

# 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

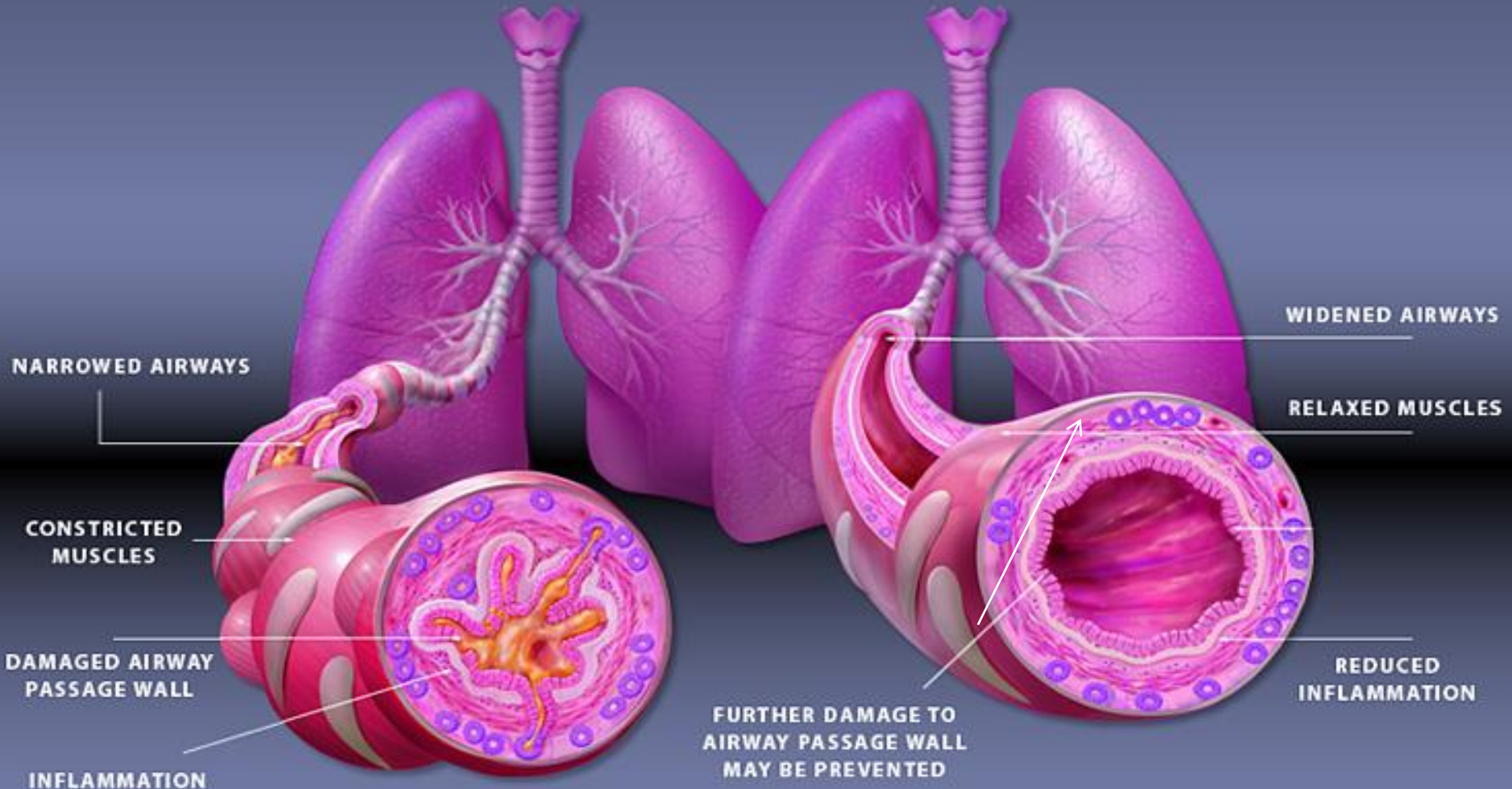
UNTREATED LUNG AIRWAY  
WITH ASTHMA

[www.asthmameds.ca](http://www.asthmameds.ca)



