



LECTURE 1

IMMUNOLOGY OF ASTHMA

“IT’S ALL ABOUT INFLAMMATION” – DR. ZAHID SHAKOOR

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**.

VIDEO

Mechanism of Allergy

<http://www.youtube.com/watch?v=-m1e5r8BP9U>

Watch it, it's very short.

Clinical Features

Episodes of *reversible* airway obstruction

Increase bronchial reactivity

Airway inflammation

Symptoms

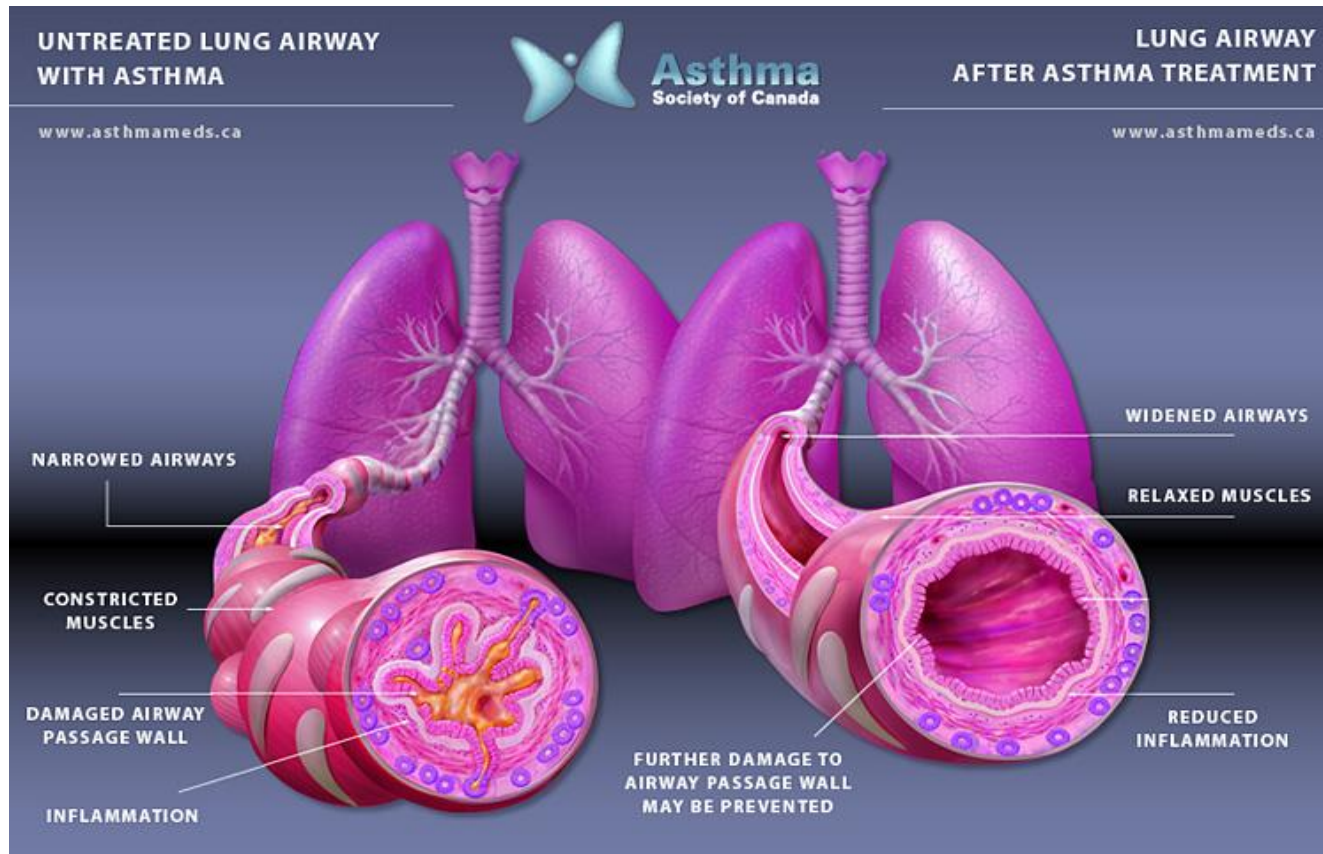
Breathlessness

Wheezing

Persistent cough

Chest tightness

AIRWAY OBSTRUCTION



Bronchial Asthma has:

- Thick mucosa (mucosal membrane)
- Inflammatory reaction
- Bronchial spasm (constricted muscles)

CLASSIFICATION

	Intrinsic (non-atopic)	Extrinsic (atopic)
Cause	Unknown	Allergy
Percentage of Asthmatics	10-33%	60-90% Children 50% Adults
Target Patients	Elderly	All
Skin Test Result	Negative	Positive (immediate)
Serum IgE Levels	Normal	High
Clinical/Family History	None	Yes
Severity	More severe	Less severe

Note: The symptoms of both types are the same.

ALLERGENS

INDOOR

1. **Dust mites**
2. **Pets** (cat fur & dander)
3. **Insects** (cockroaches)
4. **Fungal spores** (mold)

OUTDOOR

1. **Grass, tree & weed pollens**
2. **Fungal spores**
(e.g. *Alternaria*)

Allergen sensitization is linked to the risk of developing asthma

INDUCTION OF ALLERGIC INFLAMMATION

- **In Predisposed Individuals:**

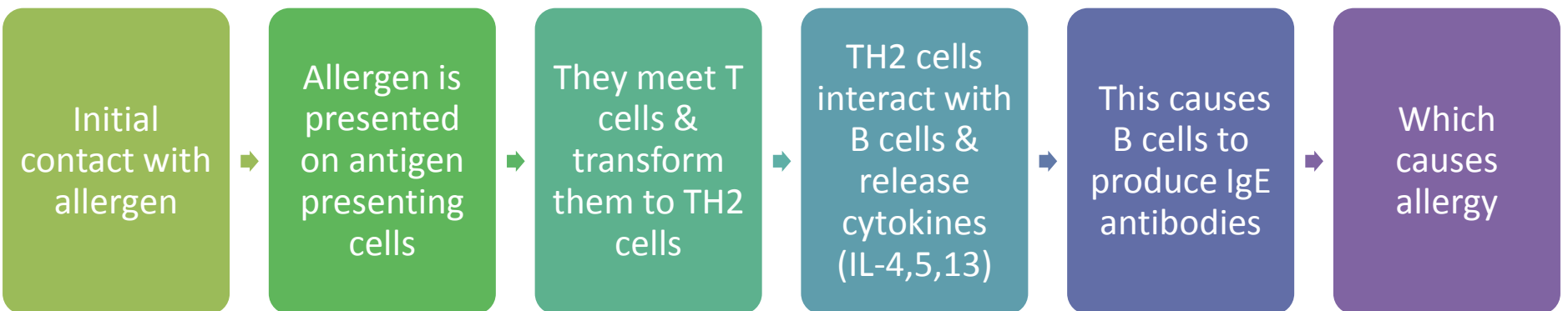
First encounter with allergens stimulates production of allergen specific *IgE antibodies* by B cells (allergic sensitization)

