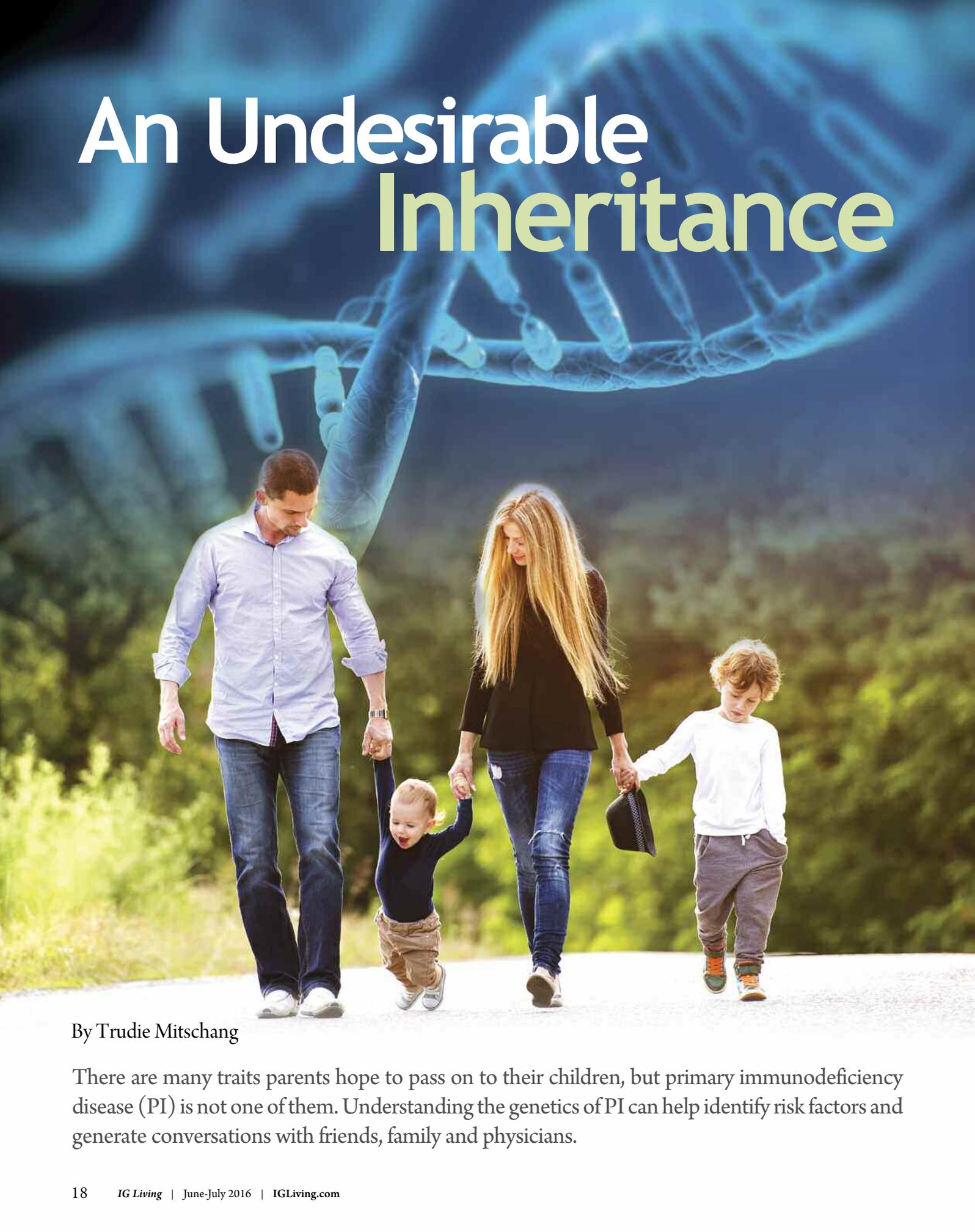


An Undesirable Inheritance

A photograph of a family of four walking on a paved path outdoors. The father is on the left, wearing a light blue button-down shirt and dark jeans, holding the hand of a toddler. The mother is on the right, wearing a black long-sleeved shirt and blue jeans, holding the hand of a young boy. The toddler is in the center, wearing a dark blue shirt and tan pants. The young boy is on the far right, wearing a white long-sleeved shirt and grey pants. In the background, there is a large, glowing blue DNA double helix structure against a dark blue sky. The overall scene is bright and sunny.

By Trudie Mitschang

There are many traits parents hope to pass on to their children, but primary immunodeficiency disease (PI) is not one of them. Understanding the genetics of PI can help identify risk factors and generate conversations with friends, family and physicians.



