THE IMPORTANCE OF Genetic SCREENING

By ANDREA JACOBS
Steven Senft, development director for Judaism Your Way, was born in Bogota, Colombia. He moved to Denver with his wife Daniela Loeble, a native Israeli from a Peruvian family, in June, 2016.

“When I was an undergrad in college, a representative from JScreen spoke to our class about getting genetic testing to make sure we have healthy babies,” he says. “Jews are vulnerable to so many diseases.”

Senft, who wasn’t in a serious relationship at the time, put the advice on hold. “But I knew I would have to do this one day.”

Married to Daniela for two years now, the couple hopes to start a family in the foreseeable future.

Senft chose JScreen, a program of Emory University, to test for 226 diseases even though Jewish genetic disorders comprise only a fraction of the panel.

“The test is really very simple and painless,” he says. “You receive the kit in the mail. There’s a small testing tube attached to a receptacle. You spit into it, close it, mix with fluid that you swish around to balance with your pH, drop it in a FedEx drop and wait for the results.”

Senft, who had not yet received his results, says genetic screening is about ensuring the health of the baby.

“We want our child to have the best life possible,” he says. “If we can’t have a child, we’re realistic. It would be devastating, but it is a possibility. It’s not a given that everyone can bring children into this world.

“If that’s the case, we would adopt.”

Brooke Berry Soltanovich, 33, has lived in Denver since 2008, earned

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Brooke Berry Soltanovich

Out of 226 tests on the JScreen panel, he tested negative for 225.

He is a carrier for a variant on one gene (protected here for privacy reasons). However, there is insufficient evidence that individuals with the requisite two copies for this variant are at risk for the syndrome.

If his wife tests negative for the mutation, the couple’s reproductive risk would be 1/160,000.

“Right before the consultation, Daniela and I discussed potential results and what to do,” Senft says. “It’s always hard to think in ‘what if’ terms, but we both agree that we would like to bring a healthy baby into the world.

“If we are not able to do this, I’m sure we’ll evaluate all of our options and even consider adopting one of the many children looking for a good home.

“But I’m sure we’re going to be fine.”

Steven Senft

problems that manifest in patients who have the same background as I do,” says Elias, who has worked in the field for 37 years.

“As more information became available, it was obvious that genetic disorders in people with Ashkenazi Jewish backgrounds were personally and medically important.”

To provide background on this complicated subject, Elias describes the nature and purpose of genes.

“We all have genetic information that we pass on to our offspring,” she says. “That genetic information is carried in your DNA, which is made up 23,000 messages that tell your body how to make protein.

“If you have a change in a gene, the message telling your body how to make that protein is also altered. Your body might not be able to make that protein properly — and you need all the proteins to work correctly for you to be healthy.”

The vast majority of Ashkenazi

Dr. Ellen Elias, director of the special care clinic for children at The Children’s Hospital in Denver and a full professor in pediatrics and genetics at the CU Medical School, is an Ashkenazi Jew.

Elias, now in her 60s, first gravitated toward genetics because she specialized in children with disabilities, “and it turns out that there’s an underlying genetic cause in many disabilities,” she says.

“It became clear to me that it was important to find this connection to better understand and care for my patients.

“And I’ve always been interested in
Most people who are carriers don’t know it, or don’t know if their partner is a carrier

“Generations are inherited in an autosomal recessive pattern, meaning the mother and father must both be carriers for a disease to pass it to their offspring.

“Everybody has little changes in those 23,000 genes we have, and that makes us unique individuals,” Elias says. “But one out of five people of Ashkenazi Jewish descent is a carrier for a gene mutation for diseases in that specific population.

“That’s a pretty high percentage.”

If you happen to be a carrier, “no problem,” she says. “You’re a normal person, because everyone has two copies of every gene. You got one from your mom and one from your dad.

“As long as one of those copies is normal, you’re a healthy human being.”

When both parents carry the same mutation, there is a 25% risk that one of their children will get the disease.

Elias focuses on the glass-half-full scenario without diminishing the seriousness of the situation.

“You could be a carrier and your husband could be a carrier,” she says. “But 75% of the time you’re going to have nice healthy children.

“That’s why most people who are carriers are in the dark, or have no idea that their partner is a carrier for the same gene — unless they are screened.

“It’s incredibly important to get screened to see whether you are a carrier.”

Elias says some people suffer from the Ostrich Phenomenon, the head-in-the-sand “it’s better not to know” attitude that rejects genetic testing.

“I’ve heard, ‘Oh, there’s nothing like that in my family so I’m not worried.’ That’s the problem with these disorders, because there is no family history.

“For the most part, carriers look normal and only have a 25% chance of having an affected baby. Many people are lucky.”

But anyone equating a visible absence of disease in the family with carrier status is making a big, poten-
The ideal time for Ashkenazi Jewish genetic testing is prior to pregnancy and childbirth. While post-childbirth options are available, pre-pregnancy is optimal.

