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:

- Episodes of reversible airway obstruction
- Increased bronchial reactivity
- Airway inflammation

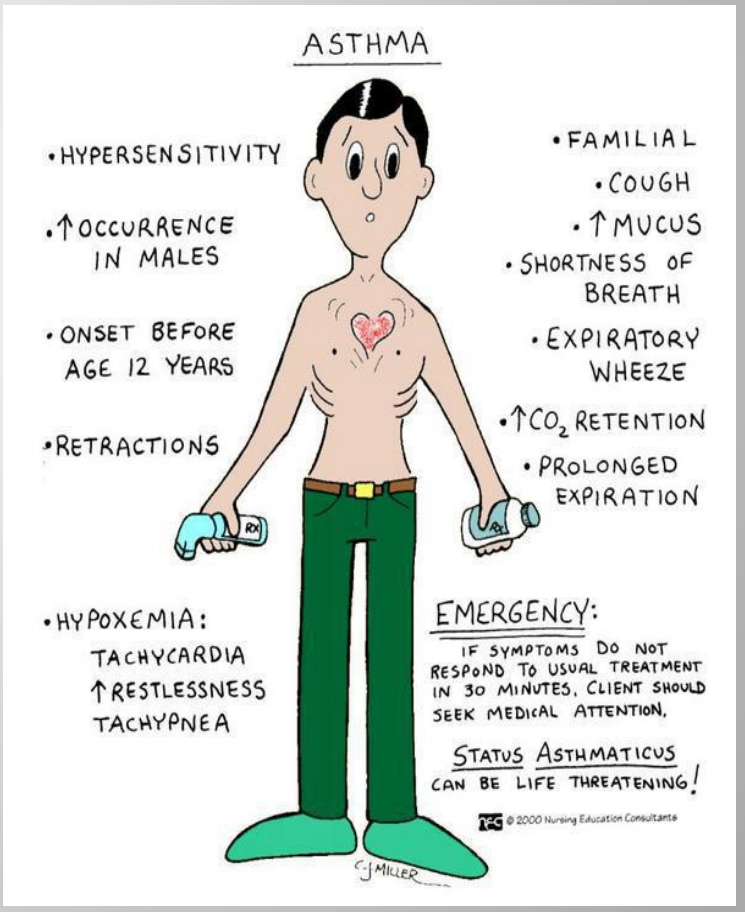
Symptoms :

