



Severe Combined Immunodeficiency

Background

Severe Combined Immunodeficiency (SCID) is a group of disorders characterized by the absence of both humoral and cellular immunity. Infants with SCID die of infections by age two years unless immunity is reconstituted by treatment. The defining characteristic for SCID is always a severe defect in T cell production and function, with defects in B-lymphocytes as a primary or secondary problem and, in some genetic types, in NK cell production as well. SCID is also commonly known as the “bubble boy” disease.

Clinical

Infants generally have a normal physical examination result before the onset of infection. The pathophysiology and molecular biology vary among different forms of SCID, however, the lack of T-cell and B-cell function is the common endpoint in all forms of SCID. Lymphopenia usually occurs from the absence of T cell, and sometimes from the absence of natural killer cells. Functional antibodies are decreased or absent. Infections are usually serious, and may include pneumonia, meningitis or bloodstream infections with average age at the onset of symptoms at two months.

Testing

T-cell Receptor Excision circles (TRECs) are circular DNA fragments generated during T-cell receptor rearrangement. In healthy neonates, TRECs are made in large numbers, while in infants with SCID they are barely detectable. Real-time quantitative PCR assay is used to determine the TREC copy number in blood, which can be used to distinguish T-cell lymphopenic SCID infants from healthy babies. However, low TRECs copy numbers can also be the results of other immunodeficiency, such as DiGeorge Syndrome, and sometimes as a result of the use of immunosuppression drugs. Confirmatory tests are needed for the diagnosis of SCID and for the determination of the form of SCID.

Treatment

Infections are treated with specific antibiotic, antifungal, and antiviral agents and administration of intravenous immunoglobulin. Restoration of a functional immune system is essential. The preferred treatment is bone marrow/stem cell transplantation. Early detection and treatment can result in markedly improved survival rates. Enzyme replacement therapy is available for adenosine deaminase deficiency (a form of SCID). Gene therapy is still in the experimental phase.

Inheritance

SCID occurs in approximately 1 in 50,000-100,000 live births. Over 10 different genetic defects have been identified that account for SCID in humans. The most common type is linked to the X chromosome, making this form affect only males. This X-linked form accounts for approximately 50% of SCID cases. Other forms of SCID usually follow an autosomal recessive inheritance pattern or are the result of spontaneous mutations. Approximately 25% of the patients with an autosomal recessive SCID are JAK3 deficient, and 40% are adenosine deaminase deficient.