“The far and away best time to learn whether you are a carrier — remember, one out of five us is a carrier for something — is when you’re a young person in college, and before you’re pregnant,” Elias says.

She strongly suggests that couples visiting their rabbis for pre-marital counseling ask about genetic testing, as well as women seeing their OB-GYNs.

“That’s when you want to find out, is there a problem? Are you at risk?”

Rabbis meeting with engaged couples prior to marriage “are the first line of defense,” says Elias, who has addressed the Rocky Mountain Rabbinical Council on the necessity of testing.

Obstetricians who are current on medical testing share that first line of defense.

Genetic testing is recommended for individuals of Ashkenazi Jewish descent; if there is one Jewish grandparent in the family; and for anyone unsure about his or her familial history.

“A lot of people don’t think they need to be screened because their partner isn’t Jewish,” Elias says. “But that’s not true.

“In the old days, when we lived in small villages somewhere in Europe, Russia or other regions, Ashkenazi Jews married people of similar backgrounds. Now, especially in the US with its high rate of intermarriage, that’s not necessarily the case.

“Our policy is recommending testing even if only one of the partners comes from an Ashkenazi Jewish background because these diseases have spread into other populations,” she says.

“The Ashkenazi Jewish individual is tested first. If he or she is a carrier, we will screen the non-Jewish partner for that specific mutation.”

Elias, who will soon celebrate her 40th wedding anniversary, says that only one test was available when she got married, “and that was for Tay Sachs.

“Do you have any idea how many diseases we can screen for now? There are 49 diseases on the most updated Ashkenazi Jewish genetic panel, and that number is a moving target because it keeps going up.”

(Currently, the Ashkenazi panel ranges from 49 to 60 to 89 disorders.)

Individuals using JScreen or other testing venues may request the 200+ disease panel, which screens for Ashkenazi Jewish diseases as well as those in the general population.

Elias says it’s crucial to realize how dramatically the Ashkenazi panels are changing in order to ensure you are getting the most updated test available.

“If you were tested prior to 2010, it’s probably advisable to get retested,” she says.

Elias says that Ashkenazi Jews considering screening must carefully research the disorders because prognoses are far from identical.

For example, Tay Sachs, Canavan Disease, Niemann-Pick and mucolipidosis IV are severe, progressive in childhood and always fatal.

Treatment for cystic fibrosis, once a death sentence for children, has extended life into early adulthood.

Enzyme replacement therapy has improved the outlook for many patients with Gaucher disease.

“People need to know what test they want to do and what lab they’re allowed to use, which is dictated by health insurance,” Elias says.

A sophisticated Ashkenazi Jewish
genetic panel screens for all these diseases simultaneously — with the major exception of Tay Sachs.

“Tay Sachs is not a DNA test,” Elias says. “It’s a separate enzyme protein test.

“It’s important to know that.”

Most marriageable-age Orthodox men and women meet each other through a shadchen, or matchmaker. A good match leads to marriage, which typically produces many children.

Dor Yeshorim: Committee for the Prevention of Jewish Genetic Diseases, a matchmaking service and preventative health organization based in Brooklyn, provides anonymous genetic testing to Orthodox clients in the US, Canada, Israel and elsewhere.

The goal is to negate the risk that two carriers will marry one another.

Founded in 1983, Dor Yeshorim assists Orthodox Ashkenazi and Sephardic Jews who want to know whether they carry genes that could endanger future offspring.

Unlike Jews who are tested at hospitals, medical clinics, JScreen or other venues, Dor Yeshorim’s users never learn their carrier status.

According to Tablet’s 2014 excellent article on Dor Yeshorim (which did not return the IJN’s calls), a male voice answers the automated hotline.

“To submit a request for compatibility, press 1.”

“To check compatibility, you will need to submit both the male and female’s nine-digit Dor Yeshorim ID number and both their dates and months of birth, excluding the year.”

The only information released is whether a pair is compatible, meaning both parties are not carriers for the same offending gene mutation.

Confidential personal results are withheld from all individual users.

Anonymity ensures no one is stigmatized as a carrier because that might diminish his or her chances for a future match.

While some may take issue with Dor Yeshorim’s refusal to divulge results to the person who underwent screening, the practice has a noticeable health benefit.

“Segments of the Orthodox community have virtually eradicated Tay-Sachs births by an ingenious method of preventing carriers from marrying,” Dr. Daniel Eisenberg wrote in an article for Aish.com.

Eisenberg also examined whether genetic screening, which did not exist until relatively recently, is hinted at in the Torah.

“While the Torah obligates us to guard our health, it does not necessarily follow that testing ourselves for recessive genetic traits [that do not directly affect our health] is included in the mitzvah,” he wrote.

“Nevertheless, the late halachic authority Rabbi Moshe Feinstein favored Tay Sachs testing and considered the possibility that testing might be a moral obligation.”

