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Too Much Information

By Amanda Schaffer on December 17, 2013

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Pregnant women and their partners can already peer at an unborn child's chromosomes: with amniocentesis, they can learn about the presence or, more likely, absence of large-scale genetic defects, often gaining peace of mind. But only a small percentage of parents-to-be take the opportunity, because the procedure is invasive and uncomfortable – a large needle is inserted into the amniotic sac – and causes miscarriage in roughly one in 400 cases.

Researchers have long hoped to develop a noninvasive alternative. Ever since scientists discovered, in the 1990s, that pregnant women's blood contains substantial amounts of fetal DNA, they've theorized that they could use this genetic material to test for fetal abnormalities like an extra copy of chromosome 21, which causes Down syndrome.

That technology has now arrived (see "Prenatal DNA Sequencing," May/June 2013). Several companies have introduced genetic tests that use blood drawn from the mother. These tests can be performed earlier in pregnancy than amniocentesis is usually done, which means that if the results suggest an abnormality, women and their partners have more time to grapple with whether to have an abortion or prepare for a child with special needs. If the results are reassuring, the cloud of anxiety dissipates sooner.

Given that the risks of having blood drawn are minimal, the tests are likely to be widely used. While today fewer than 5 percent of pregnant women undergo amniocentesis, "I think we could see 50, 60, 70, 80 percent of American pregnancies getting genetic testing," says Hank Greely, director of the Center for Law and the Biosciences at Stanford.

Thing reviewed
Noninvasive prenatal screening

The catch, though, is that as the accuracy of these tests continues to improve, they will be able to detect a greater range of genetic variations, including some with murkier implications. For example, rather than indicating something with certainty, they could reveal elevated risks for certain diseases or disorders. These advances could collide with the politics of abortion and raise the ugly specter of eugenics. When, if ever, should parents terminate pregnancies on the basis of genetic results? Do we have the wisdom to direct our own evolution? And perhaps most important, are there limits to how much data parents should have – or want to have – about their children before birth?

Corporate contenders

The first noninvasive tests to reach the market have screened for the largest-scale genetic defects – namely, abnormal numbers of chromosomes. Sequenom Laboratories, Verinata Health (part of Illumina), Ariosa Diagnostics, and Natera all offer tests that look for trisomies – an extra copy of chromosomes 13, 18, or 21, which cause Patau syndrome, Edwards syndrome, and Down syndrome, respectively. Some also identify an aberrant number of sex chromosomes. This fall, Sequenom

expanded its test to encompass additional trisomies as well as selected microdeletions (in which DNA is missing), including those known to cause DiGeorge syndrome, -Cri-du-chat syndrome, and Prader-Willi or Angelman syndrome. The various companies' tests range in price from less than $1,000 to almost $3,000, though they are covered by some insurance plans. So far, these offerings have not replaced amniocentesis, which remains the gold standard for accuracy. But they can be performed as early as 10 weeks into pregnancy and can help identify women who may need the more invasive test.

Companies will modify these tests to flag an increasing number of genetic conditions, including some that are quite rare. The trend is toward "detecting smaller and smaller mutations," says Jonathan Sheena, chief technology officer of Natera, who predicts that noninvasive identification of inherited single-gene diseases like cystic fibrosis, Tay-Sachs, and neurofibromatosis will soon become commercial reality. In the laboratory, meanwhile, researchers have already used noninvasive methods to sequence a whole fetal genome. In 2012, geneticist Jay Shendure's group at the University of Washington analyzed blood from the mother as well as a saliva sample from the father to reach this goal. Also in 2012, Stephen Quake's group at Stanford used a maternal blood sample alone to derive the fetal exome, which consists of the coding parts of genes. "That's pretty much the whole ball of wax," Quake told me. (Shendure and Quake are advisors to Ariosa Diagnostics and Verinata, respectively.) These laboratory efforts were not cheap: Shendure says it cost him around $50,000 to do the full genome. But they represent a clear proof of principle. And as the costs of sequencing continue to plummet, far more parents-to-be will potentially have access to far more genetic data about their future children.

Quake says he hopes the technology will be used to identify and manage conditions that are well defined and for which early intervention can make a difference; he points to metabolic disorders like phenylketonuria, in which children require a strict diet, and certain immune disorders that can respond to early treatment. If babies' problems can be diagnosed prenatally, he says, "you're not putting them in distress for the first few weeks" while everyone is "running around trying to figure out what is wrong." Another example is a condition called dilated cardiomyopathy, in which the heart is enlarged and weakened. This disorder can go undiagnosed until its victims find themselves short of breath or have a heart attack as teenagers or young adults. By treating them from a young age with drugs, physicians can "dramatically change outcomes," says Euan Ashley, a Stanford researcher who cofounded Personalis, a genetic screening company.

Credit: Illustration by Gracia Lam

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