Bob Barrett: This is the podcast from *'Clinical Chemistry',* I am Bob Barrett. Noninvasive prenatal diagnosis has developed substantially since the discovery that appreciable amounts of free fetal DNA occur in maternal plasma. This discovery rapidly paved the way for the detection of paternally inherited alleles in maternal blood, including, Rh blood group, fetal sex, and single-gene disorders.

In the April 2012 issue of '*Clinical Chemistry*', Dr. Neil Avent, a Professor at The School of Biomedical and Biological Science at Plymouth University in the United Kingdom, provided his thoughts on a recently published study in the same issue of the journal by Jessica van den Oever and her colleagues that utilized Single Molecule Next-Generation Sequencing to detect Trisomy 21 in maternal plasma samples.

Dr. Avent is our guest in this podcast. Doctor, what would be the impact of noninvasive prenatal diagnosis?

Dr. Neil Avent: Well, the main impact is, it would eliminate the risky procedures of amniocentesis and chorionic villus sampling, which have roughly a 1% risk of loss of fetus during the procedure. So any procedure which eliminates the need for that method is obviously very beneficial.

Bob Barrett: Is the risk of fetal loss due to amniocentesis high?

Dr. Neil Avent: It's roughly about 1%, but it can vary between different senses, that's sort of generally how we figure about 1%, but it can be higher than that and it can be lower, but generally the numbers of fetuses that are diagnosed with down syndrome are lower than those lost for the procedure itself. So that just gives you a feel for the impact of the risk.

Bob Barrett: Why have there been such problems implementing noninvasive prenatal diagnosis for aneuploidy?

Dr. Neil Avent: Well, the main focus of noninvasive prenatal diagnosis have been fetal DNA and maternal bloods, that is an admix of both fetal DNA about 3-6% fetal DNA and the remainder is derived from the mother.

So the main problem there is the amount of maternal DNA that's there, and it's very difficult to actually assess for aneuploidy because of that large mix of maternal DNA you can't -- count the proportion of fetal DNA which has got say Trisomy 21. So that's the main issue, is the admix of maternal and fetal DNA in the sample.

Bob Barrett: How has NGS impacted on this problem?

Dr. Neil Avent: Well, NGS is extremely powerful because it is able to count the number of different targets that you have in a sample. Because the proportion of fetal DNA is relatively high, you are able to see a higher number of targets from say chromosome 21 and the trisomy 21 fetus. So that the chromosome counting ability of NGS has actually got around that issue and it is extremely powerful.

Bob Barrett: Doctor, why is single molecule sequencing more powerful?

Dr. Neil Avent: Single molecule NGS as compared to the first generation, next generation sequencing, is much more powerful because there is no modification of the DNA at all, it is much more ready to actually assess the complete DNA that's there, there is no artifacts associated with it. So it appears in a recent paper in '*Chemical Chemistry*' that this is the way to go and it is leading to much more sensitivity for trisomy 21 investigations.

Bob Barrett: Can you foresee a mass move towards NGS-based diagnosis for aneuploidy?

Dr. Neil Avent: Absolutely, I can. It is moving in that direction and several countries in the world know that it's happening in Europe and possibly the States. So this is the way forward, digital counting of different chromosome abnormalities is going to replace, I believe, it's going to replace amniocentesis and CVS sampling in the medium term.

Bob Barrett: What about the cost, would the high cost of this be a roadblock?

Dr. Neil Avent: Yes, it is, I guess at the moment the cost is over $1000 per sample, so it would need to come down for it to be beneficial. But I have seen estimates of the cost tumbling recently, and certainly it seems very, very economic to do this, and then the risk of course is much less, so it will certainly impact.

Bob Barrett: Well Doctor, let's look ahead, are there any cheaper alternatives to NGS on the horizon?

Dr. Neil Avent: The comparable technology is digital PCR, microfluidic-based PCR where you do thousands of different PCRs in that simple reaction, that's an alternative. The costs are roughly the same to NGS, but that certainly is an alternative technology, proves to when that technology is yet to be seen, we've got to view the experiments I guess on a large number of clinical samples. But the possibility of purification of fetal DNA from maternal blood would give some very cheap assays. So that's another possibility in which we'll see a massive reduction in costs. So all three of those could win out in the end.

Bob Barrett: Dr. Neil Avent is a Professor at The School of Biomedical and Biological Science at Plymouth University in the United Kingdom. He's been our guest in this podcast from '*Clinical Chemistry.*'

I am Bob Barrett, thanks for listening!

Total Duration: 5 Minutes