LUNG AIRWAY  
AFTER ASTHMA TREATMENT

[www.asthmameds.ca](http://www.asthmameds.ca)



NARROWED AIRWAYS

CONSTRICTED  
MUSCLES

DAMAGED AIRWAY  
PASSAGE WALL

INFLAMMATION

WIDENED AIRWAYS

RELAXED MUSCLES

REDUCED  
INFLAMMATION

FURTHER DAMAGE TO  
AIRWAY PASSAGE WALL  
MAY BE PREVENTED

# 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**

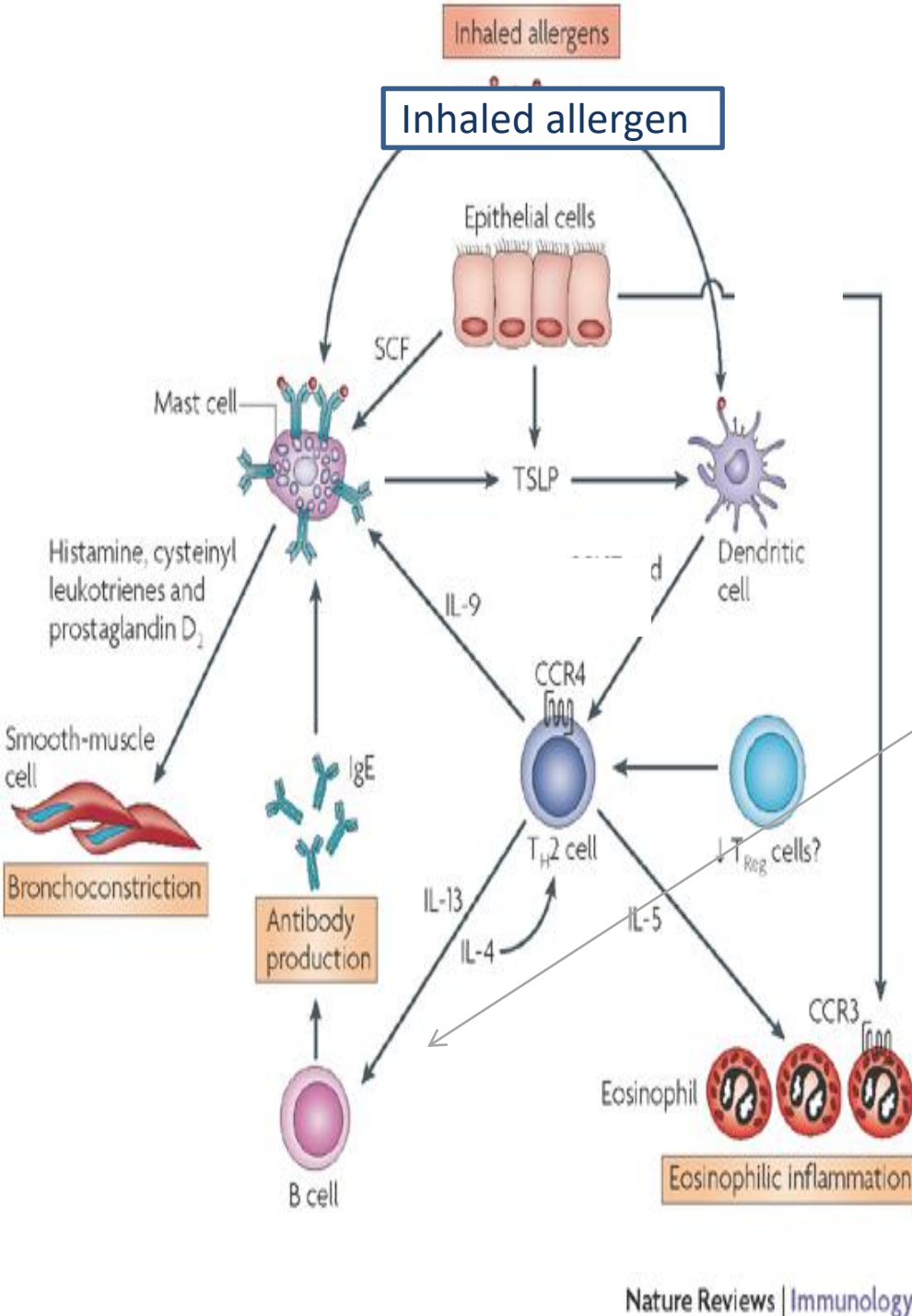


**Tree pollens**

# 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)** aide in respiratory **tolerance** to allergens



## In susceptible individuals

First encounter with allergens activate B-cells to produce IgE

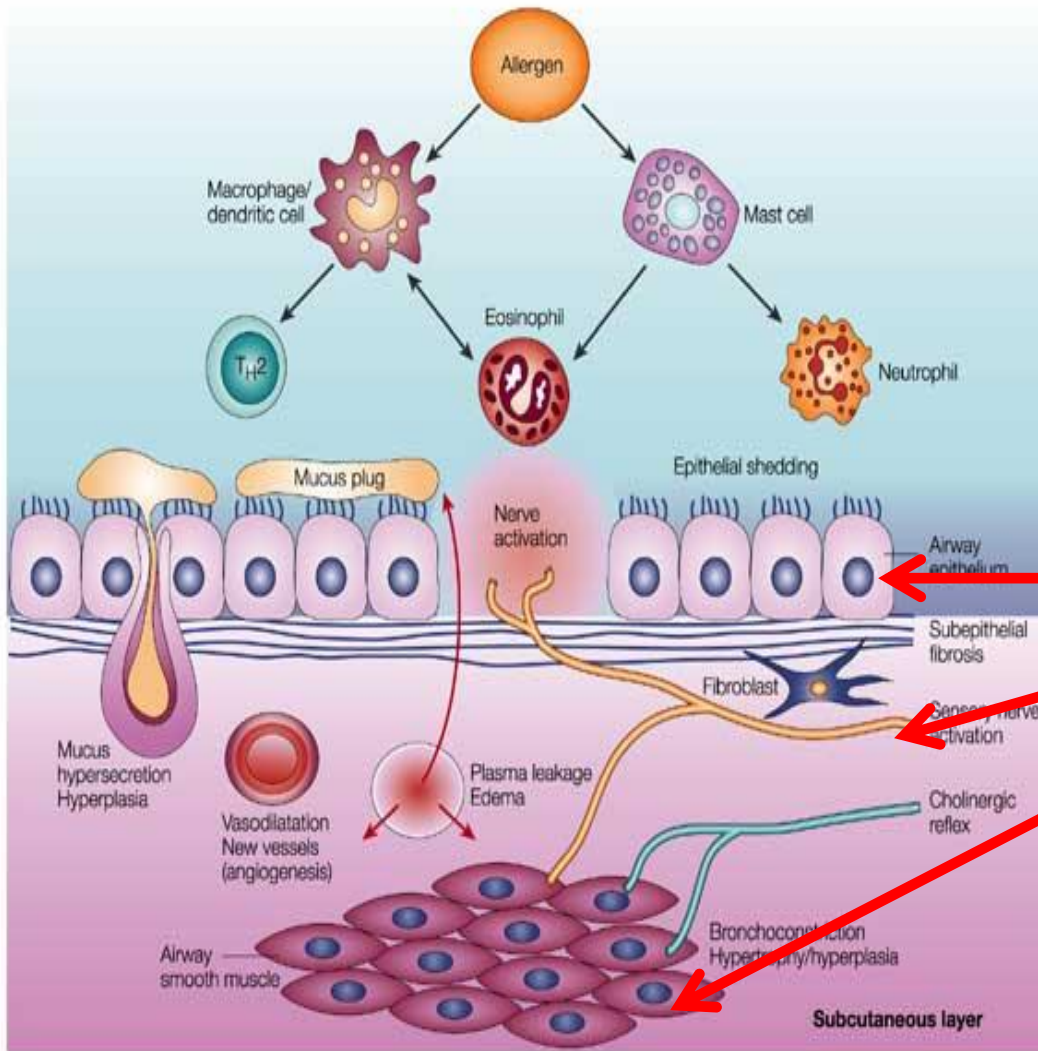
## Subsequently:

Inhaled allergens activate submucosal mast cells in the lower airways

Mediators are released within seconds causing:

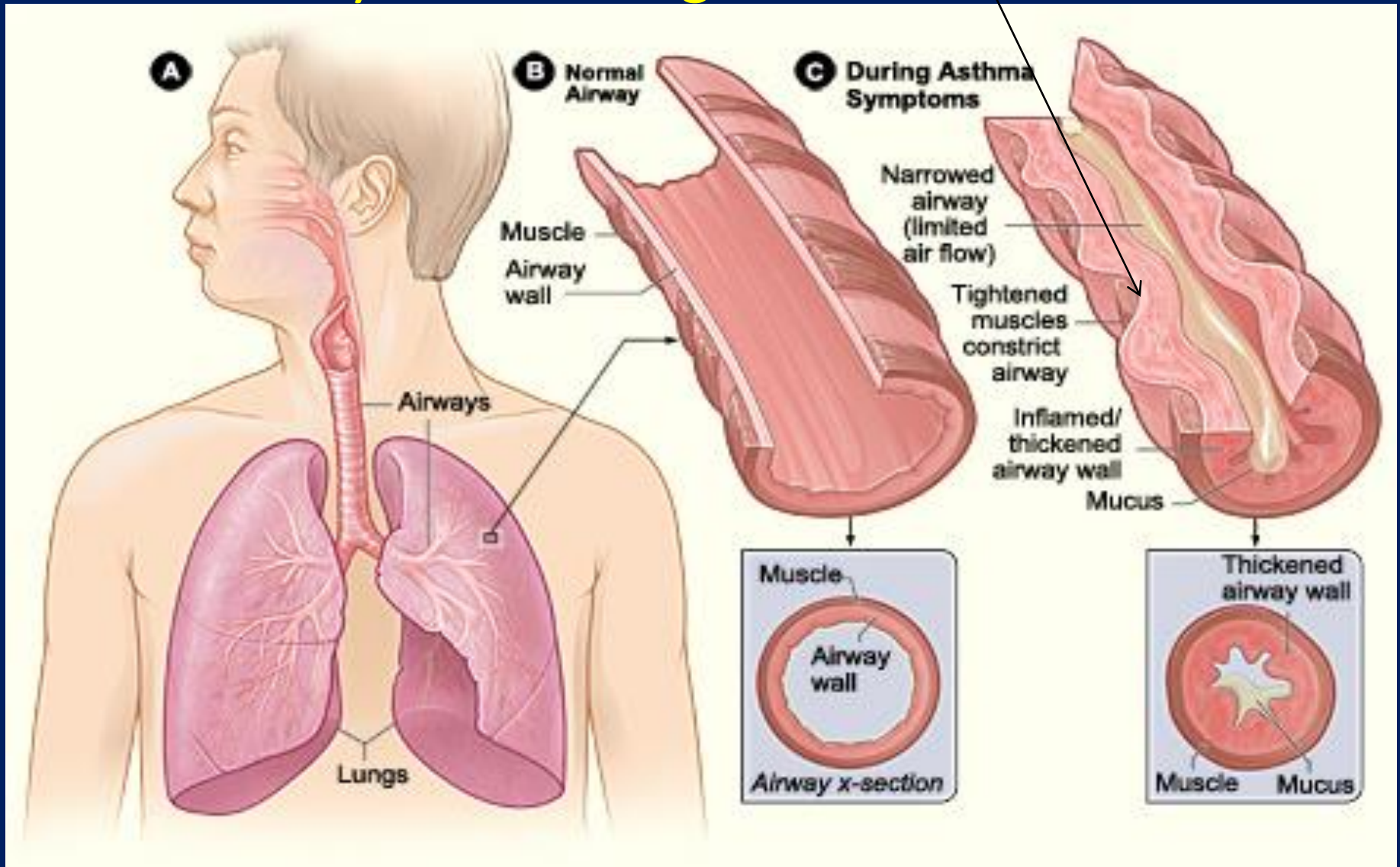
1. Bronchoconstriction
2. Influx of eosinophils & other inflammatory cells

