Respiratory Block

Immunology

Lecture 3

Immunology of Asthma.

In this document you will find some main points gathered from the 1st lecture..This document is NOT a replacement for the lecture..If you need additional information go back to the lecture or use a book as a reference so you understand everything correctly.

Hopefully all the information is correct and Hope you find them useful.

Good Luck to everyone.

430 Immunology Team Members

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Immunology

Immunology of Asthma.

Some main points you can go through and revise from:

Note:
People with asthma have a very sensitive air way can be triggered by any thing

Note:
Asthma→inflammation on the lung by an allergen or any disease

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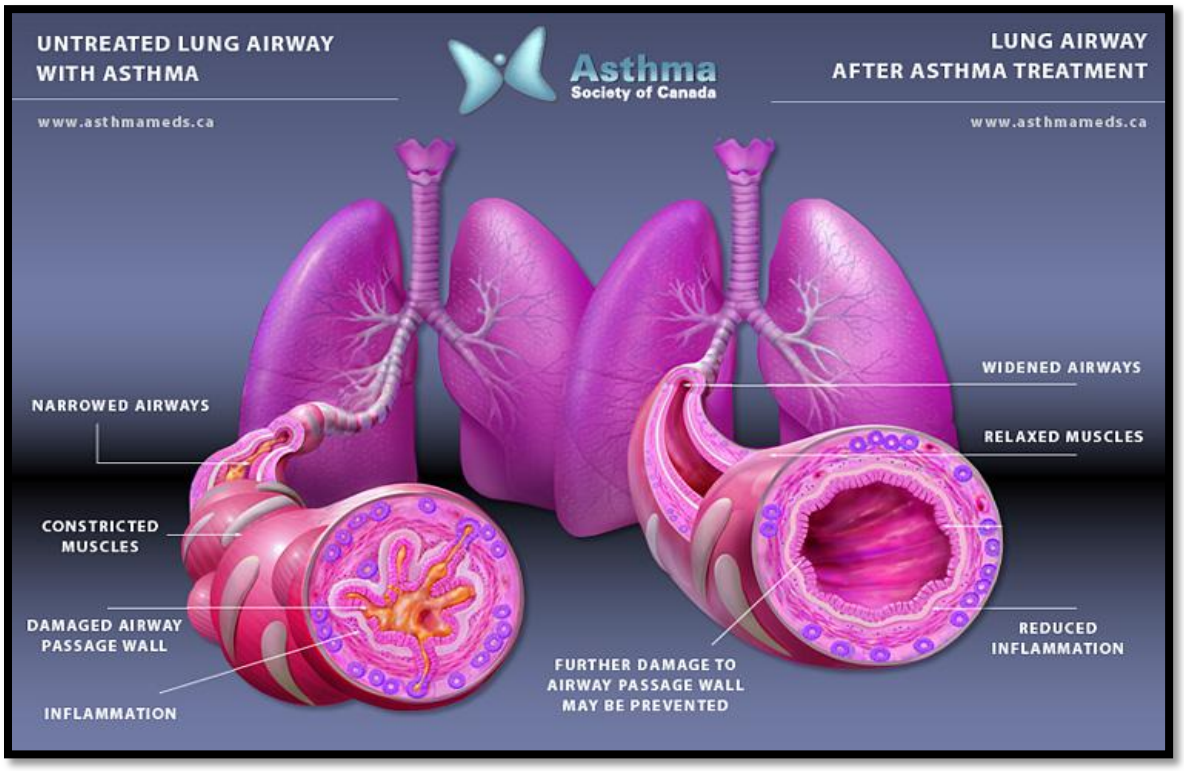
Asthma is a clinical syndrome characterized by :

- Episodes of reversible airway obstruction.#(important in diagnosing asthma)
- Increased bronchial reactivity.
- Airway inflammation

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

- breathlessness (difficulty in breathing).
- Wheezing .
- persistent cough. (the common symptoms of asthma)
- chest tightness

Note:
Reversible Airway Obstruction→(an important feature of asthma)



Classification of asthma :

- Extrinsic (atopic).#Main type
- Intrinsic (non-atopic).

Note:
Atopy → A genetic tendency to develop allergy

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

- ! Negative skin tests .
- ! No clinical/family history of allergy
- ! Serum [IgE] is normal .
- ! Older patients .
- ! More severe .

Atopic (extrinsic) asthma .

*Allergies trigger asthma attacks in :

- Children (60-90%)
- Adults .(50%)

Note:

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

#Some Allergies get treated by the increase of hormones at puberty

Role of Allergens in Asthma

#Allergen sensitization is linked to the risk of developing asthma.

