This figure also shows the changes that occur during the early phase which are :-



1-Sensory nerve activation and plasticity

2-Plasma leakage and edema

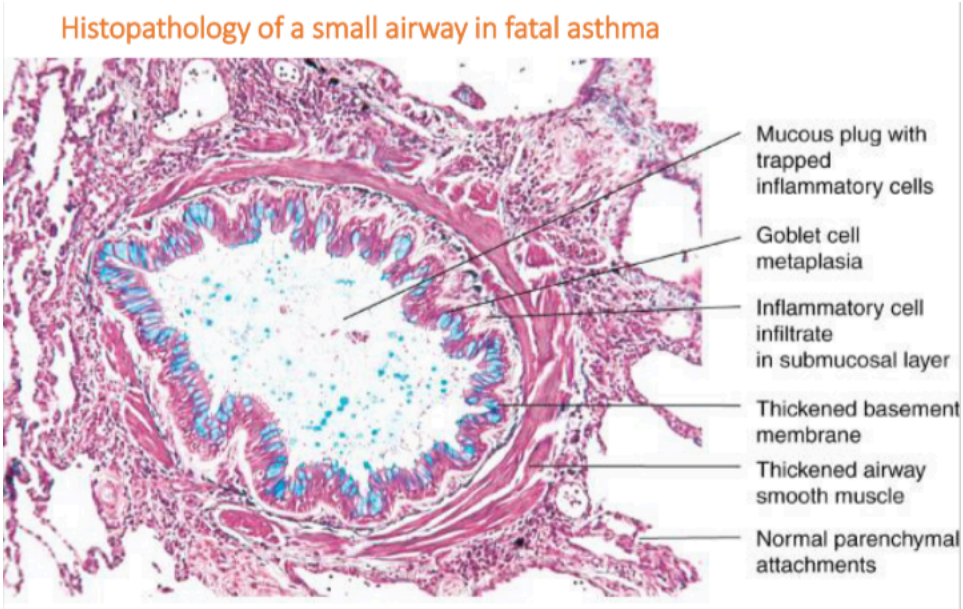
3-Epithelial shedding

4-Vasodilation

5-Sub-epithelial fibrosis

6-Parasympathetic nerve activation and plasticity

And remember that the inflammatory cells involved are mast cells , macrophages and other inflammatory cells .



Memorize the figure and remember PATHOLOGY

Asthma Triggers (remember it is variable) :

Exercise / cold air / Cigarette smoke (VIP) / Stress -anxiety situations /Animal dander's (cats, dogs etc..) / Allergens (grass, trees, molds, cockroach) /Pollutants (sulfur dioxide, ozone, etc...) / Fumes/toxic substances / Medications (ASA, NSAID's, others).

Diagnosis of Asthma- Subjective

1-Cough (remember that cough could be related to other conditions) - usually in spasms and to the point of vomiting - nighttime worse than daytime . Cough may follow exposure to cold air, exercise, a URI (common cold), or allergen (one of the asthma triggers)

2-Dyspnea > cough or wheezing > sputum.

3-Past history of bronchiolitis as a child (small airway disease that lasts for a week ,the child is usually hospitalized).

4-Family history of asthma is common.

Diagnosis of Asthma – Objective

1•Diminished Peak Expiratory Flow Rate (PEFR)

2•Reduced mean and Forced Expiratory Flow Rate (FEFR)

3•Reversibility with Bronchodilators

4•Heightened response to Methacholine Test (Methacoline is a bronchoconstrictor , the patient will inhale a small amount of it ; if the patient is normal ,the constriction effect of Methacoline is not significant , but if the patient is asthmatic , the bronchoconstriction will be significant and it will initiate the symptoms of asthma) .

5•Increase in expired Nitric Oxide (VIP the high percentage of nitric oxide in the expired air is an indicator for the presence of asthma) .

6•Increase in Inflammatory Mediators and their metabolic products in body fluids.

Factors in the treatment strategy :

➢Asthma is a chronic condition (it is a life-long condition).

➢The goal of the therapy is normalizing the lung function .

➢The Condition is heterogeneous in terms of:

1▪Cause or trigger mechanism.(it is variable between patients , for example certain smells are the trigger in some asthmatic patients whereas stress could be the trigger for other asthmatic patients …etc)

2 ▪Extent of bronchoconstriction

3 ▪Degree of inflammation.