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



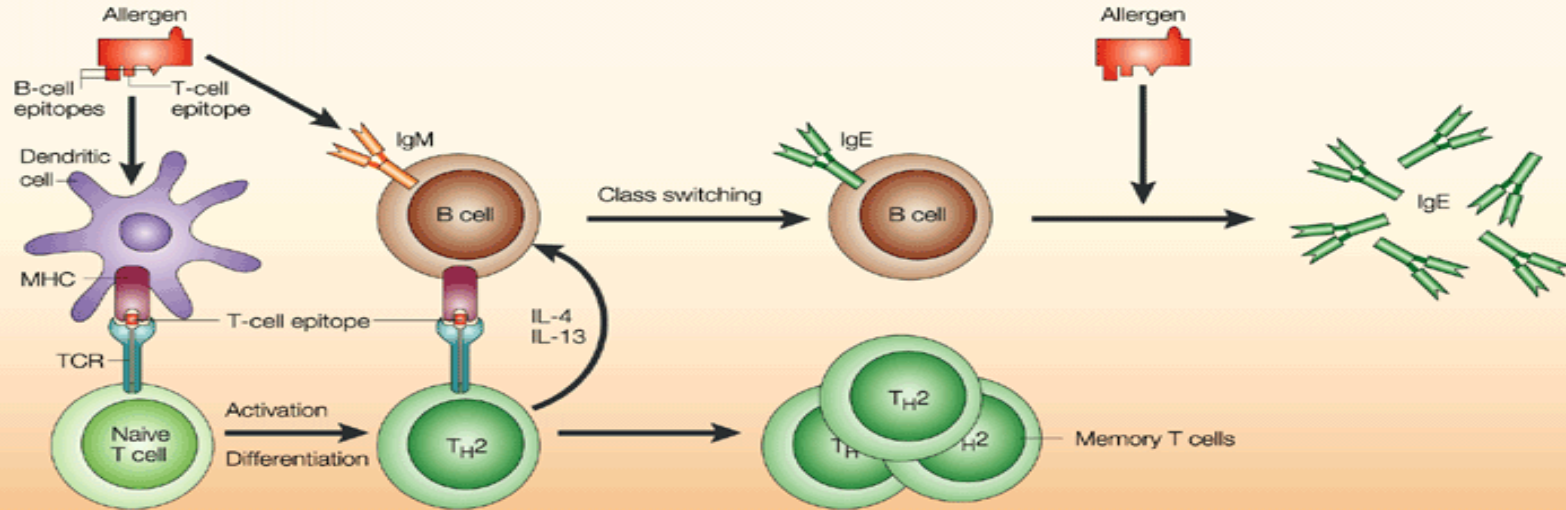
1. Airway epithelium
2. Nervous system
3. Bronchial smooth muscles