Indoor allergens #Patient would present with asthma all year long

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

Outdoor allergens : #Patients present with asthma at certain times of the year

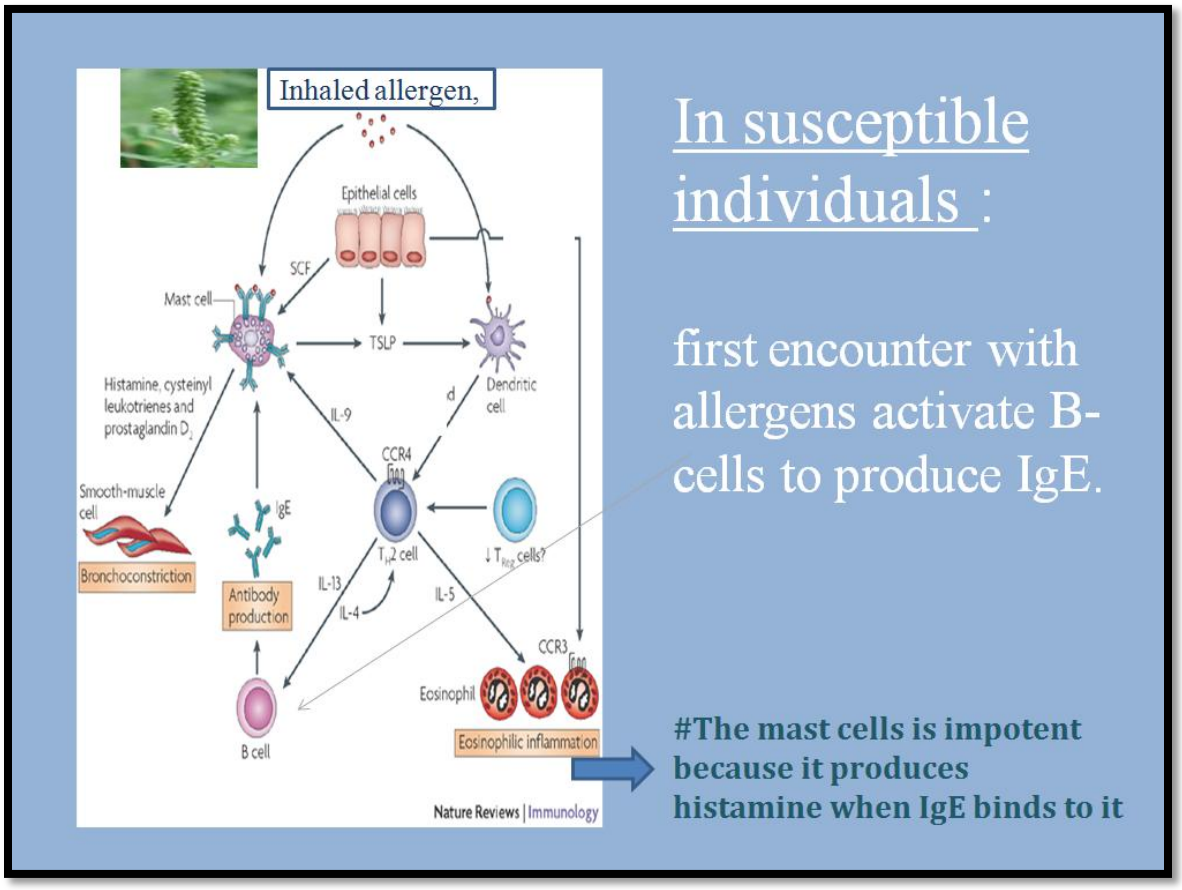
- Fungal spores :(e.g. Alternaria) .
- Grass, tree & weed pollens.

Antigen presenting cells (APC) in the lung :

#Cell mediated immunity

Two subsets of dendritic cells in the lungs.

- Respiratory tract myeloid DCs (mDCs) aid in the development of asthma symptoms→ #Causes Allery
- Plasmacytoid DCs (pDCs) aid in respiratory tolerance to allergens. → # Does not cause allergy

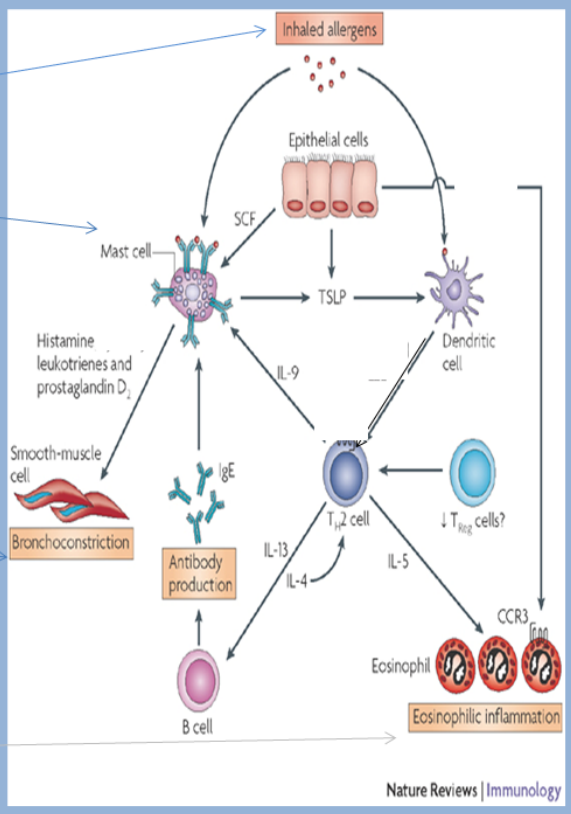


Subsequently:
inhaled allergens activate submucosal mast cells in the lower airways .

mediators are released within seconds & lead to :

1.bronchoconstriction.

