LECTURE 25

RESPIRATORY IMMUNE DISEASES

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Objectives:

- Identify different categories of immune mediated respiratory diseases.
- Discuss immune mechanisms involved in some respiratory diseases.

Impact of hypersensitivity reactions on respiratory tract .

Hypersensitivity diseases are conditions in which tissue damage is caused by immune responses. They may result from uncontrolled or excessive responses against foreign antigens or from a failure of self-tolerance, in which case they are called autoimmune diseases.

Examples :

- **Bronchial asthma**
- **Allergic rhinitis**
- **Goodpasture disease**
- **Farmer's lung**
- **Tuberculosis**

Classification of Immunologic Diseases

Disease	Type of hypersensitivity	Immune mechanism	Mechanisms of Tissue Injury
Bronchial asthma	**Immediate (type I)**	Activation of Th2 cells resulting in the production of IgE which in turn binds to FcεR on mast cells, basophils and eosinophils	**Immediate reaction** • Degranulation and release of vasoactive amines (ie. histamine) and proteases **Late-phase reaction** • Synthesis and secretion of prostaglandins and leukotrienes • Cytokine-induced inflammation and leukocyte recruitment
Good Pasture syndrome	**Antibody-mediated (type II)**	IgM and IgG against surface (cell surface or extracellular matrix)	**Complement-mediated (cytotoxic)** • Opsonization and enhances phagocytosis • Recruitment and activation of inflammatory cells **Non-cytotoxic** • Change in physiologic behavior of a cell
Farmer's lung	**Immune complex–mediated (type III)**	Deposition of immune complexes comprised of IgM or IgG and soluble antigen	Complement-mediated recruitment and activation of inflammatory cells .
Tuberculosis	**Delayed-type hypersensitivity (type IV)**	Inflammatory cytokines, IFN-γ and IL-17, produced by CD4+ Th1 and Th17 cells, respectively.	**Cytokine-mediated tissue damage** • IFN-γ activation of macrophage • IL-17 recruitment and activation of neutrophil **Direct killing** • CTL-mediated cellular death

✓ Bronchial Asthma

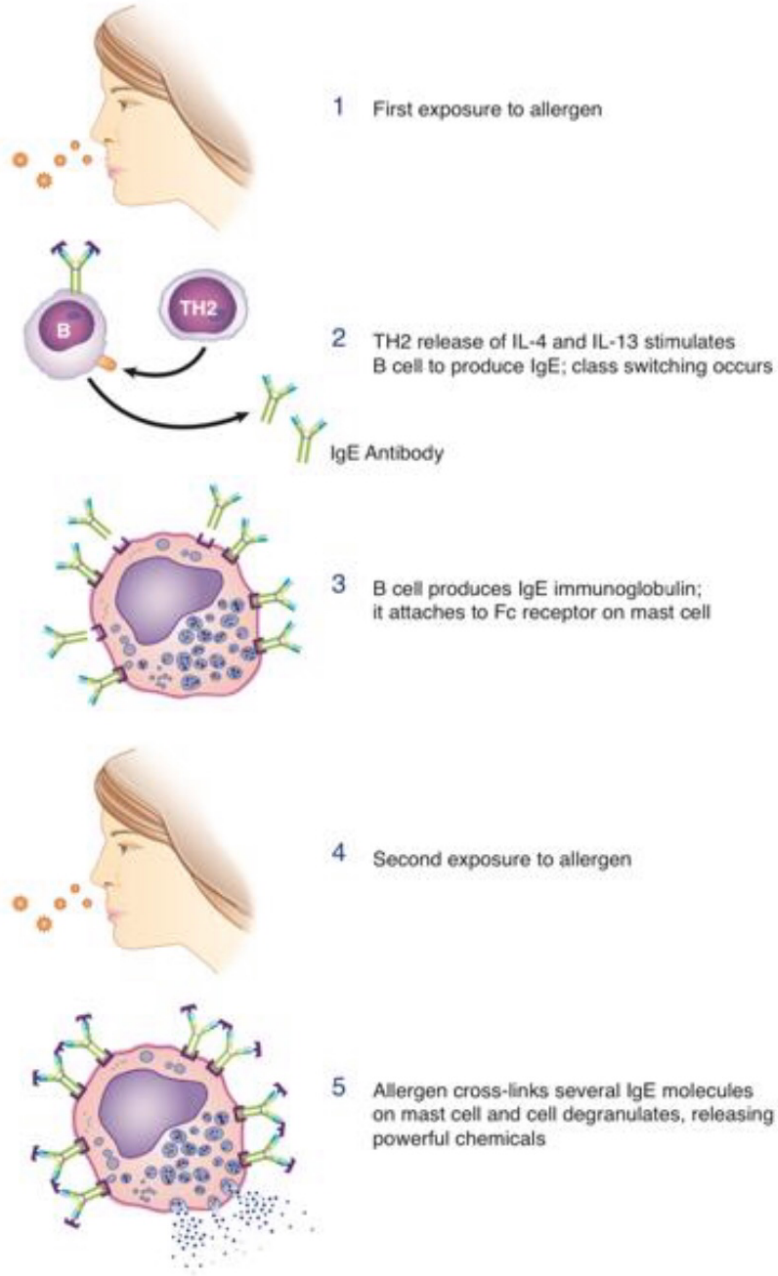
It is a clinical syndrome characterized by:

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

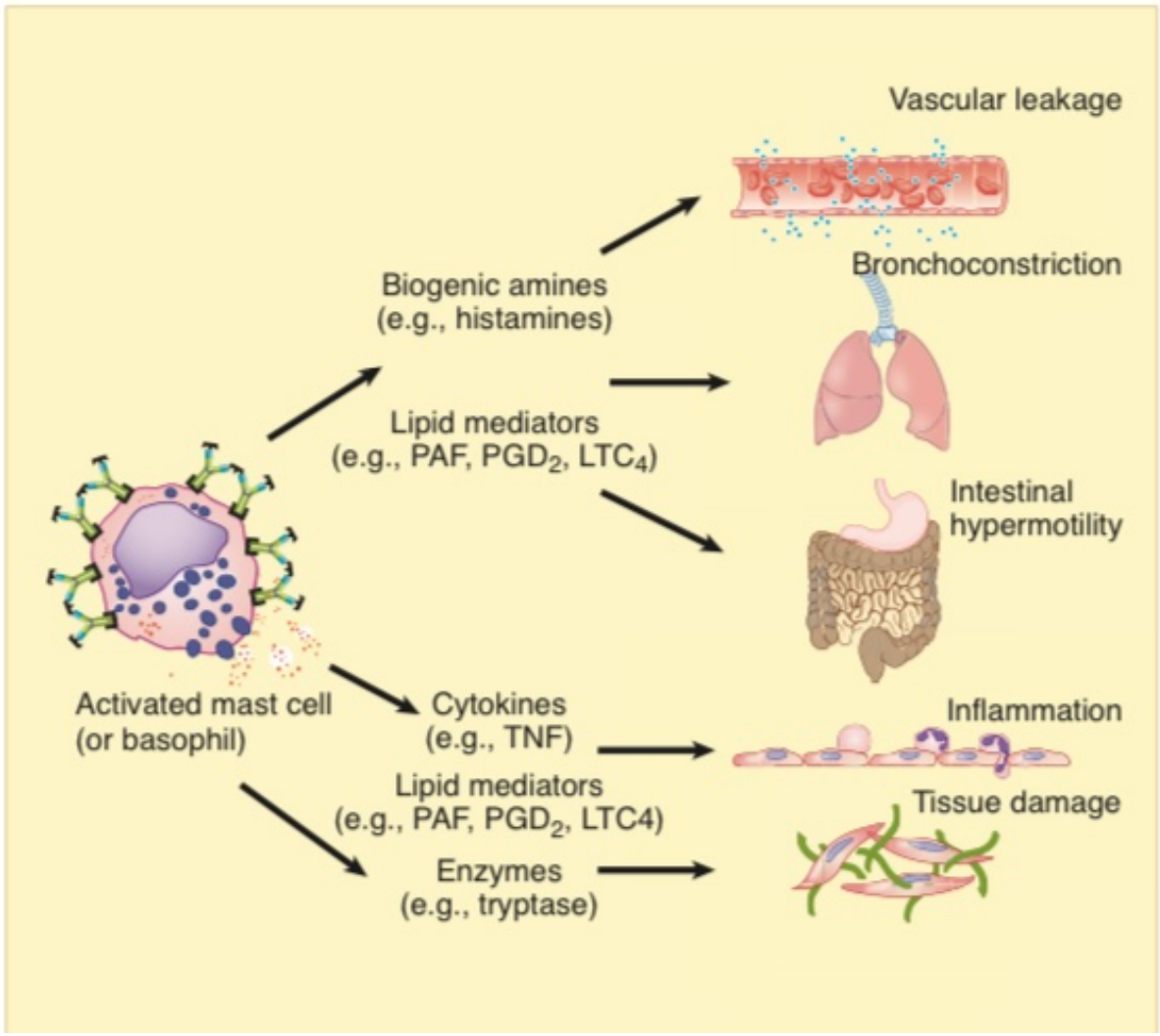
TYPE I (IMMEDIATE) HYPERSENSITIVITY

is the only type of hypersensitivity mediated by IgE antibodies and mast

cells. It is manifested within minutes of the reexposure to an antigen. The effector cells of the immediate hypersensitivity reaction are mast cells, basophils, and eosinophils. The soluble substances they release into the site cause the symptoms of the reaction. Approximately 2-4 hours after the immediate response to release of these mediators, a late-phase reaction is mediated by products of the arachidonic acid cascade.



Development of the Immediate Hypersensitivity Reaction



Mediators of Type I Hypersensitivity

✓ Good pasture's syndrome

TYPE II (ANTIBODY-MEDIATED) HYPERSENSITIVITY

Good pasture's syndrome (anti-glomerular basement membrane disease) involves diffuse pulmonary haemorrhage, glomerulonephritis, or both, often presenting simultaneously, in association with circulating antiglomerular basement membrane antibodies.

• The characteristic anti-glomerular basement membrane autoantibodies bind to an endogenous antigen ; type IV collagen, normally present in lung alveoli and kidney glomeruli .

These antibodies can cause tissue damage by 3 main mechanisms:

• Opsonization of cells

• Activation of the complement system which recruit neutrophils and macrophages that cause tissue damage

• Possible binding to normal cellular receptors and interference with their function.

✓ Farmer's lung

TYPE III (IMMUNE COMPLEX) HYPERSENSITIVITY

1. Farmer's lung is **a type of hypersensitivity pneumonitis**, also known as **extrinsic allergic alveolitis,** is an immunologically mediated inflammatory disease of the lung involving the terminal airways. The condition is associated with intense or repeated exposure to inhaled biologic dusts coming from hay dust or mold spores or other agricultural products

2. The classic presentation of farmer's lung results from repeated inhalational exposure to thermophilic Actinomyces species or mold spores occasionally from exposure to various *Aspergillus* species.