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

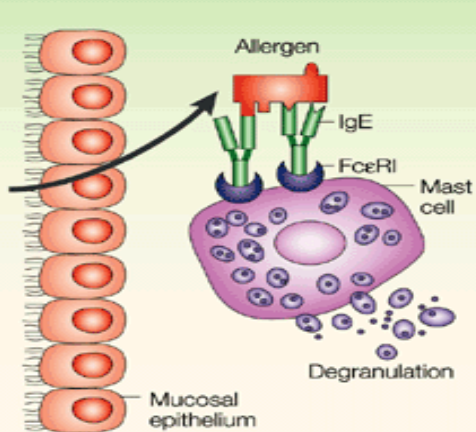


# Response to allergen occur in two phases

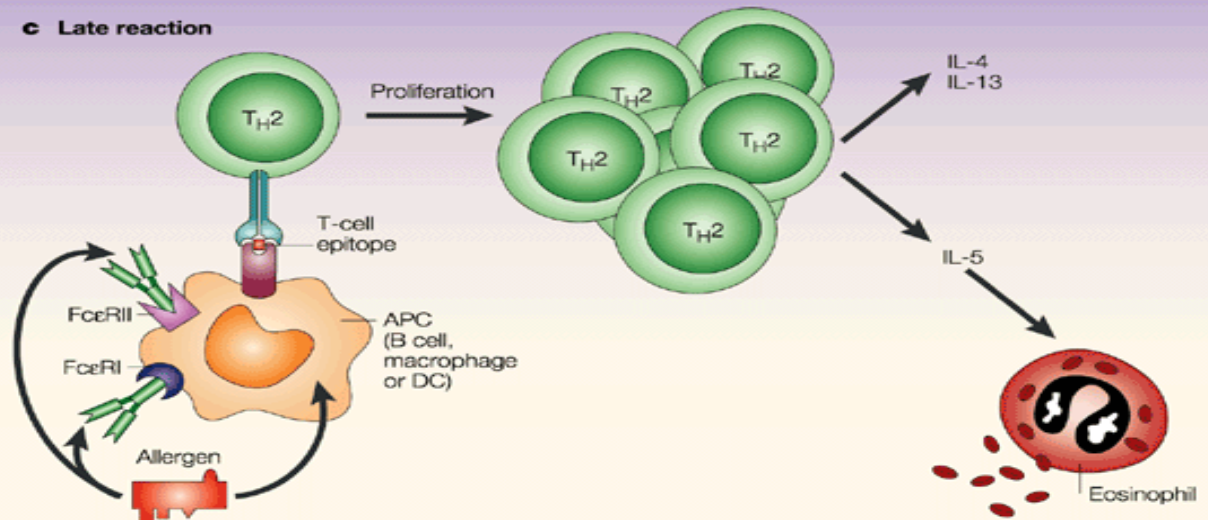
## a Sensitization and memory



## b Immediate reaction



## c Late reaction



# 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

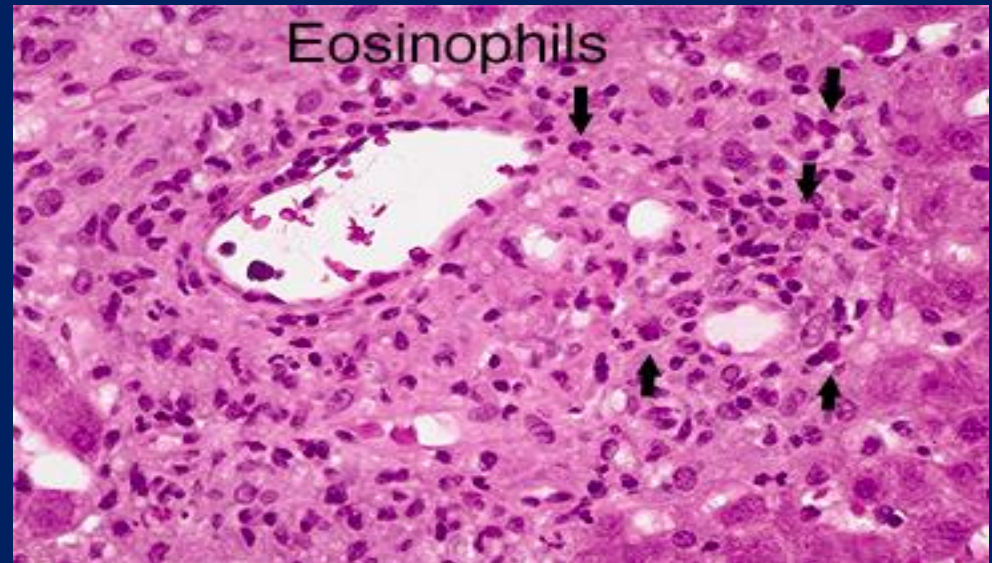
1. IL-13 induces inflammation
2. Stimulates mucus hypersecretion
3. Induces sub-epithelial fibrosis

