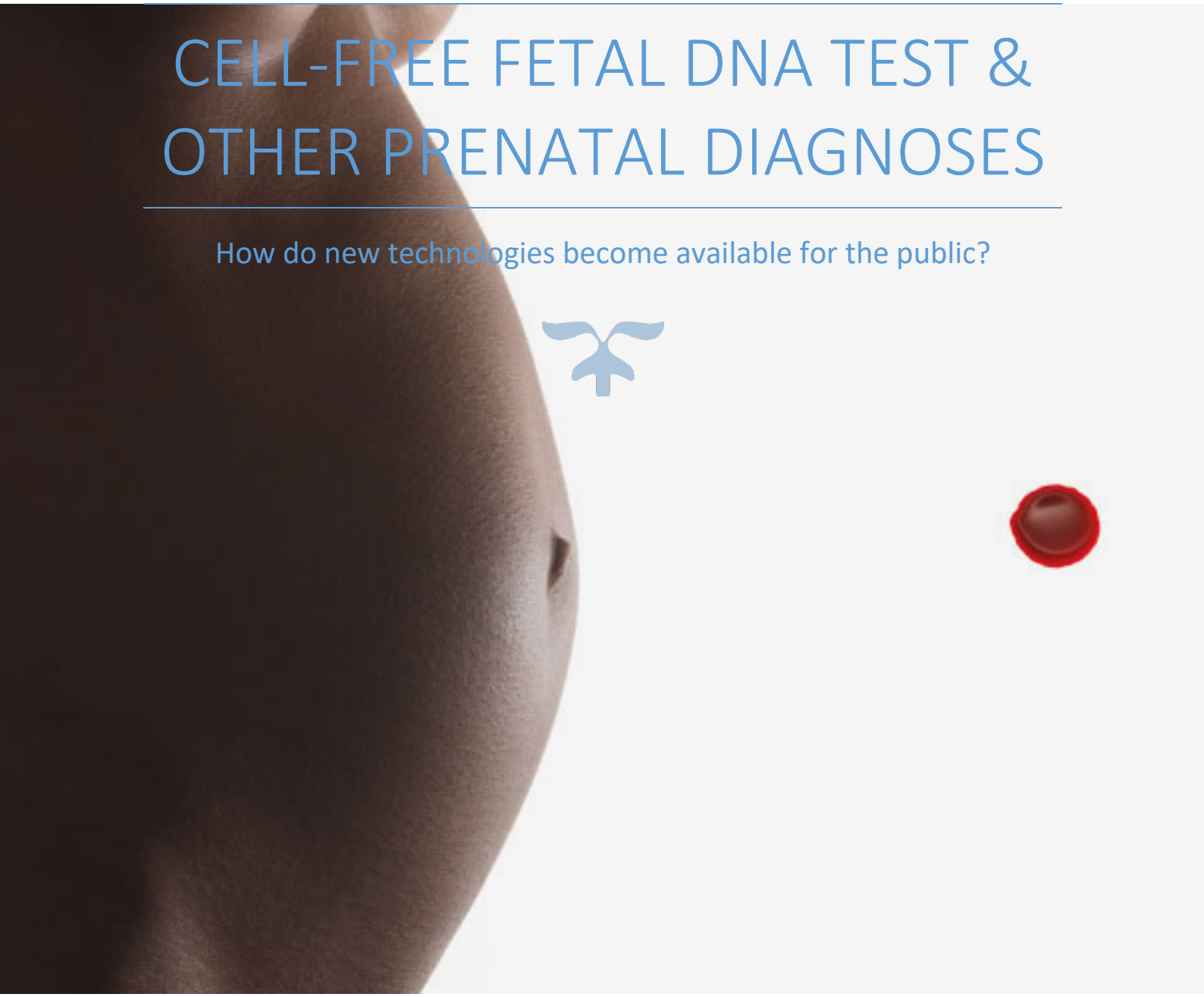

CELL-FREE FETAL DNA TEST & OTHER PRENATAL DIAGNOSES

How do new technologies become available for the public?

