Clinical Chemistry

Male infertility and microchips

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Guest:
Dr. Jason Park is the Director of the Advanced Diagnostics Laboratory at the Children's Medical Center, Dallas and Assistant Professor of Pathology of the University of Texas Southwestern Medical Center.

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

In the March 2013 issue of *Clinical Chemistry*, Dr. Yuan Chen and colleagues of the National Taiwan University demonstrated a new miniaturized device that performs most of the key semen analyses that predict male infertility. The same issue included an accompanying editorial by Dr. Jason Park, Director of the Advanced Diagnostics Laboratory at the Children's Medical Center, Dallas and Assistant Professor of Pathology at the University of Texas Southwestern Medical Center.

Dr. Park is our guest in this podcast. Doctor, can you please describe the need for tests for male infertility?

Dr. Jason Park: Well, Bob, infertility is generally defined as the inability of sexually active non-contraceptive using couples to achieve pregnancy in one year. In the United States, infertility affects 10% or approximately 6.1 million women. Now, the difficulty in becoming pregnant is due to female factors about one-third of the time, male factors in another third, and the last third is a combination of other factors.

In male infertility, there are number of causes for reduced fertility. This includes congenital abnormalities of the testicles which produce the sperm or the vas deferens which is the key duct through which the sperm pass. Mechanical obstructions to the passage of sperm, increases in scrotal temperature, endocrine abnormalities or immunologic factors may also play a role. In approximately 50% of cases of male infertility, no discrete cause is found.

A key step in determining male infertility is the analysis of semen. Semen is the body fluid that contains sperm. The key features of semen that are analyzed include: semen volume, total sperm number in an ejaculate, sperm concentration, motility, vitality of the sperm, and sperm

morphology. Normally a sperm has a single head and a single tail. But occasionally sperm may have heads that are too small or too large, or two heads or two tails. A comprehensive analysis of male infertility includes the measurement of all these features of semen and sperm.

Bob Barrett: Please describe for us the current types of semen analysis, and is this something that could be done at home?

Dr. Jason Park: In clinical laboratories, the gold standard analysis of sperm is by observation under a microscope. Many laboratories use commercially available semi-automated systems known as CASA, otherwise known as Computer Assisted Semen Analysis. These systems use digital image analysis to rapidly perform a complete analysis of sperm. In terms of doing this at home, there are several different types of devices that can be bought at your local pharmacy. These devices are simplified and usually focused on a single aspect of semen analysis. To perform a complete comprehensive clinical analysis, this is usually done in a clinical laboratory.

Bob Barrett: Please describe and tells us about the device created by Dr. Chen and his colleagues.

Dr. Jason Park: In the current issue of *Clinical Chemistry*, Dr. Yuan Chen and colleagues demonstrate a novel microfabricated device that does not rely on optical images of the sperm. The key feature of their miniaturized device is a straight channel that has the width of approximately a single human cell; this channel is etched in silicon and capped with glass. As sperm moves through the channel, it causes measurable changes in voltage in the device. These changes in voltage reveal the various properties of individual sperm. Not only is sperm motility derived from the changes in voltage, but also additional features such as concentration, total number of sperm, and sperm head morphology can be determined.

Bob Barrett: What's novel about the device in Dr. Chen's paper?

Dr. Jason Park: The key advancement of this device is the demonstration that the sperm head morphology can be measured electrically. This has previously only been performed by visual assessment. Now, it is important to point out that paper did not directly measure abnormal sperm morphology, but rather they performed a "proof of concept," by measuring microparticles that would simulate abnormal sperm heads. The possibility of determining sperm head morphology electrically is exciting because it has not been done before and it could lead to smaller devices that do not require optical imaging. The methods for sperm analysis up to this point have all required optical measurements of sperm morphology, either by direct visualization through a microscope or by digital imaging. Dr. Chen and colleagues

have created a microchip that can perform the major semen analyses by electrical measurements alone.

Bob Barrett: Is the use microchip devices a new development in semen analysis?

Dr. Jason Park: Microfabricated chips for semen analysis have been around for 20 years or more. One of the first examples was published in *Clinical Chemistry* in 1993 by Drs. Larry Kricka and Peter Wilding at the University of Pennsylvania. Their original device was comprised of silicon, etched with microchannels and capped with glass. Since that time, more complex semen analysis devices have been demonstrated.

In essence, many of these devices are akin to obstacle courses for the sperm. The devices contain many physical, electrical or chemical barriers that the sperm must traverse to prove their fitness. What is important to note is that despite several decades of demonstrations of the possibilities of performing complex semen analyses on microchips, there are no commercialized examples of semen analysis microchips.

Bob Barrett: Is the lack of commercialized analytical microchips a problem specific to semen analysis?

Dr. Jason Park: No, Bob, the lack of commercialization is a problem that has been identified within the entire field of analytical microchips. Every month, novel analytical microchips are demonstrated, but there are few examples of successful commercialization and adaption in clinical laboratories with a wider healthcare market. So we probably won't be seeing the semen analysis microchip described in this paper in the clinical laboratory anytime soon.

Bob Barrett: Well finally, Doctor, what will it take to see wider use of analytical microchip devices such as the semen analysis device we heard about in this issue of *Clinical Chemistry*?

Dr. Jason Park: There have been a number of conceptual proposals and sponsored agreements between industry and the research community. At first, the focus was on so-called “killer apps,” finding an important application that needed an analytical microchip and that was so novel and important that every laboratory would need to use it. This has had some success with preparative techniques such as sample purification or quality assessment for genomic analysis.

Recently, in the journal *Lab on a Chip*, a new concept has been described for microfluidic apps. The concept is derived from the revolution in smartphone apps. Smartphones have become general platforms for running many different kinds

of independently designed software applications. Similarly for analytical microchip devices, if researchers design their novel devices to work on the standardized platform, a key hurdle to widespread adoption would be removed. The cost of developing and implementing analytical microchips includes not only the novel microchip, but all of the ancillary equipment needed to run the microchip.

Furthermore, having a standardized platform for microchips would decrease the need for new expensive ancillary equipment for each new analytical microchip. Instead, all analytical microchips could run on a common platform. Thus, there is promise to the wider use of analytical microchip devices, if there is an adaption of a standardized platform interface that allows developers to focus on innovative microfluidic or analytical microchip applications.

Bob Barrett: Dr. Jason Park is the Director of the Advanced Diagnostics Laboratory at the Children's Medical Center, Dallas and Assistant Professor of Pathology of the University of Texas Southwestern Medical Center. He's been our guest in this podcast from *Clinical Chemistry*. I'm Bob Barrett. Thanks for listening.