Wheezing

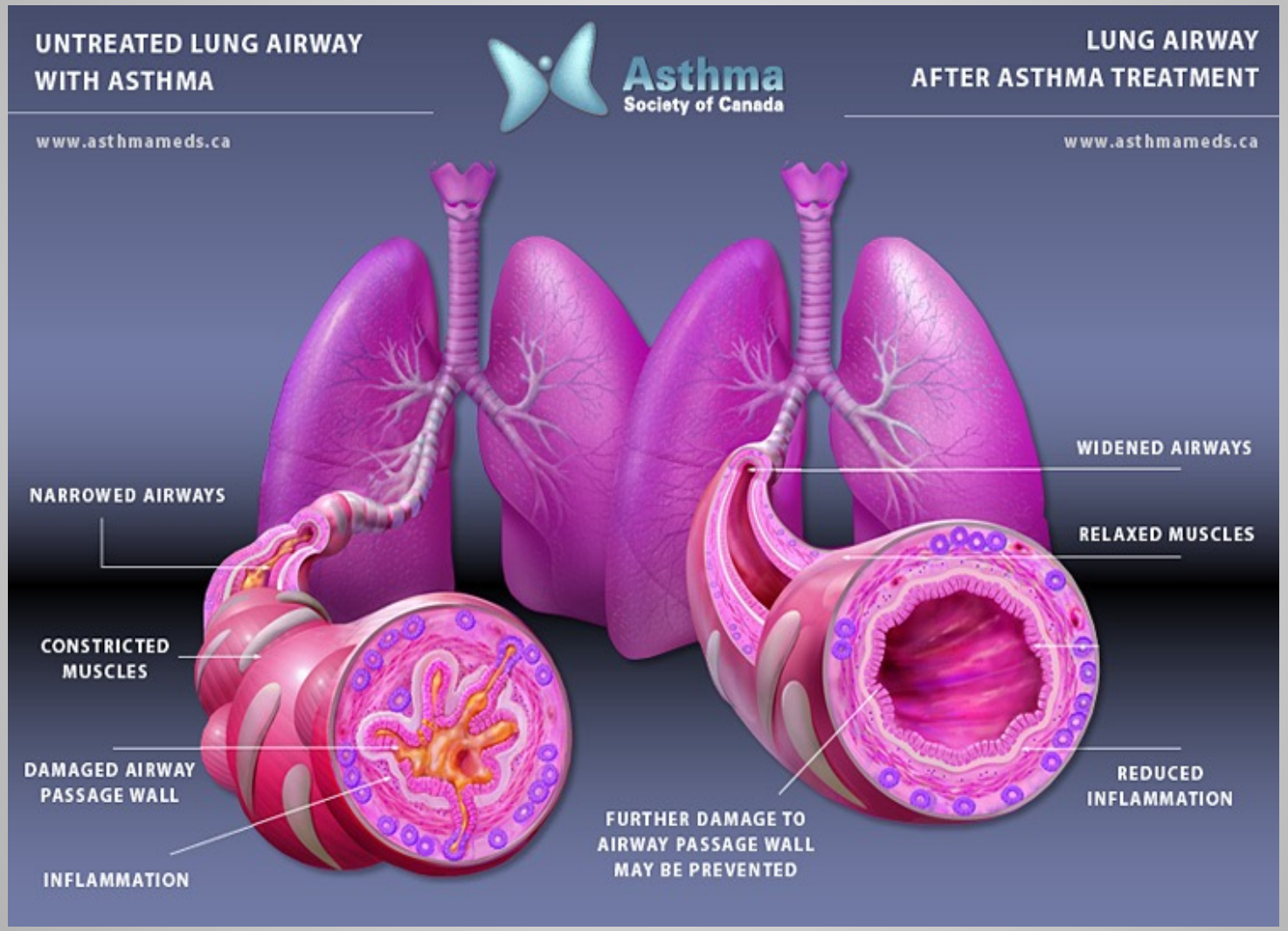
Breathlessness

Persistent cough

Chest tightness



Airway obstruction in Asthma



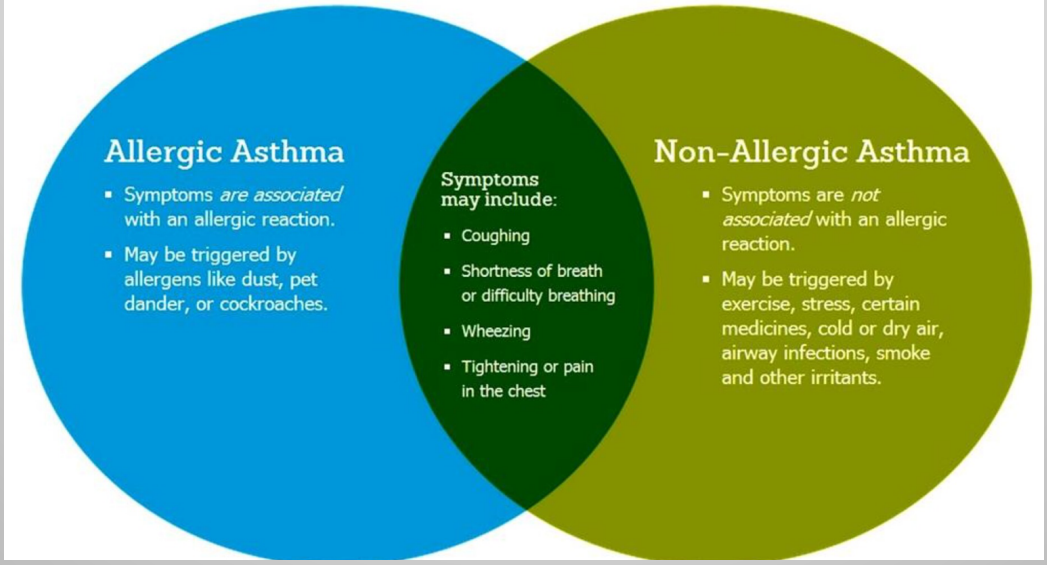
Classification of Asthma

Extrinsic (atopic)

Atopy: genetic tendency to develop allergy

Intrinsic (non-atopic)

Is not caused by exposure to an allergen



ATOPIC VS NON-ATOPIC ASTHMA

	EXTRINSIC (ATOPIC)	INTRINSIC (NON-ATOPIC)
SKIN TEST	Positive	Negative
FAMILY HISTORY	Associated with family history of allergy	No history of allegry
NOTES	• 60 - 90% Children • 50% Adults • Approximately 75 - 85% of patients have positive skin test to various allergens • ↑ serum IgE Levels	• 10 – 33% of asthmatic patients • More sever than Atopic • Normal serum IgE levels • Occurs during adulthood

Role of allergen in asthma

- What is an allergen?

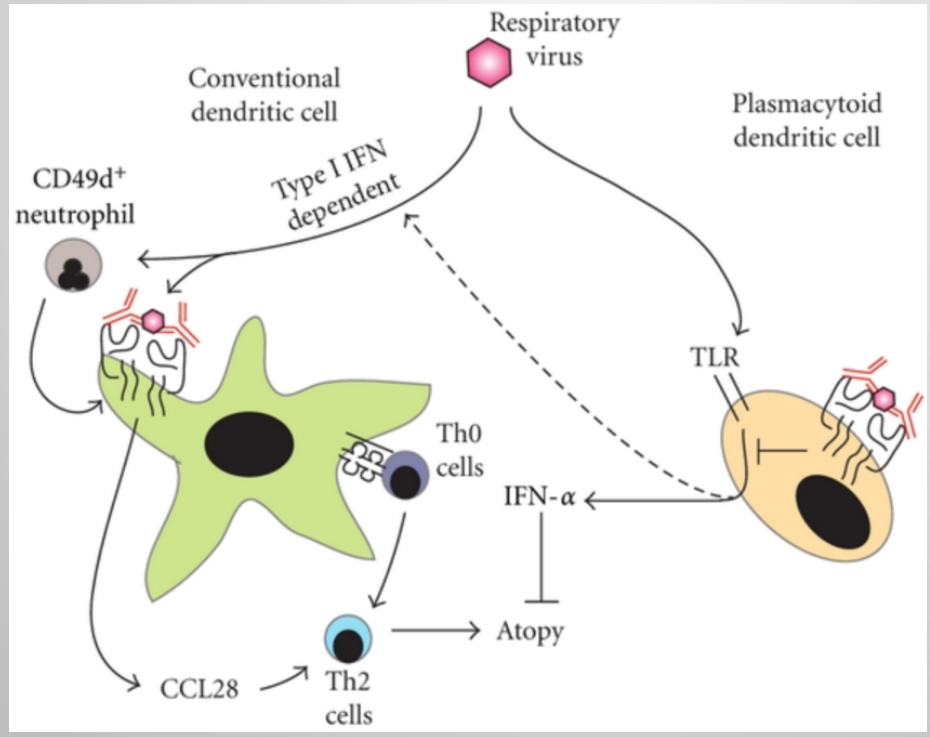
Is an antigen that triggers an allergic reaction, it's the main cause of hypersensitivity type 1 (allergy).
In bronchi asthma it's a hypersensitivity type I

