
بسم الله الرحمن الرحيم

إن الذين آمنوا و عملوا الصالحات إنا لا نُضَيّع أجر مَن أحسن عملاً

الكهف:30

Bronchial Asthma

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Definition

- **Asthma is a chronic inflammatory disease of the bronchial tree characterized by hyper responsiveness to broncho-constricting stimuli with episodic air flow limitation that is reversible either spontaneously or with therapy.**
- **Another def. "Asthma is a lung disease with the following characteristics:**

  1) Air way obstruction that is reversible either spontaneously or with drugs.

  2) Air way inflammation.

  3) Air way hyper responsiveness to a variety of stimuli.

Aetiology

- **The aie of Asthma are not fully understood. Asthma appears to be a *multi factorial* disorder with both *Genetic* and *Environmental* causes and is likely to be a *Clinical Syndrome* in which various precipitating factors result in similar clinical and pathologic manifestation. e.g., Childhood-onset atopic asthma, Adult-onset asthma in a middle aged ex-smoker without apparent allergies,**

and Asthma developing in the setting of occupational exposure to toluene di-isocyanate are likely to result from different cellular and molecular abnormalities despite their common characteristics of airway hyper responsiveness, air way inflammation, and variable air way obstruction.

- ***Genetic factors*: Asthma is familial. Recent genetic epidemiological studies have mapped a gene for asthma to a focus on chromosome 5, where numerous genes encoding inflammatory cytokines are located. Asthma is frequently associated with clinical manifestation of *Atopy* (Familial allergy to common allergens) and elevated serum total IgE concentration, but some evidence suggests that asthma and allergy may be inherited independently.**

Pathogenesis

- The *Eosinophil* is a major effecter cell in asthmatic air way inflammation, but the *Mast* cell and *T lymphocyte* also play crucial roles.

***A- Mediators in the biology of Asthma*: The** inflammatory response in asthmatic airways is extremely complex. It is characterized by varying degrees of mononuclear cell and eosinophil infiltration, epithelial desquamation, mucus hyper secretion (airway plugging), smooth muscle hyperplasia, and airway remodeling with sub epithelial fibrosis.

1-Cytokines:

-They are low molecular wt. protein molecules that are produced and secreted by all nucleated cells.

-Cytokines regulate inflammation and the immune response.

-Principle cytokines implicated in asthma pathogenesis are: Interleukin-1B (IL-1B), IL5, IL3, IL4, and tumor necrosis factor-α (TNFα). They are produced by mast cells, T lymphocyte (TH2), macrophages and epithelial cells.

-Cytokines have the following effects:

1) Recruit eosinophils to the airways and perpetuating eosinophilic inflammation in asthma.

2) Increase expression of adhesion molecule on endothelium which enhances inflammatory cell migration into the airway.

3) IL4 plays a key role in initiating IgE synthesis and TH2 lymphocyte development.

2-Histamine:

-Histamine is primarily a product of synthesis from histidine in the Golgi apparatus of mast cells and basophiles.

-It is released on activation of mast cells primarily through IgE-receptor interaction.

-Histamine has direct vaso-active and smooth muscle spasmogenic effects.

