Obstructive Pulmonary Diseases (Asthma)

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Asthma

❑ It is a chronic inflammatory airway disease characterized by:

o Airflow limitation which is usually reversible spontaneously or with treatment.

o Airway **hyper-responsiveness** to wide range of stimuli.

o Periodicity & diurnal variability of symptoms.

❑ **Airway obstruction occurs due to a combination of:**

• Smooth muscle contraction.

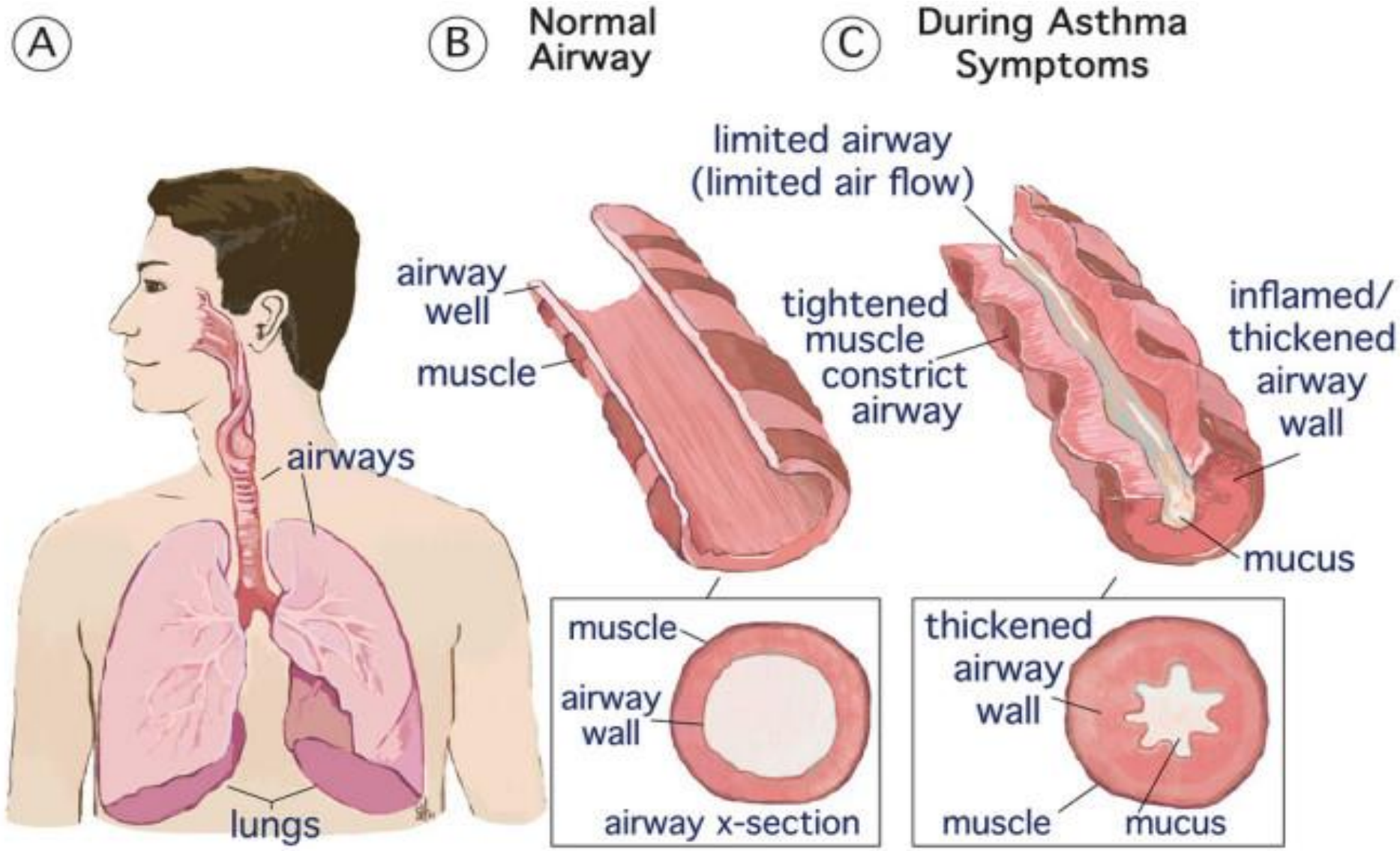
• Airway lumen secretions.

• Edema of bronchial mucosa & accumulation of inflammatory cells.