- Allergen sensitization is linked to the risk of developing asthma

Antigen presenting cells (APCs) in the lung:

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

respiratory tract myeloid DCs (mDCs)	• help in the development of asthma symptoms.
plasmacytoid DCs (pDCs)	• aid in respiratory tolerance to allergens.



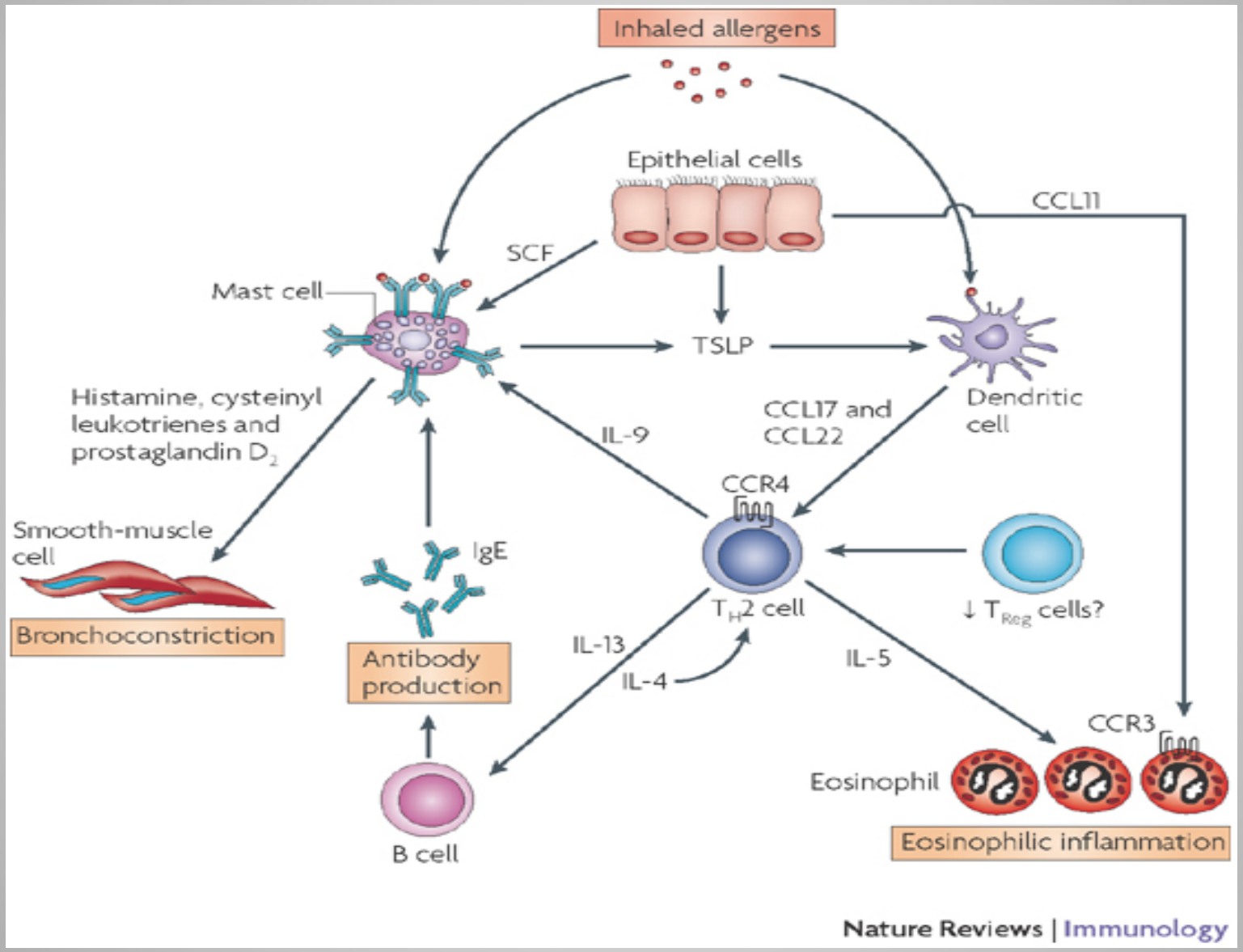
In susceptible individuals (predisposed individuals)

- First encounter with allergens activate B-cells to produce IgE (allergic sensitization)