- As a result therapy must be individualized.

➢The course of treatment is unpredictable ; because it depends on the response of the patient .

Risks of Not Treating Asthma:

1• Poor or no control of the patient's asthma.

2• Accelerated decline in the function of the patient's lungs

3• Increased number of asthmatic attacks .

4• Poorer response to therapy if started late.

5• Increased mortality from asthma.

Goals of Therapy in Asthma

(We should keep in mind that our goal is not fully treating the condition because as we said it is a chronic condition , but our purpose is to improve the patient's life quality).

1•Minimal symptoms even during sleep.

2•No, or infrequent, acute episodes.

3•No ED (Emergency Department) visits or missed days in school or work.

4•Rare need for beta-agonist inhaler therapy.

5•No limitation of activities – even sports.

6•Peak flow rate variability less than 20% .

7•No or minimal adverse effects from drugs. (And this is done by decreasing the frequency and the dose of the drug taken)

Myths and Misconceptions

Points that should be emphasized to the patients before starting the treatment journey :

✓**Patient and physician "Steroid-o-phobia"** , a lot of patients have fear from taking steroids , so as a physician **if the patient's state require treatment by steroids** we should explain to the patient the importance of taking such medications.

✓**Asthma is an emotional illness.** (it means that it is triggered by STRESS , so we should emphasize this point to the patient if he/she experience stress frequently)

✓**Asthma is an acute disease.**

✓**Asthma medications are addictive.**

✓**Asthma medications become ineffective if they are used regularly.**

✓**Asthma is not a fatal illness / It does not kill.**

Survey of the changing therapy of asthma by decade

1960's : Aminophylline, Epinephrine, Ephedrine are used to treat asthma.

1970's : Beta-agonists (Bronchodilators) , Theophyllines, Beclomethasone, Cromolyn, Ipratropium.

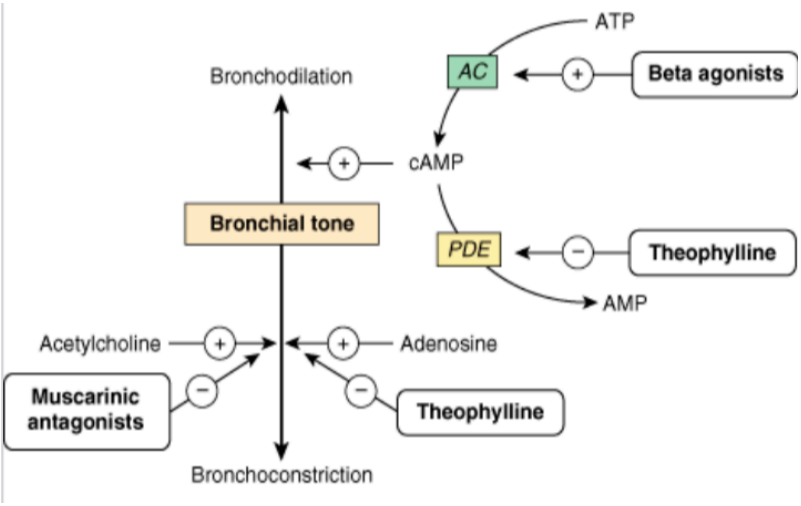
1980's : Beta-agonists, Inhaled Corticosteroids, Cromolyn, Ipratropium

1990's : Inhaled Corticosteroids, Beta-agonists, Theophylline, Leukotriene Inhibitors .

2000's : Corticosteroids + LABA (Long Acting Beta-Agonists , bronchodilators) , LTRAs (Leukotriene Antagonists : their effect is a combination of anti-inflammatory effect and bronchodilation effect) , Theophylline, Cromolyn, Ipratropium,

