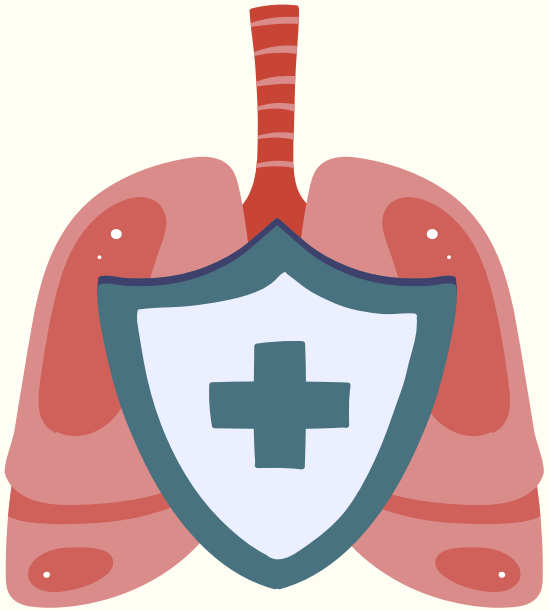
Immunology of bronchial asthma



Color Index:
-Main Text -Important -Notes
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Editing File

objectives

01 To identify the difference between extrinsic and intrinsic asthma

02 To be familiar with types of allergens and their role in allergic sensitization

03 To understand the inflammatory processes operating in allergic asthma

04 To know about the airway remodeling

Asthma (الربو) is a clinical syndrome It's a chronic inflammatory disorder of the airway, and is recurrent.

characterized by:

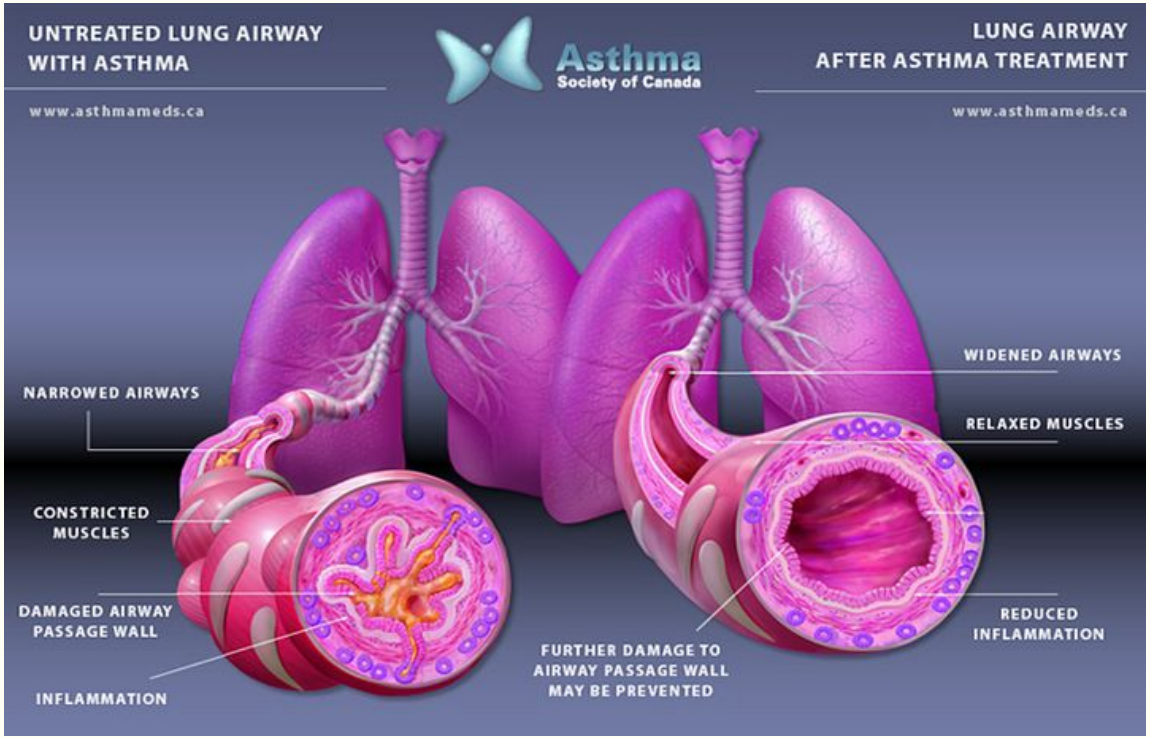
1. Episodes of reversible airway obstruction
2. Increased bronchial reactivity
3. Airway inflammation