Subsequently : Inhaled allergens activate submucosal mast cells in the lower airways

Mediators are released within seconds causing:

1. Bronchoconstriction
2. Influx (Recruitment) of eosinophils& other inflammatory cells


Inhaled allergens
Epithelial cells
CCL11
SCF
Mast cell
TSLP
Dendritic cell
Histamine, cysteinyl leukotrienes and prostaglandin D_2
IL-9
CCL17 and CCL22
CCR4
Smooth-muscle cell
IgE
T_H2 cell
↓ T_{Reg} cells?
Bronchoconstriction
Antibody production
IL-13
IL-4
IL-5
CCR3
Eosinophil
B cell
Eosinophilic inflammation
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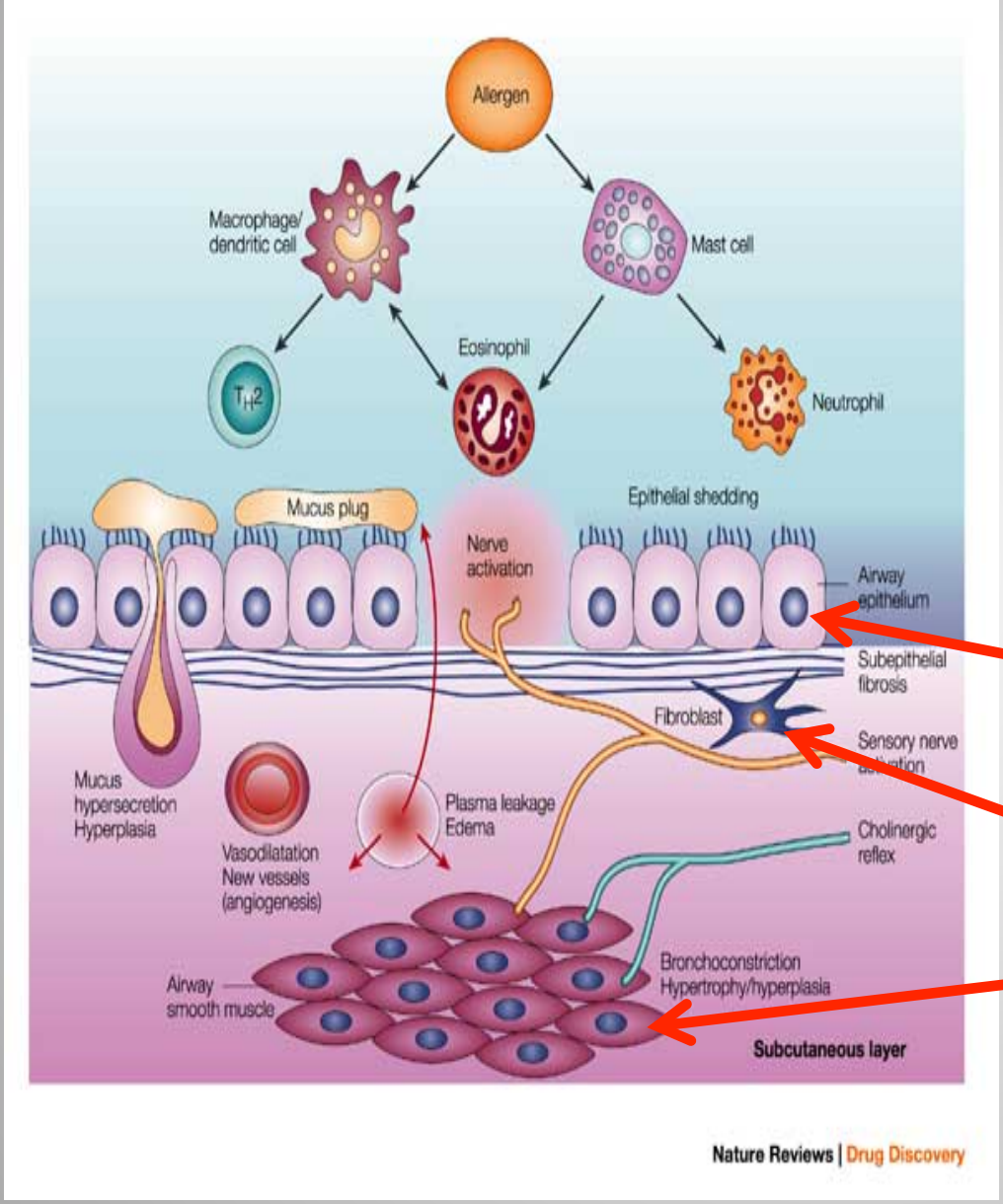
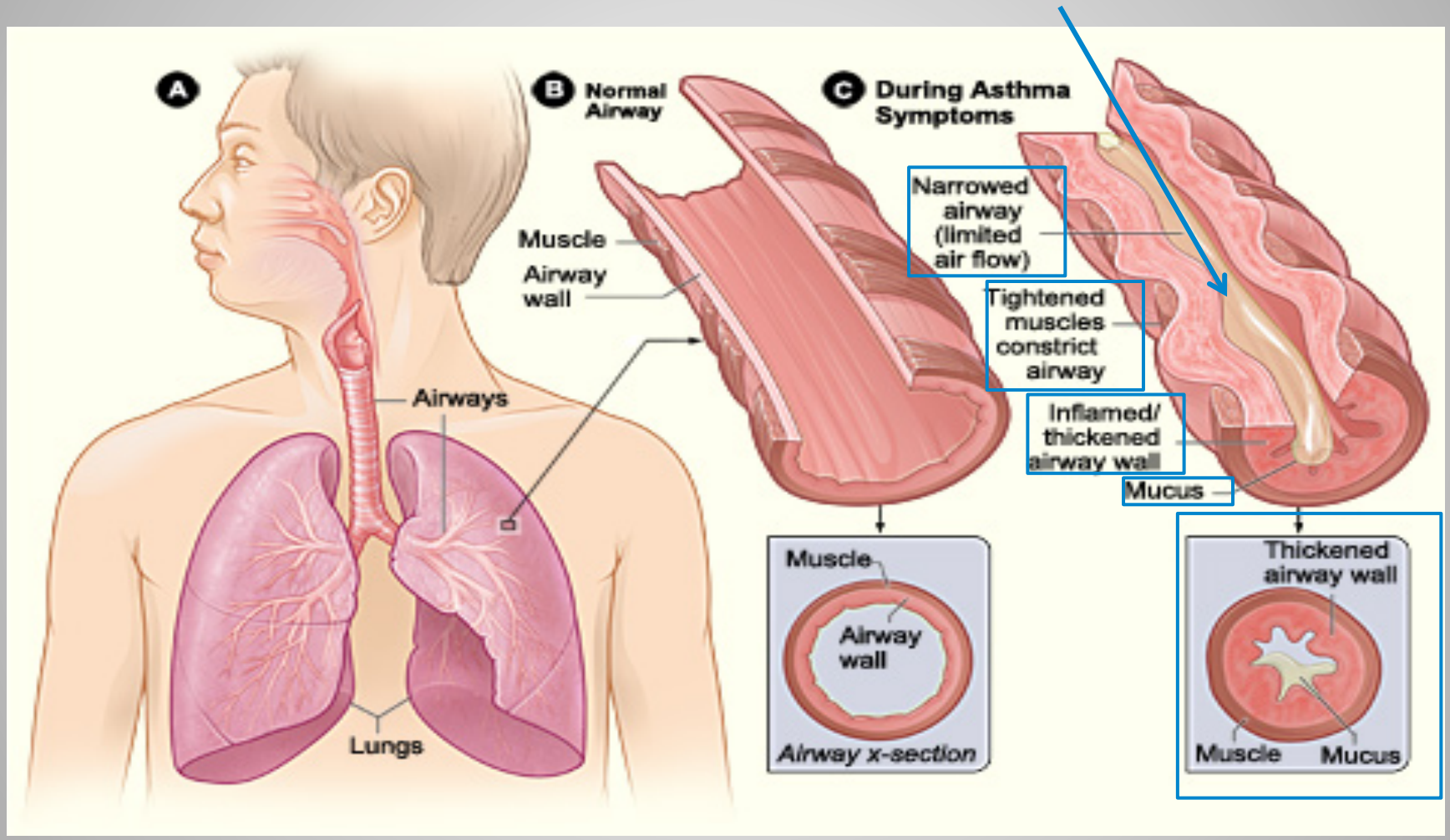