## 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**

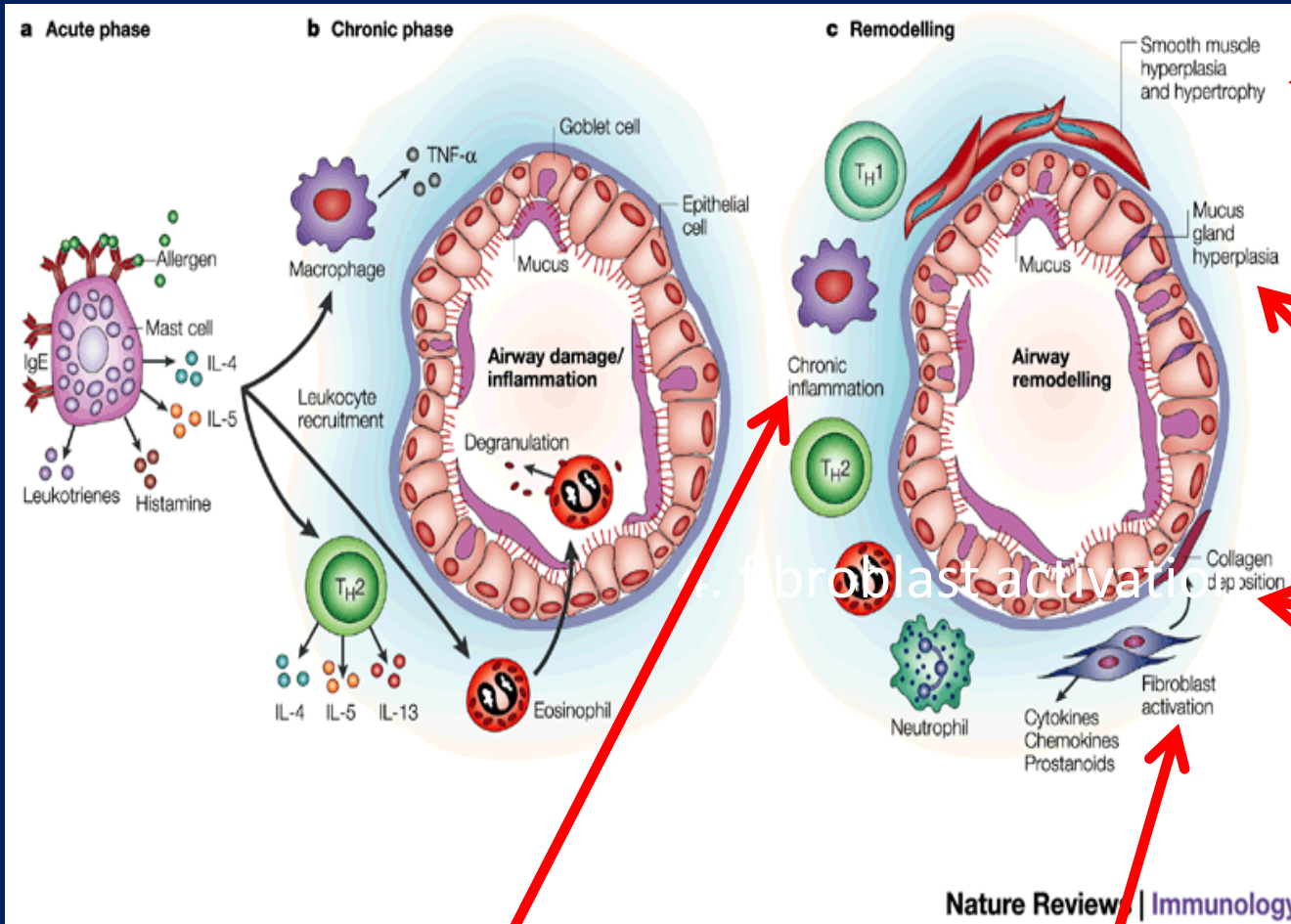
Products of the inflammatory cells act on :

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

4. Fibroblast activation

# Inflammatory cells & their mediators



Airway inflammation

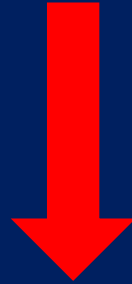


Increased bronchial  
reactivity



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 reversible