Protect Yourself From a Lapse in Coverage

CSL Behring AssuranceSM

CSL Behring Assurance is designed to help ensure that people who rely on CSL Behring Ig therapies can continue to receive treatment even if they experience a lapse in third-party, private health insurance.

- **Earn CSL Behring Assurance points** for every month of continuous Ig product use
- **Points are redeemable** for Ig therapy in the event you **lose insurance coverage**
- **Enroll as soon as possible** because points are issued from the date that enrollment eligibility is approved

“No one wants to think they will lose their insurance—even briefly—but when you’re dealing with a chronic disorder you always have to be prepared for the unexpected.”

— Lori K.
Parent



1-877-355-4447
Monday – Friday
8 AM to 8 PM ET

CSL Behring AssuranceSM is a service mark of CSL Behring LLC.
Biotherapies for Life[®] is a registered trademark of CSL Behring LLC.

©2016 CSL Behring LLC
1020 First Avenue, PO Box 61501, King of Prussia, PA 19406-0901 USA
www.CSLBehring-us.com HIZ16-04-0017 5/2016

A Gap in Your Insurance
Coverage Shouldn't Mean
a Gap in Treatment



Zero Cost. Zero Worries.

How to enroll:

- Call the toll-free IglQ Hotline at **1-877-355-4447**

Earning and redeeming points is easy.

- Earn a point for every consecutive month of CSL Behring product use
- Redeem 3 points for a one-month supply of your CSL Behring product*
- Should you suffer a lapse in your insurance, simply contact a IglQ Care Coordinator and we will take care of the rest



“At the Immune Deficiency Foundation, we often talk to patients who lose their insurance coverage and we see firsthand how stressful this situation can be. This program not only helps people continue their life-saving treatments but also provides security for the future. It is a valuable option for our patient community.”

— Marcia Boyle
President and Founder, Immune Deficiency Foundation

*Certain limitations apply—see program Terms and Conditions at www.cslobehringassurance.com.

CSL Behring AssuranceSM is a service mark of CSL Behring LLC.
Biotherapies for Life[®] is a registered trademark of CSL Behring LLC.

©2016 CSL Behring LLC
1020 First Avenue, PO Box 61501, King of Prussia, PA 19406-0901 USA
www.CSLBehring-us.com HIZ16-04-0017 5/2016

WHEN COUPLES DREAM of starting a family, they delight in imagining the physical traits their child will inherit. Will the baby have Mom's blue eyes, Dad's prominent nose, Grandpa's slim physique or Grandma's curly hair? Unfortunately, when one or both parents carry the genetic makeup of a primary immunodeficiency (PI), passing along DNA from parent to child can go from joyful anticipation to fear and dread. And, in some cases, if one of the parents is merely the carrier of a genetic disorder, the devastating news of a diagnosis does not come until one or more children are already exhibiting symptoms.

Tragedy Leads to Diagnosis

Jessica Johnson was unknowingly a carrier of X-linked agammaglobulinemia (XLA), a condition that affects the immune system and occurs almost exclusively in males. Children with XLA are usually healthy for the first 1 month or 2 months of life because they are protected by antibodies acquired before birth from their mother. Later, as the maternal antibodies diminish, the affected child begins to develop recurrent infections. "When our first child, Emma, was 2 years old, we had Andy. And although Emma was always very healthy, Andy started to get sick at the age of 4 months," says Johnson. "He suffered from frequent colds, ear infections and sinus infections. He would get 105-degree [Fahrenheit] fevers, and his white cell count could be through the roof."

Jessica's third child, Ethan, wrestled with the same cycle of infections as his 2-year-old brother, and tragically succumbed to complications from his illness just prior to a diagnosis. Armed with medical information and still grieving the loss of Ethan, Jessica and her husband, Bart, made the controversial decision to have a fourth child, Gavin, who also has XLA. "I struggled quite a bit with the decision to have more children after our sons were diagnosed, because the diagnosis came at the same time as my son Ethan's death," she recalls. "We lost him and got the diagnosis of XLA at the same time." While Johnson wasn't done having kids, she wondered whether she could survive XLA taking away another child.

Understanding the Genetics of PI

A short review from high school biology class helps explain the basics of genetic influence on offspring. In the human body, each cell contains 23 pairs of chromosomes, hence 23 sets of genes. One of each pair of chromosomes is inherited from the mother, while the other is inherited from the father. One gene from each biological parent determines characteristics like eye and hair color. All of the chromosomes except the sex

chromosomes are called autosomes and are numbered from 1 to 22 according to size. One additional pair of chromosomes determines the sex of the individual. These are called the sex chromosomes and are of two types, X and Y chromosomes (females have two X chromosomes, and males have an X and a Y chromosome). The sex of the baby is determined by which type of sperm (X or Y) fertilizes the egg.¹