30. APRIL 2014

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Inhalt

Preface

Prenatal diagnosis plays a huge part in modern society. In countries such as China, where having a son is a far bigger advantage for the family than having a daughter and due to the one child policy the parents have only one chance, parents often check what gender the unborn is. Should it be a boy, the parents are happy and the mother will give birth. However, if the unborn is female, the parents will almost certainly get an abortion. They will even go as far as to get an illegal abortion, should a legal one be impossible. This is all due to prenatal diagnosis. As a group, we are both shocked and amazed by this topic. The fact that it is 'abused' by people in countries such as China and India is horrible. But there is always a bright side, in this case being the very early diagnosis of diseases. We want to explore how accurate these measurements are, and what the dangers are. We are also interested in how many different diseases and conditions can be determined, and how prenatal diagnosis works. Could there be a future where only healthy and genetically 'perfect' humans exist? Is this possible with what procedures and technology we have today? These are but a few questions we hope to answer in this paper.

Introduction

Prenatal diagnosis is a very present topic all over the world with parents who want to know whether or not their future baby is going to be healthy or not. Doctors have been trying to look inside the womb of pregnant women since 1895, when x-rays were discovered. Since then, many different techniques for the determination of gender, chromosomal abnormalities, genetic diseases and other conditions of an unborn foetus have been developed.

We will also discuss about the repercussions, the knowledge that these test can give, can have for all those involved.

And how new technologies such as the Cell-Free Fetal DNA Test become available to the public in non-first world countries like India and China.

Techniques

Ultrasonography

Ultrasonography is without a doubt the most common technique used for prenatal diagnosis. First introduced by Ian Donald in 1958, this technique is not harmful to both mother and unborn child. Back then it was far more difficult as it is today, but

the principal stayed the same: Sound waves are used to produce an image of the foetus, which can be measured thereafter. First and foremost the gender can be defined simply by looking at the sexual organs of the foetus. But also conditions like trisomy 21 (Down syndrome) can be determined, though not with the precision of some of the methods described in this chapter. This is because a picture of the foetus does not show its genes.

Error Rate False positives for Down syndrome: ~6 percent; false negatives: ~20 percent

Chorionic Villus Sampling (CVS)

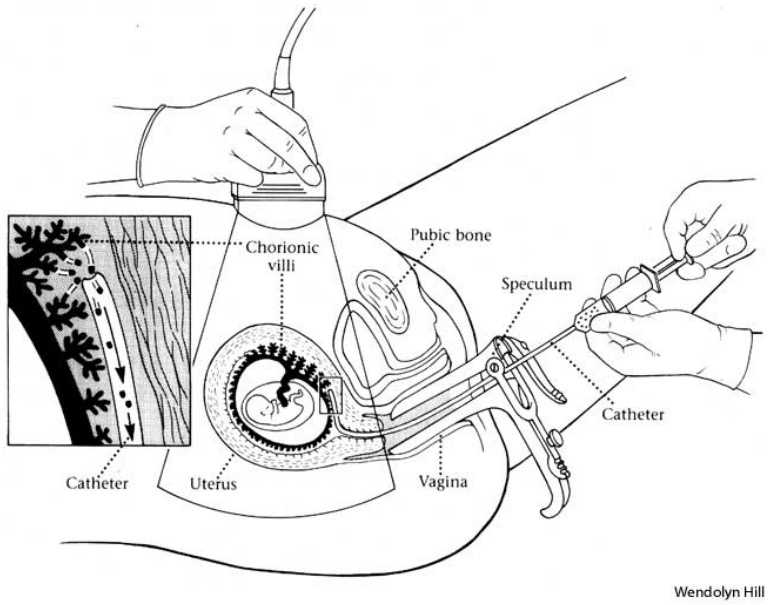
This technique involves taking a sample of the chorionic villus (placental tissue). It is used to determine chromosomal abnormalities with great accuracy, as well as all other genetic disorders. CVS is usually performed in the 10^{th}, 11^{th} or 12^{th} week. Though this technique is very accurate and effective and is considered a safe procedure, there are dangers as with all other procedures of this kind. Statistically 1 in a 100 procedures goes wrong and results in a miscarriage.

There are two ways of collecting the necessary samples.

Trans abdominal: A needle is inserted into the placenta through the abdomen and uterus to collect a sample.

Trans cervical: This method requires a catheter to be inserted through the cervix to obtain the tissue sample.