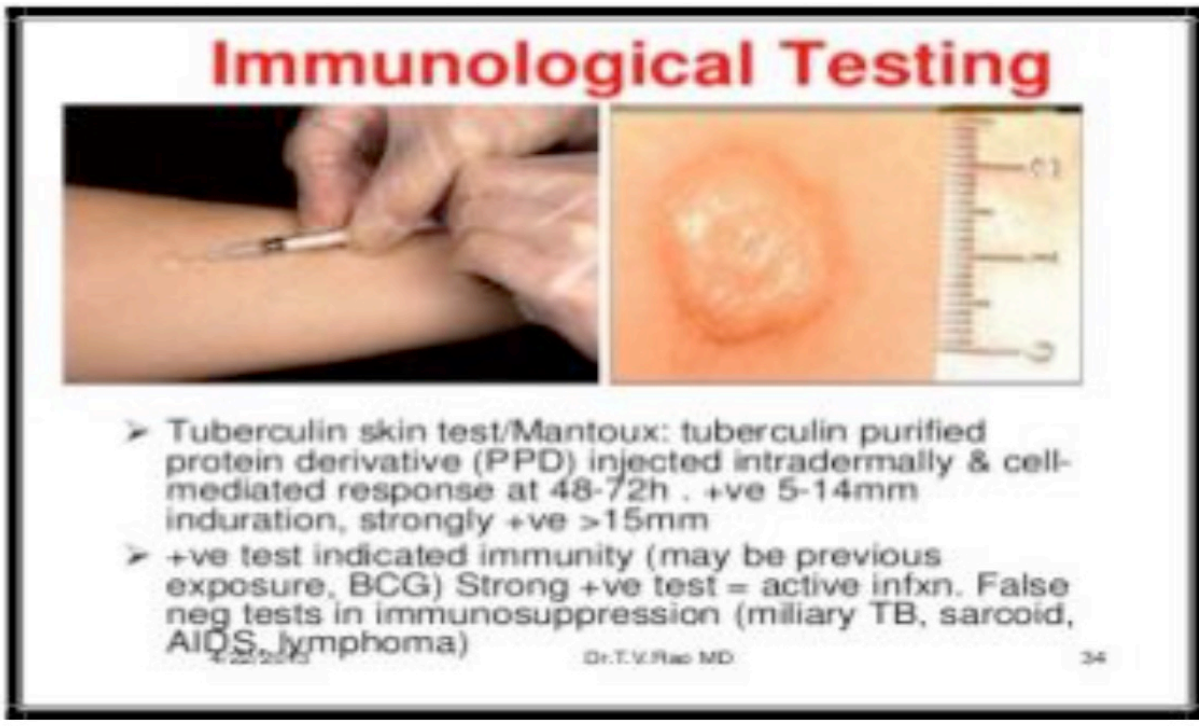
3-Immune complexes are formed in the walls of the lung alveoli . This causes accumulation of fluid, protein and cells in the alveolar wall which slows blood- gas interchange and compromises the function of the lung.

C/P: Acute stage , subacute stage and chronic stage

✓ Tuberculin test

TYPE IV (T-CELL–MEDIATED) HYPERSENSITIVITY

T lymphocytes may cause tissue injury by triggering delayed-type hypersensitivity (DTH) reactions or by directly killing target cells. The reactions are elicited by CD4+ Th1 cells, or CD8+ CTLs, which activate macrophages, recruit neutrophils, and induce inflammation. These T cells may be autoreactive or specific against foreign protein antigens bound to tissues. T-cell-mediated tissue injury is common during the protective immune response against persistent intracellular microbes.



Tuberculin Skin Test

Autoimmune Interstitial Lung Disease

- Interstitial lung disease (ILD) is a category of conditions that cause inflammation and scarring in the lungs. This can lead to difficulty breathing and, eventually, heart failure. Autoimmune ILD is a specific type caused by autoimmune disorders (**connective tissue diseases**), such as lupus, rheumatoid arthritis, and more.

Causes

While there are many different causes for ILD in general, autoimmune ILD is caused specifically by autoimmune diseases. These are conditions in which the body's immune system attacks its own organs. They can include the following:

- Dermatomyositis
- Lupus
- Mixed connective tissue disease
- Polymyositis
- Rheumatoid arthritis
- Sarcoidosis
- Scleroderma
- Sjogren's syndrome

Immunodeficiency of the Respiratory System

Background:

- Different Ig isotypes are dominant in different parts of the lung in the airways: the respiratory surface in the upper and lower airways is covered predominantly with secretory IgA (sIgA) and IgM, while in the alveolar space, IgG is the dominant isotype.

- sIgA prevents bacterial adhesion or neutralizes toxins without causing an inflammatory response.

- IgM activates the complement system, which enhances opsonization of pathogens. Due to its multimeric structure, IgM is highly effective for agglutination, especially of viruses.

- Alveolar IgG originates from the systemic circulation by passive diffusion and effectively prevents bacterial infections such as pneumonia.

- In most patients with primary antibody deficiency (PAD), both systemic IgG and local IgA are absent or dysfunctional.

- Patients with common variable immunodeficiency (CVID) have low IgA and/or low IgM .

- **Reference**

KAPLAN Medical, USMLE Step 1 Lecture Notes 2021, Immunology and Microbiology, p:110, 113, 114, 115, 116, 117, 119 ,122

Question:

Release of which of the following immunoglobulins can cause urticaria, itching, and shortness of breath after a bee sting?

A. IgD

B. IgM

C. IgE

D. IgA