2. Influx of eosinophils & other inflammatory cells.



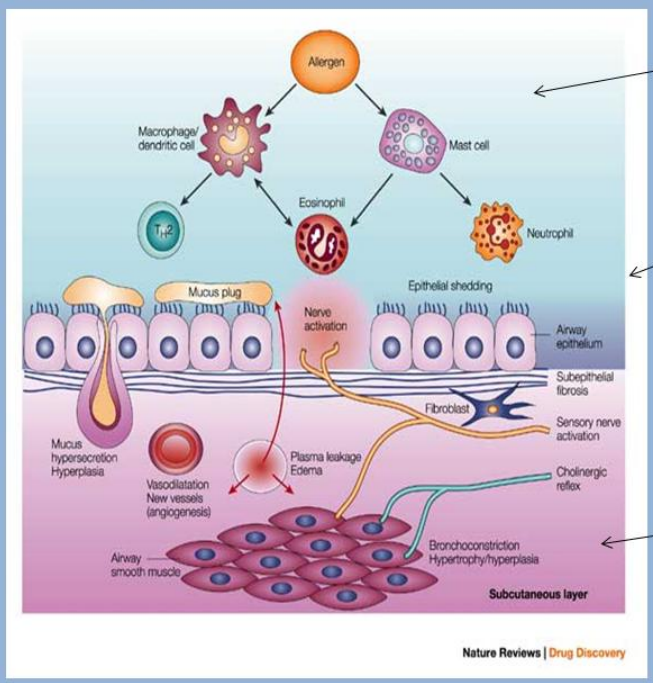
Asthma results from complex interactions of among the

Inflammatory cells and :

