

## Questions about Severe Combined Immunodeficiency Disease

### **Why have medical professionals called Severe Combined Immunodeficiency Disease (SCID) a pediatric emergency?**

SCID is a group of inborn disorders, all of which result in failure of affected infants to develop T- cells, a critical component of the immune system. As a result, the condition is fatal in infancy unless treated with bone marrow transplantation, or in some cases enzyme replacement or gene therapy. If diagnosed within the first 3 1/2 months of life before infections develop, the cost of this treatment can be as low as \$50,000 for each infant. By contrast, treatment costs can exceed \$1,000,000 for each infant diagnosed late, primarily due to costs of treating infections that can leave the child with long-term medical complications. Without a bone marrow transplant in those crucial 3 1/2 months, many of these infants die of infection even if a bone marrow transplant is attempted later. The diagnosis of SCID very early in life is a true pediatric emergency.

### **How common is SCID?**

It is not possible to know the true prevalence of SCID incidence until all 50 states are screening. It is estimated to be 1 in 55,000 births with more frequent incidences found in the Hispanic and Native American populations. SCID is a rare condition, but is as frequent as some conditions that newborns are currently tested for such as PKU, biotinidase deficiency or certain metabolic disorders. On the other hand, researchers have no clear idea of how many babies are not diagnosed and die of SCID-related infections each year. The actual number of cases is most likely higher.

### **How is SCID diagnosed?**

Fewer than 20% of infants with SCID have a family member with the condition that allows doctors to suspect it and test at birth. Early diagnosis of SCID is rare because doctors do not routinely count each type of white blood cell in newborns. As a result, the average age at which babies are diagnosed with SCID is just over six months and some are diagnosed much later, usually because of recurrent infections and failure to thrive. Blood tests for SCID typically reveal significantly lower-than-normal levels of T cells and a lack of germ-fighting antibodies. Even if B cells are present in the blood of SCID patients, they do a poor job of producing antibodies. Low antibody levels and lack of specific antibodies after vaccination or a natural infection are characteristic features of SCID.

### **Is there effective treatment for SCID?**

The most effective treatment for SCID is transplantation of blood-forming stem cells from the bone marrow of a healthy person. Bone marrow stem cells can live for a long time by renewing themselves as needed and also can produce a continuous supply of healthy immune cells. A bone marrow transplant from a tissue-matched sister or brother offers the greatest chance for curing SCID. However, most patients do not have a matched sibling donor, so transplants from a parent or unrelated matched donor are often performed. All transplants done in the first three months of life have the highest success rate.

## Facts about Severe Combined Immunodeficiency Disease and Newborn Screening

- SCID, or severe combined immunodeficiency disease, is a treatable illness in which an infant fails to develop a normal immune system. After successful treatment, people with SCID lead normal lives.
- SCID is a pediatric emergency, and newborn screening offers an opportunity to catch the disease early when treatment is most effective and cost efficient.
- A wide range of viruses, bacteria and fungi that are normally controlled by a healthy baby's immune system can cause serious infections in SCID babies.
- If undetected and untreated, SCID typically leads to death before the baby's first birthday.
- If diagnosed and treated in the first weeks or months of life, infants born with SCID can live healthy productive lives.
- One form of the disease can be treated with an injectable medication.
- Newborn screening would provide a rapid indication of a possible immune problem soon after birth while the infant is still protected by the mother's antibodies.
- Research shows that bone marrow transplants in the first three months of life have a higher rate of efficacy than transplants at a later age.
- Early treatment for SCID can also reduce medical costs – the cost of a transplant in the first three months of life can be measured in tens of thousands, but the cost of delayed care can reach into the millions for seriously ill patients with less guarantee of success.
- The poor quality of life in late-diagnosed SCID patients, often caused by complications of infections that started before diagnosis, can eventually lead to disability or even death.
- Immune Deficiency Foundation (IDF) applauds the Secretary of Health and Human Service's inclusion of SCID in the **new** national standards.
- IDF asks every state to include SCID Newborn Screening on their newborn screening panel immediately to save lives.

