ASTHMA

By Dr. Swathi Swaroopa. B

- Bronchial asthma defined as

- "A chronic inflammatory disorder of the airways in which many cells and cellular elements play a role, in particular, mast cells, eosinophil's, T lymphocytes, and epithelial cells."

- This inflammatory process produces recurrent episodes of airway obstruction, characterized by wheezing, breathlessness, chest tightness, and a cough that often is worse at night and in the early morning.

- Based on the stimuli initiating asthma it is categorized in to
    - **Extrinsic (allergic, atopic) asthma**
    - **Intrinsic (idiosyncratic, non-atopic) asthma**
    - **Mixed type**

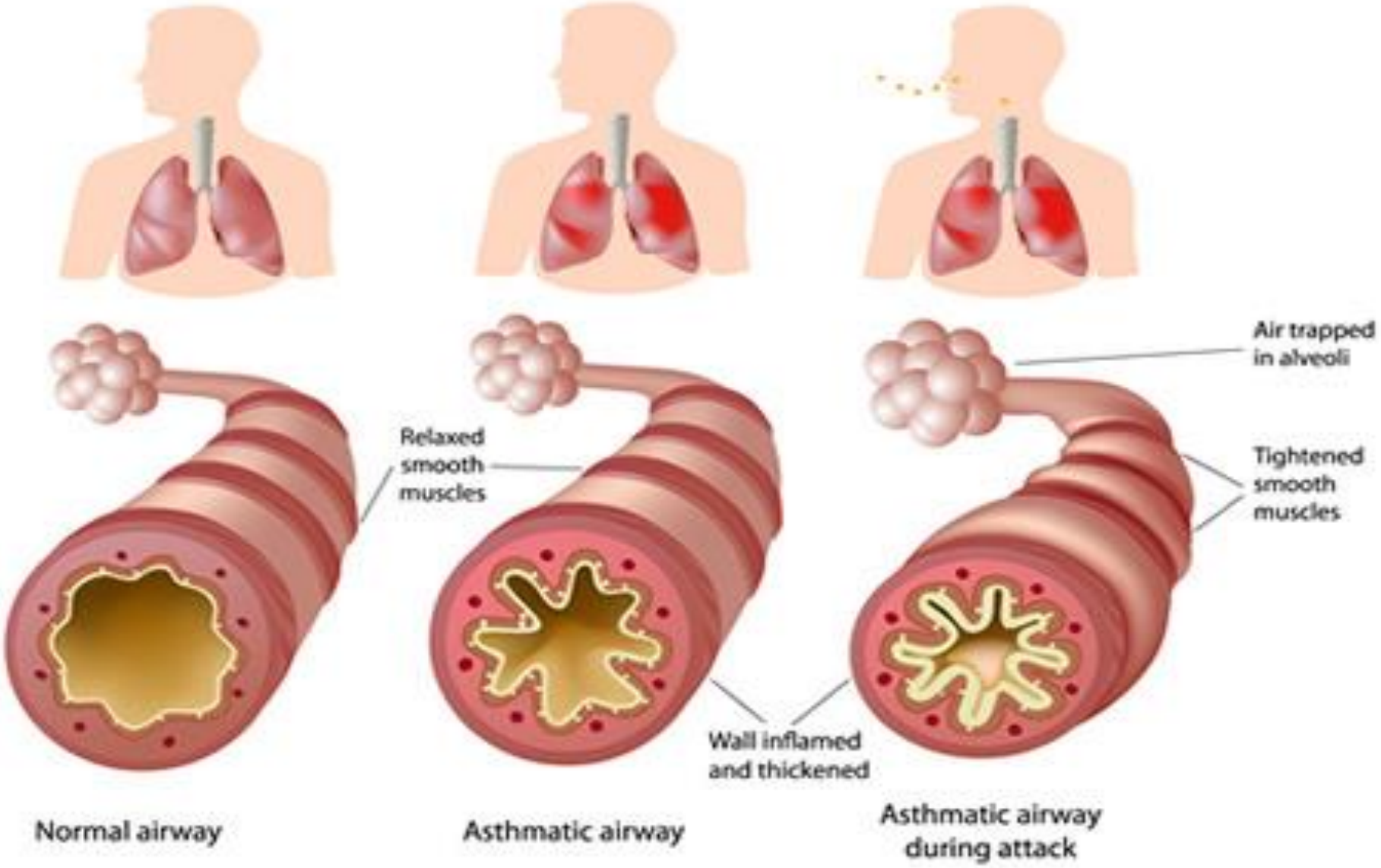
Extrinsic/atopic:

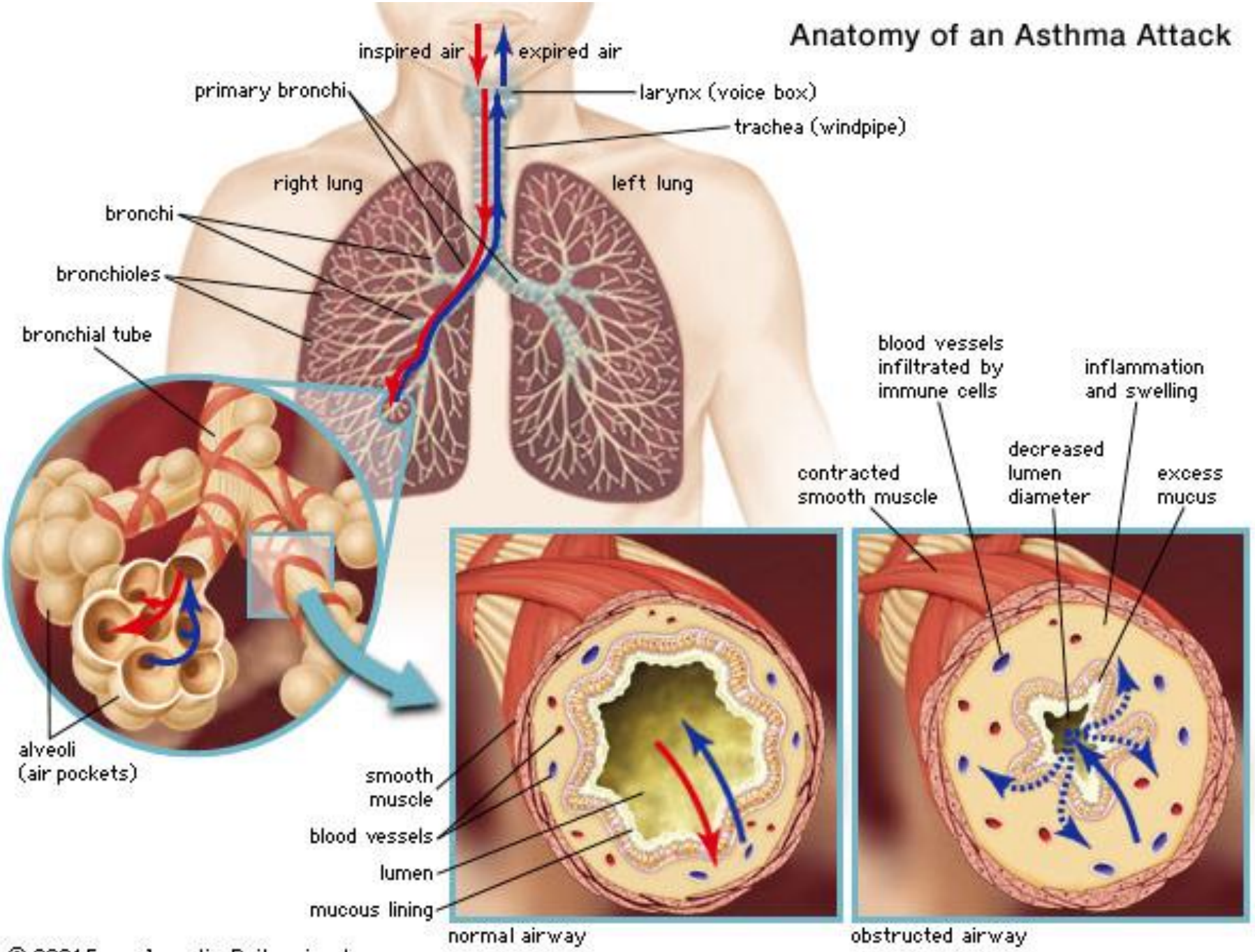
- Initiated by type I hypersensitivity (IgE mediated) reaction induced by extrinsic antigen or allergen
- Usually its onset is in childhood or adolescence
- Seen in persons with family history of atopic allergy.
- Eg: house dust, pollens, animal danders, moulds, fumes, gases,
- Mechanisms after exposure to antigen is expressed as
    - Early/acute-phase response
    - Late-phase response

