Provider fact sheet for severe combined immunodeficiency (SCID)

What is severe combined immunodeficiency (SCID)?

Severe combined immunodeficiency (SCID) is a group of rare, sometimes fatal, congenital disorders characterized by little or no immune response. The defining features of SCID are defects in the specialized white blood cells that defend people from infection by viruses, bacteria, and fungi. Individuals with SCID have few or absent T lymphocytes and B lymphocytes that are either absent or non-functional. When these cells are not working correctly, an affected baby is susceptible to recurrent infections including as pneumonia or bronchitis, oral thrush, and diarrhea.

SCID is caused by defects in a gene essential for immune cell development. The most common type of SCID is due to mutations in IL2RG (interleukin 2 receptor gamma), a gene on the X chromosome that provides instructions for the gamma receptor protein, which must be present on the surface of lymphocytes to allow them to mature and function. An X-linked gene defect causes disease in males, who have only a single X chromosome, while females, who have two X chromosomes may be carriers without symptoms if one of their X chromosomes is defective.

Other forms of SCID follow an autosomal recessive inheritance pattern and occur in males and females. Adenosine deaminase (ADA) is an enzyme that is required for recycling components of the cell, including DNA; when it is deficient deoxyadenosine builds up and is toxic to lymphoctyes. Other forms of SCID are caused by mutations in recombinase activating genes known as RAG1 and RAG2, the gene that encodes the alpha chain of the IL-7 receptor, the Janus kinase 3 enzyme, DNA repair genes such as Artemis, and other genes essential for lymphocyte development.

What are the treatments for SCID?

Treatment is essential to establish a durable, functional immune system before devastating infections occur. The standard treatment for SCID is hematopoietic stem cell transplant, or HSCT, or bone marrow transplant, in which blood-forming cells from a healthy donor are given to the affected child. These cells reproduce and create a functional immune system. HSCT is successful when undertaken early and before serious infections occur.

Gene therapy, correcting the child's own blood forming cells, shows promise because most infants with SCID lack a tissue matched related donor, and this approach avoids incoming donor attacking the child's tissues (graft vs. host disease). Gene therapy has been effective in clinical trials for X-linked, ADA and Artemis SCID gene. PEG-ADA, an enzyme replacement therapy, is available for ADA SCID.

Until SCID patients undergo HSCT or gene therapy, they must be isolated from exposure to infection and must receive supportive care with antibody infusions, and prophylactic antibiotics and antifungals.

For more information about SCID please refer to the following resources:

- The National Human Genome Research Institute of the NIH (www.genome.gov/13014325)
- Baby's First Test (www.babysfirsttest.org/newborn-screening/conditions/severe-combined-immunodeficiency-scid)
- SCID Compass (www.scidcompass.org)

California Department of Public Health
Newborn Screening Program (www.cdph.ca.gov/NBS)