

# Learning Genetics

*Finding sparse, uncoordinated research on their children's rare disease, a couple starts their own organization to jumpstart hopes for the future.*

BY SHARON F. TERRY

*PREFACE: The promise that genetics holds for improving the diagnosis, prevention, and treatment of disease is staggering if not yet fully realized. Such hopes are based on the successful mapping of the human genome and discovery of the genes that mark us for particular maladies—developments that someday could lead to cures for diseases such as cancer, Alzheimer's, or diabetes. With this new knowledge and the technology to apply it, however, come questions about what we do with what we know. A host of moral, ethical, and legal uncertainties, at both the policy and personal levels, surrounds the use of genetic technologies. After Sharon Terry discovered that her children had a rare genetic disease, she and her husband took a crash course in genetics, founding an organization whose aim is to accelerate research on their children's condition. Her story reveals the power that proactive parents can wield in expediting research while protecting the privacy of affected families. For all of its potential to cure disease, however, genetic technology also equips us with painful knowledge. Writer Lisa Sweetingham tells us about a couple facing agonizing decisions because of what genetic testing could reveal about their unborn baby's health.*

**I**N 1994 WE DIDN'T KNOW a gene from a hubcap. We thought we didn't need to know. The brave new world of genetics was vaguely interesting but not part of our world—not until our children were diagnosed with a rare genetic condition and we were thrown headlong into a chasm. The chasm was really a threshold. We crossed it, abandoning our ignorance of medical research and clinical treatments for the other side—a desperate need for those systems to perform exceptionally well. The leap across that threshold took seconds, but learning the realities of these systems was an arduous, eye-opening journey that led us to start a foundation and a new model for accelerating research.

Our children, Elizabeth and Ian, now ages fifteen and thirteen, have pseudoxanthoma elasticum (PXE), a rare genetic condition that causes vision loss, premature wrinkling, and cardiovascular and gastrointestinal disease. The condition's worst complication is vision loss, devastating people with PXE when they are between thirty and forty.

Two days before Christmas 1994, I brought Elizabeth, then age seven, to a dermatologist. She had small bumps on the sides of her neck that had not disappeared since I had first spotted them a year before. Our pediatrician didn't think they warranted attention and assumed that my

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worry was spurred by the recent death of my brother from a brain tumor.

The dermatologist knew immediately that these bumps were a sign of PXE. Glancing at Ian, then five, he said, “Ah, he has it too.” He asked if he could biopsy Elizabeth’s neck and examine her eyes. Confused and terrified, I consented. Why would a dermatologist examine eyes for a skin condition? I learned all too quickly that many skin problems are part of larger, systemic conditions. I also learned that we were fortunate that the dermatologist we chose, who happened to be a neighbor, also happened to be an ophthalmologist. He could do a preliminary assessment of the disease’s effects on my children’s eyes.

### Distrusting The System

I CAME HOME NUMB AND TERRIFIED. I called Pat, my husband, desperately wishing he had come to the appointment with us. When you ask our children what they remember from that day and the following weeks, they reply, “The best Christmas ever! We got every toy we asked for!” We recall this period as a time of great fear and confusion as we delved into a morass of medical literature, trying to sort truth from fiction. Popular medical resources such as the *Merck Manual* described the condition in dire terms, including the possibility that our kids would die at age thirty. What most jarred us was the realization that the research-medical system was not a well-oiled machine. We began to understand that we could not expect accurate information or a course of treatment.

The only light in the season was our dermatologist, Lionel Bercovitch, who lived a few houses away and knew of our shock and sadness. He suggested we talk about the diagnosis and offered to meet with us at a neighbor’s house, so that our children would not overhear our discussion. And so on Christmas Eve we learned about genes, recessive inheritance, pedigrees, and mutations. The doctor was frank about the limited understanding of the condition. A sense of foreboding began to overlay this already traumatic journey, which was starting to resonate with another experience—my brother’s death.

My brother had died a year earlier of a lethal form of brain cancer, at age thirty-three, leaving behind a young wife and baby daughter. I accompanied my brother and his wife through his diagnosis, treatment, and death. All along the way the doctors treating my brother at a major teaching hospital assured us that he would survive. After his death, I learned that his cancer is always lethal, but there were avenues we didn’t explore because we trusted his doctors to lead us down the right paths.