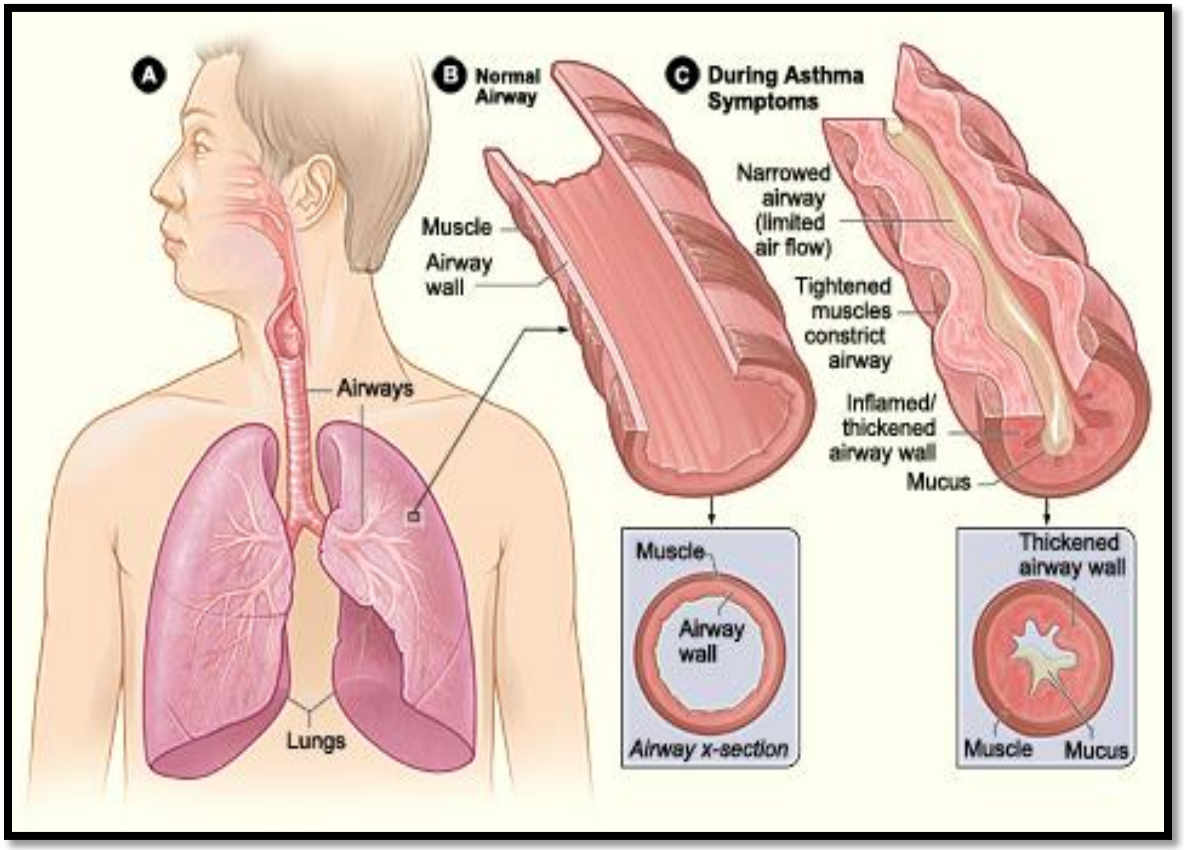
1. Airway epithelium

2. Nervous system #Mast cells stimulate it

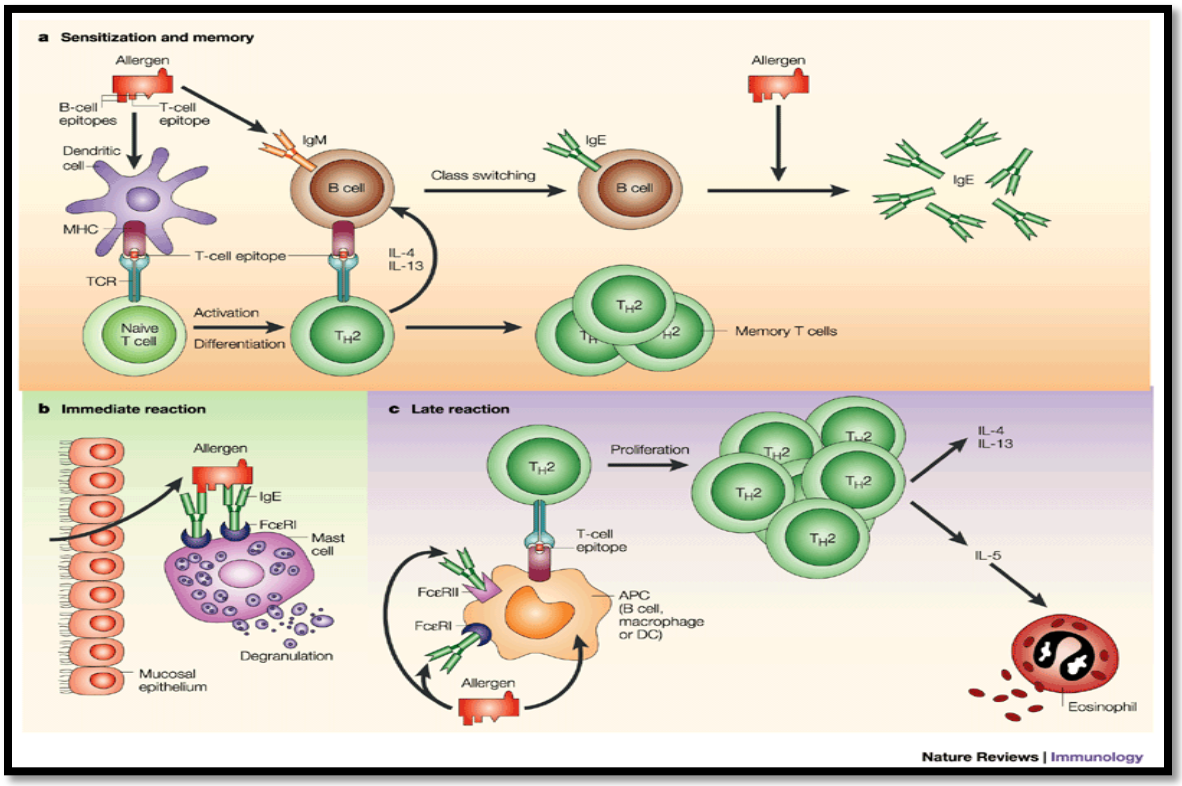
3. Bronchial smooth muscles



Factor contributing to airflow obstruction leading to difficulty in breathing



Response to allergen occurs in two phases.



Early allergic response :

- Occur within minutes.
- manifest clinically as :
  - bronchial constriction .
  - airway edema .
  - mucus plugging .

*respond to bronchodilators .

Late allergic response :

- Appear 4 to 10 hours later.
- Result from infiltration by inflammatory cells.
- Activation of lymphocytes & Eosinophils .

*respond 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 :

- B-cell IgE production.
- eosinophil attraction.
- airway inflammation .
- increased bronchial reactivity .

Role of IL-4 in allergic asthma.