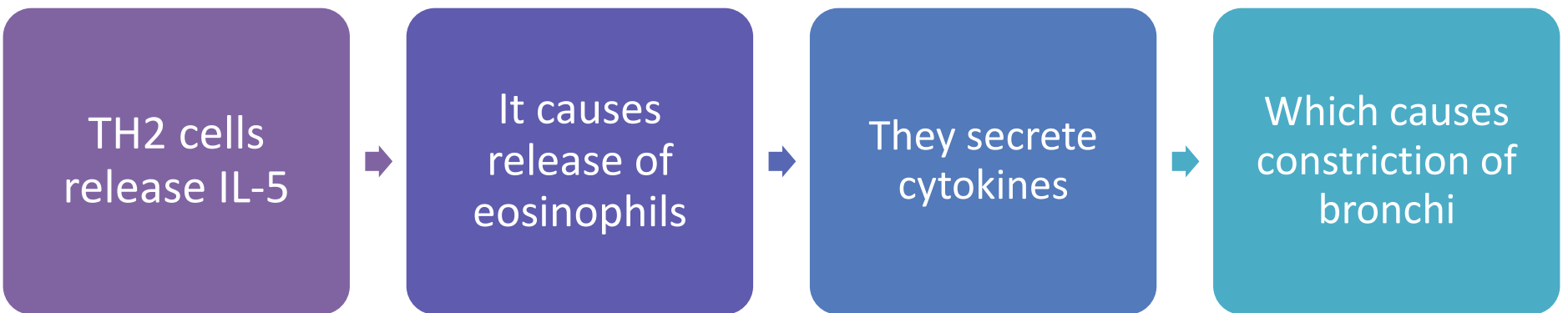
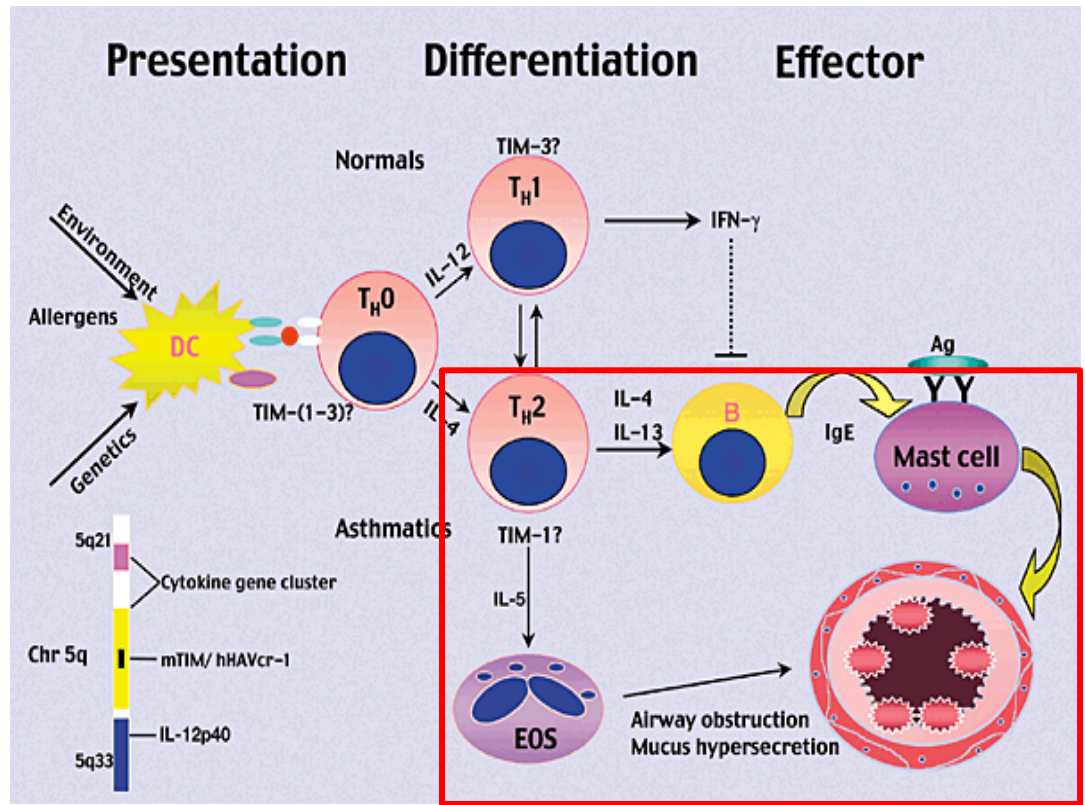
- **Subsequently:**

Inhaled allergens activate *sub-mucosal mast cells* in the lower airways resulting in release of mediators instantly causing:

- ❖ Recruitment of eosinophils & pro-inflammatory cells
- ❖ Bronchoconstriction

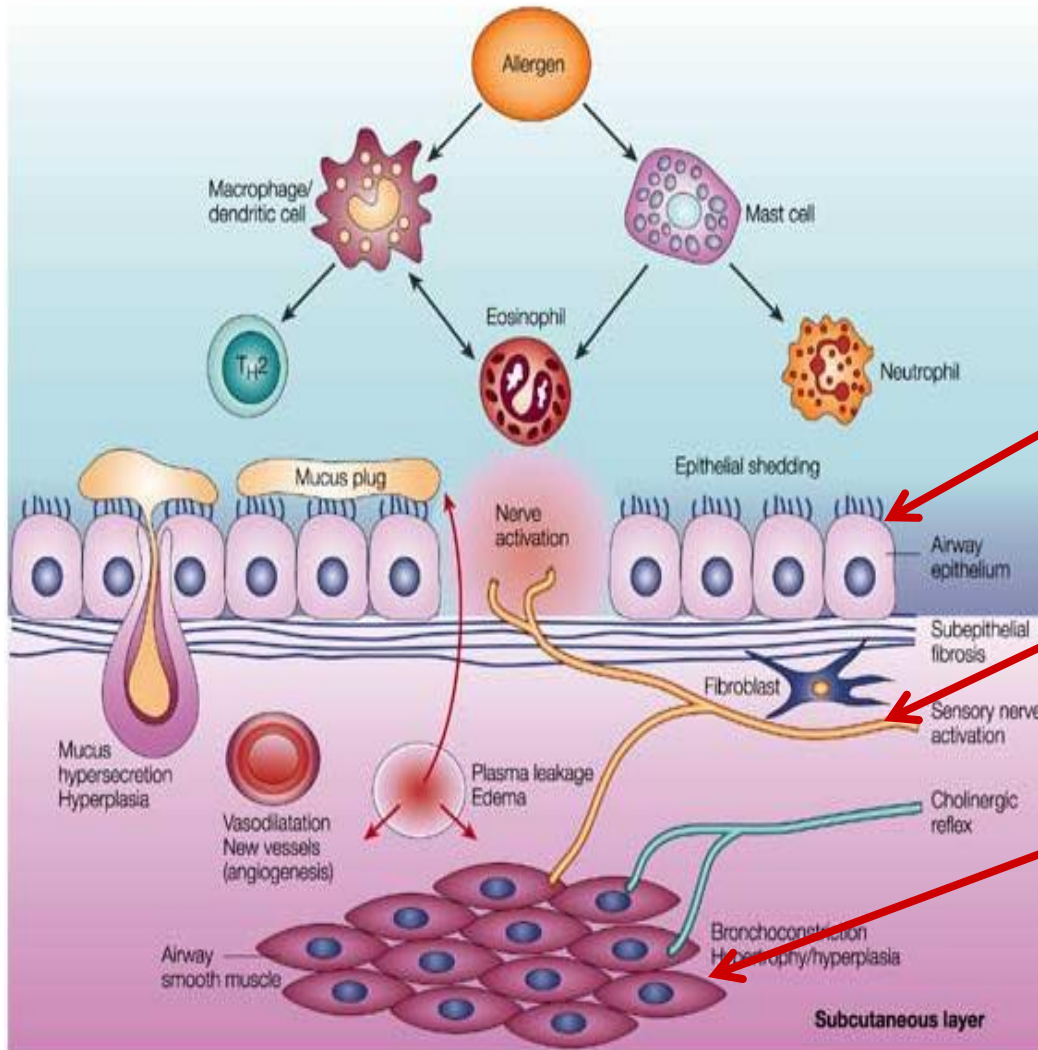
MECHANISM OF ACTION





INTERACTIONS

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



Airway Epithelium

Nervous System

Bronchial Smooth Muscles

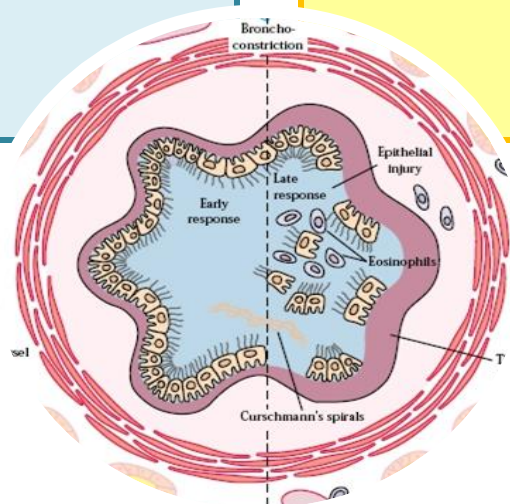
RESPONSE TO ALLERGEN

EARLY PHASE

1. Occurs within minutes
2. Manifests clinically as:
 - Bronchial constriction
 - Airway edema
 - Mucus plugging
- Is reversible and responds to bronchodilators