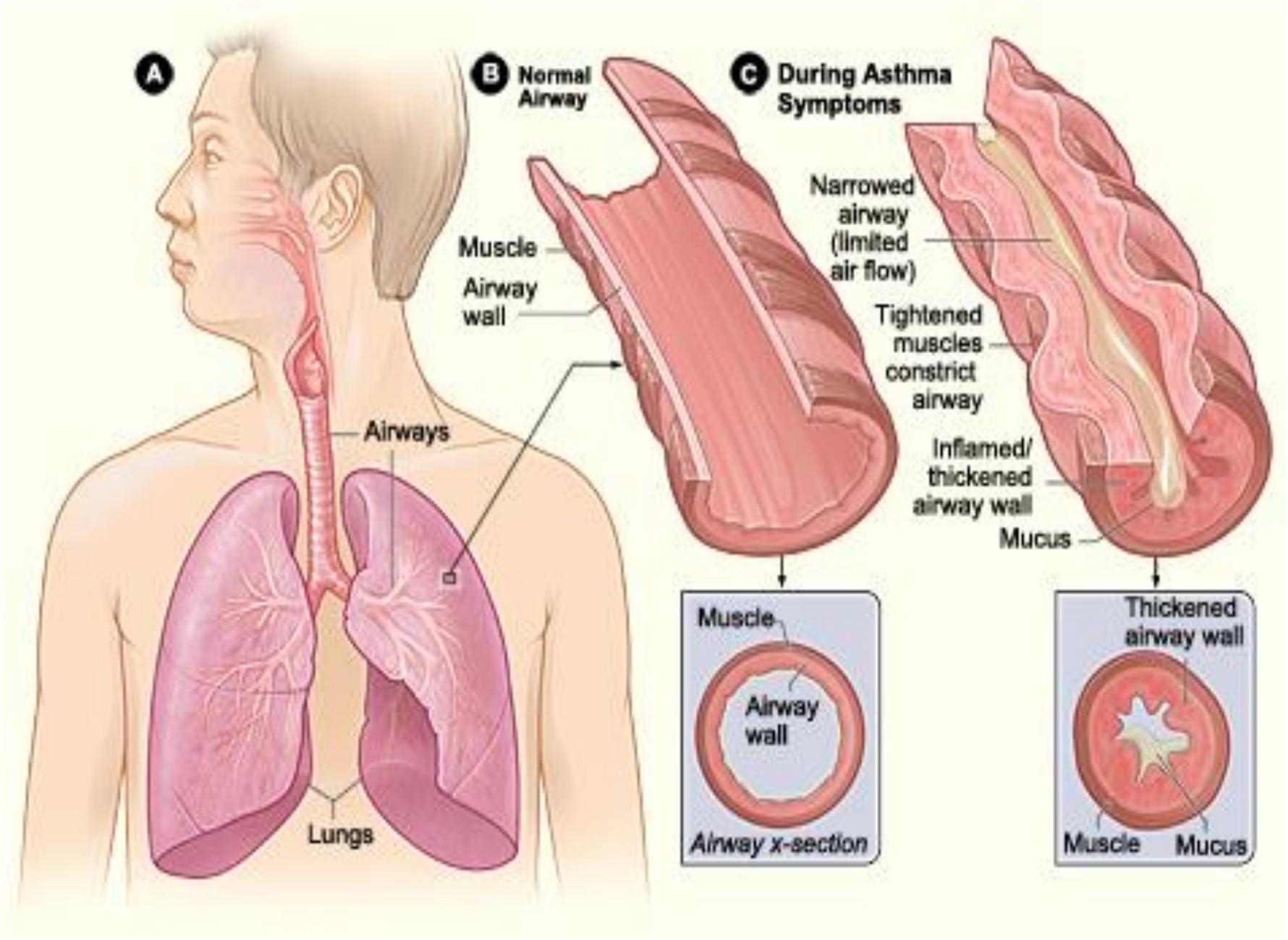
Intrinsic/non-atopic:

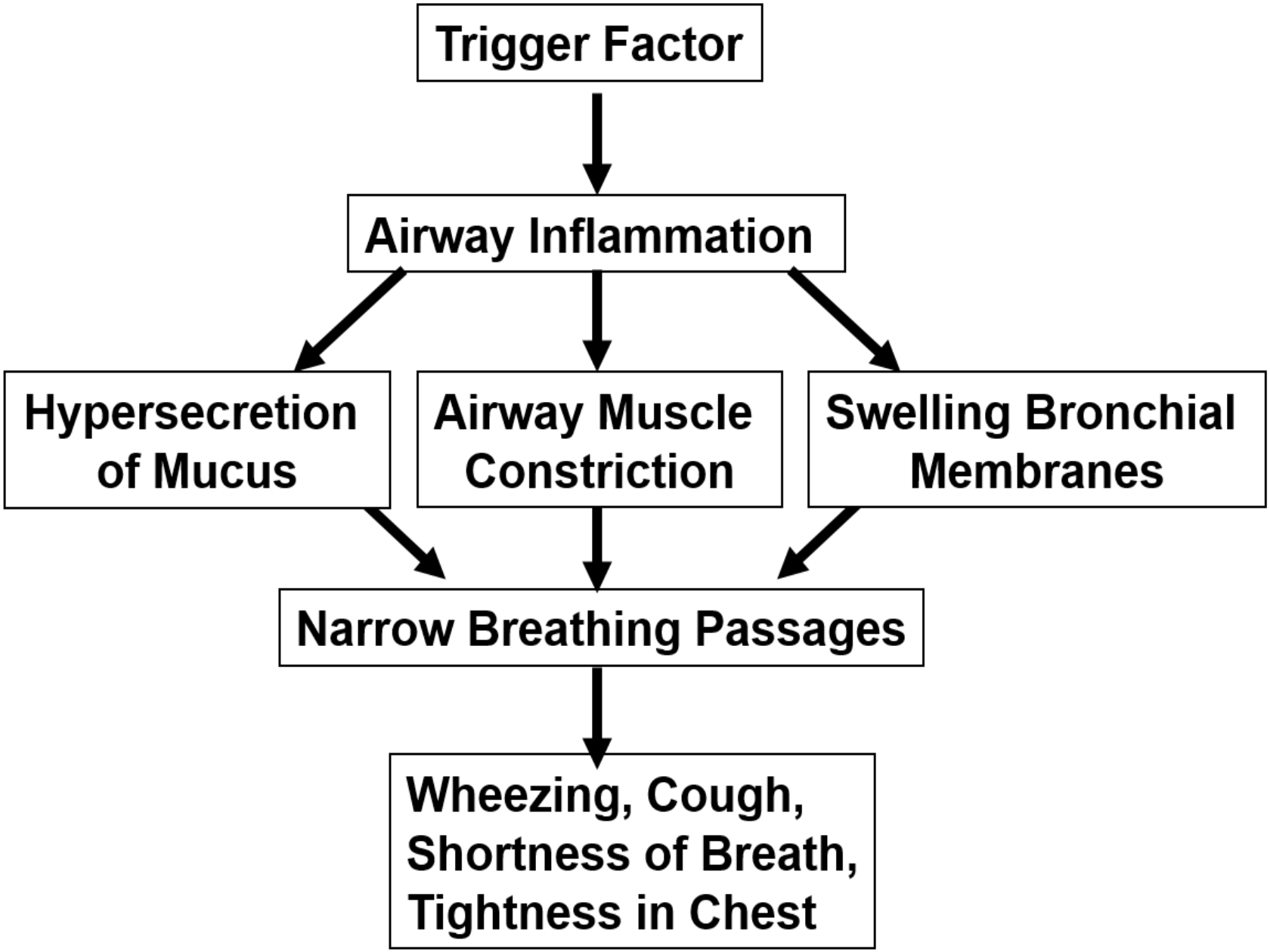
- Initiated by diverse non-immune mechanisms, including respiratory tact infections, exercise, emotional stress, ingestion of aspirin, exposure to bronchial irritants cigarette smoke.

