بسم الله الرحمن الرحيم

Physiology

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

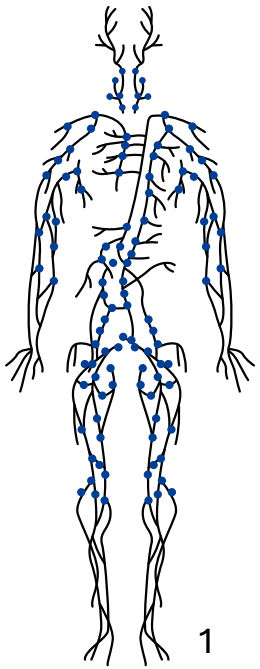
ربنا آتنا من لدنك رحمة وهيئ لنا من أمرنا رشدًا

MID | Lecture 7

Allergy and Immunity (Pt.2)

Written by: Deema Nasrallah
Heba Suliman

Reviewed by: Sara Masadeh



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.

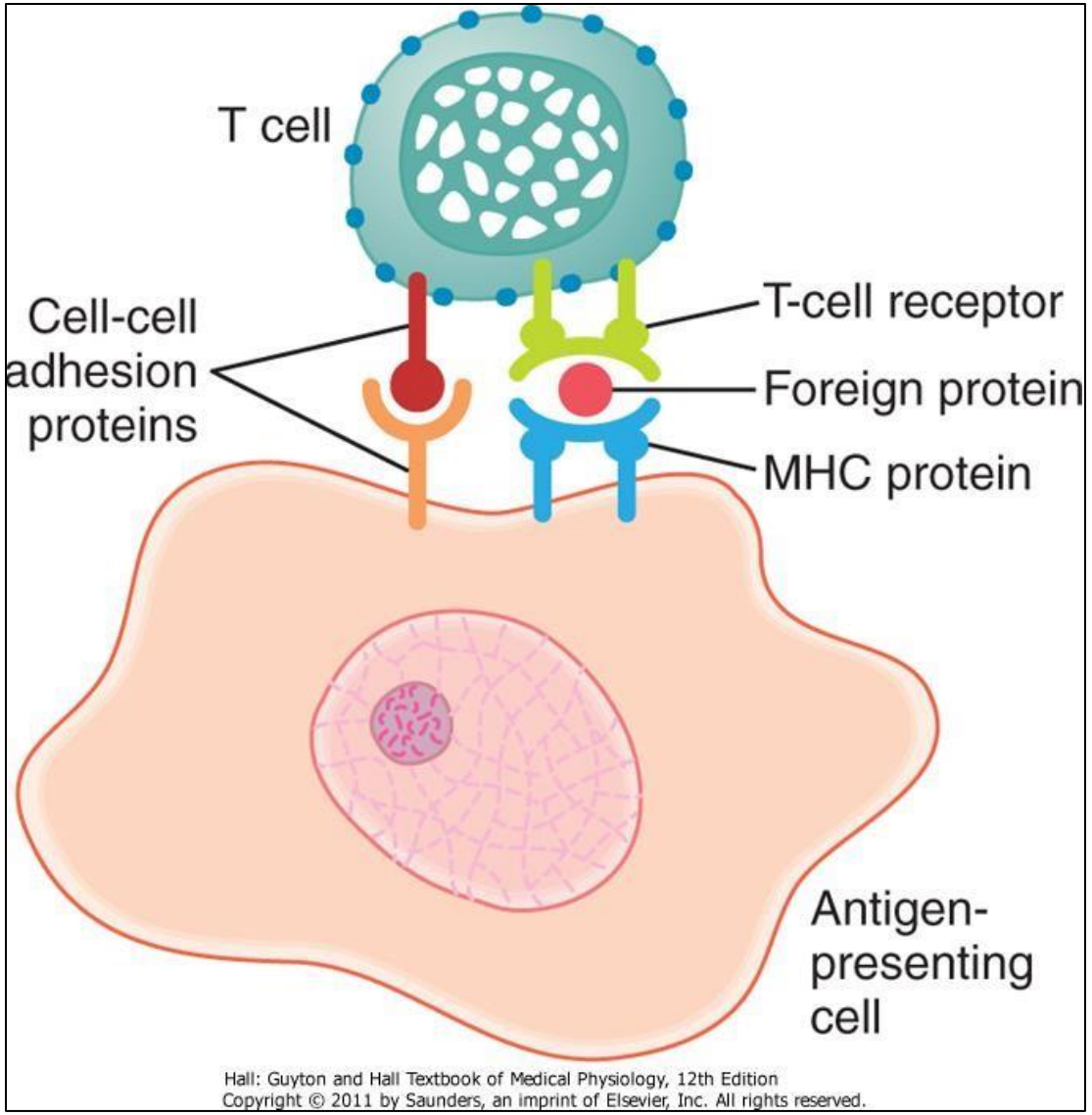
MHC Proteins

- **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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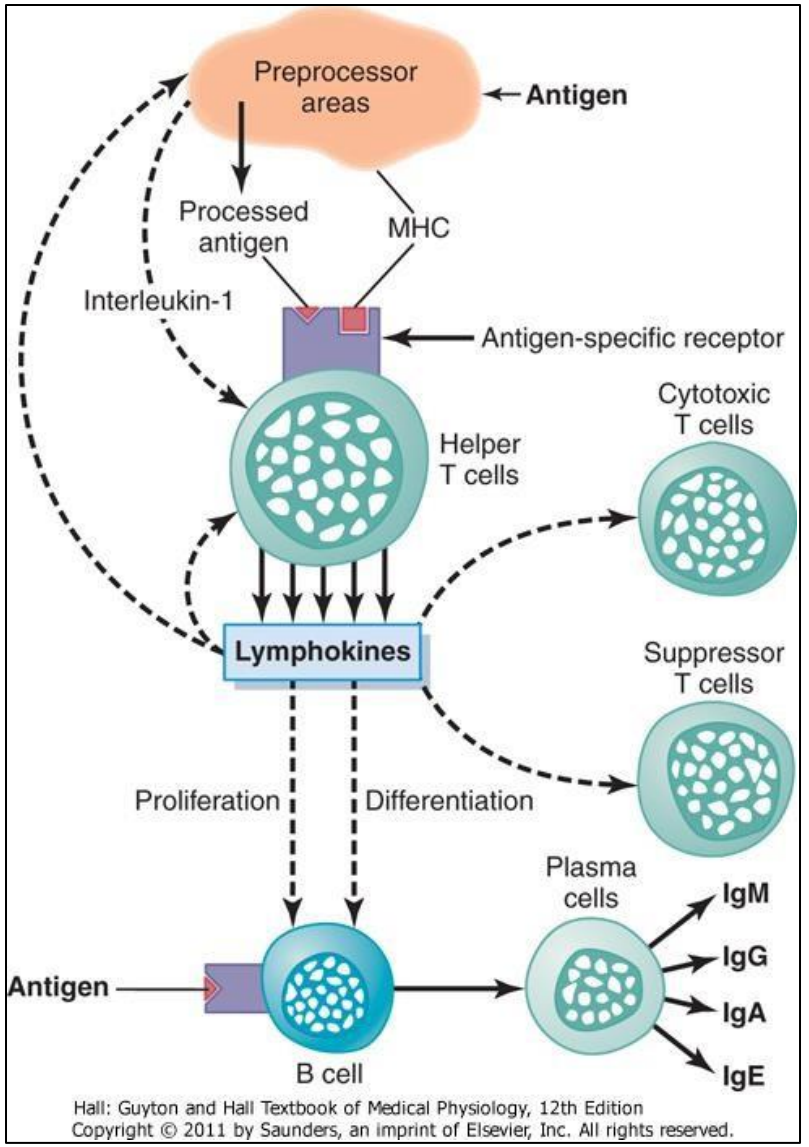
T cell help for immune response

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.

