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Jewish Genetics: To Test Or Not To Test? That Is The Question — And The Answer

By Rita Rubin

Hila David always knew she wanted a big family. Five kids would be perfect.

But when things started getting serious with her boyfriend, Jon Creme, he decided it was time to discuss something that might derail her dream.

Creme's 22-year-old half-brother, Shaul, had died in 2002 of cystic fibrosis, the most common fatal inherited disease in the United States. Cystic fibrosis is a recessive genetic disorder, which means that people with the disease must have inherited two copies of the mutated gene that causes it, one from each parent.

Like Shaul Creme's parents, about one in every 31 Americans — or more than 10 million individuals – carry one normal copy of the cystic fibrosis gene and one mutated copy. Carriers don't have symptoms and might never know their status unless they conceive a child with another carrier. There is a 1 in 4 chance with each pregnancy that the child of two carriers will inherit the mutated gene from both parents, as Shaul Creme did.

But screening, using either saliva or blood, can reveal whether healthy individuals carry any of hundreds of recessive genetic diseases, some of which are more common among Ashkenazi or Sephardic Jews than in other population groups. One of these diseases, familial dysautonomia, is seen almost exclusively in Ashkenazi Jews, while others, such as cystic fibrosis, are almost as common in many other ethnic groups as they are in Ashkenazi Jews.

An estimated 1 in 5 to 1 in 4 Ashkenazi Jews carry at least one of the Jewish genetic diseases. Couples who learn before they get pregnant that they both carry the same genetic disorder can take steps to ensure that their children do not inherit it. They might choose to adopt or use a sperm or egg donor. Or they could opt for in vitro fertilization with pre-implantation genetic diagnosis, in which embryos are analyzed

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Photo by Hannah Broder

Mitchell Eisenberg, 30, and Gabrielle Schechter, 29, complete consent forms for JScreen carrier testing at Adas Israel Congregation in Washington, D.C. The couple is planning a September wedding.

genetically, and then only those with one or no copy of the mutation are transferred to the mother's womb.

Without pre-conception carrier screening, expectant couples wouldn't learn that they carry the same disease unless late testing, such as amniocentesis, showed their fetus had a recessive genetic disorder. At that point, the only way they could avoid giving birth to an affected child would be to end the pregnancy.

"Doing genetic testing does not obligate you to do anything you're not comfortable with," beyond getting the results, Dr. Evelyn Karson, a Bethesda, Maryland, obstetrician-gynecologist and geneticist, said at a recent program on the subject at Adas Israel Congregation in Washington, D.C. That means a couple once informed they are at risk may decide to take their chances and conceive naturally or use a donor egg or sperm or adopt.

Clergy in Agreement

Associations of rabbis and cantors all support the need to educate couples planning marriage to get carrier screening for Jewish genetic diseases.

"You call the caterer, you call the band, and you call the Victor Center," says genetics counselor Deborah Wasserman of the Victor Center for the Prevention of Jewish Genetic Diseases, a nonprofit based at Miami's Nicklaus Children's Hospital.

Photos by Hannah Broder

Hillary Kener of JScreen points out the amount of saliva that must be deposited into the collection tube for carrier testing.

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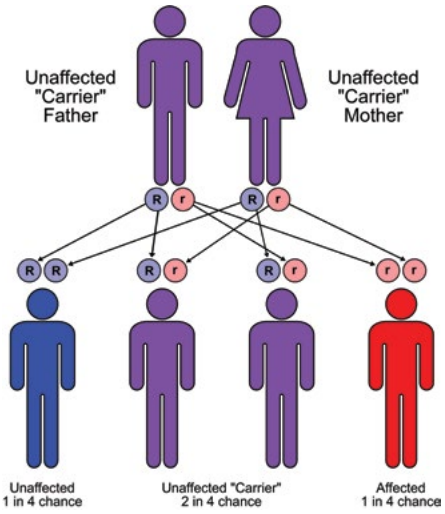

Familial Dysautonomia is inherited in an autosomal recessive pattern, depicted here. Parents each carry one copy of the mutated gene but typically do not show signs and symptoms of the condition.

