بسم الله الرحمن الرحيم

Physiology

﴿ وَقُل رَّبِّ أَدْخِلْنِي مُدْخَلَ صِدْقٍ وَأَخْرِجْنِي مُخْرَجَ صِدْقٍ وَاجْعَل لِّي مِن لَّدُنكَ سُلْطَانًا نَّصِيرًا ﴾

ربنا آتنا من لدنك رحمة وهيئ لنا من أمرنا رشدًا

MID | Lecture 7

Allergy and Immunity (Pt.2)

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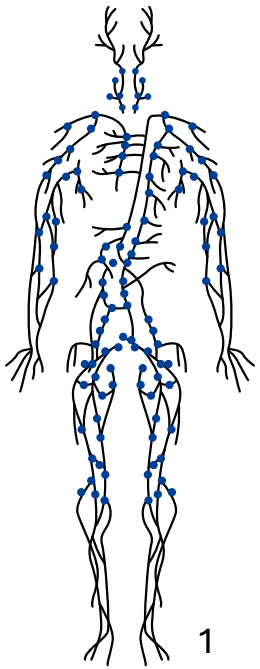


T cell activation

(Important for T cell activation)

- Binds to cognate antigen presented by antigen-presenting cell.
- After activation, the **first** response is rapid expansion of **T helper (CD4) cells**.
- T helper cells produce cytokines that stimulate the whole immune system.
- Drives expansion of both T helper (CD4) and cytotoxic (CD8) T cells, CD8 plays an important role in the destruction of the pathogen.
- Both types of cells also generate clonal memory T cells, which are retained for future exposure to the same antigen. This enables a faster and more robust response in the future.