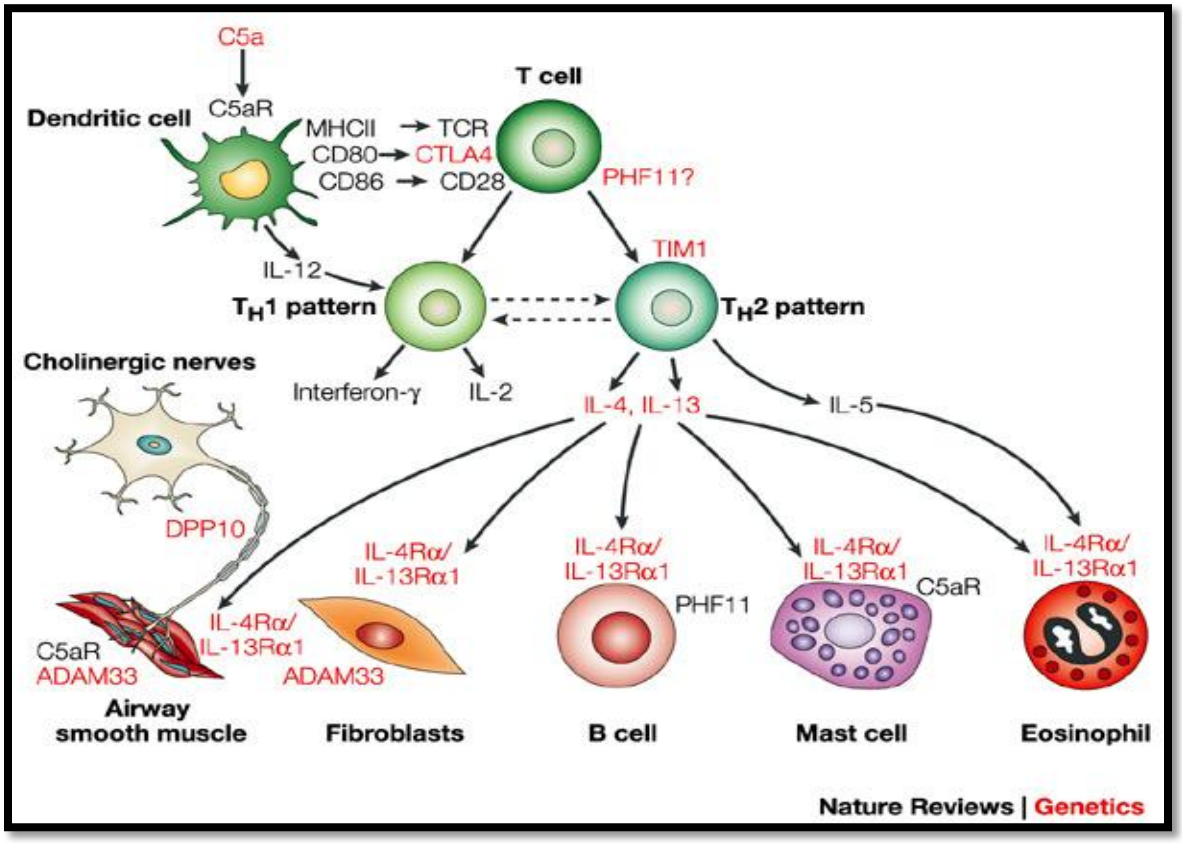
The main role of IL-4 is carried out during the initial priming of Th2 cells:

- Regulate isotype switching in B cells to IgE. #When B-Cells are stimulated by IL-4 they form IgE
- Induce MHC II on antigen-presenting cells .
- Induce adhesion molecule expression.
- Activate mast cells and eosinophils .

Role of IL-13 in allergic asthma .

- IL-13 induces inflammation.
- Stimulate mucus hypersecretion.
- Induce subepithelial fibrosis. # The fibroses of the tissue is irreversible and will deposit in the bronchi which leads to the narrowing of the air way
- stimulate eotaxin production.

IL-4 & IL-13 act on: Eosinophils. Mast cells, B-cells, fibroblasts and airway smooth muscles.



Role of IL-5 in allergic asthma .

- IL-5 induces an increase in eosinophil production in the bone marrow.
- release of eosinophils from the bone marrow into circulation .

Role of eosinophils in allergic asthma .

- Eosinophils play a prominent role in initiating asthmatic symptoms by causing tissue damage in the airways of the lungs.

Role of IL-10 in allergic asthma.

