جامعة الملك سعود
King Saud University

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Immunology of Asthma

Color code:
Important in red
Extra in blue

Immunology
MED438

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Editing file

Objectives

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

Immunology of Asthma

Asthma is a clinical syndrome characterized by:

1- Reversible airway obstruction **2-** Increased bronchial reactivity **3-** Airway inflammation

Symptoms:

1- Breathlessness **2-** Wheezing **3-** Persistent cough **4-** Chest tightness

Classification	Non-atopic asthma (intrinsic)	Atopic asthma (extrinsic)
Severity	Very severe	Less severe
Prevalence	Older patients (10-33% of asthmatics)	60-90% children 50% of adults
History of allergy	Not needed	Needed
Serum IgE	Normal	High
Skin test	Negative	Positive (in 70-85%)

Atopy: genetic tendency to develop allergy.

Atopic: asthma caused by an external allergen.

Non-atopic: asthma triggered by internal factors.

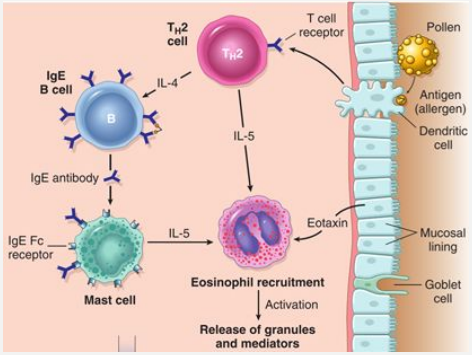
Allergens are linked to the risk of developing asthma.

- **Indoor:** Dust mites, pets, cockroaches, mold.
- **Outdoor:** Spores (Alternaria), grass, weed pollens.

APCs and allergic response

There are 2 different types of APCs present in the lung:

1. **Myeloid Dendritic cells**: they develop asthma symptoms.
2. **Plasmacytoid Dendritic cells**: They aid in respiratory tolerance to the allergen. (They suppress the allergic immune response)



Allergic response

Sensitization	Response
• The allergen binds to the dendritic cells, pushing it to activate Th2 cells. • Th2 cells release multiple cytokines, including IL-4-5-9-13. • Il-4 activates B-cells, Causing a class switch and releasing IgE, which will bind with mast cells.	**Early:** • Allergen will bind with mast cells, releasing mediators such as histamine and prostaglandin. • This causes bronchoconstriction, edema and mucus plugging. • Occurs within seconds or minutes. • Reversible and responds to bronchodilators **Late:** • Eosinophils released by IL-5 and T-lymphocytes are stimulated, causing inflammation. • 8-10 hours after early response. • Responds to steroids

None of the symptoms will manifest in this phase because the mast cell won't release any mediators.

Class switching is when the IgM on the B-cell switches to IgE.

The Role of Cells & Cytokines in Allergic Asthma

Th2 cells during allergic asthma secrete:

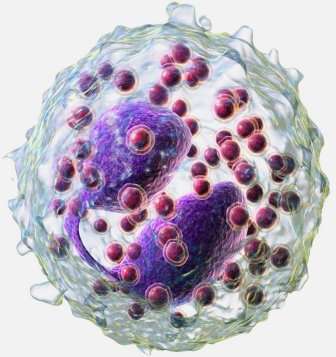
- Interleukin (4,5,9 & 13)

This causes:

1. Production of IgE
2. Eosinophils attraction
3. Airway inflammation
4. Increase in bronchial reactivity

The inflammatory cells interact with:

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



Cytokines

IL-4	-Regulates isotype switching to IgE in B cells. -Induces MHC II (in antigen presenting cells) -Induces adhesion molecules. -Activates mast cells and eosinophils.
IL-5	-Increases eosinophils production. -Release eosinophils from bone marrow.
IL-13	-Induces inflammation. -Stimulate mucus hypersecretion . -Induces subepithelial fibrosis.

Cells

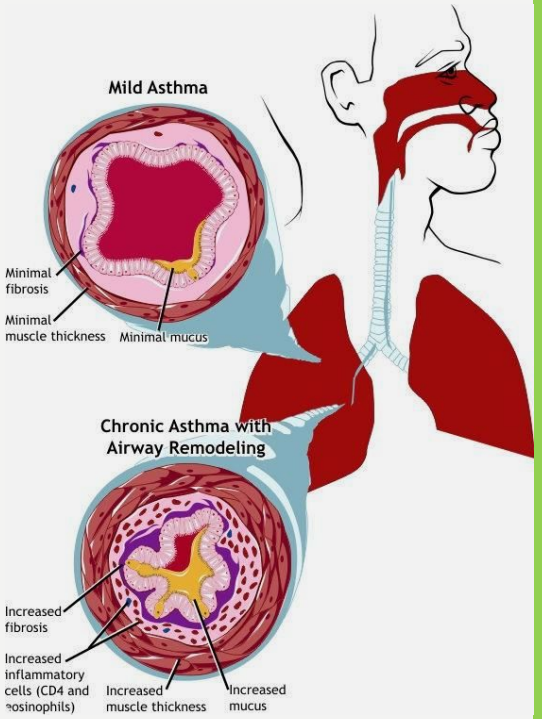
Eosinophils	-Initiate asthmatic symptoms by causing tissue damage. -IL-10 can inhibit eosinophils' production
Regulatory T-cells	-Suppress asthmatic symptoms. -Some asthmatics lack this function.

Airway inflammation and Bronchial Reactivity

Activation of inflammatory cells (eosinophils and mast cells) and their mediators will act on:

1. Airway and smooth muscles → hyperplasia and hypertrophy
2. Mucous glands → hyperplasia
3. Lung Fibroblasts → activation and collagen deposition (fibrosis)
4. Airway → chronic inflammation

This will cause airway remodeling and bronchial reactivity, which will eventually lead to chronic inflammation.



Outcomes

Airway Remodeling (hyperplasia, hypertrophy & fibrosis)	Bronchial Reactivity (airway chronic inflammation)
Leads to <u>fibrosis</u> and <u>irreversible airway obstruction</u>	Bronchus becomes more reactive to some non-specific irritants and cause asthma attack. <u>**Non-specific irritants include:**</u> • Chemicals, smoke, strong perfume, sulphur dioxide, air pollutants and infections

Take Home Message

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

Quiz:

1. Which of the following is released by mast cells at the end of the sensitization phase?

a) prostaglandin
b) Histamine
c) Both A&B
d) None of the above

2. Which of the following cytokines inhibit the production of eosinophils?

a) IL-5
b) IL-10
c) IL-4
d) IL-13

3. The antibody present on T-cells switches from… to..

a) IgD-IgE
b) IgM-IgE
c) IgE-IgM
d) None of the above

4. A 45 year-old male came into the ER complaining of dyspnea and a bad cough. IgE levels were elevated, and a skin-prick test was positive for dust mites. What is the most likely diagnosis?

a) Intrinsic asthma
b) Extrinsic asthma
c) Drug-induced asthma
d) COPD

5. In the first encounter with allergens, they initially bind with?

a) Myeloid dendritic cells
b) Mast cells
c) Plasmacytoid dendritic cells
d) T-helper cells

6. If asthma has fibrosis, does it become a restrictive disease like pulmonary fibrosis?

a) Yes, asthmatic fibrosis will impair the lung's ability to fully expand
b) No, pulmonary fibrosis is in the airway while asthmatic fibrosis is in the alveoli
c) No, pulmonary fibrosis is in the alveoli while asthmatic fibrosis is in the airway
d) Asthma has no fibrosis

1.D 2.B 3.D 4.B 5.A 6.C

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