Most PIs are inherited in one of two ways: X-linked recessive or autosomal recessive. Recessive genetic disorders occur when an individual inherits two copies of an abnormal gene for the same trait, one from each parent. If an individual receives one normal gene and one gene for the disease, the person will be a carrier for the disease but usually will not show symptoms. The risk for two carrier parents to both pass the defective gene and have an affected child is 25 percent with each pregnancy. The risk of having a child who is a carrier, similar to the parents, is 50 percent with each pregnancy. The chance for a child to receive normal genes from both parents and be genetically normal for that particular trait is 25 percent, and the risk is the same for males and females.¹

MOST PIs ARE INHERITED IN ONE OF TWO DIFFERENT WAYS: X-LINKED RECESSIVE OR AUTOSOMAL RECESSIVE.

Rarely, the inheritance of a genetic disease is autosomal dominant. Dominant genetic disorders occur when a single copy of an abnormal gene is necessary to cause a particular disease. The abnormal gene can be inherited from either parent or can be the result of a new mutation (gene change) in the affected individual. The risk of passing the abnormal gene from the affected parent to offspring is 50 percent for each pregnancy, and again, the risk is the same for males and females.¹

Of course, statistics can never predict every possible variable when it comes to conception, pregnancy and childbirth. Even when the odds seem to be in favor of delivering a healthy baby, genetic outcomes can be wildly unpredictable.

Terry Harville, MD, PhD, medical director of the Special Immunology Laboratory at the University of Arkansas for

Medical Sciences and a consultant for immunodeficiencies, autoimmunities and transplantation, has decades of experience working with families who have wrestled with family planning issues. In his opinion, denial of risk is often a driving force behind the decision to have children once the possibility of an inherited PI has been established. “In situations where the risk of passing on the disease is 50/50 for each pregnancy, parents who are optimistic by nature will still believe the odds are in their favor with the coin flip,” he explains. “Sometimes, when they already have one or two affected children, they believe they’ve used up all of the potential ‘bad luck.’”

TREATMENT OPTIONS LIKE IG CAN POSITIVELY INFLUENCE FAMILY PLANNING DECISIONS, ESPECIALLY WHEN COUPLES HAVE QUALITY-OF-LIFE CONCERNS REGARDING CHILDREN WITH GENETIC DISEASES.

Joanne Pease, the mother of three adult sons with XLA, agrees with that assessment. “Our oldest was 2 years when he was diagnosed, and our second son contracted polio from a live vaccine before we knew he also had XLA,” she recalls. “When I got pregnant with my third son, the doctors encouraged me to abort, but my husband was hoping for a girl, and we went through with the pregnancy. Who knew we’d win the XLA lottery three times in a row with another son?”

Johnson says for her family, it was also a matter of calculating the odds based on previous experience: “We were told that XLA occurs in one out of every four births if the mother is a carrier. After Ethan and Andy were both born with XLA, we figured we had more than met our quota. Unfortunately, we were wrong; we ended up with four out of five.”

Navigating Guilt

In families stricken with genetic diseases, feelings of guilt can manifest in myriad ways. Parents may blame themselves and one another. Family dynamics are also impacted; healthy siblings may feel intense shame wondering why they were spared the life-altering disorder that affected a brother or sister. Expectant parents who learn their unborn child will be chronically ill also confront feelings of guilt, whether they decide to have the child or abort. Even adult children who have accepted the ramifications of their inherited diseases may feel reluctant to discuss their health challenges with parents for fear of instilling guilt.

Experts believe understanding the many layers of guilt as it applies to families with genetic diseases may help researchers better understand the emotion, and may lead to better counseling and support systems for individuals and families. “Psychoanalytically, we look at guilt as an internal process of punishment. You’ve done something bad, and your superego says you have done something bad and need to be punished. It is an internal way of keeping us moral,” says Dr. Philip R. Muskin, a psychiatry professor at Columbia University.² “Guilt can be warranted when you’ve really done something wrong, but you can also feel it without having done anything.”

Advances in medicine have only intensified potential feelings of guilt surrounding inherited diseases. Illnesses that were once chalked up to “God’s will” or a combination of unforeseen factors can now be absolutely attributed to a single bad gene inherited from one parent. Dr. Harville has seen this scenario numerous times in his practice dealing with X-linked diseases. “Many men blame the female disease carrier for ‘giving this disease to my child.’ I tell people, you can pick your friends, you can pick your nose, but you can’t pick your relatives. You are stuck with the genetics you come with,” he says. “In spite of feeling guilt about having a sick child, with the father present, it’s important to address the tendency of the husband to blame the wife and confront that issue head-on.”

Dr. Harville notes that in terms of family dynamics, if fathers tend to place blame, mothers tend to bear the burden of responsibility: “The mother tends to ask, ‘How did this happen; what did I do to cause this?’ These questions are normal, and it’s important to work through the facts so that the family can begin to heal.”