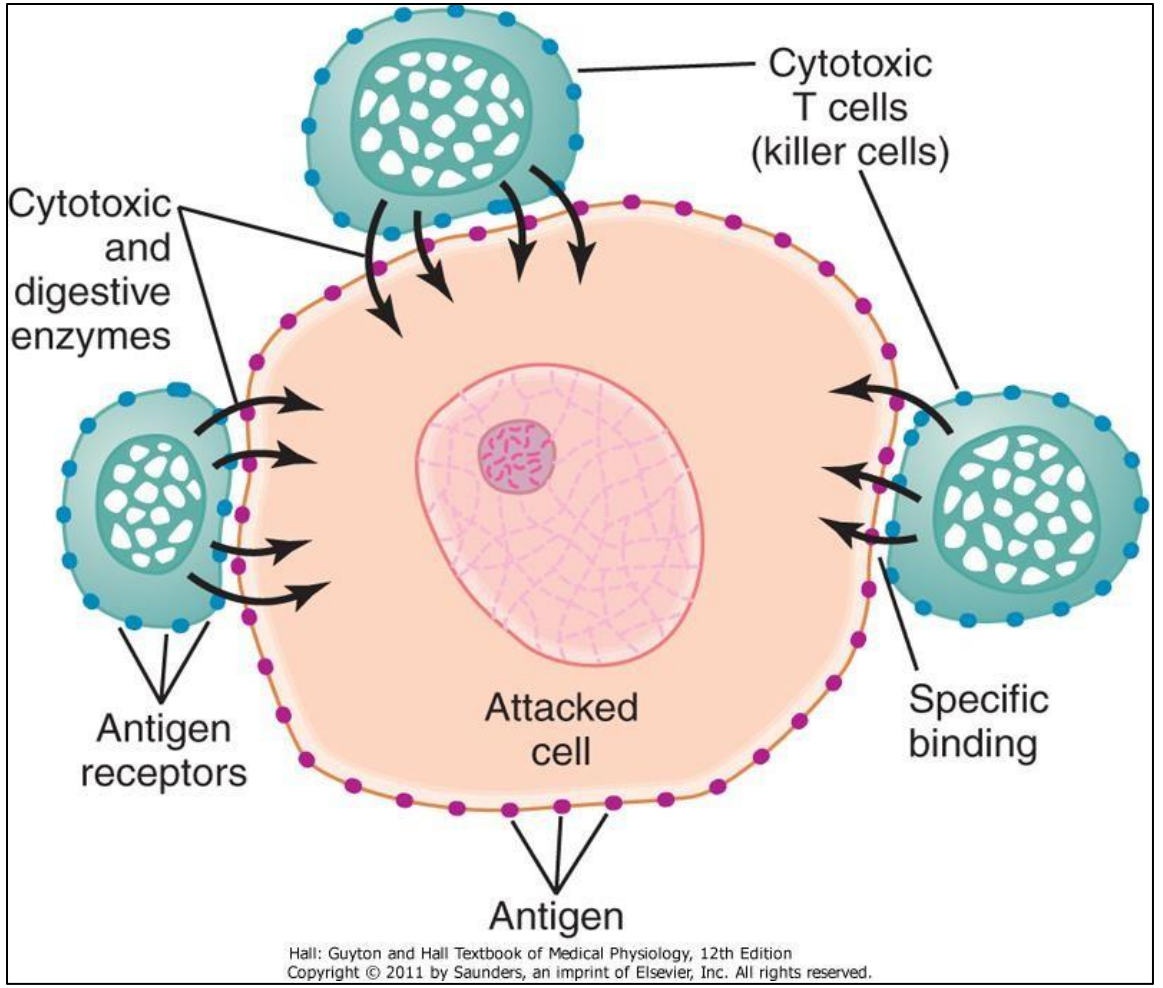
- Positive feedback for helper T cells (IL-2).
- Stimulation of cytotoxic T cells (IL-2, other cytokines).
- Stimulation of B cells (IL- 4, 5, 6 (BCGFs)).
- Macrophage accumulation, since T helper cells promote their attachment and slow their movement, leading to their accumulation at the site of infection,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

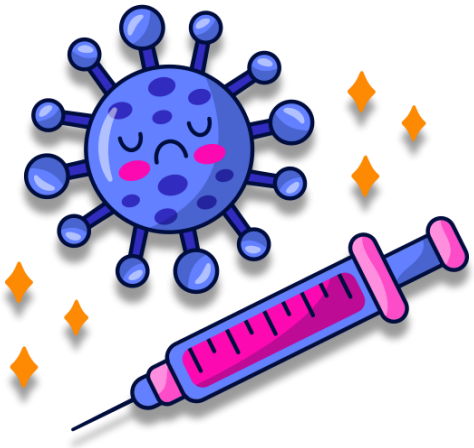
- Rheumatic fever (cross-reactivity with streptococcal antigens).
- Post-streptococcal glomerulonephritis.
- Myasthenia gravis (antibodies to acetylcholine receptors).
- Systemic lupus erythematosis (auto-immunity to multiple tissues).

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 reduce 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	20 12	to redness the immune response due to the decrease in the number of WBCs and platelets	to reduce the immune response due to the decrease in the number of functional WBCs and platelets