Hillary Kener, assistant director of outreach and marketing for the nonprofit JScreen, based at Atlanta's Emory University, echoes Wasserman, "It's becoming something that people add to their wedding checklist: You get a chuppah, you get JScreen," Kener says. Both the Victor Center and JScreen, for which Karson serves as a consultant, offer screening and genetic counseling to Jews and their non-Jewish partners nationwide. The nonprofits were founded by parents who had children with devastating recessive genetic diseases.

Reform Rabbi Peter Kasdan, an advisor for the Jewish Genetic Disease Consortium, works closely with both organizations. For years, he has required all couples who want him to officiate at their wedding to get screened and show him the results. He even arranges their screening.

"A lot of rabbis now do what I do," says Kasdan, who retired from Temple Emanu-El in Livingston, New Jersey, and now lives in Longboat Key, Florida. "We all recommend pre-conception testing, not post-conception testing, because that's where you get involved in real moral issues."

Back in 1975, the Central Conference of American Rabbis (CCAR), which represents Reform rabbis, called upon its members to educate couples contemplating marriage about premarital carrier screening for Tay-Sachs disease. Since then, the Conference has continued to urge rabbis and cantors to educate congregants about screening, and the number of genetic diseases for which screening is available has grown.

"I take this very, very seriously," Kasdan says. "Over the years, I buried eight of my students who died of one of these diseases."

Like Kasdan, Conservative Rabbi Bill Lebeau, senior consultant for rabbinic and institutional leadership for the Rabbinical Assembly, has advocated preconception carrier screening since the 1970s.

The issue turned personal for Lebeau 20 years ago, when his grandson Ezra was born with familial dysautonomia, three years before the advent of preconception and prenatal testing for the disorder. This disease affects the sensory nervous system, which controls such activities as taste and pain perception, and the autonomic nervous system, which controls involuntary actions such as digestion, breathing and the regulation of blood pressure and body temperature.

For his entire life, Ezra has received nutrition through a feeding tube because he can't swallow properly. His lungs are deteriorating, so he must be tethered constantly to a large oxygen tank, which means he can't walk long distances. After Ezra was born, Lebeau, former dean of the Rabbinical School at the Jewish Theological Seminary of America, stopped traveling on weekends so that he and his wife could give their daughter and son-in-law a break in caring for their son.

The birth of children with a genetic disease has implications not only for their immediate family but also their extended family. When carrier screening became possible, Lebeau's four other children were tested. Against the odds, none of them was found to be a carrier. Prenatal screening

Source: Wikimedia Commons

Rabbi Josef Ekstein of New York, who founded Dor Yeshorim in 1983, after four of his children died of Tay-Sachs.

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showed that Ezra's now 15-year-old sister was unaffected by it.

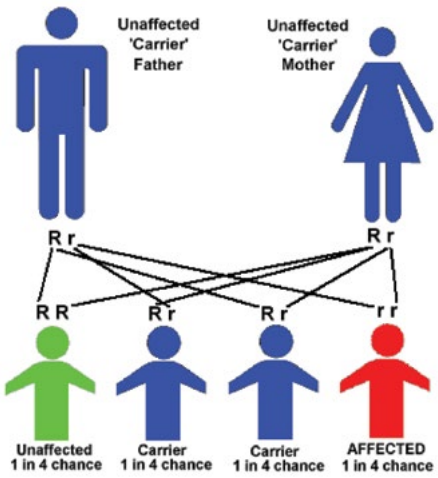
"Once you have testing, then you're in control, and I don't see a downside for any couple," Lebeau says.

Anyone who thinks carrier screening smacks of eugenics would be sadly mistaken, Kasdan says. "It's not a question of creating a perfect child. I'm not a proponent of parents being able to pick out the color of the child's eyes or whether the child will be an athlete."

The oldest and largest carrier screening organization focusing on Jewish genetic diseases is Dor Yeshorim, founded in 1983 by Orthodox Rabbi Josef Ekstein of New York after four of his children died of Tay-Sachs. "I am a Holocaust survivor. I was born in the middle of the Second World War. I hope that I am not a suspect for practicing eugenics," Ekstein told the Associated Press in 2010. "We are trying to have healthy children."