LATE PHASE

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 & ROLE OF CYTOKINES

- Allergens cause T-cells to transform into TH2 cells
- TH2 secrete cytokines **(IL-4,5,9,13)** which promote:

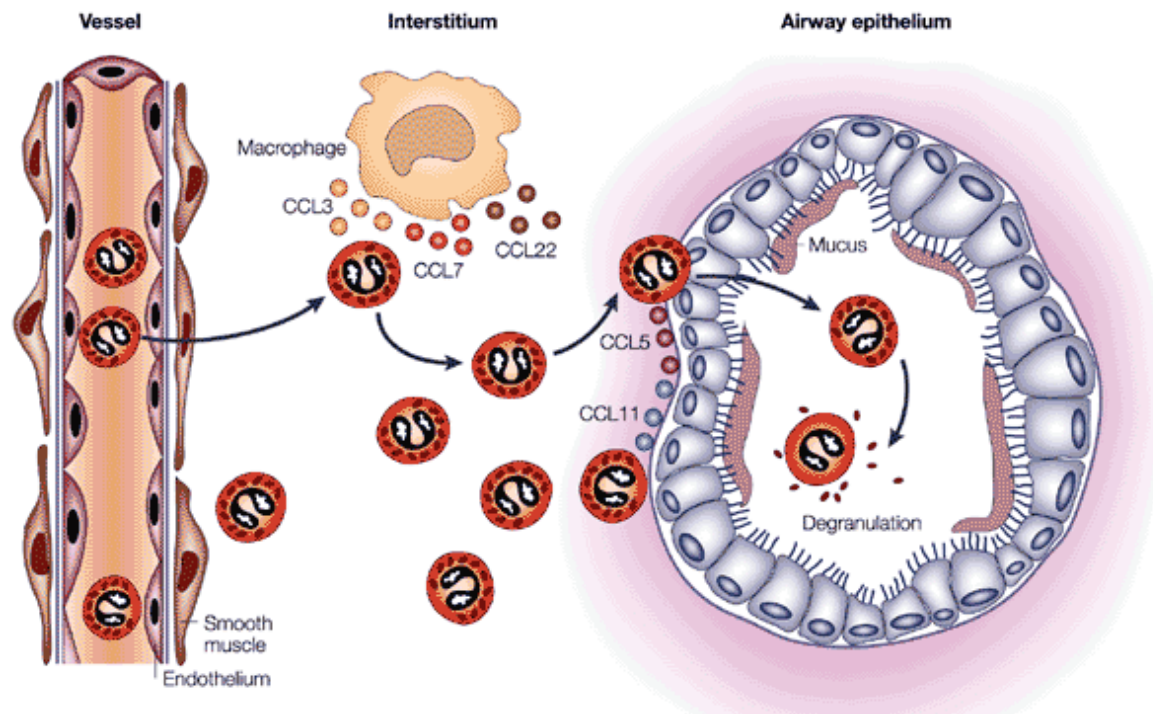
- Production of IgE by B cells
- Eosinophil attraction and infiltration
- Airway inflammation
- Increased bronchial reactivity

ROLES OF INTERLEUKINS

IL-4	IL-5	IL-9	IL-13
Regulates isotype switching in B cells to IgE	Induces increased production, terminal differentiation & activation of eosinophils	Associated with bronchial hyper-responsiveness	Induces inflammation
Induces MHC II on antigen-presenting cells		In mice it increases: <ul style="list-style-type: none"> • Lung eosinophilia • Serum IgE levels Both are clinical features of asthma	Stimulates mucus hyper-secretion
Induces adhesion molecule expression	Release of eosinophils from the bone marrow into circulation		
Activate mast cells and eosinophils	B-cell growth factor and increases Ig secretion		