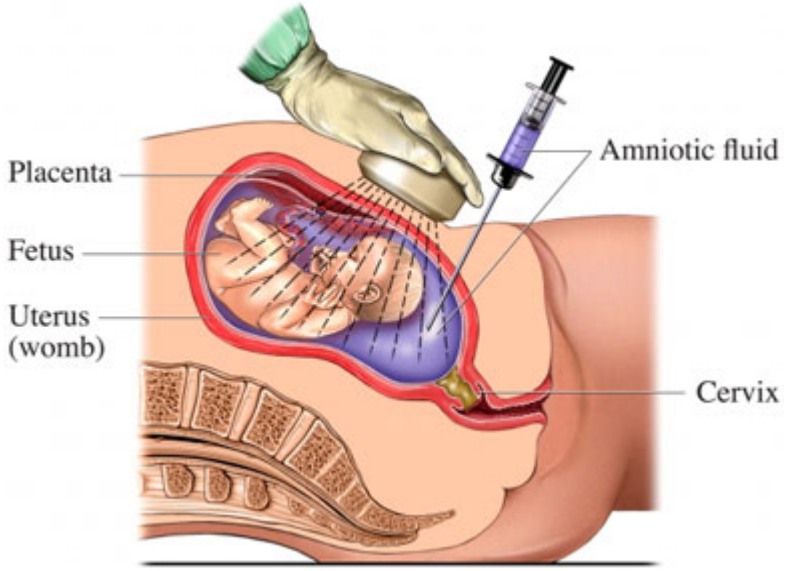
Error Rate False positives for Down syndrome: ~1 percent; false negatives: ~2 percent



Amniocentesis

In this procedure, a needle is inserted into the uterus to take a sample of the amniotic fluid. Amniotic fluid is the fluid inside the amniotic sac, and it surrounds and protects the foetus. This fluid contains foetal cells, which in turn contain the DNA of the foetus. By analysing this the health and overall condition of the foetus can be clarified. It can determine nigh every disorder, be it chromosomal or genetic, and is therefore an extremely accurate method. It can also determine neural tube defects, unlike CVS. There is a very low risk to Amniocentesis, and therefore it is a much wanted procedure. The samples are usually taken between the 14th and the 20th week of pregnancy, due to the elevated risk if you extract samples too early. Statistically, there is 1 miscarriage in ca. 300 procedures, three times as low as CVS. It is however a much slower procedure, and analysing the cells and DNA takes time. Therefore CVS is preferred in quite a few cases.

Error Rate False positives for Down syndrome: <1 percent; false negatives: <1 percent



Maternal Serum Alpha-Fetoprotein Measurement (MSAFP)

This as a somewhat more basic procedure. It also involves taking a blood sample of the mother, however instead of looking at the foetal cells, it is the maternal serum alpha-fetoprotein (ASP) levels that are looked at. This is a protein that is produced by the liver of the foetus, and can be measured in the blood of the mother. Low levels of ASP indicate trisomy 21. This information might be key to whether or not more tests should be absolved.

Cell-Free Fetal DNA Test

At 10 weeks the expectant mother, has blood drawn and that's the end of the practical procedure. They are no risks and the test is extremely exact. Cell-Free Fetal DNA Test is reliant on the fact that the pregnant woman's bloodstream is full of genetic material from her baby. This DNA is either contained inside of intact fetal cells or is of the free floating kind. As the fetus develops, the placenta will shed some of its cells, each containing 23 pairs of the baby's chromosomes. Some of these cell can migrate into the mother's bloodstream. The problem is that these cells are extremely rare and hard to isolate, from the maternal blood.

So how do you test for Down syndrome and other trisomies (trisomy is a genetic defect where the person has three copies of the chromosome instead of two). The key lies in massively parallel shotgun sequencing. Firstly millions of copies are made of snippets of DNA from the blood sample. Then you look through the mix for specific sections that only show up on chromosome 21 (Down syndrome is the presence of three 21 chromosomes). Think of it as smarties in a bowl where blue represents the presence of the 21 chromosome. You expect to find a set proportion of blue smarties some from the mom and some from the baby. But if the baby has Down syndrome then you'll have too many smarties in your bowl.

Error Rate False positives for Down syndrome: <1 percent; false negatives: <1 percent

Interview

Our topic is scientifically pretty straightforward but ethically can get really complicated. So it was essential to talk to someone who could answer my questions about the science but more importantly who could also answer my questions about the ethics.

For these reasons I consulted with Dr. Asmeeta Burra a mother of three. She is a doctor in South Africa and helped me with understanding what the situation was like from an ethical point of view and how the new Cell-Free Fetal DNA Test was being made available to the public.

In South Africa do all expecting mothers go for prenatal diagnosis?

Well certainly all women who have access to the right facilities and who regularly visit them would definitely go for an ultrasound. However like in most places we categorize our patients into high and low risk. High risk being women over 35 and/or

having a family history for children born with disabilities and/or their being signs of a disability shown from an ultrasound, are more likely be recommend an invasive prenatal test.

Who initiates these prenatal test, the patient or the doctor?