Dor Yeshorim, according to its website, annually screens more than 25,000 "young adults of marriageable age" through private appointments and mass screenings at Jewish schools in the United States, Israel and nine other countries, its approach differs from the Victor Center or JScreen. Dor Yeshorim screens for up to 19 genetic diseases that are more common in the Ashkenazi population and for up to 17 diseases that are more common in the Sephardic/Mizrahi population. (Several diseases, such as cystic fibrosis and Tay-Sachs, are on both the Ashkenazi and Sephardic/Mizrahi screening panels). JScreen and the Victor Center, on the other hand, screen for more than 200 genetic diseases.

But the biggest difference between Dor Yeshorim and JScreen and the other two screening organizations is that it does not disclose detailed screening results. Clients, many of whom are ultra-Orthodox young people working with a shadchan, or matchmaker, are given a unique ID number. When they are considering marriage, they



Tay-Sachs disease is inherited in an autosomal recessive pattern.

call Dor Yeshorim's automated hotline and enter their ID number and that of their prospective spouse. Within a few business hours, a Dor Yeshorim representative will call to say whether they are compatible, meaning they don't carry the same genetic disease, if any, or incompatible, meaning they both carry a gene for the same disorder. Counseling is provided for incompatible couples.

Tay-Sachs was the first Jewish genetic disease for which screening became possible. "Tay-Sachs really got people thinking about how families could be more proactive in understanding what their risks are," says Jennifer McCafferty, director of the Nicklaus Children's Hospital Research Institute in Miami, home of the Victor Center. "Our message is that information is powerful and empowering."

There is no treatment for Tay-Sachs, a progressive neurological disorder. Symptoms of the most common form appear at three to six months of age. As the disease progresses, children experience seizures, loss of eyesight and hearing, intellectual disability and paralysis. Those with this severe form of Tay-Sachs usually don't live beyond early childhood.

About one in every 250 people in the general population is a Tay-Sachs carrier. But among Ashkenazi Jews, French Canadians and Louisiana Cajuns, roughly one out of every 27 people carries the disease, according to the National Tay-Sachs and Allied Diseases Association (NTSAD).

Before carrier screening for Tay-Sachs began in the early 1970s, more than 100 Ashkenazi children were diagnosed with the disease in the United States every year, NTSAD Executive Director Susan Kahn says. Today, at most only a handful of children are diagnosed annually with Tay-Sachs in the U.S. Ashkenazi community, thanks to preconception testing.

To reach as many people as possible, the Victor Center and JScreen conduct educational and screening programs at Jewish community centers, synagogues, Hillels and Chabad houses. In just three days in 2016, the Victor Center screened 1,200 individuals at Yeshiva University in New York, says Wasserman.

And in January, JScreen announced it is entering into a partnership with Honeymoon Israel, which provides group trips to Israel for couples with at least one Jewish partner. Honeymoon Israel couples will receive a coupon code to help subsidize the cost of screening by JScreen, which they can use before or after their trip.

Carrier Screening Is Vital

Four out of every five babies with a genetic disease are born to parents with no known family history of it, according to JScreen.

But it was not yet available when Shaul Creme was born. Before the now 31-year-old web developer Jon Creme had even met Hila David, his brother's illness spurred him to order a test kit from 23andMe, a direct-to-consumer genetic testing company. He spit into a tube and mailed it back to the Mountain View, California, company for analysis.

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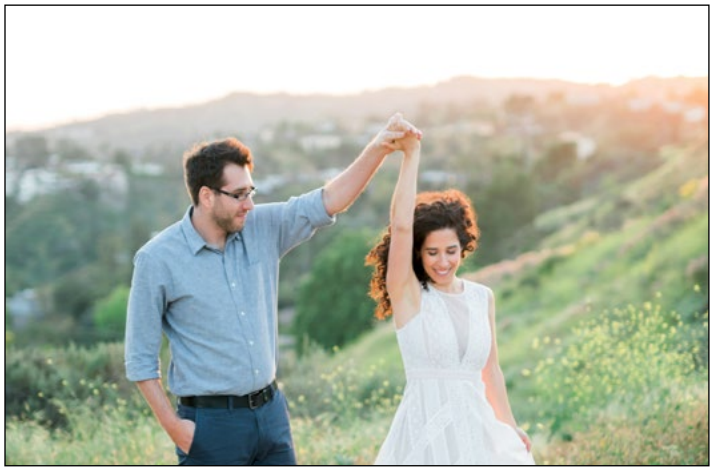

Photo by Anya Kernes Photography

Hila David and Jon Creme.