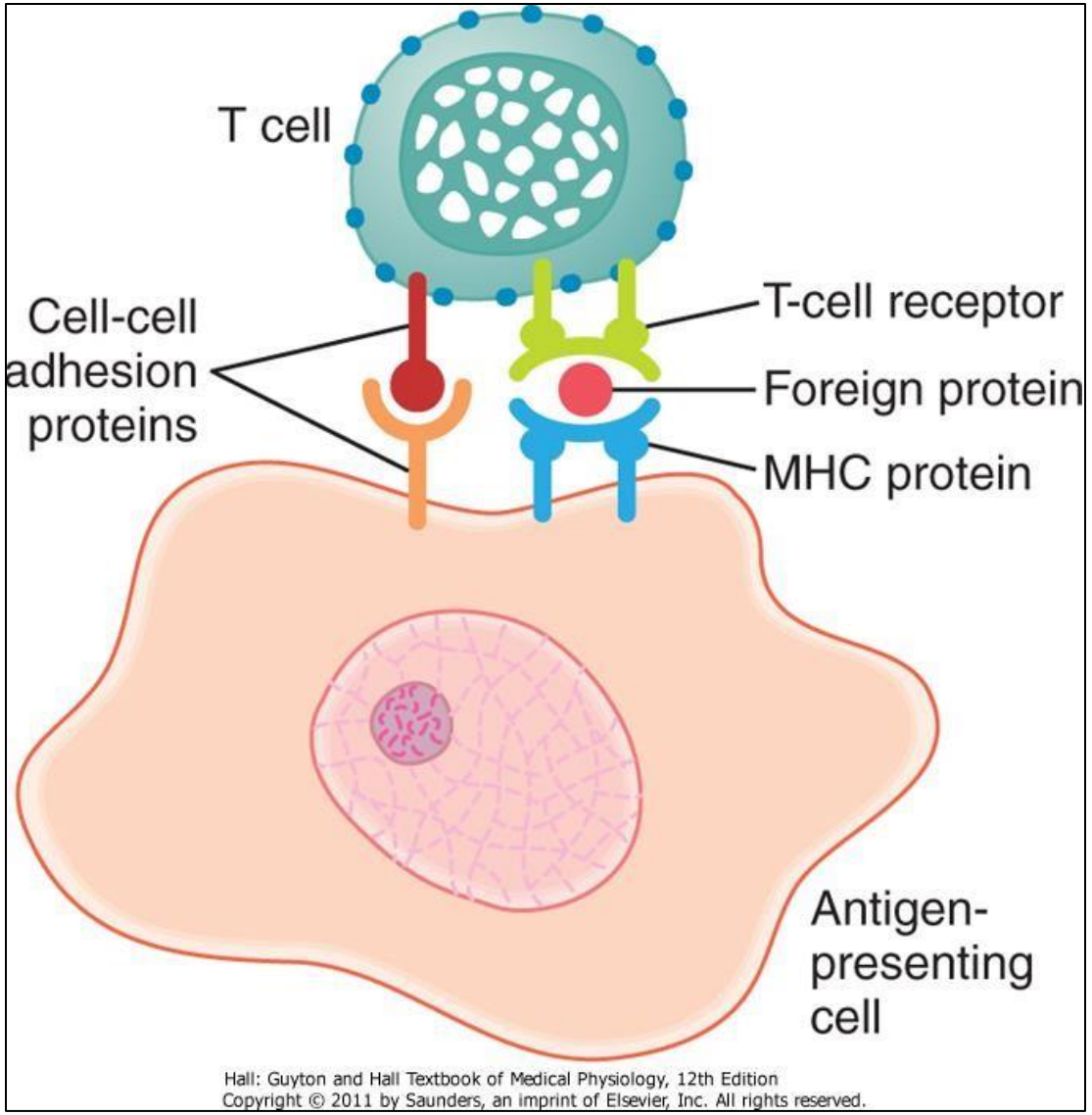
MHC Proteins

- **B cell** surface and secreted antibodies **recognize intact antigen.**
- During antigen presentation and **T cell** activation, MHC proteins play a major role, as T cells **do not recognize free** antigens. Instead, T cells **only recognize** antigen fragments that are **presented by MHC molecules** of antigen presenting cells…
  - macrophages
  - B lymphocytes
  - dendritic cells

Antigen Presentation

- As shown in the figure, the **MHC** protein is an **integral** plasma membrane protein on the **antigen-presenting cell**, that **binds** to the **foreign antigen**. This binding **allows recognition** by T cell receptors (**TCRs**), which specifically interact with the presented antigen.

- In addition, cell-to-cell adhesion proteins help strengthen and prolong this contact, facilitating effective T cell activation.



MHC Molecules

- Encoded by the Major Histocompatibility Complex:
  - MHC I – Present to cytotoxic T cells (CD8).
  - MHC II – Present to helper T cells (CD4).

- Antigen in the context of MHC is recognized by as many as 100,000 T cell receptors per cell.

Helper (CD4) T cells

It is the **dominant** type of T cells

- ~ 75% of all T cells.
- **Regulate functions** of other immunologic cells by producing cytokines…
  - Interleukin (IL-) 2, 3, 4, 5, 6, GM-CSF, Interferon-gamma.

There are different **subsets** of T helper cells each of these **subsets has major lymphokines** that are produced that are **involved in different immune reactions:**

Table 35-1 Subsets of T-helper Cells

The doctor went over the underlined notes ;)

	T_H1	T_H2	T_H17
Lymphokines that induce subset	IFN-γ, IL-12	Il-4	TGF-β, Il-1, Il-6, IL-23
Major lymphokines/ factors produced	IFN-γ, Il-2 TNF-α, GM-CSF	IL-4, IL-5, Il-6, IL-10, Il-13	Il-17, IL-22
Major immune reactions	Macrophage activation, Stimulate IgG antibody production	Stimulate IgE production, Activation of mast cells and eosinophils	Recruitment of neutrophils and monocytes