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

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

Normal classic asthma: Dry cough
Chronic asthma + persistent: ↑ secretion = sputum

Airway Obstruction in Asthma

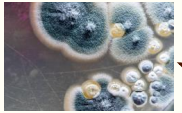


Classification of Asthma

Classification	Non-atopic (Intrinsic) (10-33% of asthmatics)	Atopic (Extrinsic) (Allergic asthma) Allergens (**Atopy:** genetic tendency to develop allergy)
Prevalence	Older patient = less common	60-90% children 50% adults
severity	More severe	Less severe
Clinical/Family history of allergy	**No** clinical/family history of allergy (negative)	**presence** of clinical/family history of allergy (Positive)
serum IgE	Usually Normal	High
skin test (skin prick test)	Negative	Positive-immediate- (in 75%-85% of patients) to various of allergens

Role of Allergens in Asthma

Allergen sensitization is linked to the risk of developing asthma



Indoor allergens

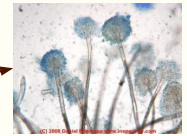
- House dust mites عث الغبار
- Domestic pets (cat fur & dander)
- Cockroaches (insects)
- Molds (fungal spores)

عث الغبار طبيعي يكون موجود بكل مكان، البيوت، الملابس... الخ

Outdoor allergens

- Fungal spores (e.g. Alternaria
- Grass pollens
- Tree pollens
- Weed pollens

Pollens = حبوب اللقاح اللي في النباتات



Antigen presenting cells (APCs) in the lung and allergic response

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

Dendritic cell is a type of APCs it will take the allergen (antigen) inside it (dendritic cell) And it has two types

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

What is immunological tolerance?

Unresponsiveness to specific antigens in an effort to prevent destructive over-reactivity of the immune system.

It is important for normal physiology

يعني قدرة الجهاز المناعي على معرفة اذا الانتجن حقه (ما يهاجمه) واذا مو حقه يهاجمه، مهم عشان الجسم ما يهاجم نفسه فإذا صار فيه مشكلة يسبب مرض مناعي

Antigen presenting cells (APCs) and allergic response

01

<u>In susceptible individuals</u> (vulnerable to allergen) :

First encounter with allergens activate B-cells to produce IgE. (Sensitization Phase)

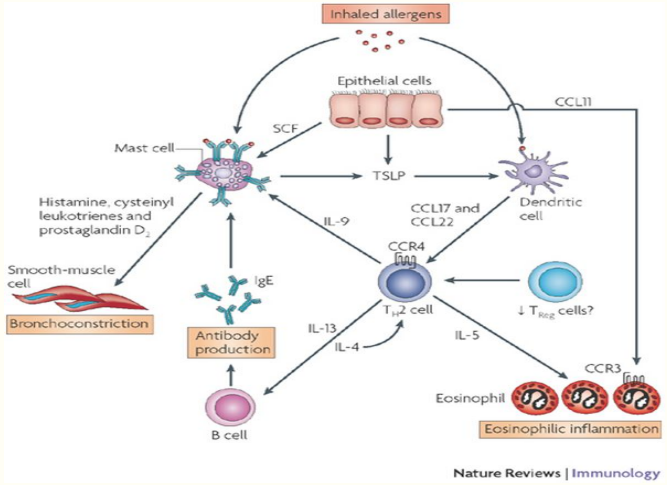
Be careful, the main cytokines responsible for the constriction are IL-4 and 13. IL-5 has an indirect effect. It's main function is explained later. #Team39