Pathology of Asthma






A
B Normal Airway
C During Asthma Symptoms
Muscle
Airway wall
Airways
Lungs
Narrowed airway (limited air flow)
Tightened muscles constrict airway
Inflamed/ thickened airway wall
Mucus
Muscle
Airway wall
Airway x-section
Thickened airway wall
Muscle
Mucus


Trigger Factor
Airway Inflammation
Hypersecretion of Mucus
Airway Muscle Constriction
Swelling Bronchial Membranes
Narrow Breathing Passages
Wheezing, Cough, Shortness of Breath, Tightness in Chest

Early- or acute-phase response (develop within 10 to 20min)

- Antigen binds to IgE-coated mast cells on the mucosal surface of the airways

- Release of chemical mediators from IgE-coated mast cells

- Opening of the mucosal intercellular junctions and enhancement of antigen movement to the more prevalent subucosal mast cells

- Stimulation of parasympathetic receptors, increased vascular permeability, increased mucus secretions

Bronchoconstriction , mucosal edema

late-phase response (**develops 4 to 8 hours after exposure to an asthmatic trigger and persist for 12-24hrs or more**

Initial trigger

- Release of inflammatory mediators from mast cells, macrophages, and epithelial cells

- Migration and activation of other inflammatory cells (e.g., basophils, eosinophils, macrophages, neutrophils and T-lymphocytes

1. Eosinophils

(migrate to the airways)

inflammatory mediators

(leukotrienes and granule proteins),

cytotoxic mediators, and cytokines.

Cell injury

2. T-lymphocyte activation

Release of [IL]-4, IL-5, and IL-13 from(TH2)

Allergic inflammation

T-helper (TH 1) cells produce IL-2 and interferon- γ that are essential for cellular defense mechanisms.

