Newborn Testing for Immune Disorders Could Save Lives

August 17th, 2008

DURHAM, N.C. - A simple, inexpensive blood test performed at birth to screen for immune disorders could dramatically increase the chance of survival for babies born with such potentially fatal disorders as severe combined immunodeficiency disease (SCID).

Physicians at Duke University Medical Center have performed stem cell transplants in 136 infants with SCID in the past 22 years. The survival rate for 38 infants receiving transplants in the first 3.5 months of life is 97 percent, but the rate drops to 69 percent for infants who were transplanted after that age, Rebecca Buckley, M.D., reports in the April 23, 2004, Annual Review of Immunology.

The main cause for the drop in survival rate is serious infections SCID babies develop in the first few months of life. Infants with SCID have little or no immune system. Without treatment, they die of infection before their first or second birthdays. But for infants without a known family history of SCID, the average age of referral for immune testing is approximately 6 months, Buckley said. "The tragedy is that most patients are critically ill by then," she said.

Buckley believes that all newborns should be screened for immune deficiency disorders at birth. "SCID is a pediatric emergency. There is no screening for any primary immunodeficiency disease at birth or during childhood and adulthood in any country. Thus, most patients are not diagnosed until they develop a serious infection, which certainly adversely affects the outcome of therapy," said Buckley, a professor in Duke’s division of pediatric allergy and immunology.

Early treatment also reduces costs — a transplant in the first three months of life can cost less than $50,000, but the cost of care skyrockets up to millions of dollars for seriously ill patients, with less guarantee of success. And SCID patients who received stem cell transplants from related donors within the first 28 days of life developed a more robust immune system, with higher levels of T cell reconstitution and output from the thymus gland. T cells are white blood cells that are essential for normal function of the immune system, Buckley reports.

Nearly all SCID cases can be diagnosed at birth by counting the number of lymphocytes, a type of white blood cell, present in umbilical cord blood, Buckley said. Infants with SCID have a profound deficiency of lymphocytes, due to the deficiency of T cells that help fight infections. Children with other immune disorders could also be identified through this test, which costs an average of $50 at a commercial laboratory. Researchers at the National Humane Genome Research Institute are developing a test for immunodeficiency disorders that could be performed on the small blood sample now taken from newborns to screen for certain metabolic disorders.

Nine forms of SCID have been identified in the past 10 years, caused by mutations of single genes. However, Buckley has treated 30 patients without mutations in the known SCID genes, making it likely other causes are yet to be discovered. The most common form of SCID is X-linked recessive, a mutation inherited on the X chromosome. Because X-linked recessive genes are expressed in girls only if a child receives two copies of the gene — one from each parent —
the disease is more common in boys, who only need one copy for an X-linked recessive gene to be expressed. SCID-X1 accounts for 46 percent of U.S. cases.

The incidence of SCID has been projected to range from one in every 100,000 to 500,000 births - more frequent than disorders such as Huntington’s disease. "However, no one truly knows how common this disease is. I suspect that it is much more common than thought because a lot of SCID patients probably die before their disease is recognized," Buckley said.

Buckley and her colleagues at Duke University Medical Center treat SCID patients via stem cell transplants derived from donor bone marrow, typically from a parent or matched sibling. Transplant recipients do not need pretransplant chemotherapy or prophylactic treatment for graft-versus-host disease. Infants with SCID have a complete absence of T cell function, so they cannot reject the transplants. The bone marrow is processed to remove T cells, preventing the donor T cells from attacking the recipient, known as graft-versus-host disease. Mature, donor-derived, T cells typically appear in SCID patients within 90 to 120 days after transplant. The success of treatment varies among different forms of SCID.

Clinicians are striving to improve the success of transplant therapy and create more robust immune systems by giving higher numbers of stem cells in preparations nearly devoid of T cells, Buckley added. "If the imperfect results seen with stem cell therapy in the past were due to an insufficient number of stem cells, this approach should result in better immune reconstitution. The only remaining obstacle would then be to ensure diagnosis is made early before untreatable infections develop," she said.

Of the 136 SCID patients treated at Duke, 105 (77 percent) are alive. None show any evidence of susceptibility to opportunistic infections and most are in good general health. The oldest is 22 years of age. All 15 recipients of marrow from perfectly matched donors and 89 of the 121 recipients of T cell-depleted marrow from related donors are among the survivors.

Of the 38 infants transplanted during the first 3.5 months of life, 37 (97 percent) survive, compared to 68 survivors among the 98 transplanted after that age (69 percent success). Twenty-four of the 31 deaths occurred from viral infections. Graft-versus-host-disease (GVHD) occurred in 40 of the 121 patients given T cell-depleted parental bone marrow, but most of the GVHD was mild and required no treatment; there were no deaths from GVHD. In 35 of 40 GVHD cases, the complication occurred when there was persistence of transplacentally transferred maternal T cells.

The source of this article is http://www.dukehealth.org