The doctor, but there is a trend that, the more educated and better of patients, seek out these tests.

Is the Cell-Free Fetal DNA Test readily available to all in South Africa?

The Cell-Free Fetal DNA Test is a very new technology and as such is not jet available to the public.

When will it be available to the public?

The problem is, is that there is a huge disparity between those who have money and those who don't. There isn't public medical care like in Switzerland as a result the private sector will be the first to have access to this Test. Over time this technology will make its way to the public sector. The fact of the matter is that most medical resource are spent on TP and Aids, due to this there is very little left over. I expect that in the next few years there should be complete access to this Test for this with the Money.

Do believe that prenatal tests can be a bad thing?

Certainly. It can occur especially among the Asian population, that women will get an abortion depending on the gender of the child.

Could you elaborate?

The female gender is seen as being inferior in these two different cultures. In the Asian community, when a woman gets married, her family has to give the grooms family a lot of valuables. This is the same as in India. However things aren't as bad as they are in India. As a result it isn't favorable for the family to have a girl. But these ritual are certainly only present among the very traditional and wouldn't be applicable to the majority of the population.

Would you say that prenatal testing is at the forefront of human engineering?

Certainly, nowhere else does the science have such a profound and visible outcome. Women decide based on these test whether or not to have their child. Of course the engineering part is very rudimental in this case, but if people are willing to have an abortion because of these tests then they probably will be open to the idea or having their child modified inside the womb. So you could say prenatal testing is preconditioning people and making human engineering something widely more accepted.

Discussion

Prenatal diagnosis is an extremely complicated topic and it has to be accepted that when discussing prenatal one will never come to a decisive conclusion.
They are very clear positive points concerning prenatal diagnosis and then they are those who abuse it. Then you have people with strong religious and moral beliefs who believe that abortion endanger their culture and way of life.
Prenatal diagnosis is a treatment as such. It helps pregnant women understand who it is inside them that is growing and how best to prepare. However like I said it's not as simple as that. Not everyone is created equal in this world and people don't all have access to same facilities. As a result it isn't unthinkable for women how cant financially take care of a child with Down syndrome or crucially who mentally can't handle a child like that, to get an abortion.
Then they are people who abuse prenatal diagnosis to determine whether or not a foetus is female or male. These people do this because there is a social and cultural pressure for women to exclusively have boy babies. I find it hard to find real fault with these people due to the extreme pressure that they are subjected to from their community and the fact that these people live in areas of low economic development. And that they probably haven't had a lot of education.
However when a women does find out she does have a child down syndrome, who is economically well and she decides to keep the child. Well then advantages are unquestionable. The parents have time to prepare and mentally get themselves ready, in case like these the benefits become very clear.
The state usually accepts if a women with a baby with a disability decides to get an abortion. The reality of the matter, is that people with a severe disability can be a financial burden to the state. This is because people with severe disabilities end up going to hospital or another state run care facility often and for long periods of time. More often than not these people aren't capable of contributing to society and are seen by some as an unnecessary burden.
Prenatal diagnosis is the first step in designing your perfect baby. Whether that is a good thing who know, it certainly is in tune with the human desire to push boundaries and what is possible and not what is acceptable.
To conclude our topic prenatal diagnosis is certainly one of the more hotly debated,

varied and controversial. The science of the fact is in this instance is fairly straightforward but it's the ethics is where the matter gets interesting.

Summary

Prenatal diagnosis can help women understand their unborn and inform them and their decision they make about them. The cons concerning prenatal diagnosis aren't really cons in themselves rather people not using the information gained properly. It certainly stimulates the imagination with all the possibilities with how we could change ourselves before we leave the womb.

References

Images

Cover picture:
http://www.wired.com/images_blogs/wiredscience/2012/12/ff_dnascreeningb_f.jpg

Pic 1: http://www.answers.com/topic/chorionic-villi-sampling-cvs

Pic 2: http://www.lifescript.com/health/a-z/treatments_a-z/procedures/a/amniocentesis.aspx

Internetlinks

http://www.wired.com/2012/12/ff-prenatal-testing/all/

http://www.discoveriesinmedicine.com/Ni-Ra/Prenatal-Diagnostic-Techniques.html#b

http://www.umanitoba.ca/faculties/medicine/units/biochem/student/prenatques.html

http://www.phil.gu.se/munthe/CRE-7.pdf

https://en.wikipedia.org/wiki/Prenatal_diagnosis

http://www.ndsu.edu/pubweb/~mcclean/plsc431/students/mclean.html