02

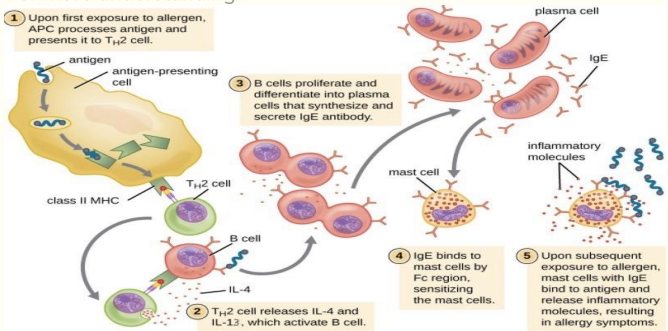
<u>Subsequently,</u>

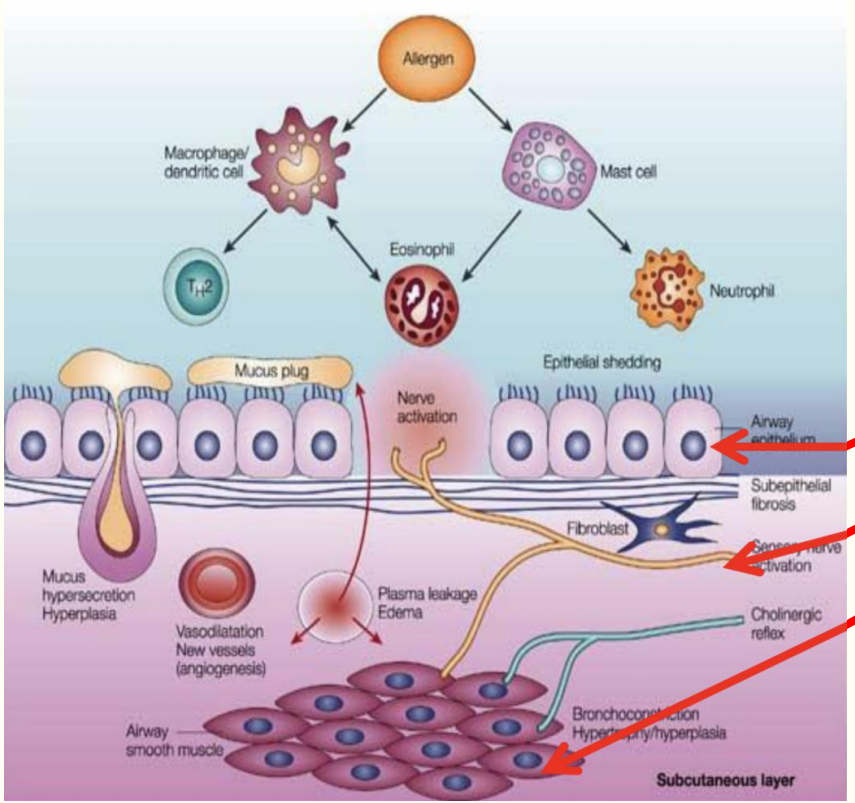
Inhaled allergens activate submucosal mast cells in the lower airways

Mediators are released within seconds causing:
1. Bronchoconstriction
2. Influx of eosinophils & other inflammatory cells



For more understanding :





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

1. **Airway epithelium (inflammation)**
2. **Nervous system (stimulation)**
3. **Bronchial smooth muscles (constriction)**

Allergic response

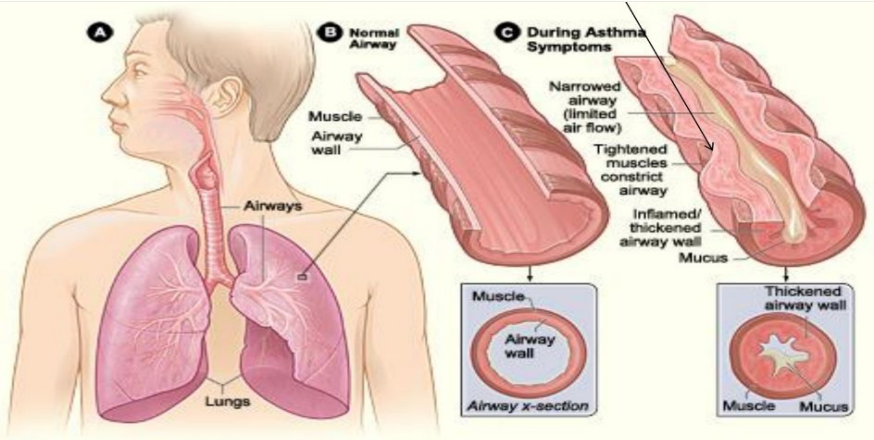
Factor contributing to airflow obstruction leading to difficulty in breathing include:

Information from the picture:

Constricted smooth muscles of bronchioles

Inflamed epithelial wall (thickened/narrowed)

Hypersecretion of mucus from mucus glad



Allergic response cont..

