Understanding SCID, or Bubble Boy Disease
By Ronale Tucker Rhodes, MS

In 1976, the world learned about a rare genetic disease, commonly referred to as the “bubble boy disease,” when the made-for-television movie “The Boy in the Plastic Bubble” (starring John Travolta) portrayed the story of David Vetter. David lived his entire life in a plastic, germ-free bubble and died in 1984 at the age of 12 from the disease, the medical term for which is severe combined immunodeficiency (SCID). Now, 35 years later, people are still familiar with the term bubble boy disease, but few really understand what it is, why it strikes and how it is diagnosed and treated.

What Is SCID?
SCID, a deficiency of the immune system, occurs in about one in every 500,000 births. Babies born with SCID lack antibodies and T cells that protect against infection. These babies typically acquire serious and even life-threatening infections, such as pneumonia, meningitis and bloodstream infections, in the first few months of life.

There are five types of SCID, each caused by a different genetic defect. X-linked SCID is the most common type, caused by a genetic flaw that damages molecules that allow T cells and B cells to receive signals from crucial growth factors. David suffered from X-linked SCID, which occurs only in males. This is because females have two X chromosomes; if they have a mutation on one X chromosome, they have a spare X that can help compensate. Males, however, with only one X chromosome and one Y chromosome, do not have a spare X chromosome to help them compensate for a mutation. The sons who inherit the mutant X chromosome will have X-linked SCID, and the daughters who inherit the mutant X chromosome will be carriers like their mother.

The other types of SCID are inherited in an autosomal recessive pattern (AR-SCID) and affect males and females equally. AR-SCID occurs if two abnormal genes, one from each parent, are present in the patient. In this case, each parent carries an abnormal gene but does not have any physical symptoms of the disorder itself.

Diagnosing SCID
Babies with SCID will normally begin showing symptoms by the time they are 3 months old. Symptoms usually include persistent thrush, extensive diaper rash, chronic diarrhea and a lack of growth or weight gain. Some children have a sharp, persistent cough with pneumocystis pneumonia, blood disorders or chronic hepatitis.

Tests to measure immune function are necessary for a diagnosis. And, because ongoing infections can interfere with results, tests may have to be repeated several times. Those who have SCID usually have a very low number of white blood cells, or lymphocytes, as well as few or no B cells and T cells. The few cells they do have often do not function properly. SCID patients also have very low levels of IgG, IgA and IgM antibodies.

Jennifer Puck, MD, professor of pediatrics at the University of California, San Francisco, has developed a method for identifying presymptomatic children with SCID using the dried blood spots already obtained from all babies for newborn screening. DNA is extracted and the polymerase chain reaction (PCR) is used to determine the number of T cell receptor excision circles (TRECs) versus a copy number of a control genomic DNA segment. Patients who lack TRECs may have SCID or other disorders with very low T cells. Pilot screening of newborns using this method is currently ongoing in Wisconsin, Massachusetts and Navajo Indian populations, where SCID incidence is high. The tests cost between $6 and $10 per sample to perform.
According to Puck, performing inexpensive quantitative PCR assays may help avert expensive and ineffective later-stage treatments for children with SCID. Currently, about 80 percent of infants with SCID go unrecognized until they develop infectious complications due to their immune deficiency.

But, an early diagnosis of SCID has traditionally been rare because doctors don’t routinely perform a test in newborns to count white blood cells. And, since babies with SCID typically appear healthy, parents and healthcare providers are unaware that these children are susceptible to life-threatening diseases. What’s more, the Centers for Disease Control and Prevention (CDC) recommends starting the first dose of vaccines when an infant is 2 months old, some of which can be contraindicated for babies with SCID. Last June, the CDC announced the addition of SCID to the list of contraindications for the two live rotavirus vaccines after several documented cases of vaccine-acquired rotavirus in infants who were undiagnosed with SCID at the time the vaccine was given.

Fortunately, screening newborns for SCID is now occurring in many states. In January 2010, the Advisory Committee on Heritable Disorders in Newborns and Children voted unanimously to add screening for SCID to the core panel for universal screening of all newborns in the U.S. Then, in May 2010, Kathleen Sebelius, secretary of the Department of Health and Human Services, announced the addition of SCID to the core panel of 29 genetic disorders as part of her recommendation to adopt the national Recommended Uniform Screening Panel. SCID is the first nominated condition to be added to the core panel of disorders. In 2008, Wisconsin became the first state to screen babies for SCID. Since then, five other states and one territory have added SCID to their panels: California, Louisiana, Massachusetts, New York, Puerto Rico and, most recently, Florida. In addition, seven other states have voted to recommend the addition of SCID to their newborn screening panels, but screening has not yet begun. These include Colorado, Delaware, Iowa, Michigan, Minnesota, North Carolina and Rhode Island.

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**Treating SCID**

The most effective treatment for SCID is transplanting bone marrow from a healthy sibling whose tissue type closely matches the patient’s. If a matched sibling is not available, a donor as closely matched as possible can be used. The earlier the diagnosis, the better chances of survival after a bone marrow transplant. The Medical College of Wisconsin recently instituted universal newborn screening, and researchers there noted that among 46 children in whom SCID was diagnosed before 3.5 months of age, 96 percent survived 26 years post transplantation, compared with 66 percent of 116 children who did not receive an early diagnosis.

Until the transplant takes effect (in one to three years), intravenous immunoglobulin (IVIG) is given to normalize antibody levels. SCID patients with adenosine deaminase (ADA) deficiency have been treated successfully with enzyme replacement therapy called PEG-ADA, a long-circulating form of ADA that almost completely corrects metabolic abnormalities, allowing the recovery of a variable degree of immune function sufficient to protect against opportunistic and life-threatening infections.

Gene therapy for correction of both forms of SCID also is under investigation. In one study, reported on in the July 22, 2010, issue of the New England Journal of Medicine, eight of nine male infants born with SCID were still alive and well nine years after they underwent gene therapy. The nine boys in the study, who had a median age of 7 months at the time they received the corrected gene (between 1999 and 2002), had normal T cell levels and were able to lead normal lives up to 11 years after the therapy. And, their weight and height were not stunted, as is usually the case with SCID. However, almost half of the participants in the study developed acute leukemia after the therapy. Three survived and one died.

In another study, performed in Italy and Israel and reported on in the Jan. 28, 2009, issue of the New England Journal of Medicine, gene therapy cured eight of 10 children with SCID. Following the patients’ progress for four years after treatment, the eight patients were no longer on medication, while the other two patients needed further treatment, and none showed signs of leukemia or other health problems from the therapy.
In October, GlaxoSmithKline reported it had licensed an experimental gene therapy from two Italian institutions (Fondazione Telethon and Fondazione San Raffaele) that aims to fix the stem cells in the patient's own bone marrow. Stem cells are removed and a healthy gene is inserted before the cells are returned to the body. The therapy has demonstrated “potential” in Phase I and II studies, according to the company.

Renewed Hope

As awareness of SCID increases and research progresses to improve diagnoses and treatments, there is renewed hope for this once-fatal disease. SCID patients no longer have to live in a bubble, such as the fate of David Vetter. Instead, they are living longer, healthier and normal lives.

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Sources