From this tragedy we found that we needed to be active participants in health care decisions, even to the point of reading the peer-reviewed literature the next time around. We learned that helping loved ones through a health crisis was not like taking a number at the deli counter. If research on PXE wasn’t being done, we couldn’t just wait until they called our number—they might never get to it. So we

spent the weeks following our children’s diagnoses in medical school libraries, which aren’t exactly lay-friendly environments. We faced steep learning curves. Pat was a design engineer for a construction company and I was a college chaplain; neither of us had any medical background. We copied every article we could find and brought them home to read, quickly learning that we also would have to invest in medical dictionaries; encyclopedias; and biology, genetics, and epidemiology textbooks. Pat poured all of his energy into understanding the science behind the research—his way of coping as a distraught dad. And every glance at the lesions on our kids’ necks renewed our fear.

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At the same time, our pediatrician discovered that a researcher at a major university nearby was conducting a research project to find the gene associated with PXE. She contacted the researcher, who came and took samples of our family’s blood. It gave us such hope to think that someone was working on this obscure disease. We were thrilled to participate, even though the researcher provided no informed-consent process. A few days later another researcher called from another major institution and asked for blood samples. We told him to get some from the first researcher. How shocked we were to find that they wouldn’t share and expected us to allow blood to be drawn from small children twice in one week. There was no central repository for the precious blood of people with this rare condition, whose numbers are 1 of every 25,000 Americans. We wondered if this was another indication of the inefficiency of the medical system.

## Taking The Reins

**P**AT WAS RELENTLESS—learning the science as quickly as he could and bringing me along. Many nights he would read aloud passages from medical textbooks. We would bat the concepts back and forth, looking them up in medical dictionaries and encyclopedias. Sometimes we’d wake up in the morning to find we had fallen asleep with books and articles strewn around the bed. Sometimes we’d fall asleep in tears after viewing photos of sagging skin or reading about the deaths of young people from heart and gastrointestinal complications. We shielded the kids from this stuff as best we could.

As we waded through the literature, it became obvious that it did not present a clear picture and usually cited case studies that even we, with our limited knowledge, thought were extreme and unrepresentative of the condition. We also noticed that the few studies that included multiple patients contradicted one another. Pat’s construction design work relied on project management and

coordination; he couldn't understand why the same principles weren't applied to medical research. We began to scheme about what we would do if we were managing research on this disease. It seemed to us that not only did PXE need a central repository for blood and tissue, it also needed a large cohort of affected people to give researchers a comprehensive understanding of the condition's manifestations and progression.

We decided to meet with as many authors of PXE peer-reviewed literature as we could. Much to our surprise, everyone we contacted agreed to see us. Their perceptions about the condition ran the gamut, from one researcher who said, "PXE research is a rat hole—no one wants to do it, it isn't worth it," to some who were overly optimistic about the results of their efforts. We joined the only support group for the condition and encouraged its founding physician to let us help set up a central registry and sample repository. He was adamantly opposed to both, not wanting to share information with other researchers because he had given much of his professional career to studying PXE. We struggled for several months to work with him, but it became increasingly apparent that his agenda and ours shared little overlap. One long night, Pat and I sat at the dining room table over a bottle of wine and agonized over what we had learned. We could not wait for one researcher to make headway while this disease progressed in our children. From our reading, Pat knew that just as he would coordinate the installation of plumbing and electricity in a building, so should the genetic studies, cell biology, animal models, and other aspects of the research progress on parallel tracks. Although it pained us greatly to do so (we had hoped that all affected people could work together), we started a new advocacy group for PXE. Pat's skills and mine complemented each other. As he laid the groundwork for the scientific endeavors of the foundation, I began to build the support structure that affected people would need.

We contacted the Washington, D.C.-based Genetic Alliance, the world's largest coalition of genetic advocacy groups. Its staff mentored us, introduced us to other lay leaders, and helped to focus our activities. With their help we were able to do a great deal in a short time. Gradually the new foundation, PXE International, took more and more of my time. I had been teaching part time and stopped doing anything except establishing the foundation. We enlisted Dr. Bercovitch and met every few nights, so that within six months we had created the PXE International Blood and Tissue Bank, laid the groundwork for an epidemiological study, coordinated dozens of volunteer outreach efforts around the world (from those of a nurse in South Africa to a mom in Romania), and begun to build the PXE International Research Consortium. This process was not easy. Only a combination of the Internet, other sup-

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port groups, and Dr. Bercovitch's help made all of this feasible. Our kids began to come to grips with PXE in their own way. Typical of children, they didn't take it too seriously and instead did things like naming a spider "pseudoxanthoma elasticum," proud to learn a Latin insect-naming technique!