## Questions about Newborn Screening for Severe Combined Immunodeficiency (SCID)

### What is SCID screening in newborns?

SCID screening in newborns became possible just a few years ago with the development of a test that can detect SCID in the dried blood spot filter cards that are currently collected from all babies to screen for a variety of inborn conditions. Prominent immunologists contend that this simple blood test could allow doctors to treat, and most likely cure, SCID in an infant at a reasonable cost, as opposed to endless, less-effective diagnostic procedures and treatments that could lead to enormous medical expenses after a child has developed an infection.

### Has SCID screening in newborns been supported by public policy?

In January 2010, the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC) recommended to the Secretary of the Department of Health and Human Services, Kathleen Sebelius, that the Federal government recommend to the States that they include SCID in their newborn screening protocols. The ACHDNC adopted a list of 29 recommended conditions for screening in September 2005. Since that time, SCID is the first condition to be added to this list for inclusion into mandatory newborn screening conducted by state public health programs. On May 21, 2010, Kathleen Sebelius, Secretary of Health and Human Services (HHS) announced her decision to concur with the committee and add SCID to the core panel of disorders for newborn screenings.”

### What is the ACHDNC?

The Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC), an evidence-based committee, was chartered in February 2003 to advise the Secretary regarding the most appropriate application of universal newborn screening tests, technologies, policies, guidelines and standards for effectively reducing morbidity and mortality in newborns and children having, or at risk for, heritable disorders. The committee unanimously voted to recommend adding SCID to the core newborn screening panel.

### The following states currently screen for SCID:

Alabama, Alaska, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Hawaii, Idaho, Illinois, Iowa, Kentucky, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Montana, Nebraska, New Hampshire, New Jersey, New Mexico, New York, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, Wyoming.

### What kind of test is used to screen for SCID?

The SCID-screening test currently utilized uses the same dried blood samples already collected from newborns. The TREC test is an assay that detects the number of T-cell Receptor Gene Excision Circles, or TRECs, that are produced during normal T-cell maturation, but that are absent or severely reduced in infants with SCID. The TREC test, which is performed on newborn dried blood samples, is very sensitive and has a false positive rate well below 1%.

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## What is Severe Combined Immunodeficiency Disease?

Severe Combined Immunodeficiency Disease (SCID) is the most serious primary immunodeficiency disorder. The defining characteristic of SCID is the absence of T-cells and, as a result, lack of B-cell function, the specialized white blood cells made in the bone marrow to fight infection. These genetic defects lead to extreme susceptibility to serious illness. Unless these defects are corrected the child will die of opportunistic infections before their first or second birthday. SCID can be caused by several different genetic defects, most of which are hereditary.

Although considered a rare disease, SCID is best known to the public from media accounts and a made-for-TV movie about David Vetter, the 'Boy in the Bubble,' a child from Texas who spent his entire life in a germ-free environment, ultimately dying after a failed bone marrow transplant in early adolescence. In the past, children with this disorder were kept in strict isolation, sometimes in a plastic isolator or "bubble." Bubbles are no longer used, but the name remains a part of the history of SCID.

Children with SCID lack immune protection against bacteria, viruses, and fungi and are prone to repeated and persistent infections that would not normally cause illness in a person with a normal immune system. In someone with SCID, these infections can be extremely serious or life threatening. SCID can affect either boys or girls, but the most common type occurs only in males (X-linked). Females can carry the X-linked trait and have a 1 in 2 chance of passing it on to each son.

There are currently 17 known genetic causes of SCID, making it possible to identify an underlying genetic defect in about 90 percent of cases. Although they vary with respect to the specific defect that causes the specific immunodeficiency, all have severe deficiencies in both T-cell and B-cell function.

SCID is estimated to occur in approximately 1 out of every 55,000 births, although we won't know the true incidence until all 50 states are screening. SCID is as common as some of the inherited illnesses – PKU, biotinidase deficiency and certain metabolic disorders – for which states currently screen all newborns.

SCID screening in newborns could potentially reveal the true incidence of children born with severe combined immunodeficiency disease.

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