IDPH
ILLINOIS DEPARTMENT OF PUBLIC HEALTH

NEWBORN SCREENING
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Severe Combined Immune Deficiency
Information for Physicians and Other Health Care Professionals

Definition
Severe combined immune deficiency (SCID) includes a group of rare inherited disorders in which genetic defects cause improper development of special white blood cells, the T lymphocytes. These lymphocytes serve as primary defenses in the identification of invading viruses, bacteria and fungi and help facilitate the immune system's response to pathogenic invasion. Individuals with SCID are very susceptible to recurrent infections and without treatment may succumb to pneumonia, meningitis or other infection related complications. All forms of SCID are inherited and not acquired as side-effects of infection or immune response suppression therapies.

Clinical Symptoms
Newborns with SCID usually appear healthy at birth and may have no family history of immunodeficiencies. Lacking adequate immune system defenses, these infants are very susceptible to multiple life threatening infections. Early symptoms may include frequent bouts of ear infections, thrush, bronchitis, pneumonia and diarrhea. Often these infections are prolonged and do not respond to usual therapies, and some may require intravenous antibiotics. Infants with SCID also may suffer from poor nutrition and "failure to thrive." Without early diagnosis and treatment, children with SCID usually succumb to infectious disease complications during the first or second year of life.

Newborn Screening and Definitive Diagnosis
In Illinois, newborn screening for SCID is performed by measuring the T-cell receptor excision circles (TRECS) in DNA extracted from dried blood spot samples. TRECS are formed during normal immune system development as T-cell lymphocytes within the thymus gland undergo differentiation and specialization following exposure to antigens. The absence of TRECS or lower numbers of TRECS may indicate the newborn has SCID or profound T-cell lymphopenia. **If newborn screening results indicate low levels of TRECS, referral should be made to a pediatric immunologist designated by the Department for diagnostic flow cytometry.** In some cases, if the newborn screening is inconclusive or the blood sample is inadequate for DNA testing, a second newborn screening sample may be requested for testing. Although newborn screening is intended to identify newborns with SCID, additional types of lymphopenia and other disorders including complete DiGeorge syndrome or congenital intestinal lymphangiectasia also may result in positive newborn screens due to the absence of lymphocytes.

Treatment
The treatment for SCID is hematopoietic stem cell/bone marrow transplant. Infants who receive a transplant within the first few months of life, especially before onset of more serious infections or complications, have a greatly improved survival rate. Live, attenuated vaccines should not be administered to infants diagnosed with, or suspect for SCID. Rotavirus vaccine is contraindicated for infants with defects in T lymphocyte production and function, and severe, prolonged episodes of gastroenteritis have been reported in infants with SCID following administration of this vaccine.

Incidence
The incidence of SCID is estimated at one in every 50,000 births. The incidence for all types of immunodeficiency may be closer to one in every 15,000 births.

Inheritance Patterns
While all forms of SCID are due to specific gene mutations, some individuals affected with the disorder have the X chromosome linked form, XSCID. In XSCID, males inherit the X-linked gene mutation from carrier mothers. Females are not affected, although they have a 50 percent chance of being carriers of the gene mutation and may pass this mutation to any future offspring. Several autosomal recessive genetic mutations also may cause SCID. **Genetic counseling services for families of infants with SCID are highly recommended.**

Pathophysiology
Genetic mutations in SCID disorders preclude normal production and maturation of T-cell lymphocytes and/or B-cell lymphocyte secretion of antibodies, thus preventing development of a normal, healthy immune system. Following birth, newborns have high levels of maternal antibodies to provide protection from pathogens until the newborn's immune system develops over the next few months. Most infants are exposed to pathogens during this period, but have some ability to fight infections as their immune system develops. Infants with SCID do not have a functional immune system response to pathogenic antigens and cannot adequately overcome infections. Parents may notice their infant has frequent, severe and long lasting infections, and often report undergoing diagnostic odysseys until their child is eventually diagnosed with SCID, usually around four to six months later.

Key Points for Parents
Try to convey to parents that although immediate referral for diagnostic testing may be necessary, newborn screening results are not conclusive, and that even if their child is diagnosed with SCID, there is an effective treatment available. If the child needs additional testing or diagnostic evaluation, make certain the parents understand the importance of promptly following the pediatrician's and/or immunologist's recommendations.

Following Confirmation of Diagnosis
These guidelines should be followed after a diagnosis of SCID has been confirmed:

1) Follow up frequently with the child's immunologist.
2) Recommend genetic counseling services to help the parents understand the complexity surrounding the carrier state and inheritance of this disease.
3) Offer parents information on support services, such as the Immune Deficiency Foundation and the local health department.
4) Additional information about newborn screening can be found at:
    - Baby's First Test: http://www.babysfirsttest.org/
      Health Resource and Service Administration (HRSA), Grant no. U36MC16509, Quality Assessment of the Newborn Screening System.

    - National Center for Biotechnology Information: http://www.ncbi.nlm.nih.gov/gtr/
      National Center for Biotechnology Information, U.S. National Library of Medicine, 8600 Rockville Pike, Bethesda MD, 20894 USA.