GENETICS

A Brief History of Genetic Testing

What the First Generation of Tests Can Tell Us About the Latest

By Ricki Lewis | Monday, May 5th, 2008 | Share This | Print

Two-thousand eight has brought a slew of Internet offerings for DNA-based tests pitched to consumers with cash and spit to spare—submit a saliva sample and learn your risk of developing everything from macular degeneration to restless legs syndrome. But the tests aren’t as simple as they seem, and their implications are potentially life-altering.

It might be wise, before indulging in a direct-to-consumer foray into one’s DNA, to consider population-wide genetic tests of times past. These efforts tracked single genes for specific mutations; many of today’s “services” instead report “associations”—patterns of genetic variation more common among people with a particular condition. Still, the past may hold valuable lessons about the human side of testing our DNA.

The Opening Salvo: PKU, Sickle Cell, and Tay-Sachs

Half a century ago, newborns began to be tested for PKU (phenylketonuria), an “inborn error of metabolism” in which an amino acid buildup in the blood causes mental retardation. A drop of blood was taken from an infant’s heel, the new parents typically oblivious. If the child indeed had PKU, strict dietary treatment preserved brain function. This earliest genetic test set a high bar—it was accurate, the disease treatable, and everyone was tested.

The 1970s saw population testing for two diseases that, like PKU, are passed from carrier parents to affected children. Yet the situations for sickle cell and Tay-Sachs diseases were quite different.

Sickle cell testing between 1970 and 1972 was mandatory in 12 states and targeted African-Americans. Misunderstanding was rampant, perhaps because the term “sickle cell trait” for carriers suggested that their condition was somehow visible. What they carried was stigma. At the time, the disease could not be prevented, tested for before birth, or treated. So why identify carriers? Fortunately the discrimination was short-lived, thanks to passage of the National Sickle Cell Anemia Control Act in 1972. By the 1980s, antibiotic treatment and bone marrow transplant became possible for this painful, but variable, disease.

In contrast, Jewish kids were tested for Tay-Sachs disease at their colleges, mostly on the East Coast, amid terrific education campaigns. Prenatal testing was available, but there was no treatment for this disease so severe that all children died young, their nervous systems shut down. A group called Dor Yeshorim took Tay-Sachs testing to a new, societal level—today they test young people for several “Jewish” genetic disorders and...
help determine potential marital compatibility for couples, identifying carriers for the same diseases. The process is anonymous, using numbers to identify people tested, and carriers are not told what they carry. Call it eugenics or artificial selection, but the diseases have disappeared from this population.

The Next Wave: NTDs, CF, HD, and BRCA

Other screens followed, and some became routine. Serum marker tests offered to all pregnant women indicate elevated risk of neural tube defects or trisomy 21 (Down syndrome) in fetuses. These are only screens, so follow-up procedures are required for diagnosis, especially for the common and worrisome false positives. Cystic fibrosis carrier screening is now routine in some obstetrics practices. If a woman is a carrier, her partner is tested, and if he’s a carrier, the fetus can be tested—or not, for CF comes in several guises depending on which gene variants are inherited, and there are treatments.

Testing for Huntington disease is more specialized, reserved for people with a family history of this disorder that typically begins near age 40 and causes uncontrollable movements and cognitive and behavioral changes. Predictive testing is chilling in its accuracy—the more copies of a telltale DNA base triplet in the implicated gene, the earlier, faster, and/or more severe the symptoms. While it is helpful to know one’s fate in time to make an informed decision about having children, it is not an easy decision. Several months of genetic counseling help families decide what to do.

Testing for BRCA1 and BRCA2 breast cancer introduced in recent years debuted a new breed of genetic test. Companies marketed this very expensive test direct to consumers through TV, print, and web ads, although a doctor is still required to order and administer the test. But the BRCA situation is tricky, scientifically, in several ways: BRCA1 and 2 account for only a small percentage of breast cancer cases. A mutation carries different risks of actually developing cancer in different populations, and a result could be “of uncertain clinical significance”—a DNA sequence out of the ordinary that may or may not cause cancer.

A Checklist for DTC Genetic Testing

The genealogy of genetic testing tracks mutations in well-studied, single genes with sometimes predictable outcomes. This is not the case for many of the conditions for which companies now offer tests, despite careful language that they provide “knowledge” or “research” and not diagnoses. The distinction between detecting specific mutations versus associations may not be clear to consumers, no matter how well-annotated a website. So here is a checklist of questions for evaluating direct-to-consumer DNA testing for health conditions, and where the lessons lie:

1) Can the condition be treated or symptoms prevented or lessened? (PKU, sickle cell, Cystic fibrosis, BRCA)

2) Does evidence support the targeting of a test for a specific condition to a specific population group, and if it does, does testing carry a stigma? (Tay-Sachs, sickle cell)

3) What are the false positive and false negative rates? (Maternal serum markers)

4) To what extent do test results predict severity of a condition? (Cystic fibrosis, Huntington, trisomy 21)

5) Are the genes tested the only ones that can cause a particular condition? (BRCA)

6) Is the extent of genetic counseling provided suited to the seriousness of the traits or disorders? (Cystic fibrosis, BRCA, Huntington)

With these considerations in mind, individuals considering the new generation genetic tests should bear in mind what we have learned from the tests that have been around for decades: Do not take DNA testing lightly!

Ricki Lewis is the author of Human Genetics, Concepts and Applications (McGraw-Hill Higher Education) and the novel Stem Cell Symphony (Available at Amazon.com, or contact the author at rulewis@nycap.rr.com). She is a fellow at the Alden March Bioethics Institute in Albany, NY.