Asthma results from complex interactions among the inflammatory cells that involve:

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

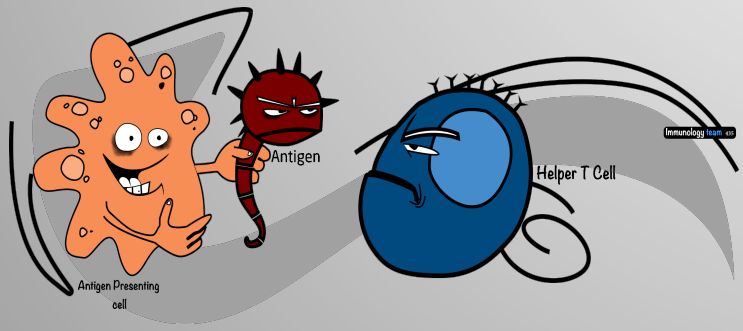
Factors contributing to airflow obstruction leading to difficulty in breathing include:



Video: Dealing with Asthma and Allergies Animations

Response to allergen occures in two phases:

Early Allergic Response	Late Allergic Response
Occurs within minutes	Appears 4 – 10 hours later
Manifests clinically as: • Bronchial constriction • Airway edema	Results from infiltration by inflammatory cells
Mucus Plugging is reversible	Activates lymphocytes and eosinophils
Reversible and Responds to bronchodilators	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

IL-9:

Associated with bronchial hyper-responsiveness

In mice it increases:

Lung eosinophilia

Serum IgE levels

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.

Production of eosinophils is inhibited by IL-10

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 hyper-secretion.

3.Induces sub-epithelial fibrosis.

Role of regulatory T – cells:

Regulatory T cells suppress the effector mechanisms that cause asthmatic symptoms.

Asthmatics may lack functional regulatory T cells that can inhibit an asthmatic response .