+ allergic reactions

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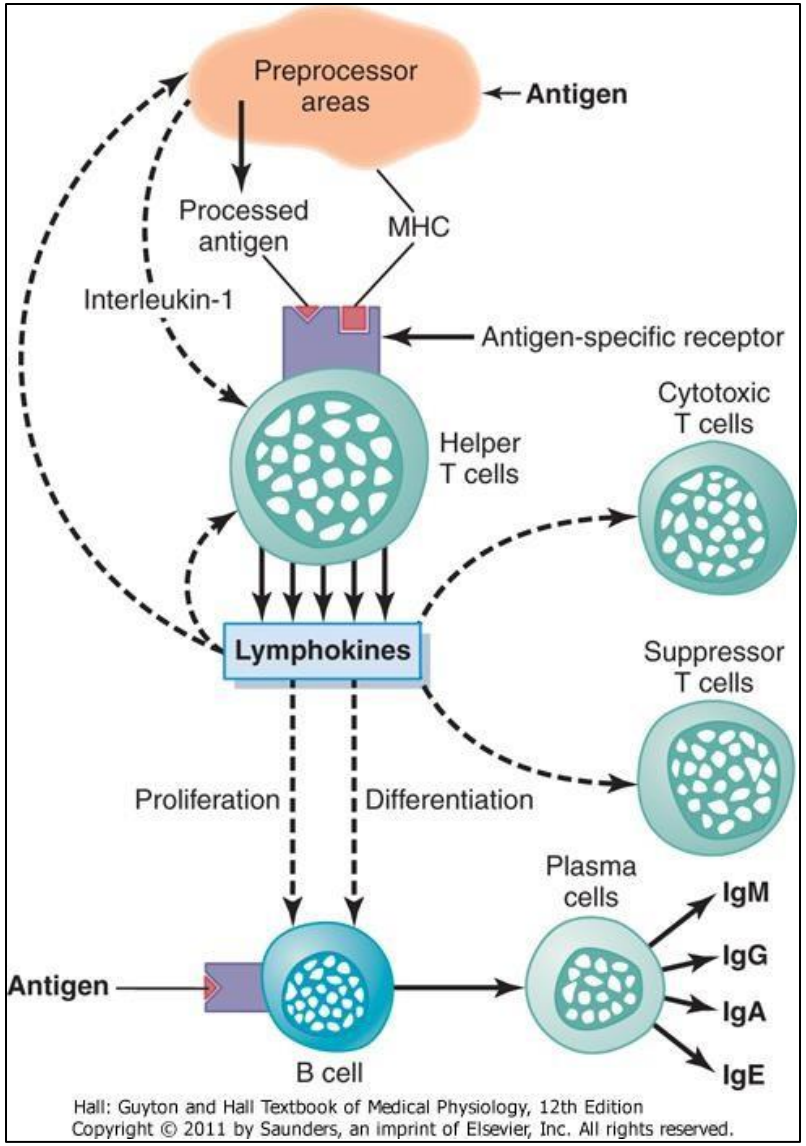
T cell help for immune response

T helper cells play a crucial role in several **positive feedback mechanisms** for cytotoxic T cells, suppressor T cells, macrophages, and their own self-regulation.

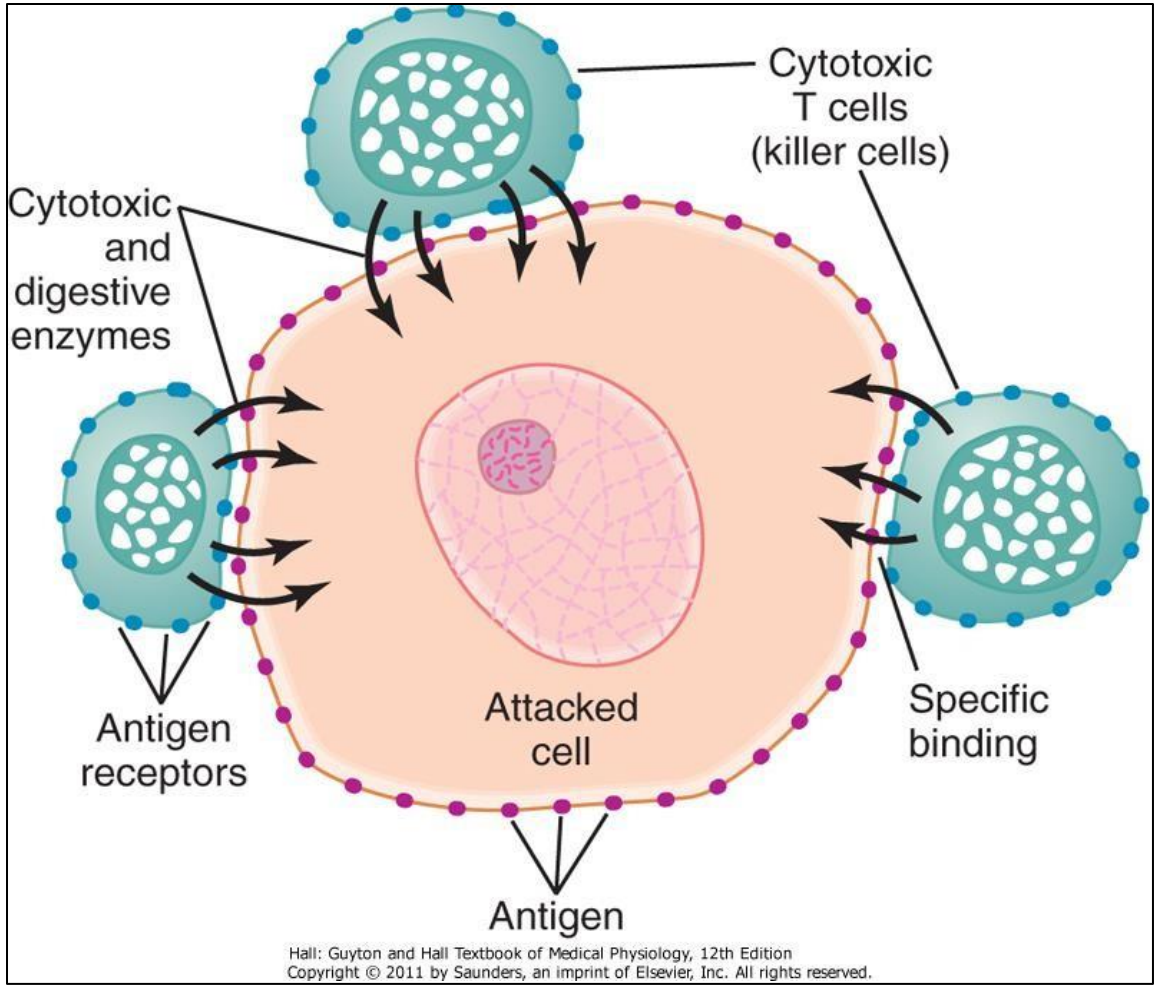
- Positive feedback for helper T cells (IL-2).
- Stimulation of cytotoxic T cells (IL-2, other cytokines).
- Stimulation of B cells (IL- 4, 5, 6 (BCGFs)).
- Macrophage accumulation, since T helper cells promote their attachment and slow their movement, leading to their accumulation at the site of infection, activation, enhanced killing, and phagocytosis functions.

