Chapter VI: Immune System Malfunction

The immune system must distinguish the self from the non-self, when this is no longer the case, chronic diseases can take hold or the immune system can turn against the body itself and destroy certain organs or induce

VI.1. Immune system deficiencies

The immune system is said to be deficient when it is unable to defend the body against aggression from the outside environment. This deficiency may be innate or acquired.

VI.1.1. Natural or primitive immune deficiencies

These disorders are genetically determined; they can occur on their own or be part of a syndrome. In 2019, the International Union of Immunological Sciences reported that 354 innate errors of immunity and 430 genes were linked to primary immune deficits. The molecular basis of about 80% of them is known.

Primary immunodeficiencies are usually manifested during infancy and childhood by abnormally frequent (recurrent) or unusual infections. Approximately 70% of patients are < 20 years old at the onset of the disorders; as transmission is often linked to X, 60% are male. The overall incidence of symptomatic disease is nearly 1/280 patients.

Primary immune deficiencies are classified according to the main component of the immune system that is deficient, absent or imperfect.

Due to advances in knowledge about these immune deficiencies, their classification according to their molecular abnormalities may be more appropriate.

Examples of innate immune deficiencies

- **Agammaglobulinemia congenital BRUTON's disease:** LB deficiency, immunoglobulin deficiency (absence of gamma globulin = IgG).

- **Thymic aplasia DIGEORGE disease:** LT deficiency and abnormal development of blood, person born with 1 thymus insufficiency.

VII.1.2. Acquired or secondary immune deficiencies

It can occur as a result of several factors:

1) Malnutrition

2) Bacterial infections: such as pulmonary tuberculosis; leprosy; parasitosis.

3) Drug infections: by immunosuppressants; cancer chemotherapy; corticosteroids.

4) Viral Infections: such as saliva-transmitted mononucleosis, AIDS.

A secondary immune deficiency is also observed in the critically ill, elderly or hospitalized patient. Prolonged severe chronic disease can decrease immune responses; the damage is often reversible if the underlying disease is cured.

Examples of acquired immune deficiencies: **Acquired Immunodeficiency Syndrome (AIDS)**

AIDS or Acquired Immunodeficiency Syndrome is a viral infection whose pathogen is HIV (Human Immunodeficiency Virus), it is a retrovirus (its genetic material is RNA).

- **Mode of HIV Affection**

HIV enters the T4 lymphocytes that are considered the conductors of the immune system and hijacks their genetic program for its benefit. Inside the host cell, HIV multiplies and emerges by budding to attack other LT4s. The LT4s, whose number is decreasing, can no longer perform their function. For the sick organism, the door is open to all infections and opportunistic diseases such as tuberculosis, pneumonia, and candidiasis.

NB: The virus can also remain latent in the lymphocytes, in this case, the subject has no symptoms of the disease; he is an HIV-positive or asymptomatic carrier.

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➢ **Modes of AIDS contamination**

- During unprotected sex
- The blood pathway: During blood transfusions.
- From mother to child: during pregnancy (at the time of delivery).

VI.2. Allergies

An allergy is an exaggerated reaction (hypersensitivity) to certain generally harmless substances to which (allergens).

Allergens are various: drugs, food, hair, dust, insect bites...

In immediate allergy, a particular class of antibodies is involved: immunoglobulins E (Ig E). Produced upon first contact with the allergen. IgE binds to particular cells, filled with histamine-rich granules: mast cells). On a second contact with the allergen, IgE causes the immediate degranulation of these cells, which release their histamine. It is she who is largely responsible for the inflammatory condition.

Allergic reactions are varied: vomiting, cough, pimples, edema, conjunctivitis..