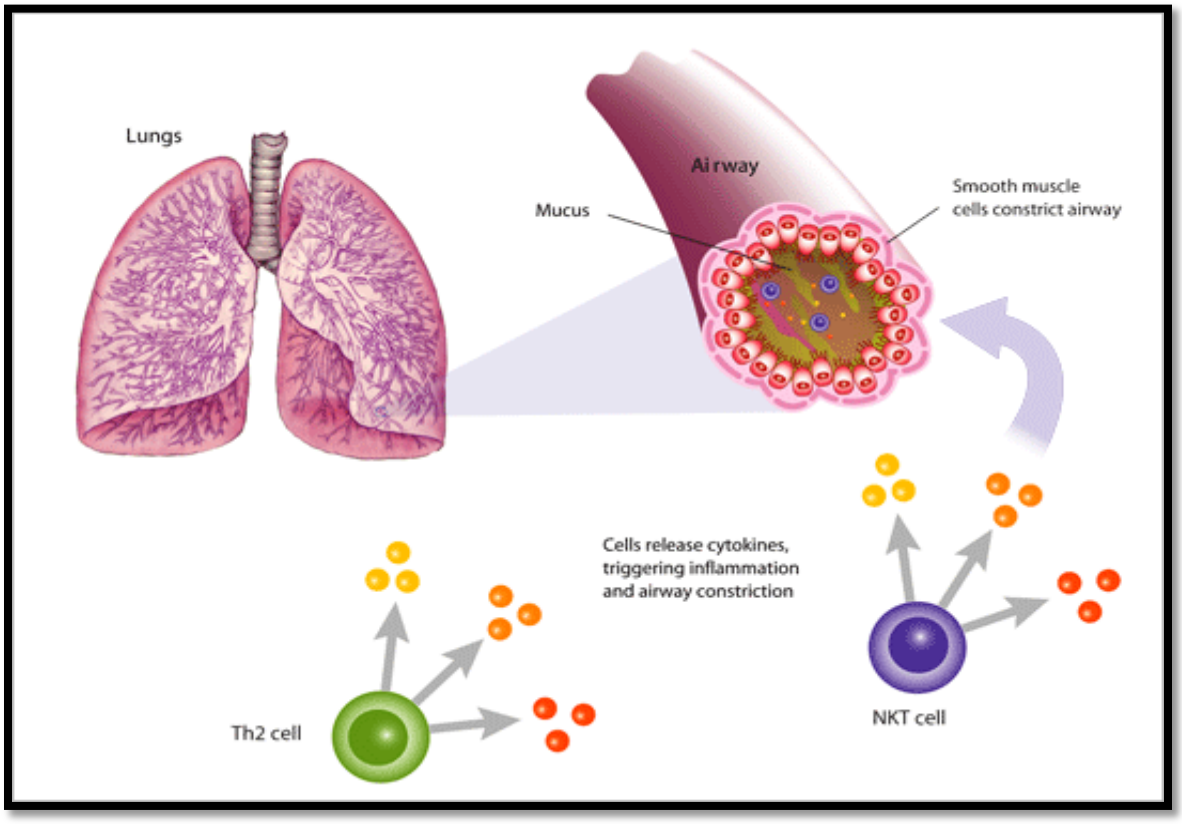
* IL-10 regulate allergic responses

- 1.IL-10 has direct inhibitory effects on APCs and T cells .
  #Inhibits the allergic reaction
- modulates eosinophil accumulation in airways by possibly inhibiting eosinophil production in bone marrow.

#Asthmatic patients have a decreased expression of IL-10 .

Role of NKT cells in asthma .

- NKT cells constitute less than 1% of CD4+ T cells in the blood and constitute 63% of CD4+ T cells in patients with moderate-to-severe asthma.
- NKT cells activate Th2 cells to secrete IL-4 and IL-13.



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 .

Airway inflammation leads to :

- Increased bronchial reactivity.

Products of the inflammatory cells act on :

- Airway smooth muscle cells . #Causes hypertrophy
- Lung fibroblasts .
- Mucous glands .

Products of the inflammatory cells cause :

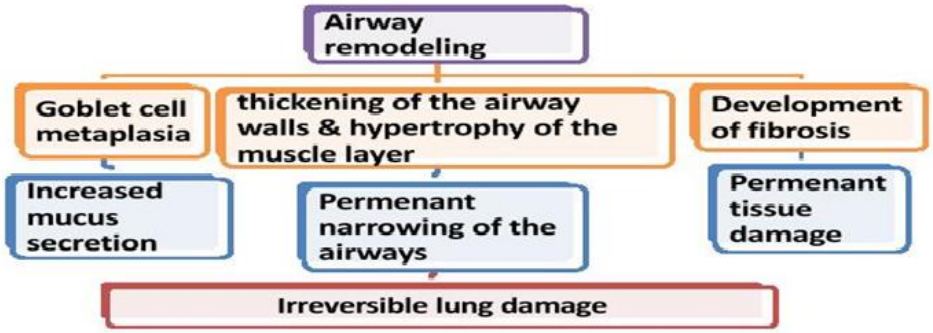
- Airway remodeling.

Products of these cells acts on:

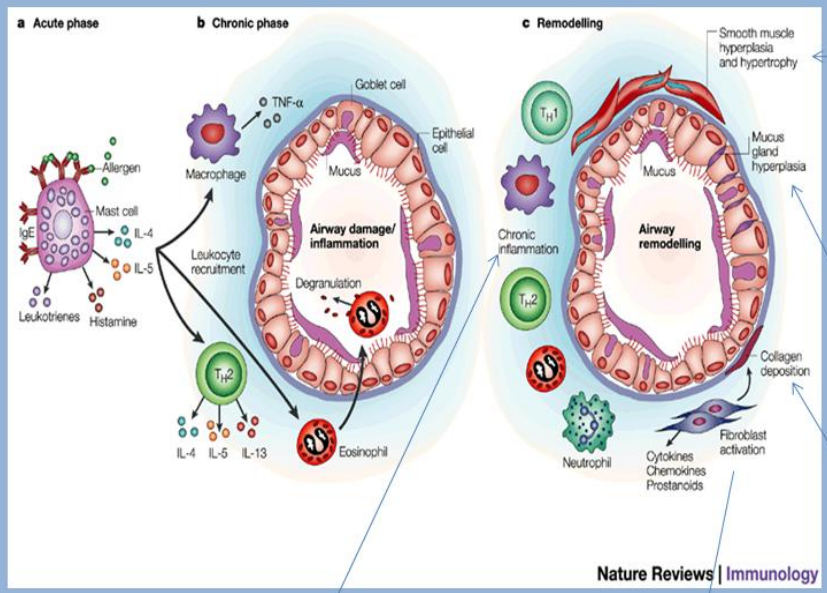
1- Air smooth muscle cells.
2- Lung fibroblasts.
3- Mucous glands.