Response to allergen occur in two phases

Sensitization Phase
(First encounter with the allergen)

1) When the allergen enters the body, it's then recognized by the dendritic cells
2) This process activates a naive T cell to become Th2 lymphocyte
3) Th2 cells release multiple cytokines(IL-4-5-9-13).
4) One of these cytokines(IL-4) activates B cells, causing a class switch (a process of converting IgM to IgE)
5) None of the symptoms will manifest in this phase because the mast cell will not release any mediators

Immediate/Early allergic response
" Challenge phase"(within minutes)
(Recurrent encounter with the **same** allergen)

1) IgE will then bind to the Allergen and set on the mast cell via the Fc Receptor

2) This stimulates the mast cells to release certain cytokines and Mediators

3)This shows some clinical features such as:
bronchial construction,
airway edema, mucus plugging

4) This stage is reversible and responds to bronchodilators (treatment)

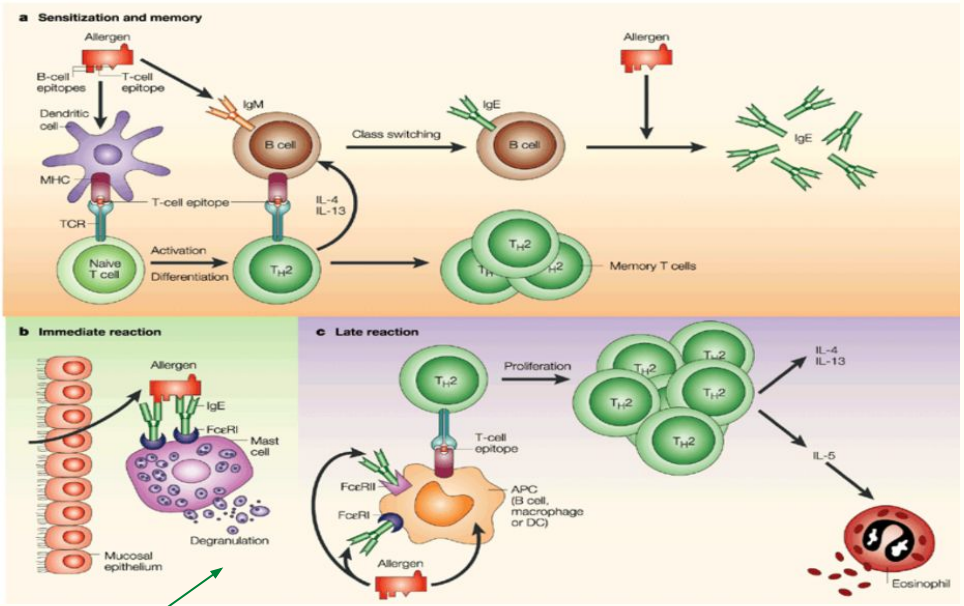
Late allergic response (4-10 hours later)

1) Results from infiltration by inflammatory cells.

2) Activation of lymphocytes & eosinophils
(Activated Th2 release IL-5 that stimulate the production and release of eosinophils)

2) Which will release granules and mediators that are toxic to epithelial cells(causing mucosal damage, edema,spasm of the small muscles fibers)
3) This stage responds to steroids (Anti-inflammatory drugs)