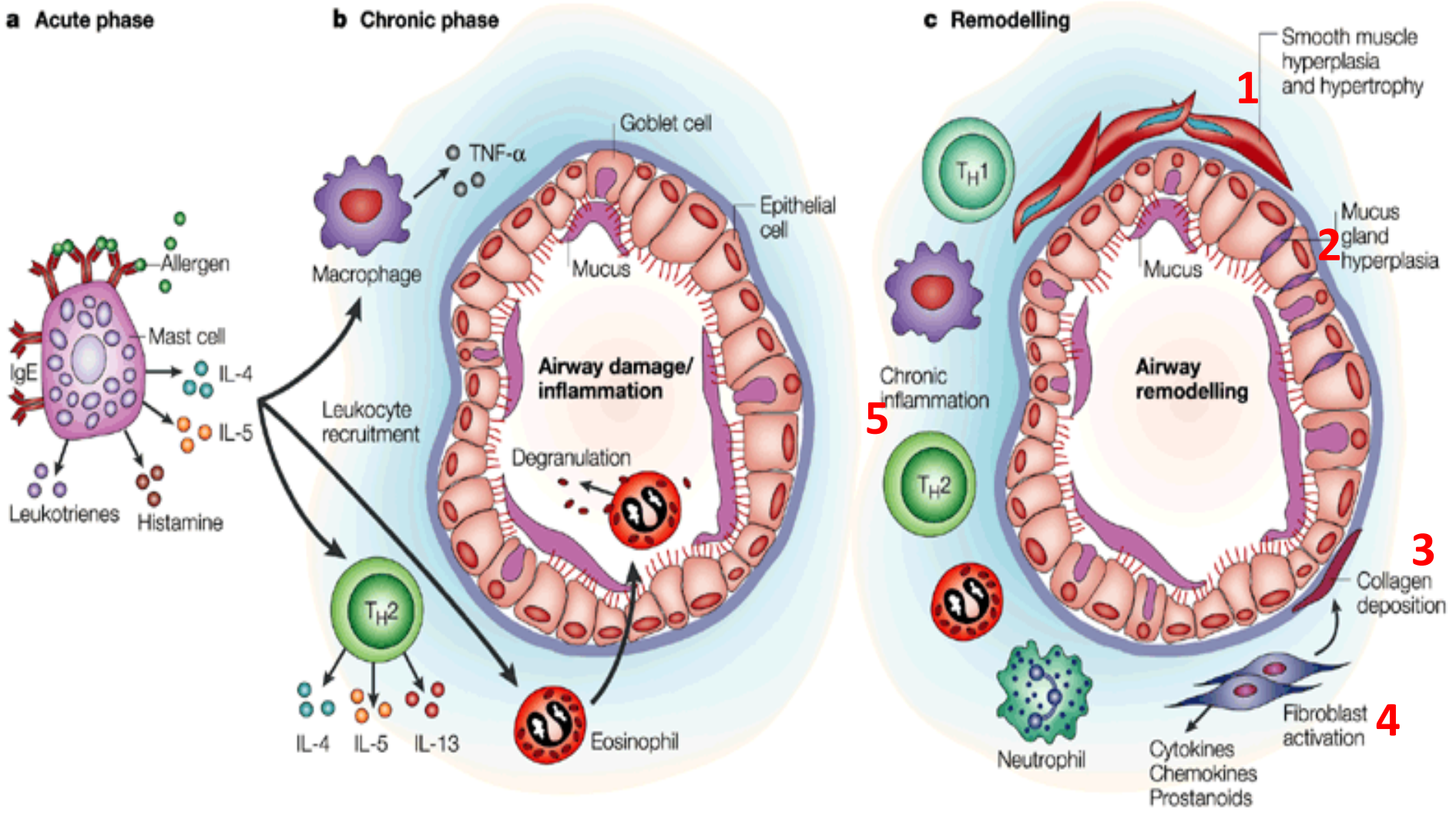
Products of the inflammatory cells act on :

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

and cause :

Airway Remodeling

Airway remodeling refers to:



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Inflammatory cells & their mediators → Airway inflammation → Increased bronchial reactivity; Airway remodeling

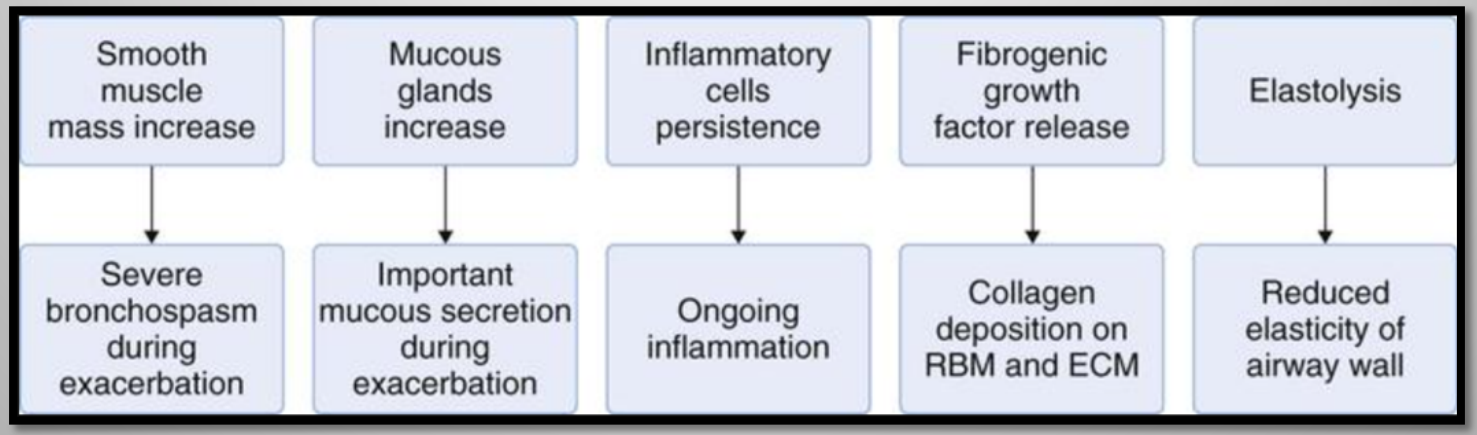
Outcome of increased airway reactivity:

Predispose patients to develop asthma attacks on exposure to non-specific irritants:

1. Chemical irritants
2. Smoke & strong perfumes
3. Sulfur 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



"MCQs"

1-Asthma is a clinical syndrome characterized by irreversible airway obstruction:
A: T B: F

2-In skin test the result of intrinsic asthma is:
A: Negative B: Positive

3- Serum IgE levels are usually abnormal in:
A- intrinsic asthma .
B- extrinsic asthma .
C- non atopic asthma .

4-which one of the following Stimulates mucus hyper-secretion:
A: IL-4 B: IL-6 C: IL-13

5-Eosinophils initiate asthmatic symptoms by :
A-release histamine.
B-tissue damage.
C-bronchodilation.

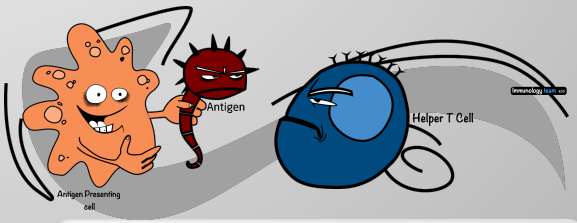
6-Production of eosinophils is inhibited by:
A: IL9 B: IL10 C: IL13

7- Airway remodeling results in irreversible airway obstruction in some asthma patients:
A: T B: F

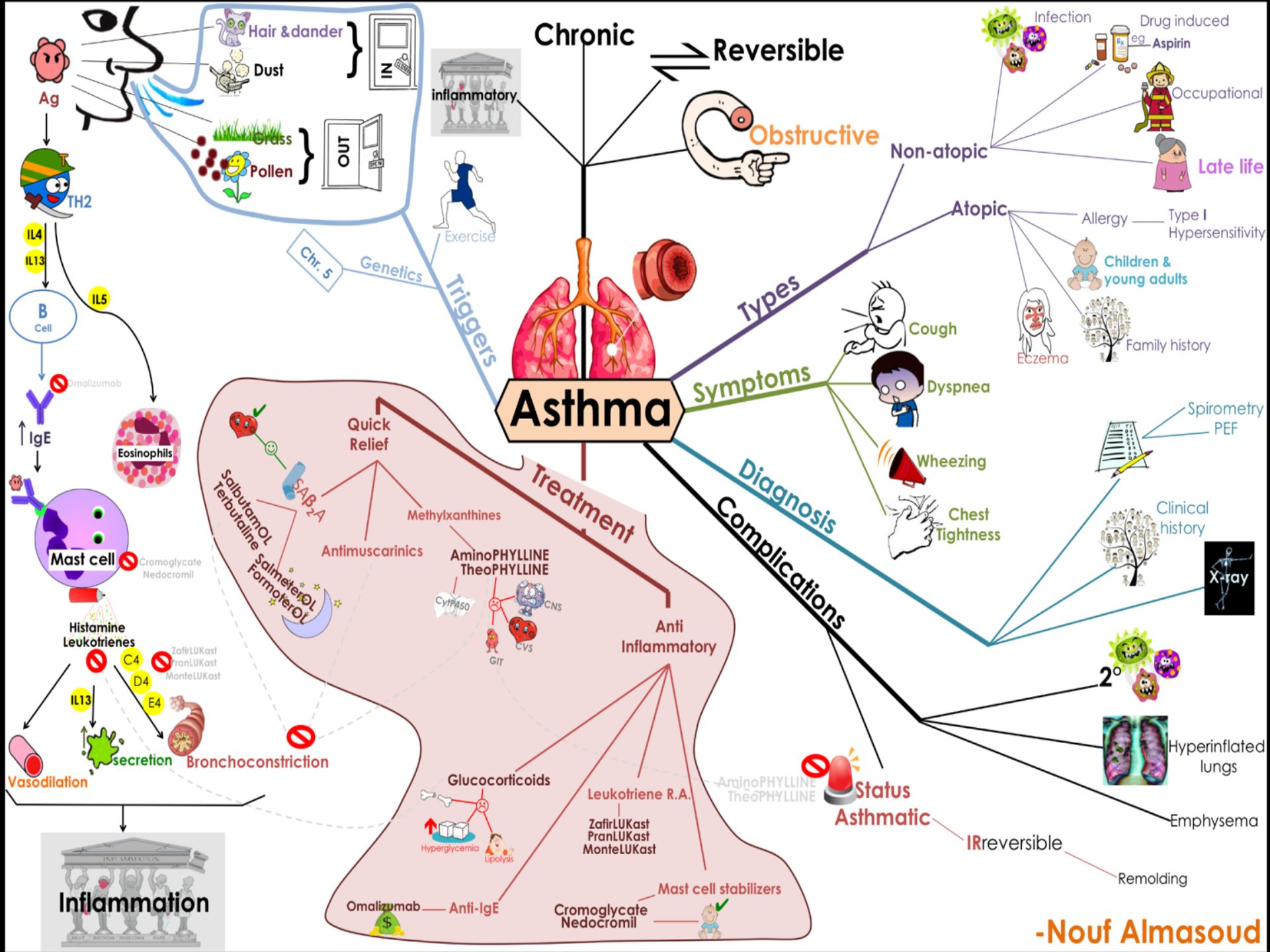
8- which phase of asthma results from inflammatory cells infiltration:
A: Early allergic response
B: Late allergic response