Elizabeth and Ian have reacted to PXE in a remarkable way. They have skin lesions and the beginning signs of eye disease (although their vision is still fine). They feel most limited by a restriction on contact sports to protect their eyes. They have grown up aware that no one knows much about PXE's progression but also with ideas about how to fight for a different future. They have testified three times before the House Appropriations Subcommittee on Labor, Health and Human Services, and Education. At age eleven, Elizabeth recommended to the subcommittee that basic research be funded to benefit all conditions, not just hers. They both think that PXE has presented them with opportunities they never would have experienced. They believe that we will make a difference, so they don't worry too much.

### Getting Researchers On The Same Page

**W**ATCHING THE DISEASE PROGRESS IN OUR CHILDREN provides us with the incentive to work long hours and craft novel solutions. Our blood and tissue bank is one result of our efforts. The need for such a bank came to us from several different directions: My ever-practical husband knew that we needed a commodity to leverage if we were to have a place at the table; competing interests of researchers don't often allow widespread distribution of samples, which can slow research; and we knew that we would be able to offer affected people a centralized bank that would afford them something that they (and we) didn't have before—confidentiality and anonymity.

Despite everything we had been through, however, new lows were yet to come. Soon after we started the PXE International Blood and Tissue Bank, the researcher in whose lab we banked our samples actively tried to thwart access to the bank by other researchers. We were appalled, maybe naïvely so, that researchers would put their needs for publications, funding, promotions, and tenure ahead of the needs of people living with disease. We apparently experienced an extreme example of this, but we and other groups have encountered variations of it repeatedly. Fortunately, this problem was counterbalanced by interactions with other researchers here and abroad, with whom real collaboration occurred. One of these relationships led to a joint application for the patent on the gene associated with PXE—the first time lay people in an advocacy group have applied for the patent. We consider ourselves stewards of the gene and know that the real issues will be played out in its licensing.

Our foundation sits at the juncture of research, education for affected people, and information for clinicians. We coordinate the PXE International Research

Consortium, in which nineteen labs work through us with one another. This allows labs to do what they do best—excellent science—while preserving the ability to publish their own discoveries. At the same time, the labs together determine the dates when information sharing will take place. This also lets PXE International see gaps in the plan and make sure that all research phases are simultaneously fast-tracked. For example, we saw that the most difficult aspect for labs was information and sample collection from affected people and their families. In an ever-tightening regulatory climate in which institutional review boards are scrutinizing all human-participant research, our organization provides a firewall between researchers and research participants. This set up protects patient confidentiality and encourages participants' involvement. It also allows us to recontact participants when necessary for research while at the same time protecting them. Participants can engage in an unrushed decision-making process with us, determining the risks and benefits of participating in the PXE International Blood and Tissue Bank, the epidemiological study that we sponsor, and other projects. They feel safe, knowing that we are all in the same boat—sharing the distress of living with PXE and searching for options.

### Consumers As Catalysts

**M**Y WORK WITH PXE INTERNATIONAL HAS TAUGHT ME that consumers can be central to the research endeavor. We can be a catalyzing force for translating research into the services we desperately need, such as treatments, technologies to alleviate suffering, and clinical methods of dealing with the conditions. I now serve as president of the Genetic Alliance. This role enables me to work with other groups so that we leverage each other's capacities to make a difference for our loved ones.

My family's experience also has showed me that we need strong protections for research participants but not overly onerous regulations that make it impossible for researchers to have access to patients. In the same way that we know that our nation's health care system needs overhauling, I am convinced that the research process in this country needs to undergo changes that will facilitate collaboration among labs and build large registries that allow discovery of the natural history and progression of disease.

We hope for a treatment that will slow down PXE and spare Elizabeth's and Ian's vision, but we know that the advances we seek are usually measured in generations, not lifetimes. For Pat, Elizabeth, Ian, and me, the journey has bonded us together in a profound way. Moreover, I know that when we shoulder our burdens with other advocacy groups, we will help to speed up research that will spare lives. It can't happen fast enough.