❑ **May become irreversible over time due to:**

• Basement membrane thickening, collagen deposition, and epithelial damage.

• Airway remodeling occurs in chronic disease, with smooth muscle hypertrophy.


A
B
Normal Airway
C
During Asthma Symptoms
airways
lungs
limited airway (limited air flow)
airway well
muscle
tightened muscle constrict airway
inflamed/ thickened airway wall
mucus
muscle
airway wall
airway x-section
thickened airway wall
muscle
mucus

Classifications:

I. Extrinsic asthma:

- In which an environmental inducing agent can be identified.
- Occurs most frequently in atopic individuals. Onset usually in childhood.
- Frequently associated with other atopic diseases e.g. atopic dermatitis, allergic rhinitis.

II. Intrinsic asthma:

- No causative agent can be identified.
- Starts usually in middle age (*late onset).*
- Not associated with other atopic diseases .

Differentiating parameters	*Extrinsic*	*Intrinsic*
- Age of onset	Childhood	Middle age
- Precipitating factor	Obvious	Not obvious
- Family history	Allergy	Bronchial asthma
- Atopic tendency	Usually apparent	Absent
- IgE level	Raised	Not raised
- Skin test	Positive	Negative
- Asthma	Intermittent	Less labile & often severe

Allergens causing asthma :

- House dust mites.
- Animal hair and bird feathers.
- Pollens.
- Fungal allergens : aspergillus.
- Rarely foods.

Triggers of asthma attacks :

- Allergens.
- Air pollution : smoking, chemical oxidants released from motor vehicle exhaust.
- Respiratory infections : especially viral.
- Iatrogenic : aspirin, β blockers.
- Occupational : occupational asthma occurs when agents at workplace cause asthma e.g., isocyanates, woods, formaldehyde, latex ... etc.)
- Cold air and exercise: due to histamine & leukotriene released from mast cells caused by post-thermal changes.

- Aspirin sensitive patients may also report symptoms following:
  - Alcohol (in particular, white wine).
  - Foods containing salicylates.
  - Other medications implicated include:
    - The oral contraceptive pill.
    - Cholinergic agents.
    - Prostaglandin F2α.
  - Betel nuts contain arecoline, which is structurally similar to methacholine and can aggravate asthma.

Pathogenesis of Asthma:

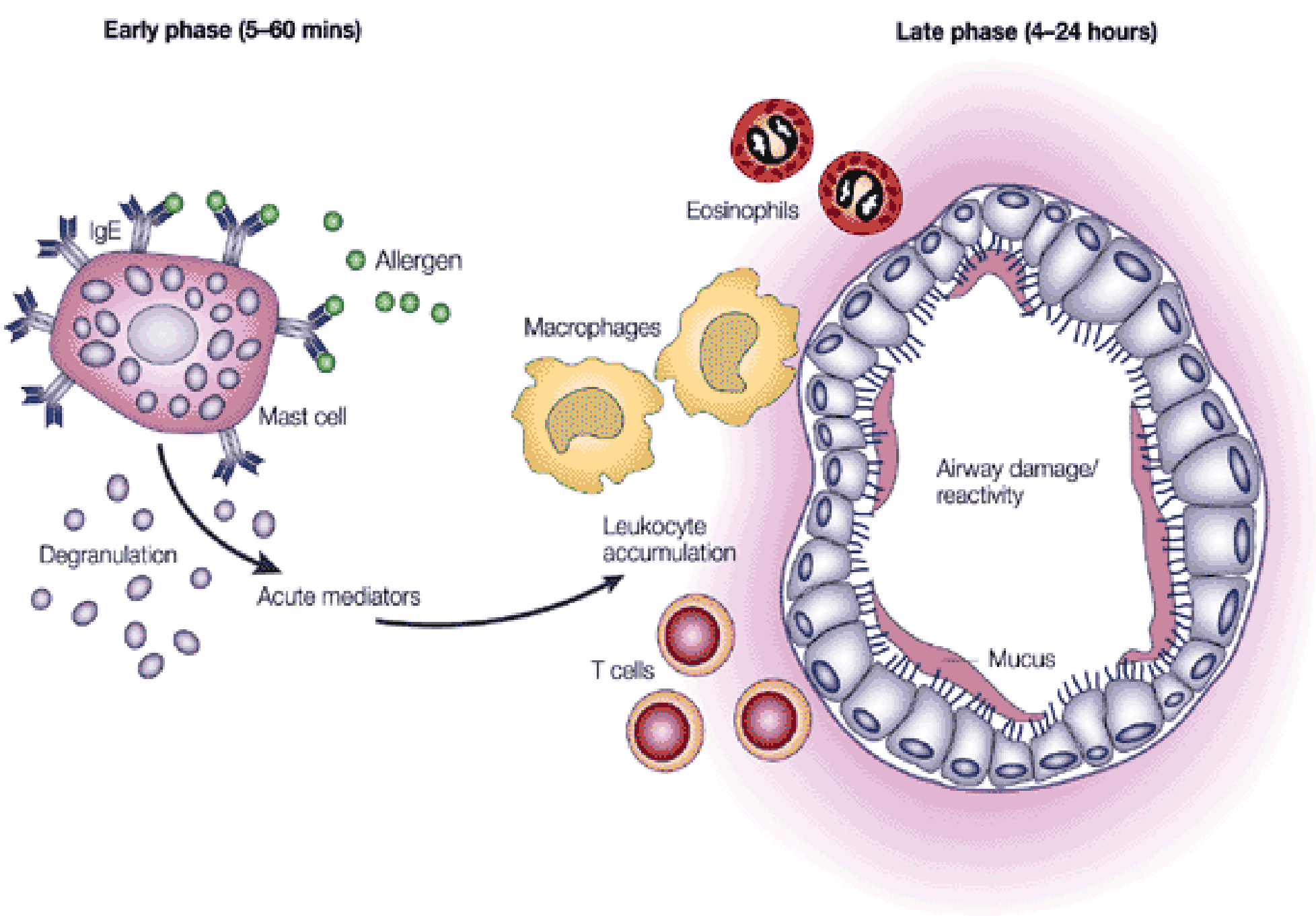
1. Immunological mechanism :