Next-Generation Considerations

Myron Anderson’s* mother has common variable immune deficiency, and he and his brother both inherited the disease.

* Name changed for privacy.

Because he was diagnosed at an early age and has lived a relatively normal life thanks to immune globulin (IG) therapy, he determined to never let his diagnosis define or limit him, and that has carried over into his views on starting a family. Recently, Anderson learned that his wife is expecting. “Having PI my whole life made me think more about what tests to have when my kids were born, but I never let my disease limit what I can do, so I didn’t let it limit me from wanting kids,” he says. “I figured if any of my kids have a PI, then I already know what to do. It did make dating harder because some women were concerned about my disease passing on to our future children.”

Treatment options like IG can positively influence family planning decisions, especially when couples have quality-of-life concerns regarding children with genetic diseases. “We believe that Ethan only died because the disease was undiagnosed and he hadn’t been receiving IG infusions,” says Johnson. “We knew our older son and future children would not have that disadvantage. XLA was something we felt we could manage, and from what we knew, the kids, if affected, could still live normal and productive lives.”

Pease agrees: “I have no guilt or regrets about my decision to have my three boys. This challenge has taught them to rely on one another, and as adults, they are extremely close.” However, she does suspect that living with XLA may have made her sons hesitant to marry and have children of their own. At 20, 26 and 33, the men remain single, preferring to share a home with one another.

Pursuing Genetic Counseling

Speaking to medical professionals who are well-versed in the risks, treatment options and quality-of-life issues of various PIs can help couples make informed decisions about family planning. Simply allowing spouses and family members to become more familiar with the genetic facts of a particular disease can help spark questions and alleviate fears. “In my experience, families often don’t know what questions to ask,” says Dr. Harville. “In cases where we are dealing with something like severe combined immunodeficiency, couples are so attuned to the fact that we are dealing with the prospect of death that fears regarding the immediate future overshadow concerns about long-term treatment and quality of life.”

Dr. Harville says that while genetic counseling can be a benefit, he advises against in utero testing unless abortion is a viable option: “The risk of damaging the fetus is too high, in my opinion.”

According to a journal article published by the Allergy Society of South Africa, due to the complexity of the genetic mechanisms involved in PIs, genetic counseling for patients and their families is recommended.³ Genetic counseling can assist affected families by helping them understand the cause of the condition and the expected prognosis, and, importantly, what the implications are for them, as well as for extended family members. Genetic counseling plays an integral part in the management of patients with PI and can facilitate genetic testing and treatment plans.

During a genetic consultation, individuals will be asked to provide a comprehensive family history and obtain a disease diagnosis, if one has not already been established. Further discussions will revolve around disease progression, risk of recurrence for future pregnancies and occurrence in other family members. Testing options may also be discussed, including testing of individuals at risk of being carriers and prenatal testing. Supporting the family may also include referrals to other professionals such as mental health counselors and parent support groups. More information on genetic counseling can be found at the National Society of Genetic Counselors (www.nsgc.org).

Whether or not families choose to seek professional advice from a genetic counselor or other healthcare professional, successfully navigating the emotional minefield of genetically inherited diseases always begins with open, honest communication. Dawn Laney, a genetic counselor, research coordinator and instructor in Emory University’s Department of Human Genetics, has written several children’s books on the topic of genetic disease. After diagnosing patients, Laney frequently has to explain the test results and potential treatment options to patients and their families. “How do you explain to a child that he or she is battling a genetic condition? It’s simple: You explain it simply.”⁴

For Anderson, the joyful anticipation of expecting his first child has pushed any fears or concerns to the background. When and if the time comes, he and his wife have a plan in place to discuss PI with their future son or daughter: “We plan on speaking to them about the risk for their kids, while emphasizing that they should not let it hold them back from fulfilling their dreams.” ■

TRUDIE MITSCHANG is a contributing writer for *IG Living* magazine.

References

1. Immune Deficiency Foundation. *IDF Patient & Family Handbook for Primary Immunodeficiency Diseases, Fifth Edition*. Accessed at primaryimmune.org/patient-family-handbook
2. Goldman, R. The Heaviest Heart: Guilt and Genetic Disease. ABC News, March 24, 2009. Accessed at abcnews.go.com/Health/story?id=7154193.
3. Wessels, TM, and Krause, A. Genetic Counseling in Primary Immunodeficiency Disease. *ALLSA Journal*, November 2012. Accessed at www.allergysa.org/Content/Journals/November2012/Genetic_counseling.pdf
4. Laney, D. Talking to Children About Genetic Conditions. Emory News Center, April 27, 2013. Accessed at news.emory.edu/stories/2013/04/talking_to_children/campus.html.