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The Genes That Bind

BY CHARLOTTE HUFF

When and how to share genetic risk with children.

For Sara Reveles-Pellegrini, one of four sisters, the fingerprint of cancer has left its imprint on her family tree and her memories, long before she learned of a gene called BRCA.

In the late 1990s, the family rallied around Pellegrini's two older sisters, Rebecca and Rachel, both diagnosed with breast cancer within a year of each other. By Pellegrini's wedding in 2000, Rebecca was quite ill, and within a few months of death. Rachel continued to battle the malignancy for years.

So Pellegrini had already developed a plan before she underwent testing in 2005 for the BRCA mutation, a gene alteration that increases a woman's risk of breast and ovarian cancers. "Seeing how aggressive the cancer was with my sisters, I knew that I wanted to remove body parts." She was 40 years old with a house filled with children, two boys and two girls, ages 4 and younger. Two of the toddlers played on the floor while the genetic counselor explained her results: positive for a BRCA1 mutation.

For the next three years, Pellegrini underwent some 30 surgeries, including the removal of her uterus, ovaries, fallopian tubes, and both breasts. Infection and breast reconstruction complications sent her back to the operating room again and again. Through it all, Pellegrini and her husband talked to their children about her proactive surgical decisions and the family's history of breast cancer, which also took Rachel's life in 2007.

Even so, Pellegrini was startled one morning last year, as she curled her older daughter's hair for a school play, when 8-year-old Antonia asked about testing for breast cancer. (She had seen a TV commercial about genetic testing.) Could she get tested as a teenager? "I was surprised and amazed and almost a little heartbroken," Pellegrini says.



Sara Reveles-Pellegrini, with her children (from left) David, Josef, Antonia, and Victoria, tested positive for a genetic mutation that elevates her risk of certain cancers. Photo by Colby Ware.

The modern-day world of genetics has created a new set of decisions and related dilemmas for parents, sometimes as they are still fighting cancer themselves. Scientists continue to identify a growing array of mutations that not only point to

elevated risk for breast cancer but also colon cancer, kidney cancer, and other malignancies.

For those impacted families, what factors should they consider as they determine whether, when, and how to share a genetic harbinger with their children? And what if their child follows in the footsteps of Pellegrini's daughter and wants to be tested?

Disclosure Timing

A few recent studies indicate that today's parents err on the side of disclosure. According to data presented at the American Society of Clinical Oncology meeting last spring, 63 percent of mothers shared their BRCA results with their children—ages 8 to 21—within a month of learning them. “Families and kids are more exposed to genetics, now more than ever,” says Beth Peshkin, CGC, a study co-author and senior genetic counselor at Georgetown University's Lombardi Comprehensive Cancer Center in Washington, D.C.

Another recent study, focused on mutations associated with a hereditary colorectal cancer condition called Lynch syndrome, sometimes referred to as hereditary nonpolyposis colorectal cancer (HNPCC), also identified a high rate of disclosure. Nearly all—98 percent of participants—told at least one first-degree relative, according to the 2008 study in the journal *Clinical Gastroenterology and Hepatology*. Nearly 90 percent of those with children shared their results; most of the remaining participants planned to once their children were older.

Genetic counselors advise parents to weigh not only their child's age and relative maturity in discussing familial genetic patterns but also the immediate relevance for that child. For example, if the parent's genetic mutation is linked to Lynch syndrome, parents have a lot more leeway since colonoscopy screening is not typically recommended until early adulthood, says Amie Blanco, CGC, a genetic counselor at the Gastrointestinal Cancer Prevention Program at University of California, San Francisco.

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Compare that scenario with another hereditary colorectal cancer diagnosis, familial adenomatous polyposis (FAP), in which colonoscopies are recommended as early as age 10, Blanco says. People with FAP may begin to develop polyps at a very young age, sometimes before their teenage years, and most patients with FAP will need to have their colon removed. Thus, it makes sense to talk to the child about genetic mutations and testing, in order to make screening decisions, she says.

Regardless of the malignancy involved, children may pick up enough bits of conversation by ages 12 or 13 to draw their own—and potentially inaccurate—picture of what's happening in the family, Blanco says. By raising the subject themselves, parents can address, and hopefully squelch, some of their

child's worries, she says.

Parents who postpone that discussion may be tempted to keep pushing that difficult conversation further down the road, Blanco says. The San Francisco-based genetic counselor has seen this occur in families with Lynch syndrome, where there is more time flexibility compared with FAP.

The reasons can stack up: children are in college; they are engaged; they have just started that first job. "There always seems to be, in this young adult group, some life transition that they are going through that parents are using as a reason for why they should hold off," Blanco says.

Occasionally the clinicians at UCSF have to be blunt, warning parents that their stalling may place their child at risk, as they move into their 20s and even beyond, Blanco says. "We say, 'How would you feel if your son or daughter is diagnosed with colon cancer and you could have prevented it?' It's a really harsh statement. But it's something they need to think about, because it's possible."

Framing The Risk

Traditionally it's been thought that children couldn't do much, at least on a practical level, with knowledge of their family's genetic risk, says Angela Bradbury, MD, director of breast and ovarian cancer risk assessment at the Fox Chase Cancer Center in Philadelphia. So she was intrigued when a study she led, published in 2009 in the journal *Psycho-Oncology*, identified some lifestyle changes among 22 young adults after learning of their parents' BRCA mutation.

Five of the seven young adults who had reported smoking said they decided to quit. "That was impressive to us," Bradbury says.

Bradbury, who is now interviewing teenagers ages 11 to 19 for another study, describes that age group as relatively mature and savvy. Already, they've developed a good "working knowledge" of genetics, she says.

When sitting down with a child, genetic counselors recommend striving to frame the news in a positive light. Don't focus disproportionately on the genetic risk, they say. Instead, describe how the knowledge can be used proactively, along with screening and medical advances, to protect the child once he or she is older. Also, healthy lifestyles that would be adopted regardless of genetic risk can be emphasized without relating it to genetic risk.

As anyone with children knows, sometimes questions can pop up unexpectedly, says Peshkin. "You don't always have to give the comprehensive answer," she says. "You can answer the question that the child has without going into more than he or she wants to know necessarily."

The parent can then circle back and revisit the subject later, either soon after or with the passing years, she says. There likely will be various opportunities, such as a news story about genetics or a family history project for school, Peshkin says. Also, keep in mind that children may process their potential genetic risk differently as they mature.

For example, a teenage girl might struggle with fatalistic fears as her body

develops, Peshkin says. “ ‘Mom had breast cancer. Grandma had breast cancer. My aunt had breast cancer. I know it’s going to happen to me.’ And sometimes they won’t verbalize that. It can be helpful, although upsetting, to feel around for some of those thoughts.”

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—Beth Peshkin, CGC

Pellegrini, who has embraced candor from the beginning, says she still didn’t expect to face her daughter’s question quite so soon. Could she foresee allowing her daughter to get tested? Pellegrini, who had been talking with Antonia sitting nearby, moved to another room before answering. The bottom line, she says, is that preventive steps cannot be taken until Antonia reaches adulthood.

“She’s 9 years old and being a teenager is not that far away,” she says. “And honestly, I don’t want to know that soon. ... I think maybe, if anything, to wait until she’s at the tail end of her teens, entering her 20s.”