Jewish genetic screening grows despite questions about breadth

In 1995, Randi Chapnik Myers chose to abort her pregnancy after a 20-week ultrasound revealed an extreme buildup of fluid inside the fetus' skull. At the time, she and her husband Rob "were told it was not genetic," recalls Chapnik Myers, a freelance journalist in Toronto. Besides, both partners had been tested as carriers for an ailment that affects the brain called Tay-Sachs disease, one of the most common life-threatening genetic disorders found to disproportionately affect Ashkenazi Jews like the Myerses. And "it didn't ever actually occur to me that there could be another genetic recessive disease that we could share," she says.

After giving birth to two healthy children in the late 1990s, the couple assumed they were in the clear. But when Chapnik Myers became pregnant again with twin girls in 2000 and the sonogram again showed the same brain swelling in one of the fetuses, the couple realized that genetics were likely to blame. Ultimately, doctors deduced that the Myerses each carried the same recessive mutation in a gene responsible for a rare genetic condition called Walker-Warburg syndrome, a severe form of congenital muscular dystrophy that causes most children to die before the age of three.

"From the day they're born, it's basically a miserable disease," says Wendy Chung, a pediatrician and clinical geneticist at Columbia University Medical Center in New York who has treated children with the disease.

Since the Myerses' harrowing experience, researchers have mapped the gene responsible for Walker-Warburg and developed a lab test to screen for the disease mutation. Recently, independent teams led by Chung and Christopher Walsh, a geneticist at Children's Hospital Boston, have also shown in separate Israeli and American cohorts that around one in 150 people of Ashkenazi descent carry the disease-causing version of the gene—about twice the rate seen in the general population (*Hum. Mutat.* **29**, E231–E241, 2008; *Prenat. Diagn.* **29**, 560–569, 2009).

Off the back of those findings, in April the Victor Center for the Prevention of Jewish Genetic Diseases, a leading reproductive screening institute based at the Albert Einstein Healthcare Network in Philadelphia, added Walker-Warburg to its list of diseases that the center recommends couples of Ashkenazi origin should be tested for before conceiving, bringing the center's panel tally up to 19 diseases.

After two more pregnancies and having lost four out of seven babies, Chapnik Myers is relieved that screening is now available—and urged—for other Jewish parents-to-be. "I'm thrilled that other women aren't going to have to go through that level of fear, worry and anxiety as their bellies begin to grow," she says.

Bliss Photography

Tried and tested: The Myers family.

Some experts, however, question the utility of screening for so many extremely rare diseases. "There's almost a sense that if you're testing for more things, that must be a better thing," says Benjamin Wilfond, director of the Treuman Katz Center for Pediatric Bioethics at Seattle Children's Hospital. "It's such an entrenched concept, but we don't know that it's a better thing."

John Mitchell, director of the carrier screening program at Montreal Children's Hospital, shares similar concerns. "Are you creating more anxiety than benefit?" he asks. "I think that's where sometimes the line has to be drawn."

Joel Charrow, a medical geneticist at Children's Memorial Hospital in Chicago and a member of the Victor Center's advisory board, also worries whether people who undergo Jewish genetic disease screening really can receive adequate genetic counseling or provide informed consent for such an ever-expanding number of tests. "I don't think we could in any meaningful way truly inform people about everything they need to know about each of these conditions before testing for them," he says.

Conflicting advice

Professional societies alike remain divided. In 2009, the American College of Obstetricians and Gynecologists recommended screening for just four of the most common diseases—Tay-Sachs, cystic fibrosis, Canavan's disease and familial dysautonomia—all of which have carrier frequencies among Ashkenazi Jews greater than one in 40 (*Obstet. Gynecol.* **114**, 950–953, 2009). In contrast, the American College of Medical Genetics (ACMG) in 2008 backed a larger panel of nine specific disorders, some with carrier rates as low as one in 100 and others that are not life threatening, with detailed criteria for adding other disorders to the list (*Genet. Med.* **10**, 57–72, 2008).

Indeed, the Victor Center used the ACMG's criteria—based on disease severity, allele frequency and assay sensitivity—in deciding to suggest screening for a total of 19 diseases. "That's the standard," says the Victor's national director Debby Hirshman. "So when we add a disease to the list it has to meet those criteria."

Walker-Warburg is also not likely to be the last addition to the panel. "At the rate we and other people are going, [the number of diseases] is only going to get exponentially higher," says Chung. In the past six months alone, for instance, researchers have discovered founder mutations in Ashkenazi Jewish populations for a blood disorder known as thrombocytopenia, a disease known as retinitis pigmentosa that causes blindness, an inherited predisposition to colorectal cancer, a brain condition that can lead to dangerous hemorrhaging, and other less severe disorders.

Meanwhile, the cost of DNA sequencing is rapidly plummeting, which will make expanded screening more available to those who seek it. "There still will be ethical questions" about the size of Jewish genetic disease panels, says Paul Wolpe, director of the Emory University Center for Ethics in Atlanta and a member of the Victor advisory board, "but they won't be as heavily weighted about finances."

Indeed, Walsh notes, "to expand the test to an additional gene is cheap, so the cost-benefit analysis usually benefits testing these really crippling diseases."

With cost out of the picture, Jodi Hoffman, director of the Victor Outreach and Screening Program for Ashkenazi Jewish Genetic Diseases at Tufts Medical Center in Boston, argues that the decision to grow the Victor's list to 19 diseases all comes down to empowering prospective parents of Ashkenazi heritage with the ability to make informed decisions about their own genetic data. "We want to allow people to have the information they need to have a healthy family," she says. That way, "you allow them to embrace the information and decide whether to bring a child into the world."

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