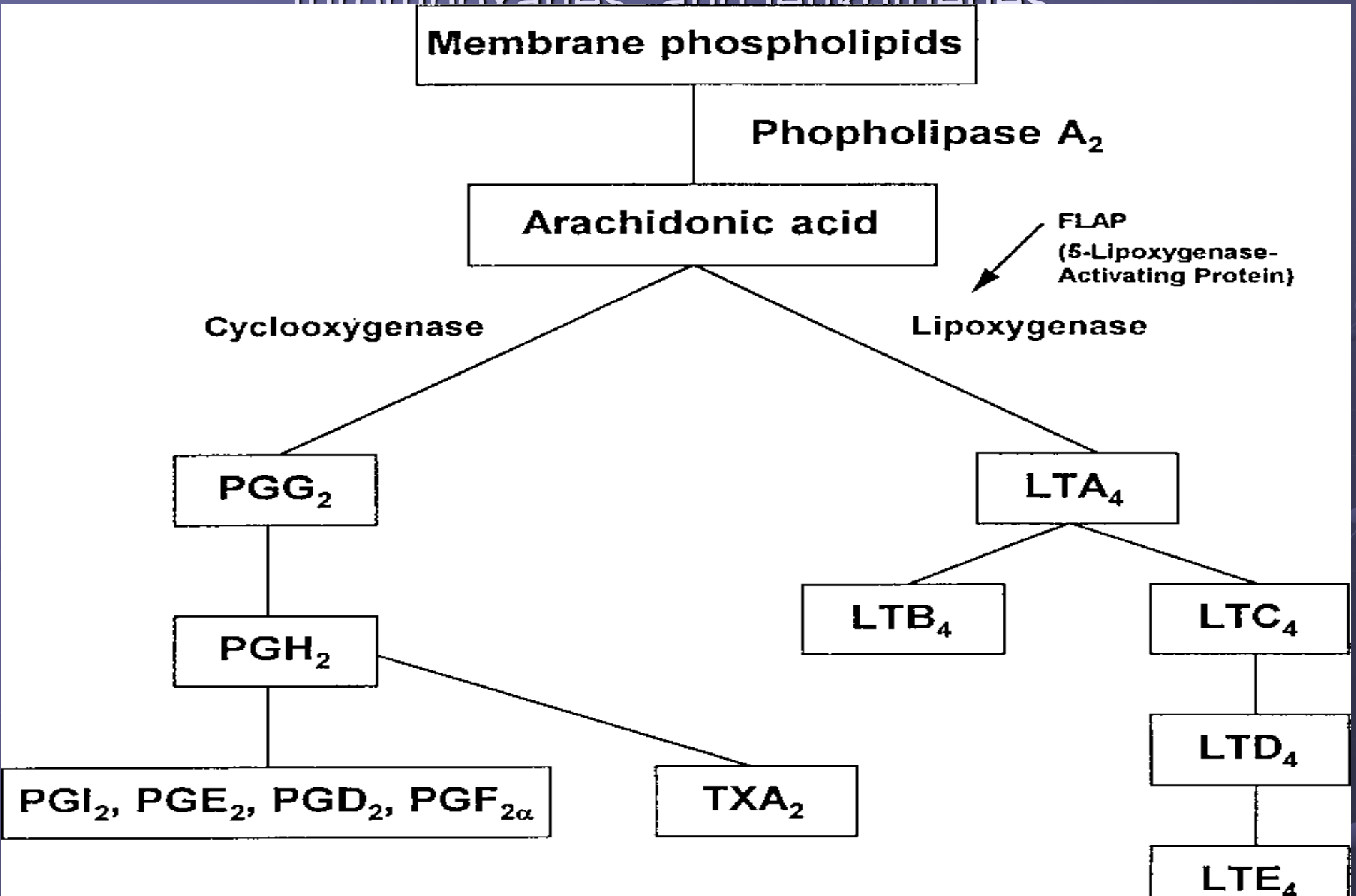
3-Arachidonic acid metabolites **i.e., Lipid mediators (PGs and Leukotriens):**

-They are produced by various inflammatory cell types, including mast cells, eosinophils, basophiles and macrophages.

-PGD2 and PGF2α and leukotriens have the following effects: 1) Inflammation.

2) Increased capillary permeability.

Figure 45-2 Pathways in the formation of prostaglandins, thromboxanes, and leukotrienes



4-Contents of eosinophil granules:

-These include 4 principle cationic proteins:

1) Major basic protein (MBP).

2) Eosinophilic cationic protein (ECP).

3) Eosinophil peroxidase (EPO).

4) Eosinophil-derived neurotoxin (EDN).

-The ECP produce the following effects:

1) Cytotoxic to respiratory epithelium.

2) Promotes histamine release from mast cells.

3) Damage myelinated neurons.

B-Airway smooth muscles:

-Bronchospasm remains an important component of asthma, particularly acute asthma.

-Smooth muscle is innervated by branches of both the parasympathetic (cholinergic) and sympathetic (adrenergic) nervous systems.

-The parasympathetic system is excitatory and vagal stimulation narrows the airways.

-The sympathetic system is inhibitory and stimulation of this system's β-receptors results in smooth muscle relaxation.

Clinical features

- **The spectrum of disease severity: Some individuals with asthma may be entirely asymptomatic between attacks provoked by specific exposures. Other asthmatics may have nearly continuous symptoms and frequent severe attacks. Episodic exacerbation of asthma range from bothersome wheezing to life threatening attacks of respiratory failure.**
- **Asthma may present at *any age* including the extremes of life.**

- **The Cardinal symptoms of Asthma include: Episodic wheezing, Dyspnea, Chest tightness, Cough and Sputum production (sputum is small amount, sticky, white or clear usually, colored if infection, rarely profuse and frothy). Other presentation of asthma such as isolated persistent unexplained cough (Cough *Variant Asthma*), Or Exertional chest tightness Or Dyspnea.**
- **N.B.: Of particular importance in diagnosis of asthma is the *Periodicity* of symptoms.**

- **Provoking Factors:**

  1) Allergy: # Over 90% of childhood asthmatic and 50% of adult are atopic.