Which will cause → Airway remodeling

Airway remodeling could cause an irreversible lung damage by:



airway remodelling refer to .



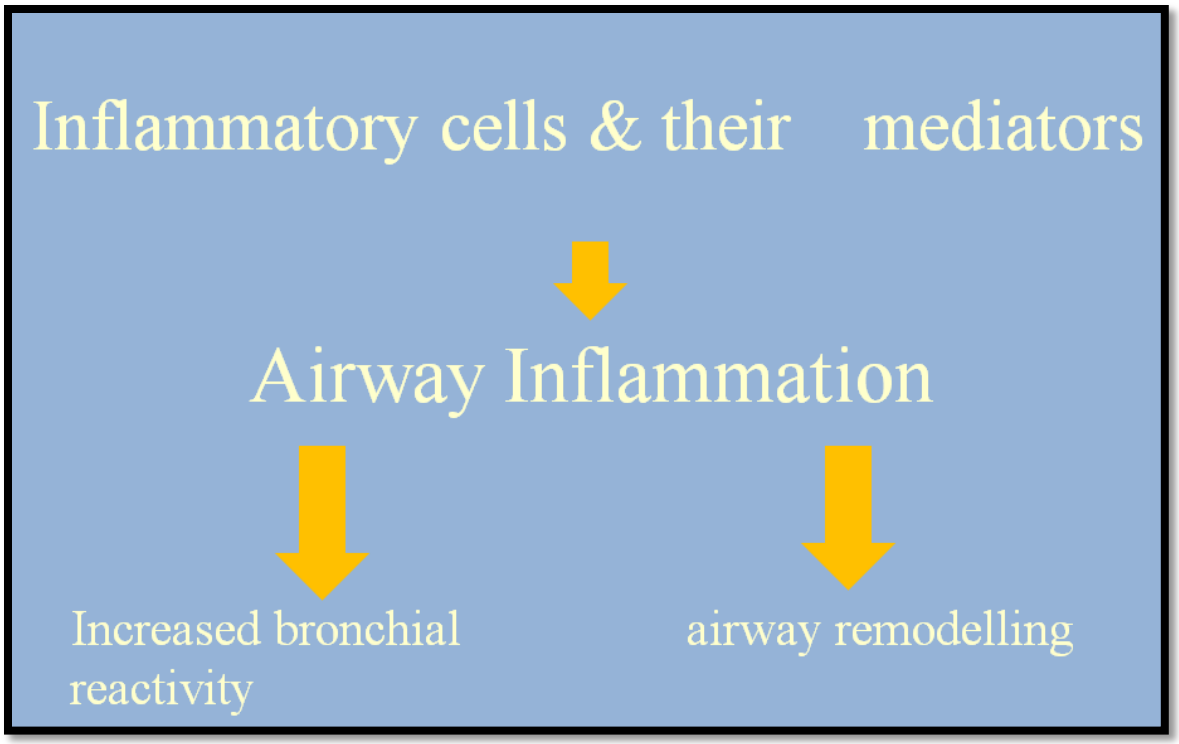
1. Smooth muscle hyperplasia & hypertrophy

