

# McCance: Pathophysiology, 6th Edition

## Chapter 08: Alterations in Immunity and Inflammation

### Key Points – Print

#### SUMMARY REVIEW

Hypersensitivity: Allergy, Autoimmunity, and Alloimmunity

1. Inappropriate immune responses are misdirected against the host's own tissues (autoimmunity); directed against beneficial foreign tissues, such as transfusions or transplants (alloimmunity); exaggerated responses against environmental antigens (allergy); or insufficient to protect the host (immune deficiency).
2. Allergy, autoimmunity, and alloimmunity are collectively known as *hypersensitivity reactions*.
3. Mechanisms of hypersensitivity are classified as type I (IgE-mediated) reactions, type II (tissue-specific) reactions, type III (immune complex-mediated) reactions, and type IV (cell-mediated) reactions.
4. Hypersensitivity reactions can be immediate (developing within minutes to a few hours) or delayed (developing within several hours or days).
5. Anaphylaxis, the most rapid immediate hypersensitivity reaction, is an explosive reaction that occurs within minutes of reexposure to the antigen and can lead to cardiovascular shock.
6. Allergens are antigens that cause allergic responses.
7. Type I (IgE-mediated) reactions are mediated through the binding of IgE to Fc receptors on mast cells and cross-linking of IgE by antigens that bind to the Fab portions of IgE. Cross-linking causes mast cell degranulation and the release of histamine (the most potent mediator) and other inflammatory substances.
8. Histamine enhances the chemotaxis of eosinophils into sites of type I allergic reactions
9. Atopic individuals tend to produce higher quantities of IgE and to have more Fc receptors for IgE on their mast cells.
10. Type II (tissue-specific) reactions are caused by five possible mechanisms: complement-mediated lysis, opsonization and phagocytosis, neutrophil-mediated tissue damage, antibody-dependent cell-mediated cytotoxicity, and modulation of cellular function.
11. Type III (immune complex-mediated) reactions are caused by the formation of immune complexes that are deposited in target tissues, where they activate the complement cascade, generating chemotactic fragments that attract neutrophils into the inflammatory site. Neutrophils release lysosomal enzymes that result in tissue damage.
12. Intermediate-sized immune complexes are the most likely to have severe pathologic consequences.
13. Immune complex disease can be a systemic reaction, such as serum sickness, or localized, such as the Arthus reaction.

14. Type IV (cell-mediated) reactions are caused by either cytotoxic T lymphocytes (Tc cells) or lymphokine-producing Th1 cells.
15. Typical allergens include pollen, molds and fungi, certain foods (milk, eggs, fish), animals, certain drugs, cigarette smoke, and house dust.
16. Clinical manifestations of allergic reactions usually are confined to the areas of initial intake or contact with the allergen. Ingested allergens induce gastrointestinal symptoms, airborne allergens induce respiratory or skin manifestations, and contact allergens induce allergic responses at the site of contact.
17. Autoimmunity is a breakdown of immunologic homeostasis, the immune system's tolerance of self-antigens. Central tolerance develops during the embryonic period. Peripheral tolerance is maintained in secondary lymphoid organs by regulatory T lymphocytes or antigen-presenting dendritic cells.
18. Autoimmune disease can be caused by the exposure of a previously sequestered antigen, the development of a neoantigen, the complications of infectious disease, the emergence of a forbidden clone of lymphocytes, or ineffective peripheral tolerance.
19. Alloimmunity is the immune system's reaction against antigens on the tissues of other members of the same species.
20. Alloimmune disorders include transient neonatal disease, in which the maternal immune system becomes sensitized against antigens expressed by the fetus, transplant rejection, and transfusion reactions, in which the immune system of the recipient of an organ transplant or blood transfusion reacts against foreign antigens on the donor's cells.
21. SLE is a chronic, multisystem, inflammatory disease and is one of the most serious of the autoimmune disorders. SLE is characterized by the production of a large variety of autoantibodies.
22. Hyperacute graft rejection (preexisting antibody) is immediate and rare, acute rejection is cell mediated and occurs days to months after transplantation, and chronic rejection is caused by inflammatory damage to endothelial cells as a result of a weak cell-mediated reaction.
23. Red blood cell antigens may be the targets of autoimmune or alloimmune reactions. The most important of these, because they provoke the strongest humoral immune response, are the ABO and Rh systems.

### Deficiencies in Immunity

1. Disorders resulting from immune deficiency are the clinical sequelae of impaired function of components of the immune or inflammatory response, phagocytes, or complement.
2. Immune deficiency is the failure of mechanisms of self-defense to function in their normal capacity.
3. Immune deficiencies are either congenital (primary) or acquired (secondary). Primary immune deficiencies are caused by genetic defects that disrupt lymphocyte development,

whereas secondary immune deficiencies are secondary to disease or other physiologic alterations.

4. The clinical hallmark of immune deficiency is a propensity to unusual or recurrent severe infections. The type of infection usually reflects the immune system defect.
5. The most common infections in individuals with defects of cell-mediated immune response are fungal and viral, whereas infections in individuals with defects of the humoral immune response or complement function are primarily bacterial.
6. Defects in B-cell function are diverse, ranging from a complete lack of the human bursal equivalent function, the lymphoid organs required for B-cell maturation (as in Bruton's agammaglobulinemia), to deficiencies in a single class of immunoglobulins (e.g., selective IgA deficiency).
7. DiGeorge syndrome (congenital thymic aplasia or hypoplasia) is characterized by complete or partial lack of the thymus (resulting in depressed T-cell immunity) and the parathyroid glands (resulting in hypocalcemia) and the presence of cardiac anomalies.
8. SCID is a total lack of T-cell function and a severe (either partial or total) lack of B-cell function. SCID can result from mutations in critical enzymes (ADA deficiency, PNP deficiency), in cytokine receptors (X-linked SCID, JAK3 deficiency, IL-7 receptor deficiency), or in antigen receptors (RAG-1/RAG-2 deficiencies, CD45 deficiency, CD3 deficiency, ZAP-70 deficiency). Other combined defects may result from deficiencies in antigen-presenting molecules (bare lymphocyte syndrome), cytoskeletal proteins (WAS), or DNA repair (ataxia-telangiectasia).
9. Almost any portion of the complement cascade may be defective. The most severe defect is C3 deficiency, which results in recurrent life-threatening bacterial infections. Defects in proteins of the membrane-attack complex usually result in unusual disseminated infections with bacteria of the *Neisseria* spp.
10. Defects in phagocyte function, which include insufficient numbers of phagocytes or defects of chemotaxis, phagocytosis, or killing, can result in recurrent life-threatening infections such as septicemia and disseminated pyogenic lesions.
11. Acquired immunodeficiencies are caused by superimposed conditions, such as aging, malnutrition, infections, malignancies, physical or psychologic trauma, environmental factors, some medical treatments, or other diseases.
12. Deficiencies in immunity usually are treated by replacement therapy. Deficient antibody production is treated by replacement of missing immunoglobulins with commercial gamma-globulin preparations. Lymphocyte deficiencies are treated with the replacement of host lymphocytes with transplants of bone marrow, fetal liver, or fetal thymus from a donor.