Tiotropium

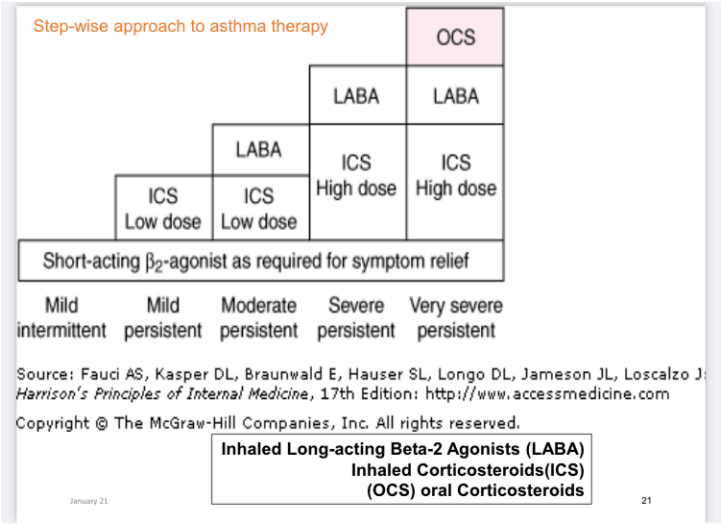
2010's : Prevention including gene therapy (under study).



Because we have bronchoconstriction (due to the accumulation of mucus and the narrowed airways) , so our aim is to dilate the airways (bronchodilation)

Notes about the figure above :-

1- **Muscarinic antagonists : they work as anti-cholinergic drugs that induce the bronchodilation .**
2- **Beta-agonist : they induce the dilation of the bronchial airways**
3- **Theophylline : they inhibit the mucus secretion and thus considered as an anti-inflammatory drug.**



Treating asthma is a step-wise approach (we start with the weakest drug and then we proceed toward the strongest) .

1-Mild intermittent symptoms :-

We give short-acting-B2-agonist as required for symptom relief during the acute attacks

2-Mild persistent symptoms :-

A-we give short-acting-B2-agonists as required for symptom relief .

B-we also give them Inhaled Corticosteroids in low dose and it is given as needed

3-Moderate persistent symptoms :-

A-we give short-acting-B2-agonists as required for symptom relief .

B- we also give them Inhaled Corticosteroids in low dose .

C-we give them LABA (Long Acting Beta Agonists) ; they prevent the asthmatic attacks .

4-Severe persistent symptoms :-

A- we give short-acting-B2-agonists as required for symptom relief .

B- we also give them Inhaled Corticosteroids but in high dose .

C- we give them LABA (Long Acting Beta Agonists) ; they prevent the asthmatic attacks.

5-Very severe persistent symptoms :-

A- we give short-acting-B2-agonists as required for symptom relief .

B- we also give them Inhaled Corticosteroids but in high dose .

C- we give them LABA (Long Acting Beta Agonists) ; they prevent the asthmatic attacks.

D- OCS (Oral corticosteroids -anti inflammatory drugs ; also prevent the asthmatic attacks.

Relievers / Controllers

1-Quick relief medications :-

A-Inhaled Short acting Beta-2 Agonists ; they are taken in urgent situations because they make a quick and rapid dilation of the bronchial airways .

B-Inhaled Anticholinergics ; they alleviate the inflammation and the mucus secretion and support the process of bronchodilation .

C-Systemic Corticosteroids ; they have an anti-inflammatory effect .

2-Long-term control medications(they prevent the asthmatic attacks and taken over a long period of time (NOT necessarily during the acute asthmatic attacks they're taken whether we have an acute attack or not). Depending on the patient's situation and depending on the severity of the asthma as well as the control on it , the patient may take a long-term control medications that are taken during or in the absence of the asthmatic attacks) :-

A-Topical (inhaled) Corticosteroids

B-Inhaled Cromolyn Na and Nedocromil (they inhibit mast cells' activity , preventing the release of histamine thus alleviating the inflammation)

C-Oral Methylxanthines (Theophyllines) [it decreases the mucus secretion and thus alleviating the inflammatory process]

D-Inhaled Long-acting Beta-2 Agonists (LABA) [they act for a long period of time , they prevent the asthmatic attacks and keep the patient under control]

E-Oral Leukotriene modifiers (LTRA)(leukotriene receptor antagonists)[they have an anti-inflammatory and bronchodilation effect , they prevent the recurrence of the asthmatic attacks]

So the treatment of asthma is divided into Short-acting and Long-acting medications, depending on the situation , and this doesn't mean that the patient only take one of the two groups ,for example the patient might take a drug form the first group for the acute attacks and from the second group for the prevention of the following attacks.