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Ectopic Pregnancy.
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Guests:
Dr. Andrew Horne is a Consultant Gynecologist at the University of Edinburgh.
Dr. Julie Shaw is from the Ottawa Hospital and the University of Ottawa.

Bob Barrett: This is the podcast from *Clinical Chemistry*. I am Bob Barrett.

An ectopic pregnancy occurs when an embryo implants outside of the uterus. Ectopic pregnancies can be difficult to diagnose, and in a question and answer feature in the September 2012 issue of *Clinical Chemistry*, four experts discussed recent advances that help us understand the etiology of ectopic pregnancy.

We are joined by two authors of that feature: Dr. Julie Shaw from The Ottawa Hospital and University of Ottawa; and Dr. Andrew Horne, a Consultant Gynecologist at the University of Edinburgh.

Dr. Horne, we will start with you. Why do we need a biomarker for ectopic pregnancy?

Dr. Andrew Horne: Well, the first thing is ectopic pregnancy is remarkably common. It's occurring in about 1 in 50 pregnancies, and it's a condition which unfortunately as well as causing problems with maternal morbidity, also still kills young women, so it's a very important clinical problem.

One of the difficulties that we have is we don't have a very good way of diagnosing it. So at the moment it's diagnosed by a combination of ultrasound scans, which often don't tell us where the pregnancy is, and repeated measurements of

the pregnancy hormone, hCG.

And so we have done a number of studies which have shown that patients require many, many visits before the diagnosis of ectopic pregnancy is made to clinicians. And this, of course, costs large amounts of money for health services and in turn costs large amounts of money for patients.

So it's really the fact that in order to diagnose an ectopic pregnancy at the moment, it takes a considerable period of time, so we desperately need some sort of biomarker.

Bob Barrett: Dr. Shaw, are there any limitations to the published studies aimed at identifying biomarkers for ectopic pregnancy?

Dr. Julie Shaw: One of the main limitations is the fact that most biopsies and blood samples are collected from women at the time of surgery for an ectopic pregnancy, so at this time it has already been confirmed that they have an ectopic pregnancy, whereas the ideal samples for studies would be collected earlier on in the pregnancy, because this is when we actually need a biomarker to help aid in determining the risk that a woman has for having an ectopic pregnancy.

Another difficulty is that not all women are treated with surgery and so when they are treated with surgery, then it's definitively known that the pregnancy is an ectopic pregnancy. But some women are treated medically and so the presence of an ectopic pregnancy is not always 100% certain, and so this can get difficult to classify women into groups, as far as miscarriages versus ectopic pregnancies.

Bob Barrett: One limitation of current studies has been the validation of candidate biomarkers using external sample cohorts. What are the challenges here?

Dr. Julie Shaw: I guess the main challenge is getting various clinical groups in different locations to work together. I mean, we need large numbers of samples to do these studies, and so we need groups to work together, and I guess the main issue is a standardized selection protocol for the way samples are not only collected, but the way that they are characterized so that they can be used for large cohort studies.

Bob Barrett: Well, realistically, do you see the diagnosis of ectopic pregnancy employing a single marker or is a multifactorial approach preferred?

Dr. Julie Shaw: I think it's very likely that it will take a combination of markers in the future to diagnose an ectopic pregnancy or to determine the risk that a woman has for having an ectopic pregnancy.

I doubt that we will identify a single marker that has this capability. This is somewhat similar to other situations where we use multiple markers, such as in pre-eclampsia, or in maternal serum screening, marker levels are combined into some sort of algorithm that's used to calculate risk.

And additionally to the marker levels, other factors are taken into account as wel,l and these algorithms, such as maternal age, smoking status, whether a woman has diabetes, this sort of thing, and the race of a patient, I think definitely that will be the sort of approach in the future.

Bob Barrett: Well, let's look ahead. Dr. Horne, do you think that the most promising markers will be biochemical or based on imaging techniques?

Dr. Andrew Horne: I think imaging techniques are advancing very rapidly. I think from a practical point of view it would be better if we could identify a marker that's either serological or perhaps a urinary biomarker.

And the reasons for this are twofold. Firstly, obviously, it's something that can be quickly performed. But secondly, increasingly with the burden on health resources, it's likely to be much cheaper than some form of imaging and could also be used in the developing world.

So I think very much we would be looking for either a serum biomarker, a blood test, or some sort of urinary biomarker; it may be even something that you could pick up in the saliva.

Bob Barrett: Well, finally, where should future biomarkers be aimed? What would be the most useful clinically?

Dr. Andrew Horne: I think for a long time people were trying to identify a biomarker that would determine the location of a pregnancy, so whether or not the pregnancy was implanted outside of the uterus commonly and with an ectopic pregnancy they are implanted in the fallopian tube, or a pregnancy that was intrauterine, and then differentiate that in turn from an intrauterine pregnancy that was viable or a nonviable intrauterine pregnancy.

But I think as time has gone on, and as Dr. Shaw pointed out, ectopic pregnancies are now treated medically or surgically, and certainly at times when perhaps we are not 100% certain where a pregnancy has implanted, we tend to revert to medical management or long-term monitoring until we know the pregnancy itself has miscarried.

So I think really what we are looking at in the future isn't a marker that differentiates where the pregnancy is implanted

but rather a pregnancy that's of high-risk to a patient and separating that woman from low-risk group of women in whom perhaps treatment or intervention isn't warranted.

So these would be women that we now classify as women presenting with pregnancies of unknown location, and then hopefully this blood test would then separate them into high or low-risk patients depending on whether the pregnancy of unknown location would ultimately require some sort of intervention, whether it be medical or surgical.

Bob Barrett: Dr. Andrew Horne is a Consultant Gynecologist at the University of Edinburgh, and Dr. Julie Shaw is from the Ottawa Hospital and University of Ottawa. They have been our guests in this podcast from *Clinical Chemistry*.

I am Bob Barrett. Thanks for listening!