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**Severe Combined Immunodeficiency (SCID)**  
(Commonly referred to as “Bubble Boy Disease”)

**Disorder family:** Primary Immune Deficiency

**SCID overview:**

Severe Combined Immunodeficiency (SCID) is a group of congenital disorders characterized by very low or absent production of the body’s primary infection-fighting cells. Infants with SCID are susceptible to life-threatening infections from microorganisms such as bacteria, viruses and fungi. Early detection and aggressive treatment, typically bone marrow transplant, is necessary to avoid deadly infections. Infants who begin treatment before infections set in have lower hospital costs, and an increased chance of survival and disease cure. Newborn screening is proving successful in other state programs, facilitating early identification, and timely treatment before patients develop life-threatening infections. In combination with advances in bone marrow transplantation and gene therapy, the survival rate for infants with SCID is greatly improved. Infants treated early now have a 94% survival rate in this previously uniformly fatal condition (Railey et al 2009).

Data from the four states currently screening for SCID suggests a frequency as high as one per 35-40,000 live births (18 SCID cases in 743,979 screened patients; data presented April 2011 at the annual Primary Immune Deficiency Treatment Consortium’s meeting). In addition, a similar number of babies with other significant immunodeficiency disorders have been identified and treated in these programs. Based on these estimates, we anticipate that in Washington State (with 80,000 to 85,000 births annually) we will identify two to three new cases of SCID, and about two other life-threatening immunodeficiency disorders per year.

**Natural History & Burden if Untreated:** For the first few months after birth, an infant with SCID is somewhat protected by infection-fighting antibodies acquired from the mother during pregnancy. However, the maternal antibodies in the infant’s circulation diminish over the first three months of life, leaving an infant with SCID susceptible to a broad range of infections. If a child with SCID contracts a common childhood virus such as chickenpox, it can be imminently fatal. Without treatment, SCID is typically lethal in early childhood (Kuehn 2010 and Puck 2007).

**Treatment for babies with SCID:** Infants suspected of having SCID are immediately begun on antibiotic, antiviral, and antifungal medications and placed in protective isolation. Contact with people, especially young children, can expose the infant to harmful infections. Immunoglobulin replacement therapy is begun in all suspected cases and offers some benefit against infections. Ultimately patients are treated with bone marrow transplantation or gene therapy, which restores normal immune function and provides a lifetime cure for the disease.

**Efficacy of treatment if identified clinically:**

In the absence of newborn screening, SCID is usually identified clinically, after life-threatening infections have already begun. Bone marrow transplantation and gene therapy are much more complicated in the setting of severe infections and are far less likely to be effective (the bone marrow transplant survival rate in late diagnoses is 70% or less) (Railey et al 2009).

**Screening test:** When T lymphocytes (a subtype of white blood cells) develop in the body, a section of the DNA that they do not need is excised and fused together to form a small circular piece of DNA. These are called TRECs (T-cell Receptor Excision Circles) and can be measured in the laboratory from the dried blood spots obtained from infants shortly after birth. The number of TRECs corresponds to the number of T-cells the body produces; babies with SCID have a very low number of T-cells and consequently, have very few measurable TRECs in the dried blood spot. The TREC test has excellent sensitivity and specificity, meaning that with newborn screening virtually all babies with SCID will be identified early with very few false positives.

**Diagnostic Tests:** If a child is identified as possibly having SCID by the screening test, flow cytometry - a specialized technique to count the infection fighting cells in the blood, can be used to confirm whether or not they actually have the disease. Further testing to identify specific genetic mutation(s) that cause SCID is also performed in most cases.

**Efficacy of treatment/benefits of early intervention:**

Early diagnosis of SCID, before an infant has had a chance to develop any infections, is critical to maximize the chance of survival, minimize severe illness, and reduce overall healthcare costs. Among babies who receive bone marrow transplant before 3.5 months of age, 94% survive, develop permanent functional immunity, and are cured of the disorder (Railey et al 2009 and Kuehn 2010). Without newborn screening for SCID, the only real chance of early identification for an affected child is to be born in a family who had a previous child with SCID. A family history of SCID alerts medical staff and can prompt the diagnosis before the new baby develops any symptoms.

Timing of Bone Marrow Transplant	Survival Rate
SCID cases age < 3.5 months	94%
SCID cases age ≥ 3.5 months	70%

**Additional benefits of SCID newborn screening:**

The TREC assay has been shown in other states to identify some immune system conditions other than SCID. Like SCID, these conditions are characterized by very low T-cells and therefore a risk of life-threatening susceptibility to infections. Babies with these related immune deficiencies also benefit from early intervention.

Infants with compromised immune systems can also be harmed from routine childhood vaccinations, particularly those for Rotavirus, Chicken pox, and Measles/Mumps/Rubella. Early identification of affected babies will also avoid complications from this otherwise beneficial public health program (CDC 2010).

**References:**

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