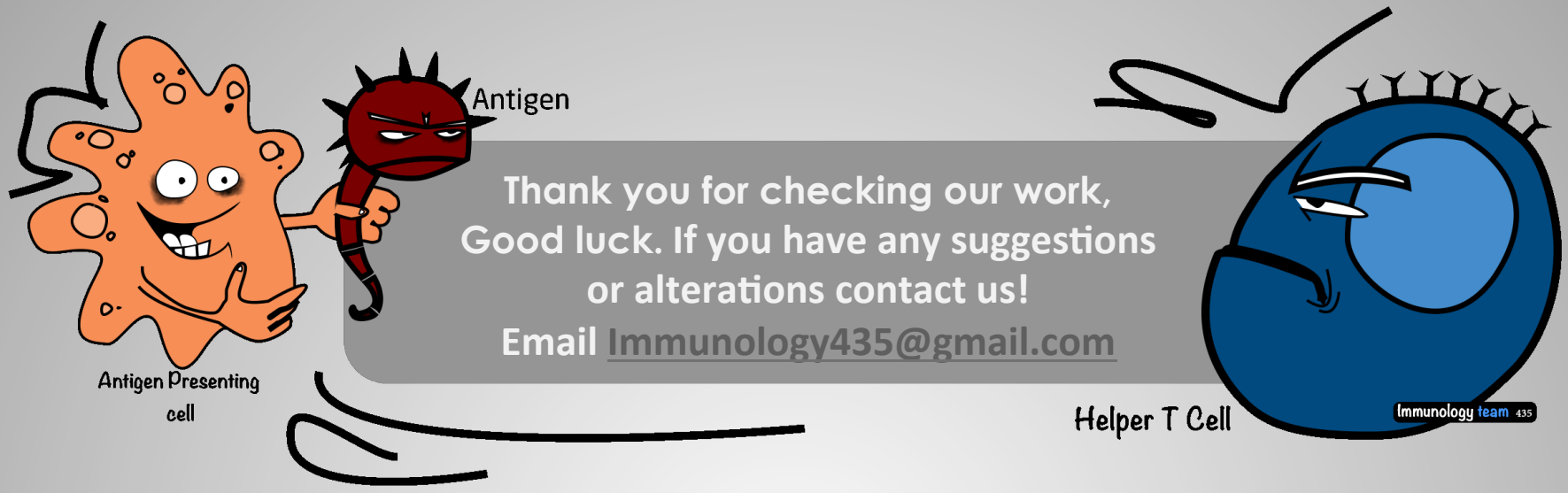
9- Plasmacytoid Dendritic Cells (pDCs) aid in respiratory tolerance to allergens.
A: T B: F

10- Asthmatics
A: have increased functional regulatory T cells
B: lack regulatory T cells
C: lack functional regulatory T cells



1-B 2-A 3-B 4-C 5-B 6-B 7-A 8-B 9-A


Asthma
Chronic
Reversible
inflammatory
Obstructive
Triggers
Hair &dander
Dust
Grass
Pollen
IN
OUT
Ag
TH2
IL4
IL13
IL5
B Cell
Omalizumab
IgE
Eosinophils
Mast cell
Cromoglycate
Nedocromil
Histamine
Leukotrienes
C4
D4
E4
ZafirLUKast
PranLUKast
MonteLUKast
IL13
secretion
Bronchoconstriction
Vasodilation
Inflammation
Exercise
Chr. 5
Genetics
Types
Non-atopic
Infection
Drug induced
eg Aspirin
Occupational
Late life
Atopic
Allergy
Type I Hypersensitivity
Children & young adults
Eczema
Family history
Symptoms
Cough
Dyspnea
Wheezing
Chest Tightness
Diagnosis
Spirometry
PEF
Clinical history
X-ray
Complications
2°
Hyperinflated lungs
Emphysema
Status Asthmatic
IRreversible
Remolding
Treatment
Quick Relief
SABA
SalbutamOL
Terbutaline
SalmeterOL
FormoterOL
Methylxanthines
Antimuscarinics
AminoPHYLLINE
TheoPHYLLINE
CytP450
CNS
CVS
GIT
Anti Inflammatory
Glucocorticoids
Hyperglycemia
Lipolysis
Leukotriene R.A.
ZafirLUKast
PranLUKast
MonteLUKast
Omalizumab
Anti-IgE
Mast cell stabilizers
Cromoglycate
Nedocromil
-Nouf Almasoud



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Good luck. If you have any suggestions or alterations contact us!
Email Immunology435@gmail.com

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