  # Episodes of wheezing and Dyspnea provoked by inhalation of airborn allergens.

  2) Infection: Viral infection

  3) Air pollution

  4) Smoking

  5) Psychological factors

  6) Gastro-esophageal reflux

  7) Exercise (*exercise induced asthma*)

  8) *Aspirin induced asthma*: charact. by Asthma + Nasal polyposis + Asp. Sensitivity.

N.B.: ***Atopic individuals*: are people who have the inherited ability to produce Igs and Abs in response to**

- Signs:

  The *characteristic* clinical finding in asthmatic patient is wheeze. **Wheezing** is caused by high velocity, turbulent airflow through narrowed airways; it is usually present *during expiration*, although it may be present during inspiration as well. Wheezing is typically *Polyphonic*, indicating their origin from many separate airways (Non-uniformity of airflow). Wheezing may be *absent* in very mild and very severe airway obstruction.

  Clinical signs of Rhinitis, Sinusitis and Nasal polyps are seen more commonly in patients with asthma.

  Patients with asthma may have entirely *Normal* physical examination *In-between Exacerbations*.

- **Acute Severe Asthma:**

  Acute severe attacks represent *progression* of an attack of *Bronchospasm* to the point where the patient is *breathless at rest* and has signs of *cardiac stress*.

  Symptoms:

  - **Increasing breathlessness.**
  - **Difficulty in talking or inability to do anything other than breathing.**
  - **Anxiety**
  - **The patient sits up in bed and chair**
  - **Wheezes are audible withoutstethoscope and the chest is is visibly over inflated**

Investigations

A. **Pulmonary function tests**: pulmonary function tests are important for **C**onfirming the diagnosis, **E**stablishing the severity of the disease, and **M**onitoring the response to therapy.

1) Spirometry: The diagnosis of asthma is usually confirmed by objective demonstration of airway obstruction by Spirometry, and evidence of significant improvement in the 1 sec. forced expiratory volume (FEV1) after bronchodilator administration.

Pattern of airflow limitation are:

→Reduction in the FEV1/FVC ratio.

→Reduced FEV1 and FVC.

→Relatively greater reduction in FEV1 than FVC.

Post bronchodilator increase in FEV1 of 15-20% is evidence of reversible airway obstruction.

3) Lung volumes: Residual volume (RV), Functional residual capacity (FRC), and Total lung capacity may increase in acute asthmatic episodes.

4) Diffusing Lung Capacity: Usually Normal in asthma

5) Arterial Blood Gases:

-Typically Normal in patients with chronic stable asthma.

-During an acute episode Hypoxemia is often present + Hypercapnia.

-Arterial PCO2is typically reduced owing to hyperventilation.

-Severe obstruction → Arterial PCO2 rise

B. Radiography:

-Because the chest radiograph is generally un remarkable in patients with uncomplicated asthma, it is used primarily to exclude other causes of respiratory symptoms.

-Non-Specific radiographic findings such as Over inflation, Prominent hilar vessels, and increased broncho-vascular markings (Dirty lung appearance).

-Over inflation has been reported in asthmatics with severe disease, chronic, persistent, rather than intermittent, and during acute exacerbation.

C. Electrocardiography:

-Asthma in remission is usually not associated with ECG abnormalities.

D. Blood tests:

-Eosinophiles may be seen in peripheral blood in both allergic and non-allergic asthmatics.

-Elevated total IgE serum level are frequently seen in allergic patients but the findings are not specific for asthma.

E. **Sputum examination:**

-Sputum eosinophilia is more charecterstically found in asthmatics than in patients with COPD.

-Neutrophiles are found more often in patients with an acute exacerbation of chronic bronchitis.

-Sputum eosinophilia can be seen in both disorders.

F. Allergy tests:

-Tests to determine whether the patient is allergic and to investigate the role of specific allergens as a cause of asthma.

-Skin Prick test is performed by putting a drop of allergen on the skin, usually the front surface of the forearm, and lifting the skin lightly through the drop with the point of an intra-dermal needle, the test should be read about 15-20 minutes later. A wheel is a positive result

G. Bronchial Challenge testing:

-Bronchial hyper responsiveness may be detected by broncho provocation tests with an inhaled pharmacologic bronchoconstrictor such as histamine or methacholine.

Differential Diagnosis

1. **COPD: Chronic bronchitis, Emphysema.**
2. **Laryngeal dysfunction.**
3. **Congestive feature failure.**
4. **Pulmonary eosinophilia.**
5. **Pulmonary embolism.**
6. **Chronic sinusitis and Gastro esophageal reflux.**
7. **Acute bronchiolitis.**
8. **Localized anatomic lesions obstructing airway, e.g., tumors, FB.**

QUESTIONS???????

Thank you,