Immunology of Asthma

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Immunology of Asthma

- Objectives:
- To the difference between extrinsic and intrinsic asthma
- To be familiar with types of allergens and their role in allergic sensitization
- To understand the inflammatory processes operating in allergic asthma
- To know about the airway remodeling

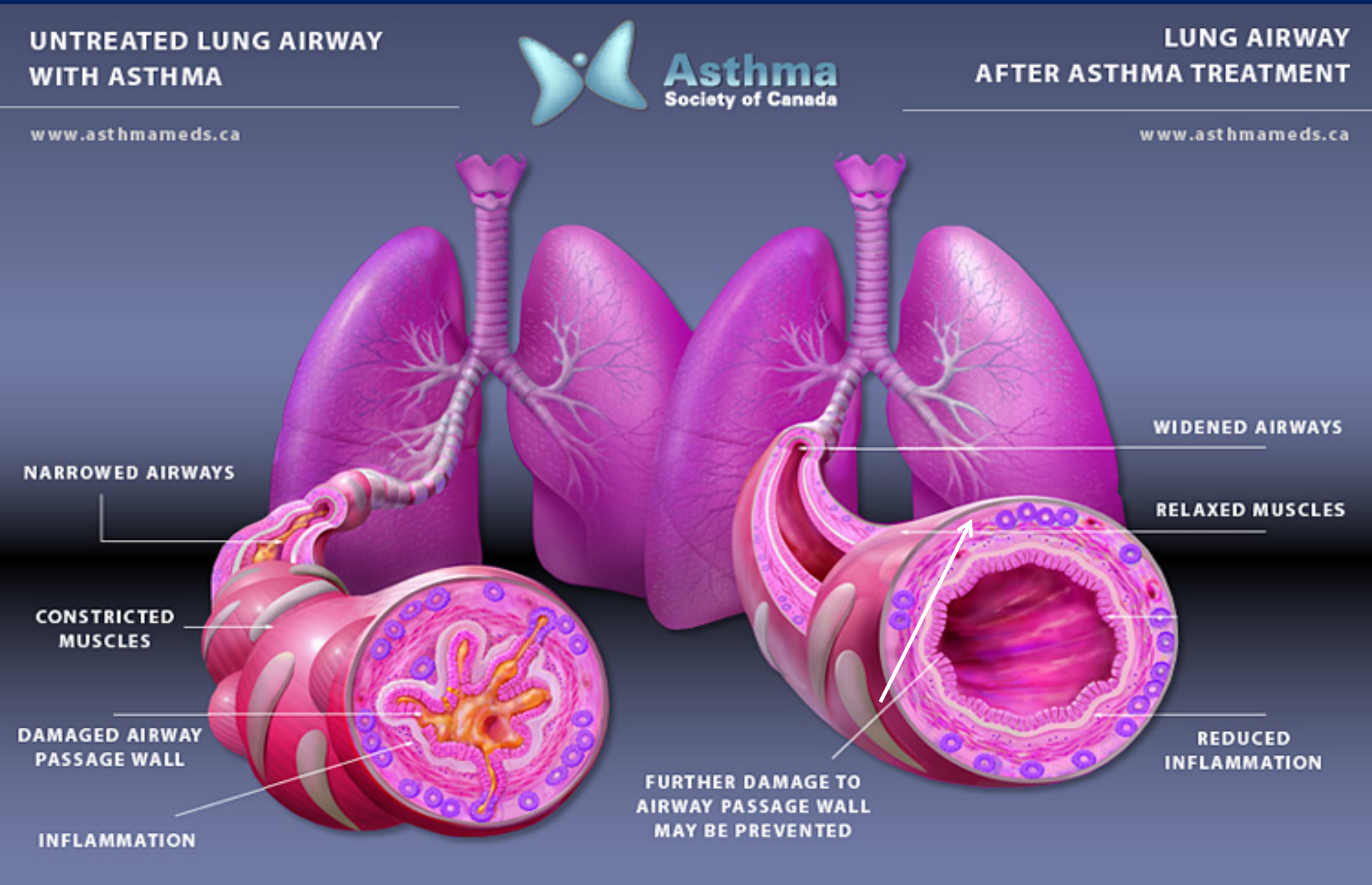
Asthma is a clinical syndrome characterized by:

1. Episodes of reversible airway obstruction
2. Increased bronchial reactivity
3. Airway inflammation

Patients with asthma present with one or more of the following symptoms:

1. Breathlessness (difficulty in breathing)
2. Wheezing
3. Persistent cough
4. Chest tightness

Airway Obstruction in Asthma



Classification of Asthma

1. Intrinsic (non-atopic)

2. Extrinsic (atopic)

   (Atopy: genetic tendency to develop allergy)

Non-atopic (intrinsic) asthma (10-33% of asthmatics)

- Negative skin tests
- No clinical/family history of allergy
- Serum IgE levels are usually normal
- Older patients
- More severe

Atopic (extrinsic) asthma
Allergies trigger asthma attacks in:

60-90% Children

50% Adults

Approximately 75-85% of patients with asthma have positive (immediate) skin test reactions to various allergens

Role of Allergens in Asthma

Allergen sensitization is linked to the risk of developing asthma

- Indoor allergens
  - House dust mites
  - Domestic pets (cat fur & dander)
  - Cockroaches (insects)
  - Molds (fungal spores)

Outdoor allergens:

- Fungal spores (e.g. Alternaria)

- Grass, tree & weed pollens

Fungal spores

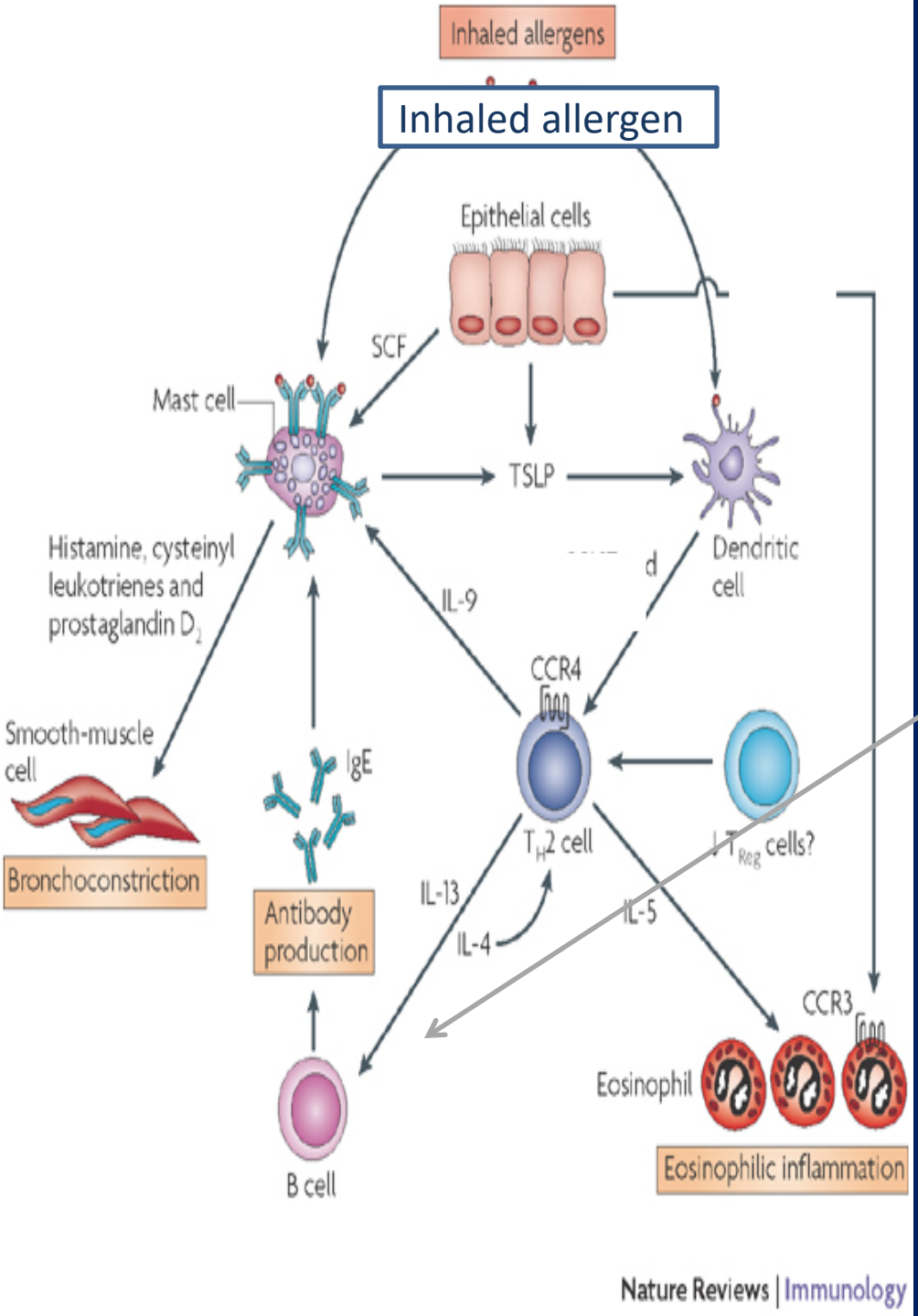
Grass pollens

Tree pollens

Antigen presenting cells (APCs) in the lung:

Two subsets of dendritic cells (DCs) in the lungs:

- One subset of DCs called respiratory tract myeloid DCs (mDCs) help in the development of asthma symptoms
- Second subset known as plasmacytoid DCs (pDCs) aid in respiratory tolerance to allergens