Imbalance between TH 1 and TH2 → Allergic asthma

3.Macrophages → PAF and leukotrienes B 4 , C 4 , and D 4

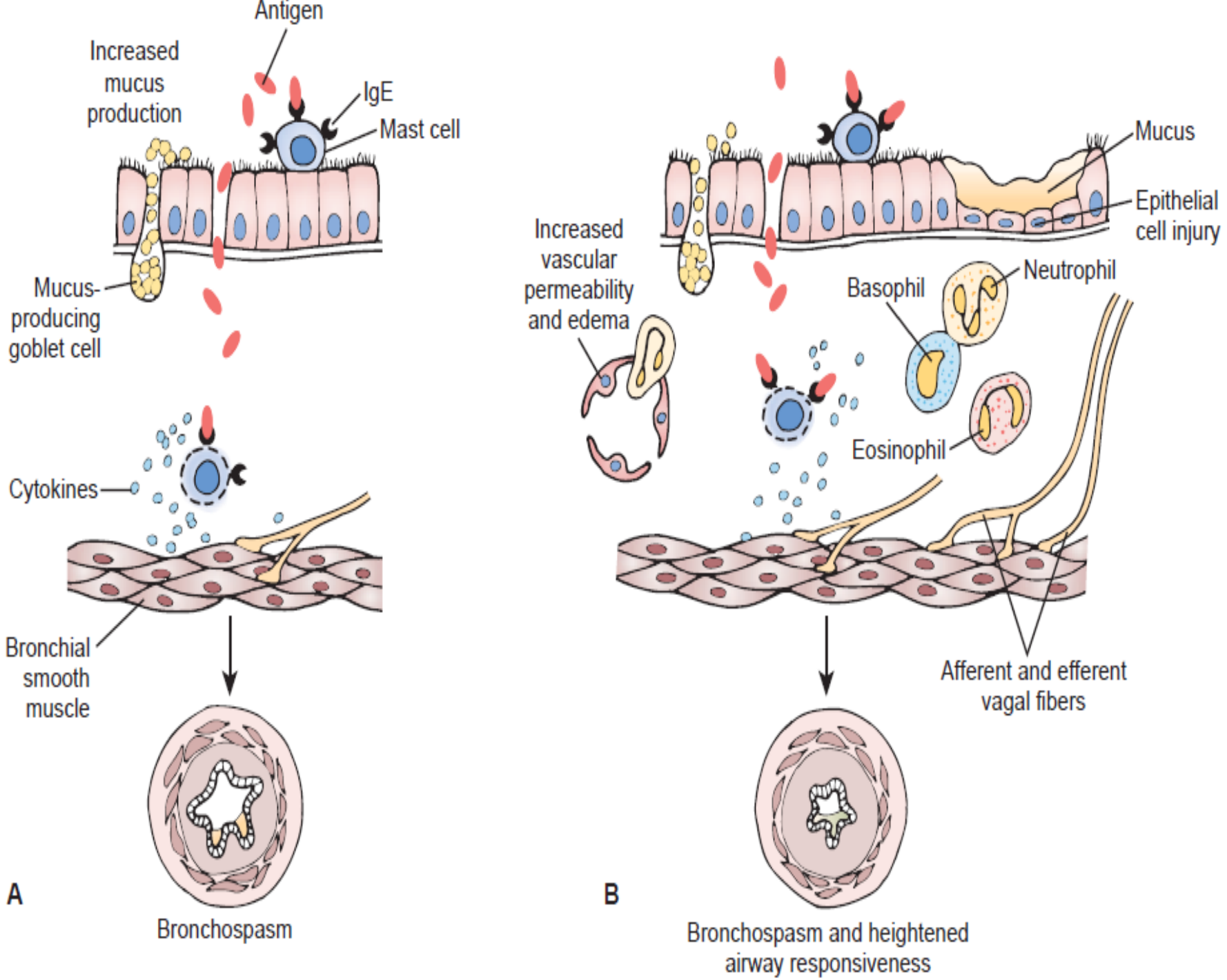
↓

Bronchospasm , mucus secretion, microvascular permeability, and airway edema.