Anonymity regarding one’s carrier status for Tay Sachs and other fatal Jewish childhood diseases averts “emotional pain before marriage,” Eisenberg wrote.

“Dor Yeshorim has prevented many genetically incompatible matches before the couples have ever met.”

Dr. Bronwen Kahn, a perinatologist at the Rose Center for Maternal-Fetal Health and the Obstetrix Medical Group of Colorado, offers the latest technology to mothers facing high-risk pregnancies.

“We talk to parents who are considering pregnancy but have already tested positive for Ashkenazi Jewish diseases,” Kahn says.

“Although we don’t do the testing, we help them work through and manage the results.”

The field of genetics and pre-conception testing are growing exponentially, she says.

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“But I do think we need to take those advances with caution.

“If you do one of those 200- or 240-disease panels, the chance of you popping up as a carrier is actually quite high. Then you have to make sure how you integrate that and not freak out.

“It’s a ton of information; hard to wade through, and very complicated.”

Obstetrix’ outside lab utilizes a panel that tests for a plethora of diseases in the general population and up to 60 Ashkenazi genetic disorders ranging from 21-Hydroxylase-Deficient Classical Congenital Adrenal Hyperplasia to Walker-Warburg.

Individuals can request the Jewish Ancestry Panel alone. Narrowing down screening options can be invaluable, Kahn says.

“I have a patient right now who took one of those tests (for 200 diseases) and found out she carries seven of them,” Kahn says. “Fortunately, her husband carries only one. We can narrow down our list of worries to that one condition.”

Kahn cites the “founder effect” to explain how and why certain illnesses impact specific groups.

“The founder effect can be traced to a population that starts off small, does not intermarry and retains its racial purity so to speak,” she says. “This can amplify the frequency of a carrier state.

“We all have little mistakes in our DNA. If we mix our blood with other groups, mistakes are less likely to be passed forward.

“You have a one in 2,700 chance that your child will actually have Tay Sachs, which has severe clinical consequences, before you’ve been tested.”

This is the baseline risk.

“If both parents are carriers, there is a 25% risk that one in four children will have Tay Sachs,” she says. “All of their offspring will have a 50% chance of being carriers when they have their own children, and another 25% would neither have the disease nor be carriers.”

Kahn says that parents who want to prevent dire percentage-based risks prior to conception can try in vitro fertilization.

Embryos undergo pre-implantation testing; only those without two copies of the mutation are returned to the uterus.

“If parents don’t want to go that far, or don’t have the money — it’s a very expensive procedure — they can get pregnant, roll the dice and hope they are in the 75% ‘good news’ category,” Kahn says.

“Doctors can perform a small placental biopsy on the fetus between 10 and 13 1/2 weeks. In the 15- to 18-week window, we could do amniocentesis and test the fetus directly to determine whether it has two mutations.”

In the worst-case, 25% scenario, Kahn says that abortion is an option.

“The assumption is that if parents are going to such lengths to do this testing, their option is abortion — which
of course is a very, very difficult emotional place to be in.”

Kahn says people who dispense with fetal testing during pregnancy in favor of accepting whatever happens might test the baby after birth, only to face the unimaginable.

While luck can be a powerful influencer, she feels that risk factors should have the upper hand.

“If your chances are one out of four for every pregnancy, it’s not going to be the same for every pregnancy,” Kahn says.

“The chances are the same, but the outcome is different.”

Full genome sequencing, which determines a person’s complete DNA sequence in one sitting, and genetic engineering that could create blue-eyed, disease-free babies, are currently out of reach.

“I think we’re a little long way from sequencing the whole genome on a routine, affordable basis,” Dr. Kahn says.

“And we’re not even close to choosing a child’s physical characteristics.

“Ethically, I’m hoping that nobody would offer that kind of engineering for trivial characteristics like eye color.”

At this point, genome sequencing is an imprecise tool, she says.

“It’s a blunt instrument, and emotionally taxing.”

Dr. Elias says that despite medical and scientific advances in genetic screening, science stands at the outskirts of the genome testing frontier.

“You can test the DNA sequence, which costs a lot of money. You could probably test everyone on the planet and find out what his or her genome is.

“But how does this help you? An individual might receive a result that says, ‘This person has an unknown variant that we can’t explain yet.’

“We still don’t know everything.”

Elias advocates stem cell research, which some Americans still view as a precursor to cloning, for humanitarian reasons.

“For the vast majority of these diseases, there is no treatment,” she says. Stem cell research may lead to new treatment modalities for genetic diseases “that would benefit my patients.

“But no, we can’t go inside and fix your genes yet.”

For more information on Jewish genetic diseases and testing contact the Victor Center at www.victorcenter.org or the Jewish Genetic Disease Consortium at www.jewishgeneticdiseases.org.

Andrea Jacobs may be reached at andrea@ijn.com.