Photo credit: Fred Marcus Studio.

Paige Aufseeser and Alan Guy.

They weren't yet engaged, but Creme already knew that he and David, who met in Tel Aviv as interns after they graduated college, might want to have children someday. That is why he felt the need to tell her that his 23andMe test revealed that he was indeed a cystic fibrosis carrier, which could present a problem if she, too, carried a genetic mutation for the disease.

"We sort of had this moment of panic," recalls David, who turns 29 in April and works in human resources for the TOMS shoe company.

She decided against testing with 23andMe, because it did not offer genetic counseling with the results. A friend recommended JScreen, and one of its genetic counselors reviewed Creme's 23andMe results and felt it wasn't necessary to confirm them with more testing. David was then screened by JScreen, which provided her with the answer she had hoped for: She is not a cystic fibrosis carrier, so none of those longed-for five children could be affected by the disease.

"JScreen made it such a smooth process," said David, who became engaged to Creme in October 2016, shortly after receiving her results. They wed in February and live in Southern California.

Carrier screening put Paige Aufseeser and Alan Guy on an unexpected path.

By their second wedding anniversary, in June 2017, the New Jersey couple began to talk about starting their family in the fall. They're both Ashkenazi, and they're both health professionals — she's an audiologist, he's a sports medicine physician — so they knew that they should be screened to see if they carried any Jewish genetic diseases.

"We weren't ever really thinking it would come back and there would be an issue," says 30-year-old Aufseeser.

But testing through her ob-gyn revealed they both carried a genetic mutation for Gaucher disease, a metabolic disorder of which there are multiple types. Symptoms of Type 1, the most common type, might not appear until adulthood and can range from mild to severe. But individuals with Type 2 can experience life-threatening problems at an early age.

"That kind of threw us into the world of in vitro fertilization, which we didn't know anything about." Aufseeser says.

Testing showed that three of their embryos didn't carry even one copy of the genetic mutation for Gaucher, let alone two. In June, one of them was transferred to Aufseeser's uterus, but it developed into an ectopic pregnancy, in which a fertilized egg implants outside the womb, usually, as in Aufseeser's case, in a fallopian tube. Ectopic pregnancies don't develop normally and must be removed.

The two other embryos that had no genetic mutation for Gaucher were less likely to result in a pregnancy because, overall, they were of poorer quality than other embryos that carried one mutation. So in September, one of the better-quality embryos with a single mutation for Gaucher was transferred to Aufseeser's

View Paige Aufseeser and Alan Guy's pregnancy announcement video.

https://www.youtube.com/watch?time_continue=1&v=SUjo8F-S1X4

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uterus, and she became pregnant. The couple's child will be a Gaucher carrier, like his or her parents. Aufseeser has dealt with morning sickness but, she says, "I worked hard to get the morning sickness, so I'm not complaining."

While progress is being made, too many Jews remain unaware of the value of carrier screening for genetic diseases, says Lois Victor.

After the death of her second daughter from familial dysautonomia, Lois Victor decided to make it her life's work to prevent other Jewish parents from dealing with a similar tragedy. Her daughters, Debbie and Linda, were born in the 1960s, long before the advent of carrier screening or prenatal testing for this disease.

Debbie lived to age 8, but Linda, who wasn't as severely affected, lived to age 35. After Linda's death, "I started thinking: What could I do to help others?" says Victor, who lives in Boca Raton, Florida. And thus, the Victor Center was born in 2002. As its founder, she serves on the Center's National Advisory Committee.

She tells of a good friend whose great-grandchild was born recently with a Jewish genetic disease to parents who had not been screened. Victor says her friend never told her grandchild about the need for carrier screening. "How can this happen to a friend of mine?"

The worst part, Victor says, is that "all of these diseases are preventable with one simple test. My feeling is we can't rest until all Jewish children are born free from these diseases."

Resource for our readers:
The Jewish Genetic Disease Consortium

For further reading:
Summer, 2016 B'nai B'rith Magazine
Genetic Testing and the Negev Bedouins,
by Michele Chabin