



No-Risk Blood Test for Down Syndrome

Mother's Blood DNA Test IDs Down Syndrome With No Risk to Fetus

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Oct. 6, 2008 -- An early-pregnancy blood test promises to tell women whether their fetus has Down syndrome without the need for risky, invasive procedures.

First- and second-trimester screening tests can detect pregnancies at high risk of Down syndrome. Many women opt to terminate such pregnancies.

But even if it never comes to having to make such a heart-rending decision, Down syndrome screening can be anguishing.

Noninvasive ultrasound and blood tests can tell women whether they need more invasive tests. These confirmatory tests mean inserting a needle into the womb to sample amniotic fluid (amniocentesis) or snipping off a small piece of the placenta for analysis (chorionic villus sampling or CVS).

The vast majority of the time, these tests go smoothly. But there's a real risk they can cause a miscarriage. Moreover, by the time all these tests confirm Down syndrome, the pregnancy is often 18 or 19 weeks along -- making the decision to terminate even more emotionally difficult.

No wonder the decision to undergo Down syndrome screening is fraught with anxiety. It certainly was an anxious time for Stanford University bioengineer Stephen Quake, PhD, and his family, when his wife underwent amniocentesis during her first pregnancy and CVS during her second.

"It was nerve-wracking for all of us, and I can only imagine how the fetus felt," Quake tells WebMD.

Safe Blood Test for Down Syndrome

Quake started looking for a better way to screen. He knew that a small amount of fetal DNA enters a pregnant woman's bloodstream. Researchers already were trying to separate that DNA from the mother's own DNA, but were having little luck.

That's when Quake had a brainstorm. Down syndrome is a genetic defect -- an extra copy of chromosome 21. Quake realized it isn't necessary to separate fetal DNA from maternal DNA. All he had to do was count the DNA that belonged to chromosome 21. Too much of this DNA signaled a fetus with an extra chromosome.

"We sequence millions of molecules from each blood sample and map the DNA back to the chromosome. And then we look to see if any chromosomes are over-

represented," Quake says.

Quake's team ran the test on small blood samples from 18 pre-selected pregnant woman and a single male donor.

Some of the women had normal pregnancies. Nine of the women carried fetuses with Down syndrome. Two of the women carried fetuses with Edward syndrome (an extra copy of chromosome 18) and one woman carried a fetus with Patau syndrome (an extra copy of chromosome 13).

The score: A plus. The test detected every genetic defect and was able to identify every normal pregnancy (as well as the male donor).

"That makes us feel pretty good. But one has to reserve judgment until this can be tested in thousands of samples," Quake cautions.

"This would be a big step forward. This is exciting stuff," says J. Christopher Glantz, MD, MPH, director of the perinatal outreach program and professor of obstetrics and gynecology at the University of Rochester Medical Center, N.Y.

Glantz, who was not involved in the Quake study, agrees that the DNA test must be tested in a very large number of women. Before it's ready for prime time, researchers will have to show that it misses very few cases of Down syndrome -- and that it sounds almost no false alarms.

"If this is confirmed to be as useful as the authors say, it would be quite a significant step forward, because women would no longer have to undergo an invasive test," Glantz says.

Quake thinks the test will be able to detect Down syndrome as early as the fifth week of pregnancy. Currently, the test would cost about \$700. But that cost would drop considerably if it were widely used.

"We are two to three years away from a viable test," Quake says. "This technology is not common in hospitals now, but we anticipate it will be soon. We are very excited about the prospects of improving health and saving lives."

Quake and colleagues report their findings in the Oct. 6 early online edition of the *Proceedings of the National Academy of Sciences*.

SOURCES: Fan, H.C. *Proceedings of the National Academy of Sciences*, Oct. 6, 2008; early edition. Ball, R.H. *Obstetrics & Gynecology*, July 2007; vol 110: pp 10-17. Malone, F.D. *The New England Journal of Medicine*, Nov. 10, 2005; vol 353: pp 2001-2011. Stephen Quake, PhD, professor of bioengineering and applied physics, Stanford University; investigator, Howard Hughes Institute, Stanford, Calif. J. Christopher Glantz, MD, MPH, director, perinatal outreach program; professor of obstetrics and gynecology, University of Rochester Medical Center, N.Y.