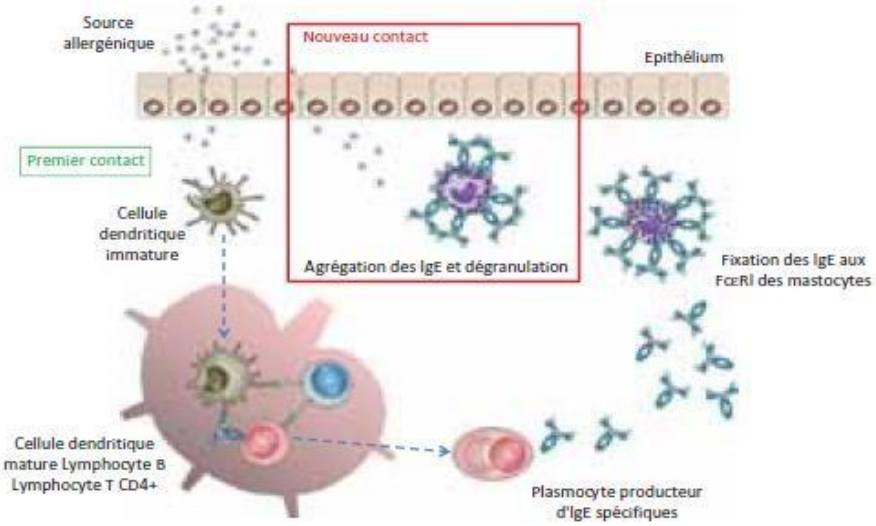

Figure 28: Cellular mechanisms of immediate allergic hypersensitivity.

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VII.3. Autoimmune diseases

Autoimmunity results from defects in establishing or maintaining the immune system's tolerance to self. In animals and humans, the disruption of self-tolerance leads to the activation of self-reactive T and B lymphocytes, resulting in the production of effector cells or autoantibodies recognizing host constituents and responsible for cell and tissue damage which in some cases can lead to clinical symptomatology responsible for autoimmune diseases.

Autoimmune diseases are common (prevalence, all combined: 5%) and represent an important cause of death in developed countries. They are very heterogeneous and are usually classified into two groups:

1. **Organ-specific diseases** in which antibodies or T cells are directed against antigens restricted to a tissue or organ distribution (examples: type 1 diabetes, Hashimoto's thyroiditis);
2. **Non-organ-specific diseases, known as**systemic autoimmune diseases, where the distribution of target autoantigens is ubiquitous and where the formation of circulating immune complexes, in particular, contributes to the development of systemic disease with diffuse and polymorphic involvement of different organs over time (example: systemic lupus erythematosus).

The causes of autoimmune diseases are many:

1. Dysregulation of the self-recognition system
2. Hereditary factors
3. Dysregulation of the target organ
4. The structural analogy between the pathogen and a molecule of the self.

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Table 3. Autoimmune Diseases.

Maladie	Prédisposition/ déclenchement	Atteinte tissulaire	Mécanismes primaires	Mécanismes secondaires	Antigènes cibles/ auto-anticorps les plus fréquents
Lupus érythémateux systémique	Maladie génétique multifactorielle	Systémique	Auto-anticorps, augmentation Interférons de type I	Formation et dépôts de complexes immuns, activation du complément	Constituants des noyaux, dont l'ADN double brin
Polyarthrite rhumatoïde	Maladie génétique multifactorielle HLA DR1/DR4	Prédominant aux articulations, possiblement systémique	Médiation cellulaire, formation de granulomes	Inflammation systémique	Antigènes non connus (collagène II ?) Auto-anticorps : facteur rhumatoïde (FR), anticorps protéines citrullinées
Thyroïdite auto-immune : maladie d'Hashimoto	Maladie génétique multifactorielle DR3	Microsomes thyroïdiens, hypothyroïdie	Production d'auto-anticorps	Infiltration lymphocytaire T	Thyropéroxydase, thyroglobuline
Hyperthyroïdie auto-immune Maladie de Graves Basedow		Récepteur de la TSH, hyperthyroïdie	Production d'auto-anticorps		Auto-anticorps antirécepteur de la TSH stimulants Thyropéroxydase (thyroglobuline)