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Congenital and Acquired Immunodeficiencies

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1. INTRODUCTION

The development of the immune system and its function are outlined in Chapter 1. Congenital immunodeficiencies are rare; more details can be found in pediatric textbooks. Here, only the most important entities are discussed. Acquired immunodeficiencies are observed in many lymphoproliferative disorders and during treatment with steroids or chemotherapy with cytostatic drugs. The deficiency of cellular immunity induced by HIV infection is a common problem in many countries. In this chapter, we describe only some hematological consequences of HIV infection.

The following are common tests of immune defense or immune status of an organism. These tests are indicated if a patient has frequent infections—bacterial, fungal, viral, or protozoan. Which tests are used depends on the clinical situation and the type of particular immune defect suspected.

1. Blood count with white cell differential count, flow cytometry: this permits exclusion of morphological abnormalities (e.g., a granulation defect of granulocytes). Full blood counts of lymphocyte, neutrophil, and eosinophil numbers are helpful. The mononuclear cell populations can be further differentiated and

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analyzed with monoclonal antibodies (*see Appendix 2, “CD Nomenclature”). This can be done both with flow cytometry or immunocytochemistry.

2. Functional studies of granulocytes and monocytes: chemotaxis (Boyden chamber), phagocytosis, bactericidal capacity, nitroblue of tetrazolium reduction, myeloperoxidase activity, CD18 expression.

3. Studies of humoral immunity: serum immunoglobulins (Igs) (IgG, IgA, IgM, IgE, IgG subclasses), isohemagglutinins (not helpful in blood type AB patients), complement levels, components of the complement cascade, levels of specific antibodies, e.g., IgG antivaccine levels: pneumococcus, tetanus, and diphtheria (depends on immunization history). In vivo studies can be done by immunizing with specific antigens (e.g., tetanus toxoid). Ig synthesis is tested in vitro by incubating B-lymphocytes with certain mitogens.

4. Studies of cellular immunity (lymphocyte subpopulations, *see Item 1*).
   - In vitro: stimulation of lymphocytes with mitogens and antigens, production of cytokines such as interleukin (IL)-2 or granulocyte-macrophage colony-stimulating factor, cytotoxic activity of T-cells, activity of natural killer (NK) cells, antibody-dependent cellular cytotoxicity activity. Measurements of T-cell effector cytokine production.

5. Further studies: sedimentation rate, total serum protein, serum electrophoresis, complement factors (total complement, CH50), classical and alternate pathway, global tests of complement (if complement defect is suspected).

2. CONGENITAL IMMUNODEFICIENCIES

Congenital immunodeficiencies are subdivided into the following:
- Defects of the phagocytic system (*see Table 1*).
- Defects of combined immunodeficiencies (*see Table 2*).
- Defects of humoral immunity (Ig synthesis) (*see Table 3*).
- Defects of cellular immunity (*see Table 4*).
- Defects of complement components (*see Table 5*).

Most congenital immunodeficiencies manifest themselves within the first 2 months of life. A defect of humoral immunity often becomes apparent several months later when Igs transferred via the placenta disappear. Tables 1–4 also indicate the clinical features and the treatment of these immunodeficiency states. The group of complement deficiencies (C1–C9) has autosomal-recessive inheritance and, in some cases, is associated with frequent infections. Some patients with complement defects suffer from autoimmune disorders. The majority of the congenital immunodeficiencies have autosomal- or X-linked-recessive inheritance. Only four congenital immunodeficiencies appear to have dominant inheritance: isolated congenital asplenia, hyper-IgE syndrome, isolated chronic