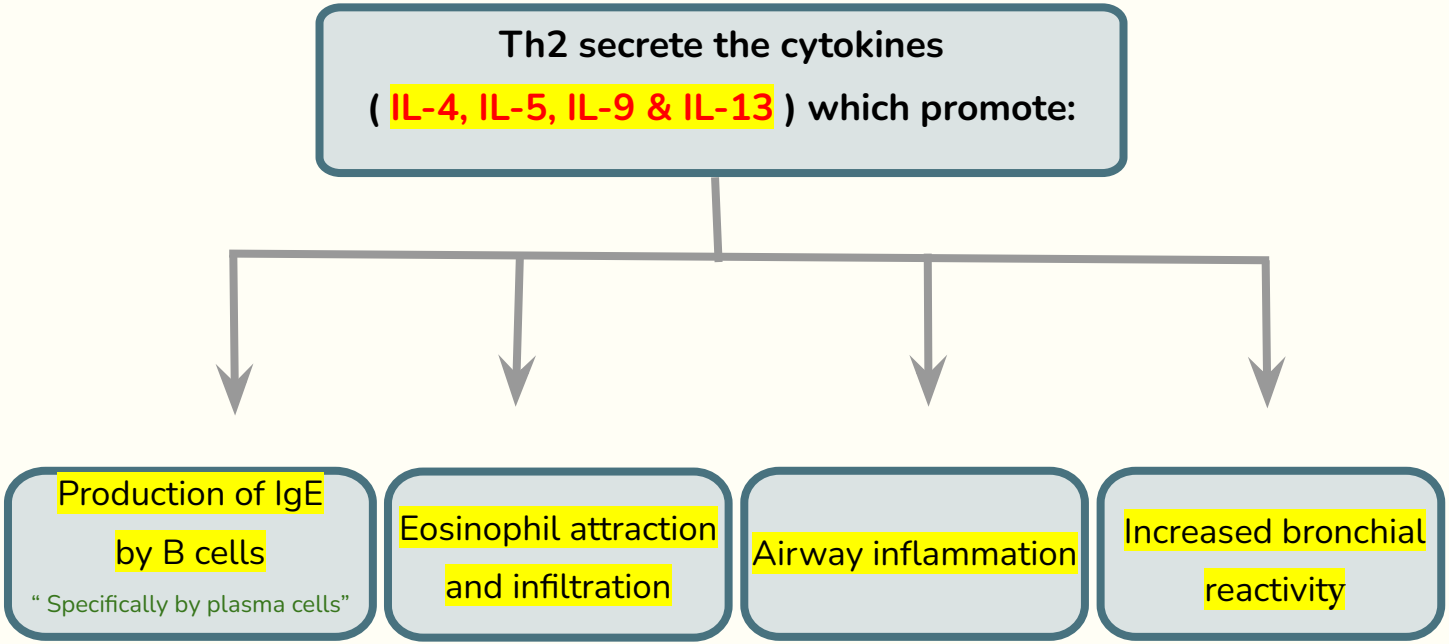
First exposure by dendritic cells
TH2 → IL4 + IL13 → activates B cell → class switching IgM to IgE



Degranulation of mast cell → histamine release = first symptom

Th2 cells and role of cytokines in allergic asthma

Allergens drive T- cells towards Th2 type:



Role of cytokines in allergic asthma

	Role in Allergic Asthma
Interleukin-4 (IL-4) **(during the initial priming of TH2)**	-Regulates **isotype switching** in B cells from IgM to **IgE.** - Induce MHC II on Antigen-Presenting cells (e.g. dendritic cells, mast cells). - Induces adhesion molecules expression. **-Activate mast cells & eosinophils.**
Interleukin-13 (IL-13)	**-Induces inflammation.** -Stimulates mucus **hypersecretion.** -Induces subepithelial fibrosis.**(which if not controlled, may lead to scarring and damage).**
Interleukin-5 (IL-5)	-Induces an increase in **eosinophil production** in the bone marrow. (IL5 for production while IL4 for activation of eosinophils) -Release of eosinophils from the bone marrow into circulation.
Eosinophils	- Initiate asthmatic symptoms by causing **tissue damage in the airways of the lungs.** - Production of eosinophil **is inhibited by IL-10** (anti-inflammatory cytokine) How to inhibit the production of eosinophil? By IL-10
Regulatory T-cells **(T-reg)**	**-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, which is a hallmark in asthmatic lung that leads to increased bronchial activity

Airway remodeling — **Airway inflammation** — **Increased bronchial (airway) reactivity**

(Structural changes of the Airways)

- **Airway smooth muscle cells** hyperplasia and hypertrophy (due to repeated exposure of constriction that increases demand on cells)
- **Lung fibroblast activation** (leads to fibrosis)
- **Mucous gland hyperplasia**
- **Collagen deposition**
- **Chronic Inflammation**

★ Airway remodeling can ultimately lead to **fibrosis** and **irreversible airway obstruction** in some patients.(if not effectively treated)