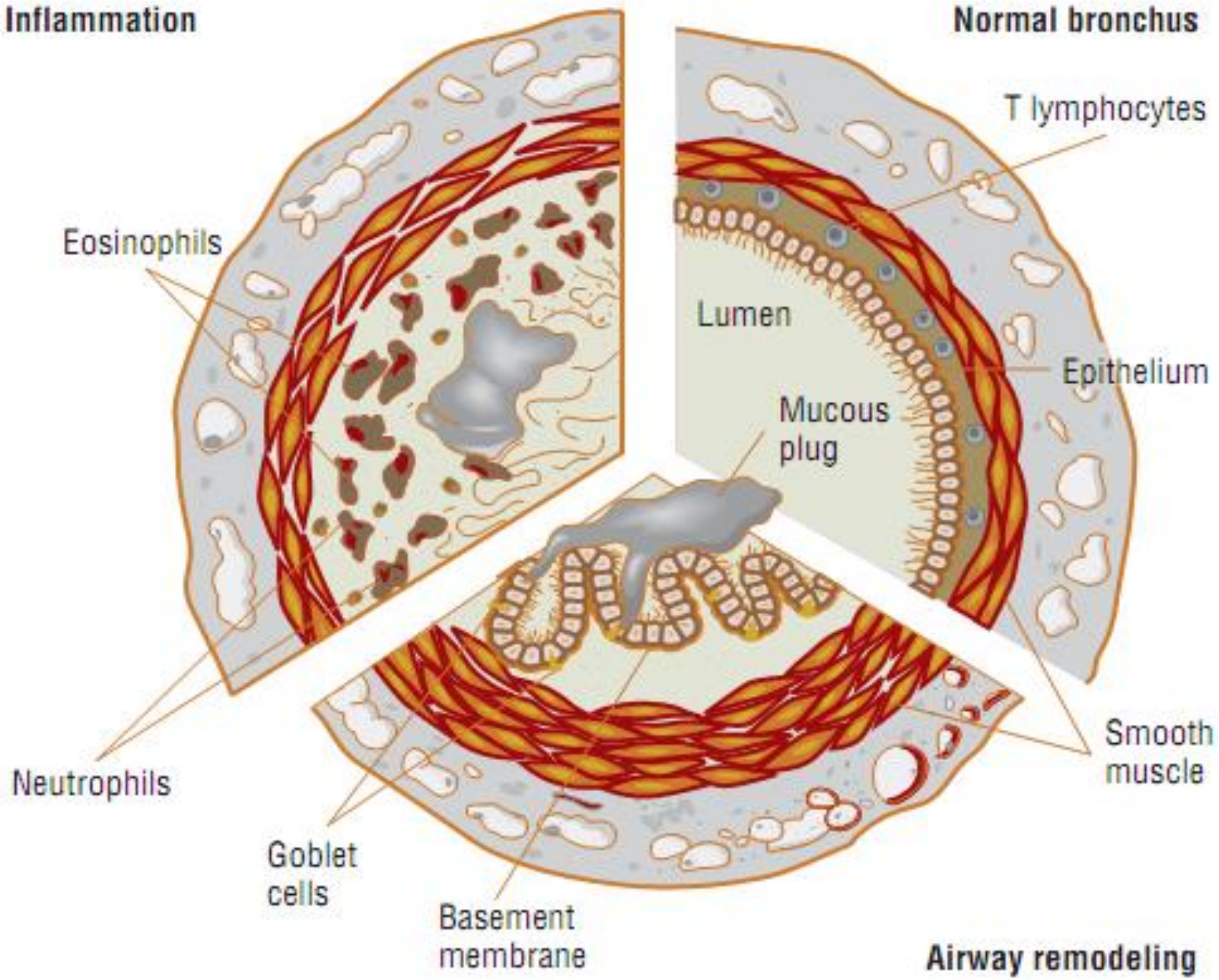
4.Neutrophils → PAFs, prostaglandins, thromboxanes, leukotrienes

↓

BHR, bronchoconstriction and airway inflammation.


Antigen
Increased mucus production
IgE
Mast cell
Mucus-producing goblet cell
Cytokines
Bronchial smooth muscle
A
Bronchospasm
Mucus
Epithelial cell injury
Increased vascular permeability and edema
Basophil
Neutrophil
Eosinophil
Afferent and efferent vagal fibers
B
Bronchospasm and heightened airway responsiveness

- Epithelial injury and edema,
- Changes in mucociliary function and reduced clearance of respiratory tract secretions
- Impaired mucociliary transport.
- Increased bronchial glands size and number.
- Sub-basement membrane thickening, sub epithelial fibrosis.
- AIRWAY REMODELLING


Inflammation
Normal bronchus
T lymphocytes
Eosinophils
Lumen
Epithelium
Mucous plug
Smooth muscle
Neutrophils
Goblet cells
Basement membrane
Airway remodeling

Intrinsic/non-atopic

1. **Respiratory tract infections** (mainly viruses)

- Epithelial damage, production of IgE antibodies, ↑ airway response to other triggers

2. **Exercise induced asthma**:

- Vigorous exercise → inhalation of increased volumes of relatively cold and dry air and loss of body heat from respiratory mucosa