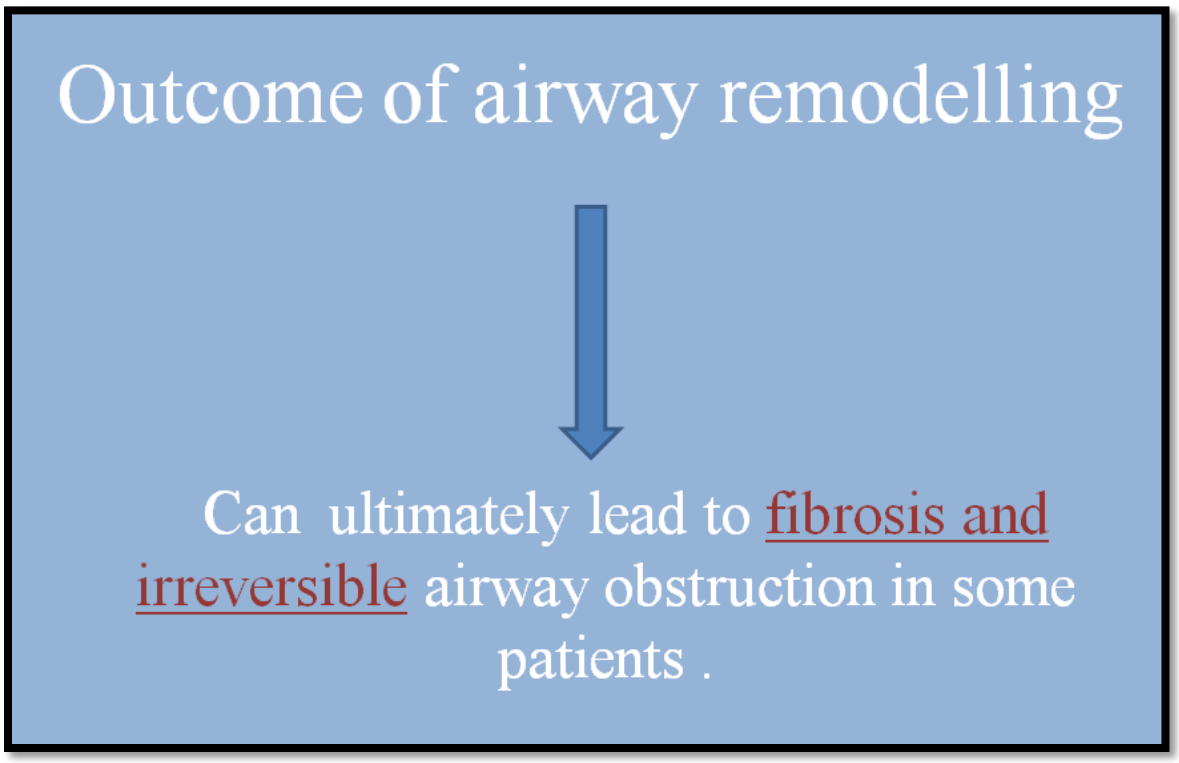
2. Mucous gland hyperplasia

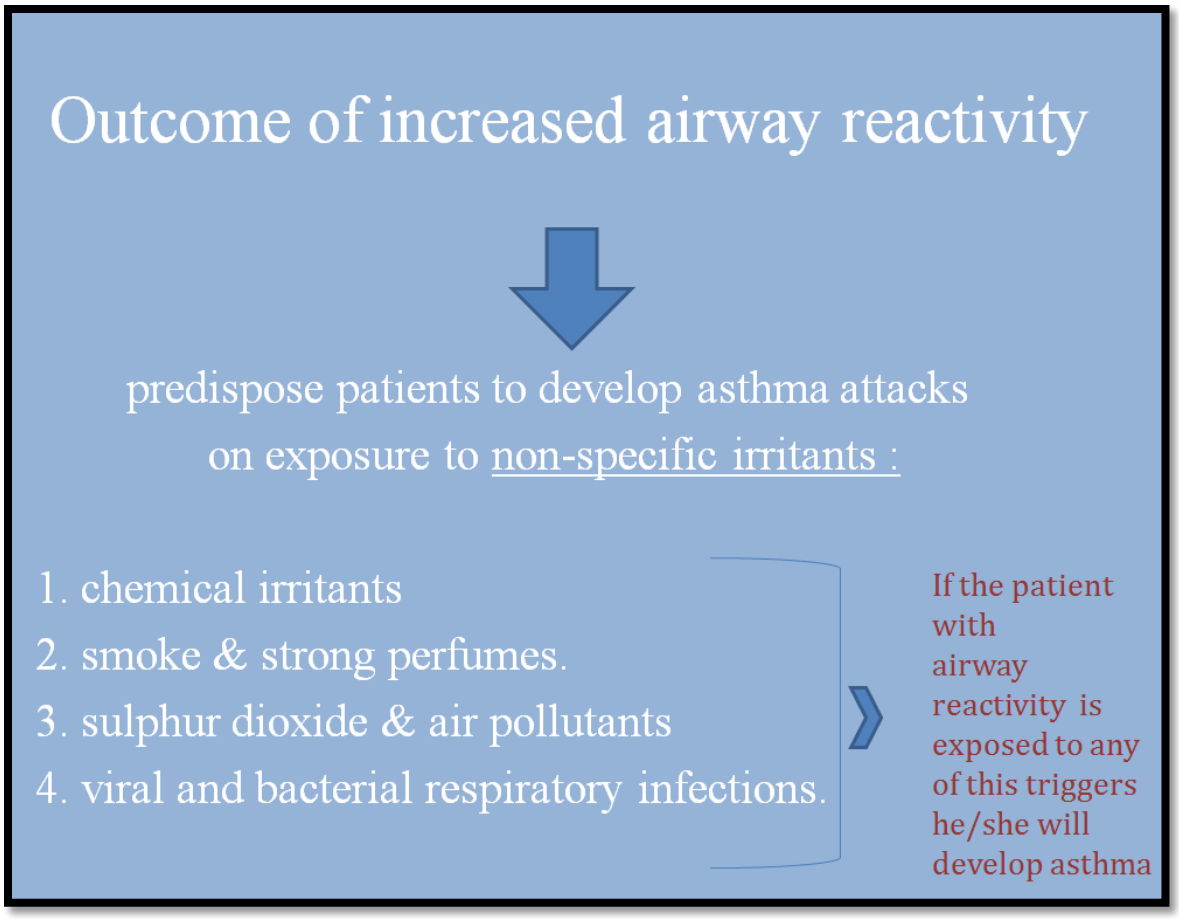
3. Collagen deposition

4. Fibroblast activation

5. Chronic inflammation


Inflammatory cells & their mediators
Airway Inflammation
Increased bronchial reactivity
airway remodelling


Outcome of airway remodelling
Can ultimately lead to fibrosis and irreversible airway obstruction in some patients .



Summary:

- Asthma is characterized by episodic reversible
- airway obstruction
- Classified in 2 types : intrinsic & extrinsic.
- 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