In susceptible individuals

First encounter with allergens activate B-cells to produce IgE

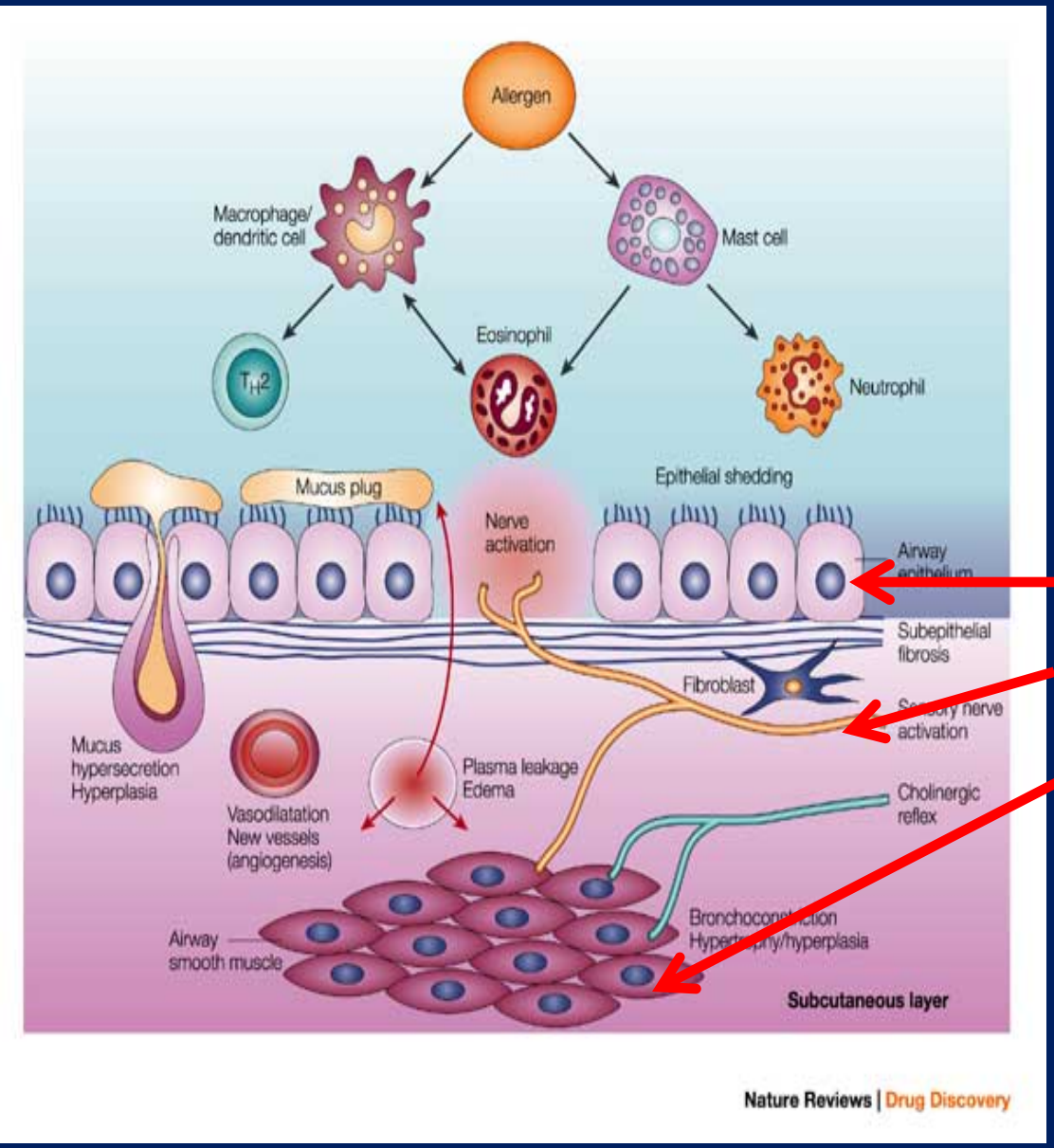
Subsequently:

Inhaled allergens activate submucosal mast cells in the lower airways

Mediators are released within seconds causing:

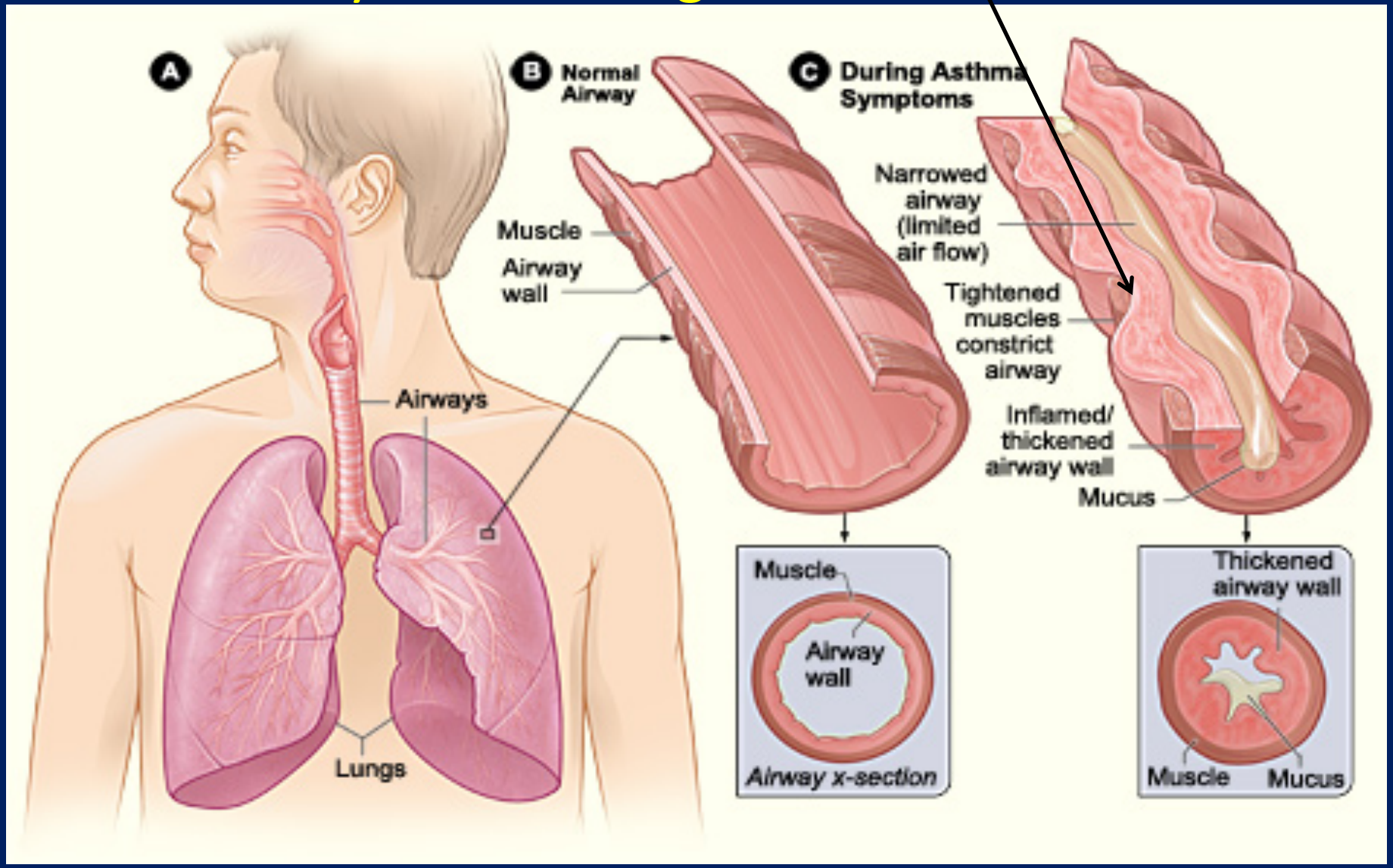
1. Bronchoconstriction
2. Influx of eosinophils & other inflammatory cells

Asthma results from complex interactions among the inflammatory cells that involve:

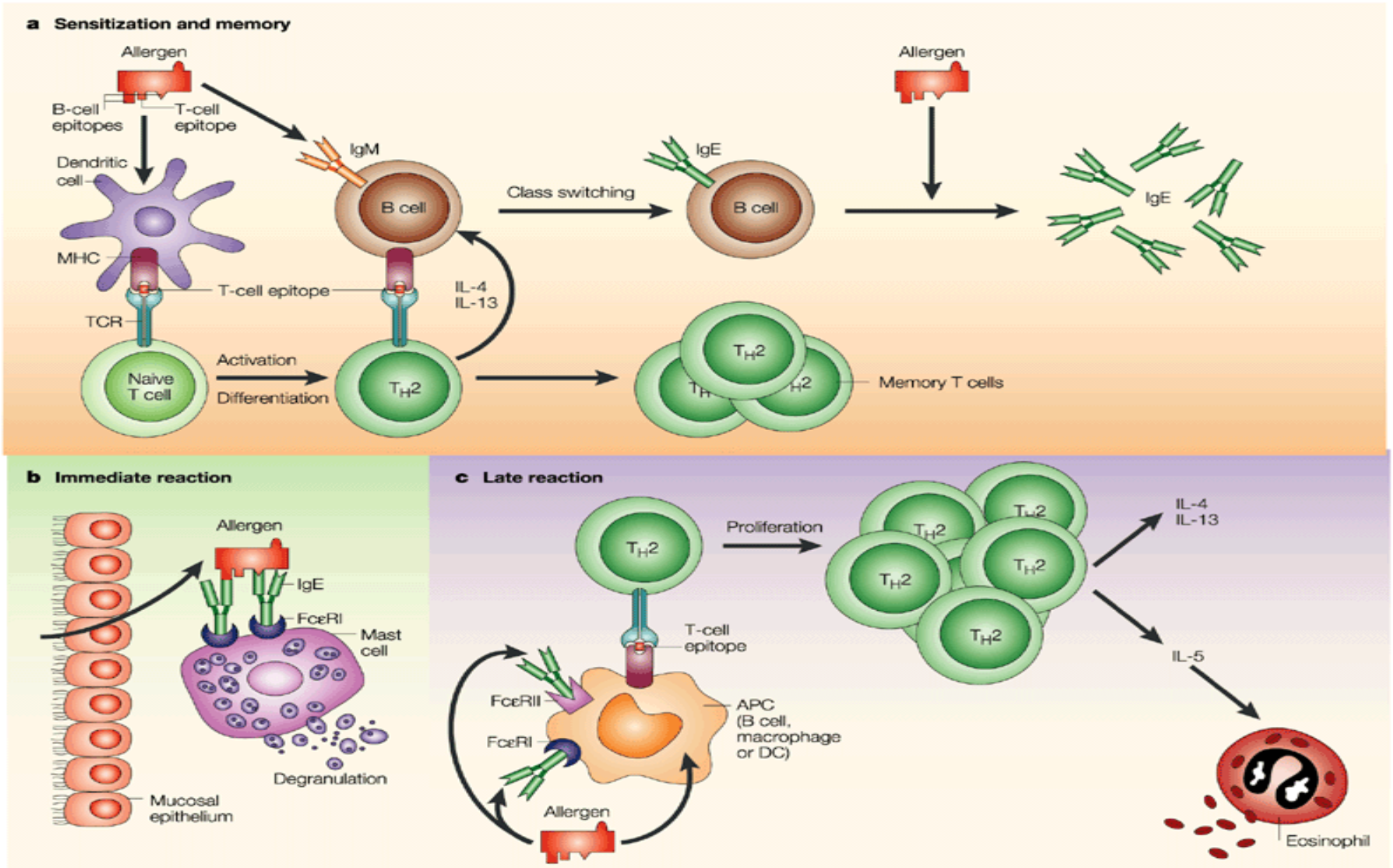


1. Airway epithelium
2. Nervous system
3. Bronchial smooth muscles

Factor contributing to airflow obstruction leading to difficulty in breathing include:



Response to allergen occurs in two phases



Early allergic response

1. Occurs within minutes
2. Manifests clinically as:
    - Bronchial constriction
    - Airway edema
    - Mucus plugging

Is reversible and responds to bronchodilators

Late allergic response:

1. Appears 4 to 10 hours later
2. Results from infiltration by inflammatory cells.
3. Activation of lymphocytes & eosinophils

Responds to steroids

(Anti-inflammatory drugs)

Th2 cells and role of cytokines in allergic asthma

Allergens drive T-cells towards Th 2 type:

Th2 secrete the cytokines:

IL-4, IL-5, IL-9 & IL-13

which promote :

1. Production of IgE by B cells
2. Eosinophil attraction and infiltration
3. Airway inflammation
4. Increased bronchial reactivity

Role of IL-4 in allergic asthma

The main role of IL-4 is carried out during the initial priming of Th2 cells :

1. Regulates isotype switching in B cells to IgE
2. Induces MHC II on antigen-presenting cells
3. Induces adhesion molecule expression
4. Activate mast cells and eosinophils

