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Too Much Information? Noninvasive Genetic Tests for the Unborn

A series of recent breakthroughs means that early, noninvasive genetic tests for fetuses may be just two years away

By Melinda Wenner Moyer | Wednesday, April 13, 2011 | 2

Today expectant parents concerned about the diseases that could afflict their unborn children don't have a lot of options. Blood tests can determine whether parents carry mutations for such genetic diseases as cystic fibrosis and Tay-Sachs, but they can't determine whether the baby will inherit them. And although fetuses can be tested for Down syndrome and other chromosomal abnormalities using amniocentesis or chorionic villus sampling, about 1 percent of procedures cause miscarriage, so many moms opt out. But thanks to a handful of recent breakthroughs, noninvasive prenatal tests may soon be available that diagnose genetic diseases before birth using samples of a mother's blood—an exciting possibility that also raises difficult questions about how they should be regulated and administered.

What makes noninvasive tests possible is that a pregnant woman's blood contains free-floating copies of her fetus's genes, as chemical pathologist Dennis Lo of the Chinese University of Hong Kong discovered in 1997. Last December in *Science Translational Medicine*, Lo reported on a method of sequencing individual fetal genes and counting individual fetal chromosomes in a mother's blood to establish whether a fetus carries disease-causing mutations or chromosomal abnormalities. Fetal genes inherited from the mother are identifiable because they are present in higher-than-normal concentrations in the mother's blood; gene variants not shared by the mother are assumed to be inherited from the father. In a follow-up article in the *British Medical Journal*, Lo tested his approach on 753 pregnant women. He counted the proportion of DNA molecules found in the mother's blood that were derived from chromosome 21—individuals with Down syndrome have three copies rather than the normal two—and accurately diagnosed 100 percent of the fetuses who would be born with the disorder. The test, Lo says, would prevent "98 percent of invasive procedures, such as amniocentesis." The trial did, however, report three false positives, so all positive results would need to be followed up with more invasive tests.

San Diego company Sequenom is developing a test based on Lo's method that should be available within two years. Tests for other conditions, including cystic fibrosis, Tay-Sachs, hemophilia and sickle cell disease, may be four to five years away.

The big question is how these tests will affect parental decisions: Will couples abort affected fetuses? How will the prevention of rare diseases affect research funding for their cures? Will tests arise that allow parents to select fetuses based on superficial traits, such as eye or hair color? Stanford University law professor Henry T. Greely says that the U.S. government is doing nothing to address these questions. In addition, doctors will need guidelines to help them counsel test takers properly. Otherwise "you will end up with families getting information they're not ready to get," says Siobhan Dolan, an obstetrician at Montefiore Medical Center in New York. In a few years, we might have too many options rather than too few.