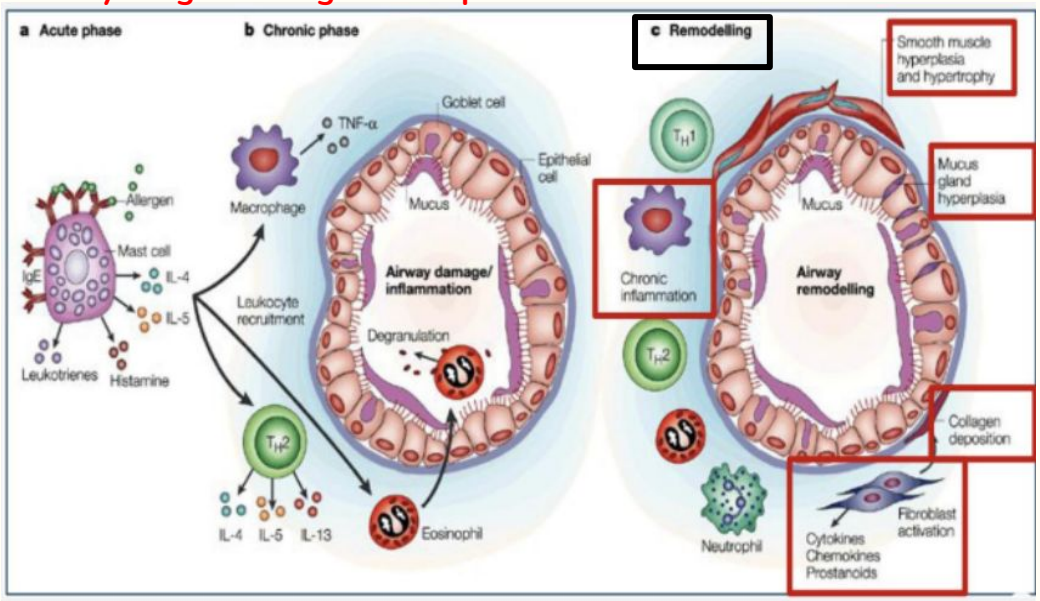
Airway reactivity is a term used to describe a set of symptoms that indicate a person is having a bronchial spasm, which happens when the bronchial tubes (airway) are irritated by something. So it's used when asthma is suspected, but not yet confirmed.

They're more likely to develop an asthma attack on exposure to **non-specific irritants:** (substances that can cause irritation or inflammation without targeting specific receptors or mechanisms.)

- **Chemical irritants**
- **Smoke and strong perfumes**
- **Sulphur dioxide and air pollutants**
- **Viral and bacterial respiratory infections**

Airway remodeling ------ **Airway inflammation** ------ **Increased bronchial (airway) reactivity**

Everything in the figure is important



- A patient with bronchial hyperreactivity should avoid exposure to nonspecific irritants to prevent developing asthma attacks.
- Allergens are specific because they will be recognized by the APCs which then will be presented to the naive T cell.
- Whereas non-specific irritants only cause asthma
attacks to patients who have bronchial hyperreactivity such as asthmatics.

*** Thanks to team 439**

Take Home Messages

- Asthma is characterized by episodic reversible airway obstruction.
- Classified in 2 types: intrinsic & extrinsic (allergens).
- In the extrinsic 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 & airway remodeling which is not revisable.

MCQs

Q1: Which interleukin regulates isotype switching in B cells from IgM to IgE?			
A- IL-3	B- IL-4	C- Eosinophils	D- IL-9

Q2: Which of the following is a type of antigen presenting cells in the lung that help in the development of asthma symptoms?			
A- T-reg	B- Myeloid DCs (mDCs)	C-Neutrophils	D- Plasmacytoid DCs (pDCs)

Q3: Production of Eosinophils is inhibited by which of the following :			
A- IL-13	B- Macrophages	C- IL-5	D- IL-10

1- B
2- B
3- D

MCQs

Q4: which one of the following considered as indoor allergens?			
A- Grass pollens	B- Mold (fungal spores)	C- Tree pollens	D- Weed pollens

Q5: Which stage is response to bronchodilators?			
A- Early allergic response	B- Late allergic response	C- sensitization phase	D- All

Q6: Which of the following is NOT true about airway remodeling outcomes?			
A- Fibrosis	B- Irreversible obstruction	C- Can be treated with steroids	D- Smooth muscles hyperplasia

4- B
5- A
6- C

Meet the team

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