Stimulus (allergen) → Bronchial narrowing

a) Exposure to specific allergen ➔ stimulation of T helper cells ➔ production of IgE (***Sensitization***)

b) Following initial sensitization, repeated exposure to allergen leads to → Antigen (*allergen*) and antibody (IgE) reactions on the surface of mast cells leads to disruption of the cells and release of *chemical mediators* (histamine, bradykinin, leukotrienes, prostaglandines, esinophils) which cause bronchoconstriction (*immediate phase*).

c) Other mediators as platelet activating factor (PAF), major basic protein (MBP) leading to edema & cellular infiltration of bronchial wall (*late phase*).


Early phase (5–60 mins)
Late phase (4–24 hours)
IgE
Allergen
Mast cell
Degranulation
Acute mediators
Eosinophils
Macrophages
Leukocyte accumulation
T cells
Airway damage/ reactivity
Mucus

2. Neural mechanism:

- Parasympathetic →bronchoconstriction & increase in mucous secretions.
- Sympathetic →bronchodilatation.

o Non adrenergic non cholinergic (**NANC)** ➔ bronchodilatation (its neurotransmitter is called vasoactive intestinal peptide, VIP). Deficiency of this system →bronchospasm.

3. Genetic factor:

o Genetic factor plays a major role in regulation of IgE production.
o Asthma is a polygenetic disease e.g.
- Chromosome 5 contains genes controlling production of cytokines.
- Chromosome 2 contains genes controlling IgE synthesis.
- Chromosome 20 contains gene called (ADAM33) which is strongly associated with airway hyper-responsiveness & airway remodeling.

Clinical Picture

Symptoms:

1. **Recurrent attacks of** :
   - o Wheeze.
   - o Shortness of breath & chest tightness.
   - o Cough.

2. **Symptoms occur or worsen at night** (and early morning) .

3. **Symptoms occur or worsen after allergen exposure, exercise, cold air, and upper respiratory tract infections.**

4. **Family history of asthma or atopic diseases.**

Signs:

- ❑ **In between the attacks:** No signs are detected.

- ❑ **During the attacks** :
  - o Hyperinflation of the chest, with an increased anteroposterior thoracic diameter and a low diaphragm.
  - o **Wheezing,** most marked in expiration, is the most characteristic breath sound of asthma but it is an unreliable indicator of severity.
  - o Vesicular breath sound with prolonged expiration due to bronchospasm.
  - o Tachycardia, tachypnea & working accessory respiratory muscles.

Complications of asthma:

1. Acute severe asthma (*Status asthmaticus*).
2. Pneumothorax.
3. Psychological troubles.
4. Respiratory failure & Cor pulmonale.
5. Complications of cough: e.g., fracture of ribs.
6. Side effects of medications: arrhythmias.