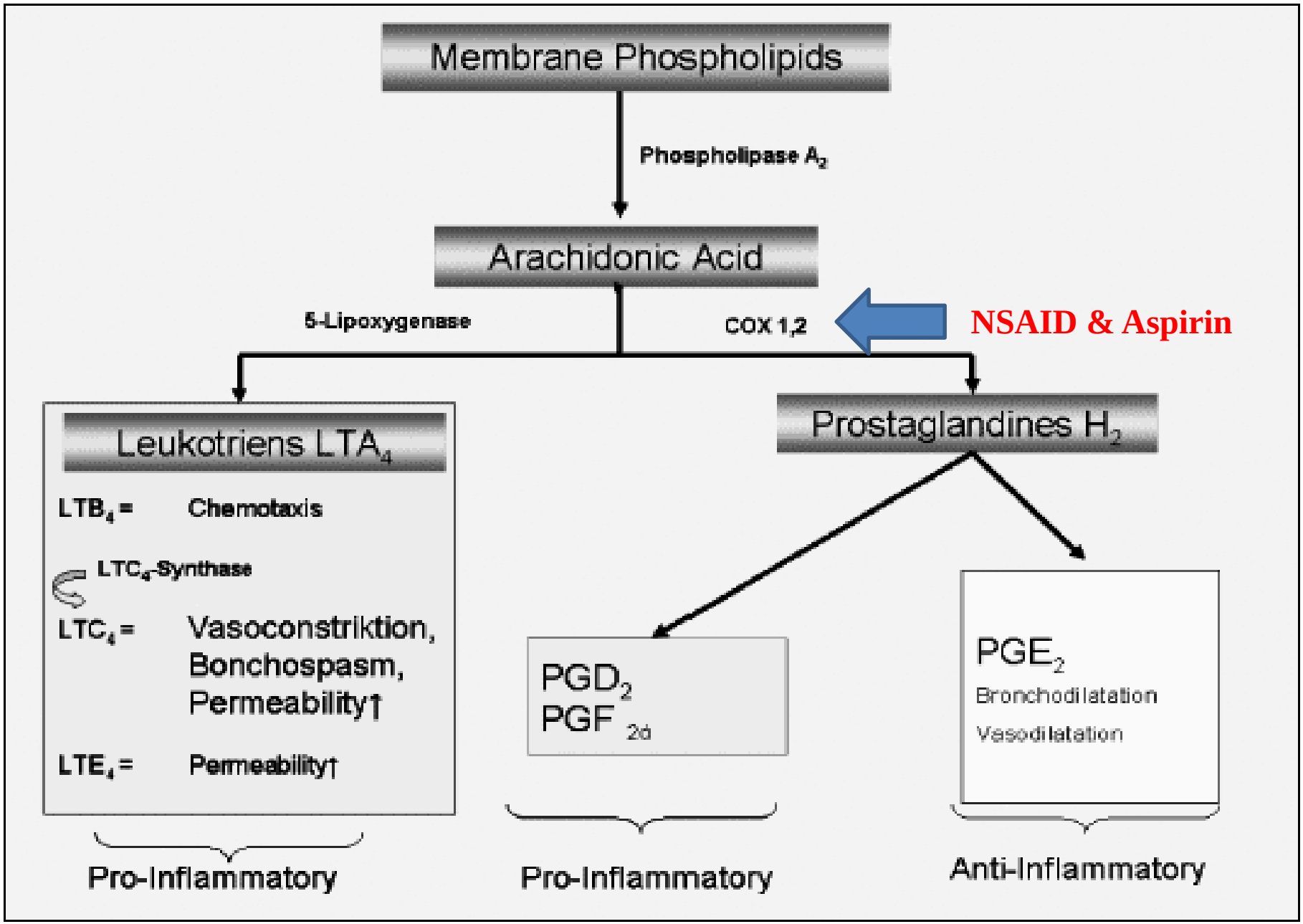
- Induces mast and epithelial cells to release proinflammatory mediators(histamine & leukotrienes)
- This occurs especially in cold climates
- Airway cooling stimulates cholinergic receptors.

3. **Inhaled irritants (tobacco smoke, strong odors)**

Activate vagal reflex and irritant receptors

Bronchospasm

4. Aspirin and NSAID



5. **Emotional factors**

Activates vagal pathway

Bronchospasm

6. **Gastric secretions**

Bronchospasmic trigger

CLINICAL MANIFESTATIONS

CHRONIC

- Persistent cough (particularly night time)
- Recurrent episodes of difficulty in breathing associates with wheezing
- Chest tightness
- Shortness of breath

Acute severe asthma

- Breathlessness at rest
- Severe dyspnea, shortness of breath,
- Chest tightness, or burning.
- Increased pulse rate, tachypnea, tachycardia
- Cyanotic skin, hyperinflated chest