BCGFs: B cells growth factors



Killing by cytotoxic T cells

- Virus-infected cells.
  - They directly interact with viral-infected cells, creating pores in the plasma membrane and infusing digestive and destructive substances that lead to the destruction of the infected cell.
- Cancer cells.
- Transplanted organs and tissues.
  - This is the underlying cause of **graft vs host disease**.



The Clinical perspective of Leukocytes and immunity

Clinical Perspective

Leukopenia

Leukopenia is never beneficial, as we know WBCs play a vital role in fighting microorganisms.

- *Leukopenia*, or low white blood cell count, is usually the result of reduced production of cells by the bone marrow.
- It can allow clinically severe infections with organisms that are not usually pathogenic.
- Within two days of bone marrow shutdown mucous membrane **ulcers** or **respiratory infection may occur.**
- **Causes of leukopenia**: radiation, chemical toxins, some medicines.
  Due to damage of the bone marrow cells and having an aplastic effects
- In most cases marrow precursors can reconstitute normal blood cell counts with proper support after the acute phase.

Clinical Perspective

Leukemias

- Uncontrolled production of abnormal immature white blood cells due to a genetic mutation.
- It is characterized by having Clonal proliferation, lineage-specific tumors, often immature cells.
- Leukemias are…
  - Lymphocytic vs. myelogenous (depending on the origin of those tumor cells).
  - Acute vs. chronic (sometimes up to 10-20 years).
- Leukemias with partially differentiated cells may be classified as the type that is more similar to neutrophilic, eosinophilic, basophilic, or monocytic leukemias.

Clinical Perspective

Clinical Effects of Leukemias

- Resulting from the overgrowth of leukemic cells in **abnormal** sites.
- **Invasion** of bone from the marrow, with pathologic **fractures**.
- Eventually **spreads** to vascular and lymphatic "filters"…spleen, lymph nodes, liver, other organs.
- **Replacement** of normal bone marrow, resulting in infection, and bleeding. (due to the decrease in the number of WBCs and platelets).
- **Wasting** because of metabolic demands.

Clinical Perspective

Immunologic Tolerance

- Host defense employs powerful destructive mechanisms.
- These must be directed at pathogens while protecting host tissues from damage. (and that is the function of the Tolerance Mechanism).
- "Tolerance" in acquired immunity is achieved mainly by clonal selection of T cells in the thymus and B cells in the bone marrow
  - clones that bind host antigens with high affinity are induced to undergo apoptosis, and are deleted.
    - The immune system selects only the clones that are reactive against foreign antigens, and that's how it works as a kind of protection for our body's tissues.

Clinical Perspective

Failure of tolerance produces autoimmunity

Such as:

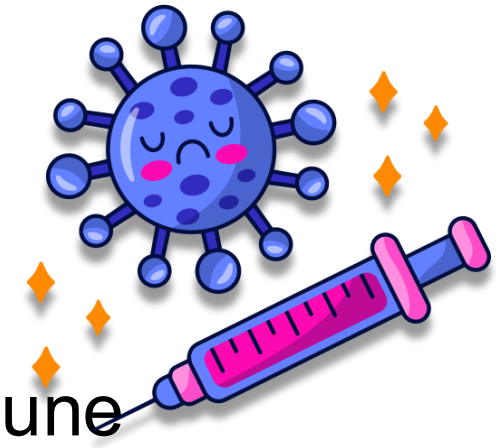
- Rheumatic fever (cross-reactivity with streptococcal antigens).
- Post-streptococcal glomerulonephritis.
- Myasthenia gravis (antibodies to acetylcholine receptors).
- Systemic lupus erythematosis (auto-immunity to multiple tissues).