Investigations

1- Pulmonary function tests : (*cornerstone of diagnosis*)

- o May be normal between the attacks.
- o **Reduced FEV1** & FEV1/FVC % during the attacks.
- o Test of reversibility (*Bronchodilator* test) : usually FEVl improve> 15 % after inhalation of short acting β2 agonist. (unlike COPD, FEVl response is< 15 %).

NOTE: Response to bronchodilators may not be present in severe chronic asthma when little reversibility can be demonstrated.

- o **Significant (> 20%) diurnal peak expiratory flow rate (PEFR) variability** on at least 3 days per week for a minimum of 2 weeks.
- o **Bronchial provocation test:** Using histamine, methacholine or exercise to induce airway hyper-responsiveness. It is used in patients with normal FEV1.

2- Chest X-ray :

o **Not diagnostic** for asthma.

✓ Normal chest X-ray is the most common finding.

✓ Lobar collapse is seen with mucus plugging of a large bronchus.

✓ Fleeting shadows with bronchiectasis on CT suggest allergic bronchopulmonary aspergillosis.

o Done mainly to exclude pneumonia, pneumothorax, or shadows e.g., allergic bronchopulmonary aspergillosis.

3- Detection of allergen :

o **Skin prick tests:** should be performed to help identify allergic cause.

o Specific bronchoprovocation test using inhaled antigens.

4- Blood picture :

o Esinophilia > 400/mm3 may be present in allergic cases.

o Leukocytosis due to infection.

5- Blood gases :

In acute severe attacks: ↓ PaO2 with normal PaCO2 • Increase in PaCO2 is a bad prognosis and considered as an indication of mechanical ventilation.

6- Sputum examination:

o Esinophils are detected in the sputum.
o Curschmann's spirals: yellow white long threads composed of epithelium, esinophils & mucous (casts of the distal airways).
o Charcot- Leyden crystals: breakdown products of esinophils.
o Creola bodies : clusters of columnar bronchial epithelium.

7- An exhaled nitric oxide level (a surrogate of eosinophilic airway inflammation) of 40 or more parts per billion in a glucocorticoid-naïve adult or a peripheral blood eosinophilia may support the diagnosis of asthma.

8- ECG : to exclude cardiac causes of dyspnea .

Classifications of degree of asthma according to severity :

Degree	Days with symptoms	Nights with symptoms	PEFR or FEV1	PEFR variability
Mild intermittent	≤ 2 days/week	≤ 2 nights/month	> 80%	< 20%
Mild persistent	> 2 days/week But < 1 per day	> 2 nights/month	> 80%	20 – 30%
Moderate persistent	Daily	> 1 night /week	60 – 80%	> 30%
Severe persistent	Continual	Frequent	< 60%	> 30%

Differential diagnosis:

1. From other causes of wheezing: "All that wheezes is not asthma"

- COPD : predominantly irreversible.
- Cardiac asthma.
- Carcinoid syndrome: usually associated with stridor, not wheezing.
- Churg-Strauss vasculitis.
- Upper airway obstruction due to foreign body, tumor, laryngeal edema.

2. From other causes of paroxysmal dyspnea :

- Tetany.
- Myasthenia crises.
- Recurrent pulmonary emboli.
- Hysterical dyspnea.

3. Drug induced cough e.g., ACEIs

4. Vocal cord dysfunction (*Factitious asthma).*

Treatment

Components of Asthma treatment: 6 Points

1- Patient and family education.
2- Assessment and monitoring of asthma severity.
3- Environmental control & avoidance of risk factors (triggers)
4- Establish individual medication plan for long term management.
5- Establish individual plans for managing exacerbations.
6- Provide regular follow up care.

Goals of Treatment : 4 goals

1. Aim for no symptoms/ near normal lung function on minimal treatment.
2. Prevent asthma exacerbations.
3. Avoid adverse effects from asthma medications.
4. Prevent development of irreversible limitation.

Asthma Control Assessment

- The goal of asthma therapy is to maintain complete control:
  - No daytime symptoms.
  - No limitation of activities.
  - No nocturnal symptoms/ wakening.
  - No need for 'rescue' medication.
  - Normal lung function.
  - No exacerbations.

- Patients who have symptoms requiring rescue medication more than twice a week have partial control.
- Those with more than 3 of the previously mentioned features in any week are termed uncontrolled.