Role of IL-13 in allergic asthma

1. IL-13 induces inflammation
2. Stimulates mucus hyper-secretion
3. Induces sub-epithelial fibrosis

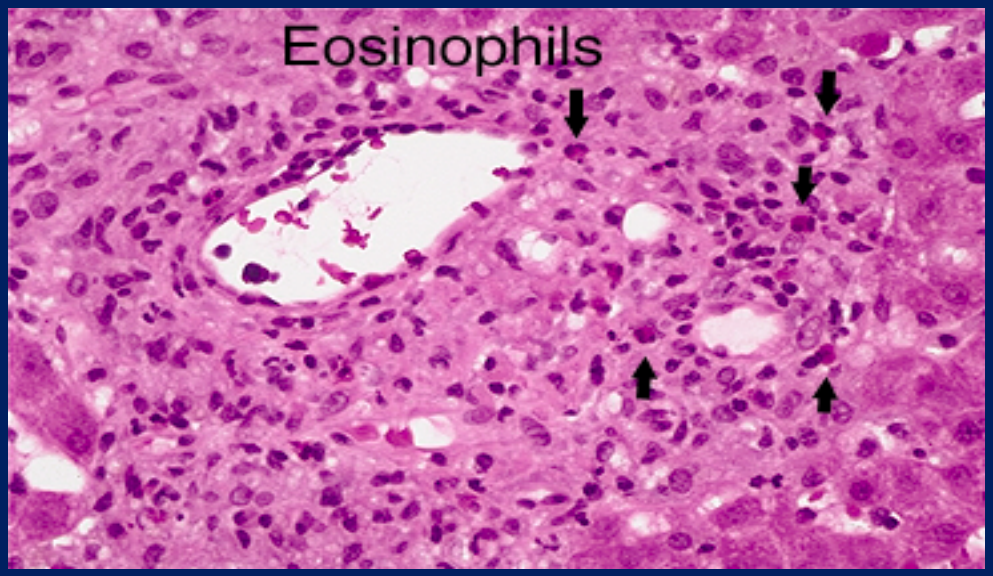
Role of IL-5 in allergic asthma

1. IL-5 induces an increase in eosinophil production in the bone marrow

2. Release of eosinophils from the bone marrow into circulation

Role of eosinophils in allergic asthma

- Eosinophils initiate asthmatic symptoms by causing tissue damage in the airways of the lungs
- Production of eosinophils is inhibited by IL-10



Role of regulatory T – cells:

Regulatory T cells suppress the effector mechanisms that induce asthmatic symptoms

Asthmatics may lack functional regulatory T cells that can inhibit an asthmatic response

Activation of inflammatory cells (mast cells, eosinophils etc,) is a major inducer of airway inflammation.

Airway inflammation is the hallmark in the asthmatic lung

which leads to :