Clinical Perspective

Immunization

Immunization is a method used to **strengthen** our immune response by **injecting** either **killed** or **attenuated** organisms at short or long intervals, **several times**. This process enhances the immune response, making it stronger and more effective in combating infectious agents.

- Injecting **killed** organisms or their products…
  - typhoid, whooping cough (pertussis), diphtheria, tetanus toxoid.
- Infection with **attenuated** organisms…
  - Smallpox, yellow fever, polio, measles, herpes zoster, other viral diseases.
- Passive immunity…
  - Infusing antibody or activated T cells from an immune individual (antibodies last 2-3 weeks),



Clinical Perspective

Allergy and hypersensitivity

Two main types:

- **T cell** mediated (delayed)…
  - poison ivy (اللبلاب) ,nickel allergies.
  - usually cutaneous; can occur in lungs with airborne antigens.

- **IgE** mediated (immediate)…

IgE-mediated allergic reactions occur when **IgE binds to an antigen**, **activating basophils** or **mast cells**. This causes an **immediate** response and is seen in allergies like eczema and hay fever. Activated cells can bind millions of IgE molecules and release **histamine**, triggering inflammation.

- typical allergies.
- a single mast cell / basophil can bind 500,000 IgE Molecules.

Clinical Perspective

Mast cell / basophil degranulation

Once these cells are activated, they release their granules, which contain the following substances:

- Histamine
- Proteases
- Leukotrienes
- Eosinophil and neutrophil chemotactic factors
- Heparin
- Platelet activating factor

Clinical Perspective

Allergic manifestations

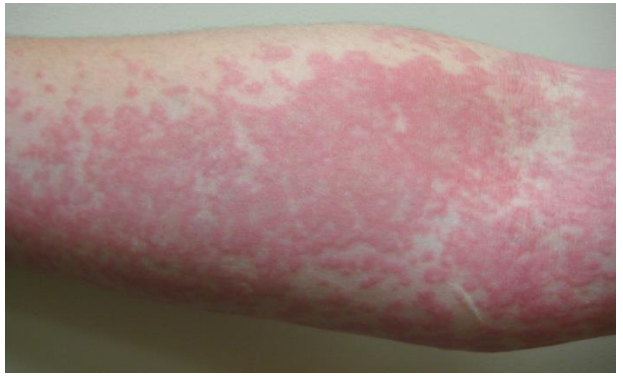
- Anaphylaxis
  - systemic, potentially fatal
  - widespread vasodilatation
  - ↑↑ Capillary permeability, volume loss, contribute to cardiovascular shock, which is a serious condition.
  - Leukotrienes released from activated leukocytes → bronchospasm, wheezing, dyspnea, and shortness of breath.

    Treatment: epinephrine (to provide sympathetic stimulation) and antihistamines.

- Urticaria
  - localized vasodilatation and red flare
  - Increased permeability and swelling (“hives”)

    Treatment: antihistamines

The Hives



Clinical Perspective

Allergic manifestations (cont'd)

- Hay fever
  - histamine mediated
  - Vascular dilatation in the nasal passages causes a runny nose. These sinuses may also become inflamed, along with redness or itchiness of the eyes.
  - leakage of fluid
  - sneezing

    Treatment: Anti-histamines, local corticosteroids (to redness the immune response).

- Asthma
  - mediated largely by leukotrienes.
  - Characterized by sustained bronchospasm.

    Treatment: β_2 agonists (bronchodilators) , inhaled steroids (to reduce airway inflammation), leukotriene receptor blockers; treat upper airway component

{وَاذْكُر رَّبَّكَ فِي نَفْسِكَ تَضَرُّعًا وَخِيفَةً وَدُونَ الْجَهْرِ مِنَ الْقَوْلِ بِالْغُدُوِّ وَالْآصَالِ وَلَا تَكُن مِّنَ الْغَافِلِينَ}

Physiology Quiz 7

Pet the Quiz Cat to
Reveal Your Challenge!

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	Quiz	The quiz cat is having a nap (Link doesn't work)	The quiz cat is ready to challenge you!
V1 → V2			