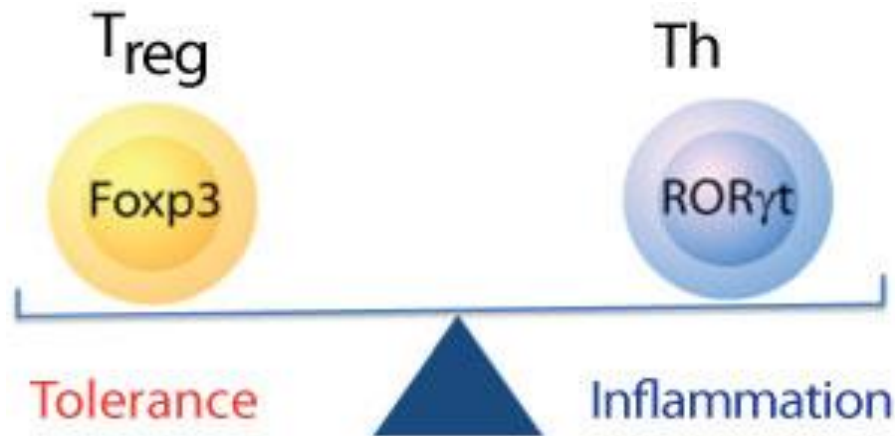
ROLES OF EOSINOPHILS

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



ROLES 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.**



Note: Regulatory T-cells keep the balance.

AIRWAY INFLAMMATION

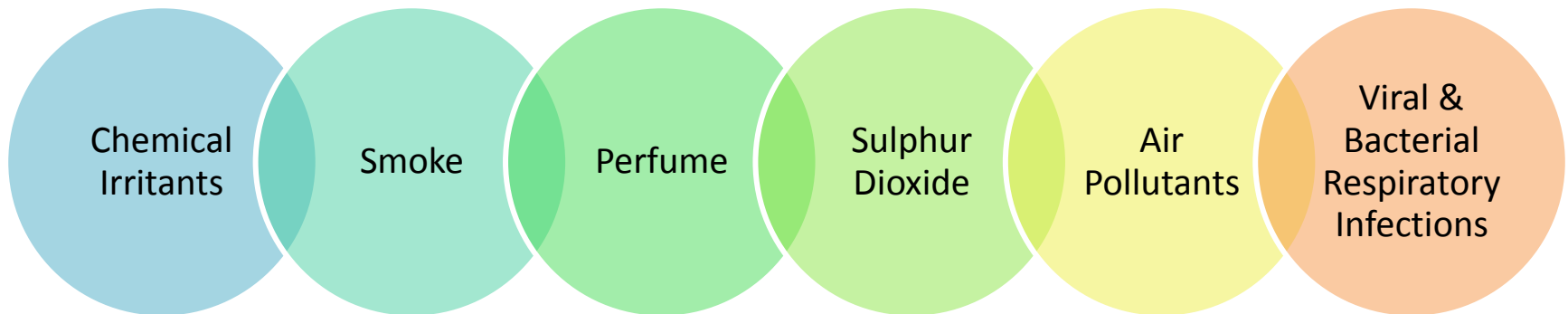
Activation of inflammatory cells (mast cells, eosinophils) is a major inducer of 'Airway Inflammation'.



INCREASED AIRWAY REACTIVITY

Outcome:

It predisposes patients to develop asthma attacks on exposure to **non-specific irritants**.