Increased bronchial reactivity

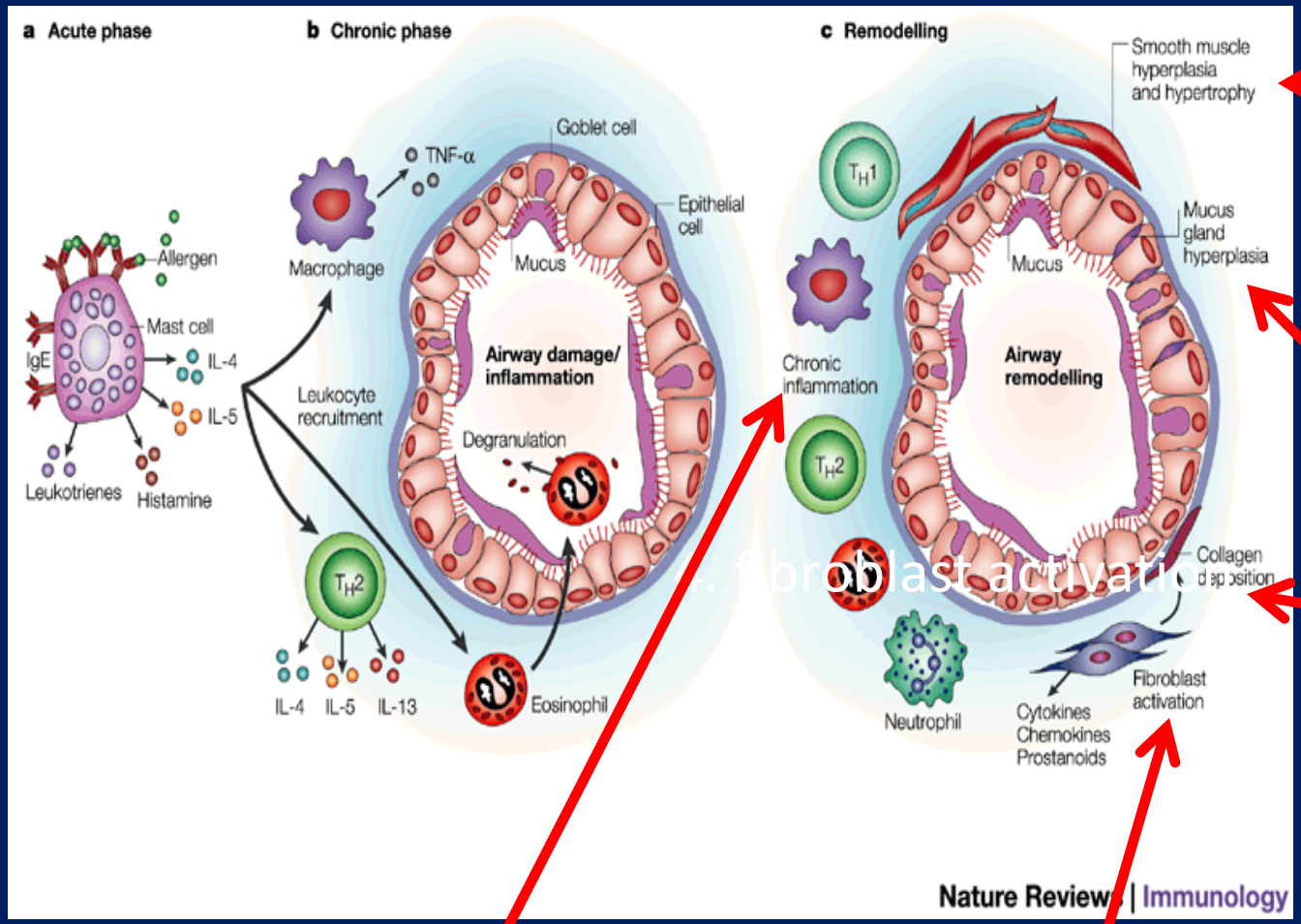
Products of the inflammatory cells act on :

1. Airway smooth muscle cells
2. Lung fibroblasts
3. Mucous glands

and cause :

Airway Remodeling

Airway remodeling refer to:



1. Smooth muscle hyperplasia & hypertrophy

2. Mucous gland hyperplasia

3. Collagen deposition

4. Fibroblast activation

5. Chronic inflammation

Inflammatory cells & their mediators

Airway inflammation

Increased bronchial reactivity

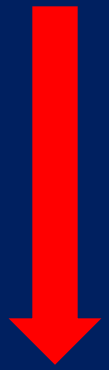
Airway remodelling

Outcome of increased airway reactivity

Predisposes patients to develop asthma attacks on exposure to non-specific irritants:

1. Chemical irritants
2. Smoke & strong perfumes
3. Sulphur dioxide & air pollutants
4. Viral and bacterial respiratory infections

Outcome of airway remodeling



Can ultimately lead to fibrosis and irreversible airway obstruction in some patients

Take home message

1. Asthma is characterized by episodic reversible airway obstruction
2. Classified in 2 types: intrinsic & extrinsic
3. In the extrinsic type allergens drive T-cells into Th2 pattern
4. Airway inflammation is a hallmark finding in the asthmatic lung
5. Inflammatory cells lead to increased bronchial reactions & airway remodeling which is not revisable