CVID and Pregnancy:
Do We Have a Problem?

By Zachary Pugh

Having a child is one of the most important events in a person's life, if not the most. This said, we want to make certain that this replication of us, this life we have created and nurtured, is introduced to our world without flaw. More important, we want to be assured that we are informed and prepared for this new familial journey. For those with common variable immune deficiency (CVID), information is imperative and preparedness is paramount.

What We Know

CVID is a term that describes a heterogeneous cluster of disorders in people who have hypogammaglobulinemia, with variable degrees of T-cell dysfunction.[1] Among the information on CVID that has been accumulated within the medical community is the fact that it is not gender-specific. According to St. Jude Children's Research Hospital, diagnosis of CVID typically becomes prevalent in men and women in the third or fourth decade of life, but it is also seen in children. CVID is often suspected when a patient possesses "low levels of antibodies in the blood stream, a poor immune response to vaccines, and a history of recurrent infections."[2]

Although the medical community has reached a consensus that heredity does pose a role in the development of CVID, there seems to be no concrete agreement on what the genetic patterns are or are not. In its publication, "The Clinical Presentation of the Primary Immunodeficiency Diseases," the Immune Deficiency Foundation (IDF) clearly affirms "there is no recognizable pattern of inheritance, although CVID may cluster in some families." St. Jude Children's Research Hospital concurs that, although genetic factors do play a part in the development of CVID, "there is no single gene mutation (mistake) that can be identified."

As a board-certified genetic counselor, mother and CVID patient, Melissa Schweitzer is well-versed on pregnancy and CVID. "I tend to think of CVID as a disease that is inherited in a 'multifactorial' way," Schweitzer says, "meaning that I think both genetic and environmental factors play a role in causing the majority of cases."

When discussing genetic factors, there is the obvious question of inheritance, which, as mentioned earlier, does play a role in the development of CVID. But how large of an influence do genes have? To date, there are no conclusive tests that have revealed a connection between one single gene and all CVID cases. However, Schweitzer does believe that single genes are responsible for subsets of the disease. Within these particular families, there are traditional patterns of inheritance such as autosomal recessive and autosomal dominant. While the autosomal recessive pattern involves the parents as unaffected carriers and a 25 percent chance of the child being affected, the autosomal dominant pattern involves affected parents and a 50 percent probability rate of inheritance.

"These subsets are caused by the single genes that have been identified…and probably other genes that have not yet been identified, but unfortunately still do not account for the majority of the cases of CVID," Schweitzer affirms.

Of these identified single genes, one is the TACI gene mutation.

In 2005, a group of researchers at the Children's Hospital Boston discovered a genetic mutation pattern in patients with CVID. Led by Raif Geha, MD, and Emanuela Castigli, PhD, this study concluded that certain mutations in the gene known as TACI contribute to the development ➢

[1] Immune Deficiency Foundation; Publications: The Clinical Presentation of the Primary Immunodeficiency Diseases www.primaryimmune.org/pubs/book_phys/phys_p06.htm.

[2] St. Jude Children's Research Hospital; Inherited Immunodeficiencies: Common Variable Immunodeficiency (CVID) www.stjude.org/disease summaries/0,2557,449_2164_6532,00.html.

of CVID and other immune system conditions. In a press release on the findings, the National Institutes of Health (NIH) summarized that "[d]efects in TACI were found in four of 19 unrelated patients with CVID and in one of 16 unrelated patients with IgA deficiency."

Upon further examination of the four individuals with TACI mutations, scientists discovered that all of them had relatives who possessed a similar mutation. "A test for TACI defects would enable the diagnosis of more children and their relatives with these immune deficiencies," Dr. Geha said in a 2005 press release. Despite this discovery, there is no agreement in the healthcare community about the likely percentage of CVID patients with TACI mutations.

Genetic Counseling

During her 10-year career in genetic counseling, Schweitzer worked as the director of patient advocacy for the IDF. Although she mentions that she was not aware of any clear and concrete links between miscarriage and CVID, "infertility and pregnancy loss [was] a concern that many women with PIDD [primary immune deficiency disease] expressed when I talked with them at IDF."

Howard M. Lederman, MD, PhD, and professor of Pediatrics and Medicine at Johns Hopkins University in Baltimore, echoes that there are no clear connections between CVID and infertility. "In general, I don't expect CVID to cause problems with infertility." He does add, however, that secondary effects of CVID, including chronic recurrent infections and autoimmune diseases such as various forms of colitis, could lead to pregnancy problems. The main thing to take into consideration is that antibody deficiency should not be an important issue.

Although Schweitzer recommends pre-pregnancy genetic counseling, if done during the pregnancy it still may be effective in determining whether or not the child will have a predisposition to CVID. "This can be done either by the patient's immunologist or by a genetic counselor who would take a detailed family history in the form of a pedigree, which is like a family tree," Schweitzer says. This method provides a way for the genetic counselor to pinpoint family inheritance patterns, even if the genetic basis for the person's individual disease is not known.

Along with determining if the child would be predisposed to CVID, genetic counseling also provides women and couples with valuable advice on testing the fetus if there is a known familial genetic mutation. "Genetic counseling would also provide information on routine prenatal screening tests for other birth defects and diagnostic tests such as chorionic villus sampling (CVS) and amniocentesis," Schweitzer suggests.

Pregnancy Management

As an expert in the field of genetics and an involved patient advocate, Schweitzer still needed guidance from her immunologist when it came to managing her own pregnancy. During her second trimester, Schweitzer's immunologist began measuring her IgG levels every month. As a patient, she suggests that pregnancy management for those with CVID "should really be discussed by an immunologist who has managed several pregnant women with PIDD. However, the main concern is maintaining the IgG at a therapeutic level in both the woman and the fetus," she explains.

In Schweitzer's case, her immunologist began measuring her IgG trough levels (the levels just before the next infusion) once a month, beginning in her second trimester. "He had a baseline to start from and then when the level started going down… and my weight was increasing… he increased my dose of IVIG." Toward the end of her term, her immunologist tried to give her an infusion as close to her delivery date as possible. "For my first pregnancy," Schweitzer recalls, "I got lucky and had gotten my infusion just a couple of days before I ended up delivering my daughter by an emergency C-section. My second pregnancy was a planned C-section, so I was able to schedule my infusion right before the C-section."

For women who plan to have a C-section, Schweitzer offers suggestions: "In order to minimize her risk of possible infection related to the surgery, she would want to have her infusion as close to her C-section as possible," adding that women should always consult with their immunologist.

"[Women] need to be sure that the person that manages their gamma globulin knows they are pregnant," Dr. Lederman says. There are "two things that will change the dose requirement for gamma globulin." The first is that "pregnant women gain weight," he explains, "and the dose of gamma globulin is based on weight. The other is that the placenta pumps gamma globulin from the mother into the baby, especially during the last trimester. You have to make sure that the dose of gamma globulin accounts for both of those things." Dr. Lederman added that it's a good idea to check IgG levels before each infusion, starting at about the third or fourth month of pregnancy so that the dose can be increased as necessary.

Schweitzer suggests that, if after your child is born and all of the tests reflect normal immunoglobulin levels, it is still important to watch for potential symptoms, because CVID and other immune deficiencies often manifest later in life. "I have always been told to keep a close eye on my children's health, and, if they start experiencing more frequent infections or other symptoms of PIDD, then it's time for more testing and evaluation." ■