Products of the inflammatory cells act on :

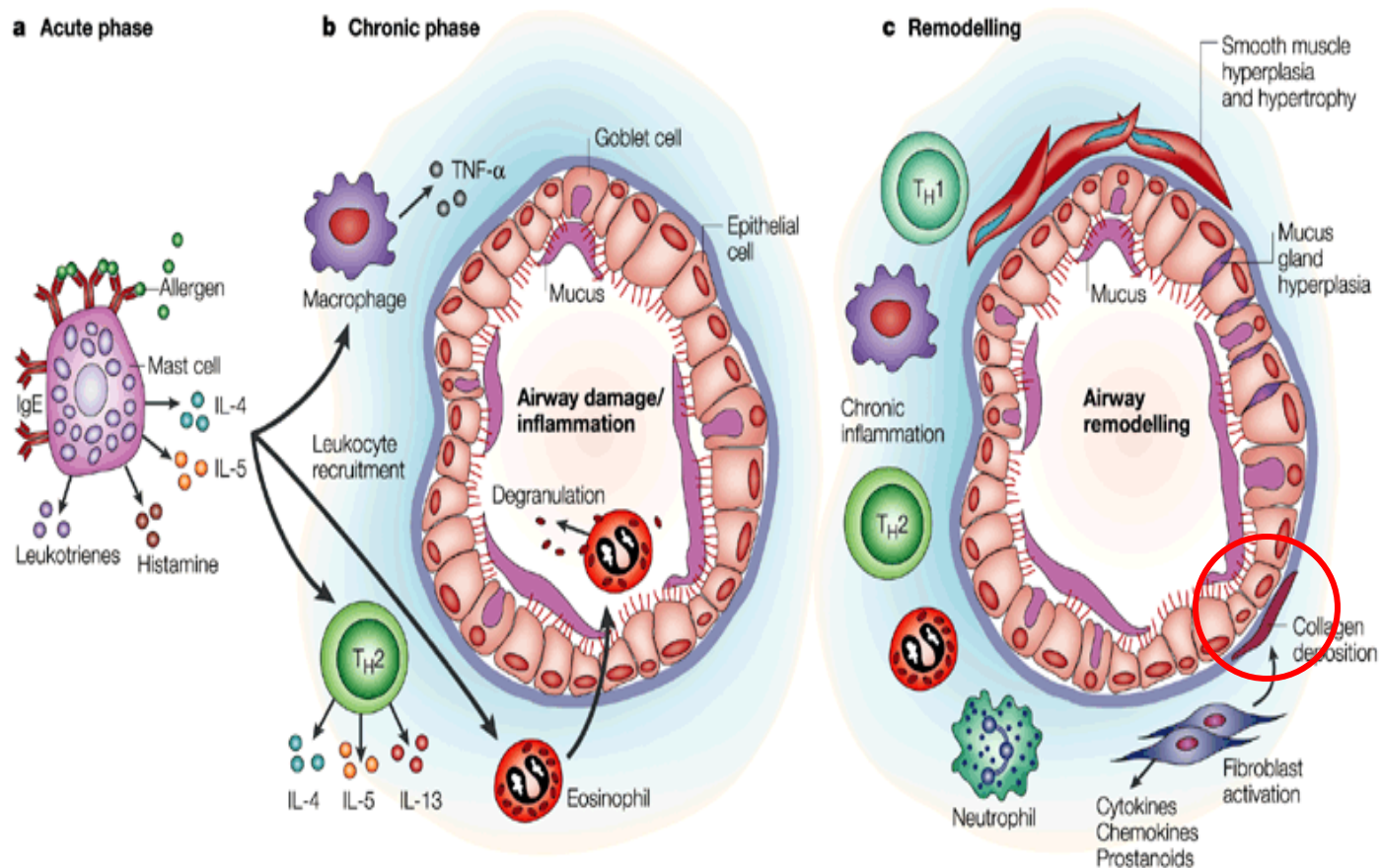
1. Airway smooth muscle cells
2. Lung fibroblasts
3. Mucous glands

They cause **Airway Remodeling**

AIRWAY REMODELING

Outcome:

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



REMEMBER

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 irreversible.

MCQS

1- In the late response, which the drug should the patient take ?

A- Steroid

B- Paracetamol

C- NSAIDs

2- Eosinophils are inhibited by ?

A- IL-5

B- IL-9

C- IL-4

D- IL-10

3- Eosinophils are produced by ?

A- IL-5

B- IL-9

C- IL-4

D- IL-10

4-Which type of allergen is cockroach?

A- Indoor allergen

B- Outdoor allergen

C- Inflammatory

Noura Ahmed

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