

## ACROSOME REACTION TESTING

The purpose of semen testing in all its forms is to answer three primary questions:

1. Does the man have sperm and are they alive?
2. Does the man have sperm that can fertilize an egg?
3. Does the man have sperm that will result in a viable embryo and live-born child?

QUESTION 1: Almost any laboratory or doctor's office with a microscope can answer the first question. A simple observation of the semen on a microscope slide will allow identification of motile swimming sperm cells. Occasionally, a sophisticated andrology (sperm) laboratory will find live motile sperm after special processing that a routine lab cannot see. However, we usually know the answer to the first question wherever the routine semen analysis is performed.

QUESTION 2: *"Does the man have sperm that can fertilize an egg?"* is a more difficult one for most laboratories. However, this question is central to the purpose of sperm analysis.

Sperm morphology has the greatest correlation with pregnancy rates and, more recently, fertilization rates of eggs with IVF than any other part of the routine semen analysis. Strict sperm morphology, a technique to determine the percentage of sperm having a "perfect" shape, allows us to identify semen samples that have a low fertilization rate in vitro. One of the initial investigators of **Strict Sperm Morphology**, Dr. Kruger (the test is often called the **Kruger Morphology Test**), demonstrated a profound decrease in fertilization (12%) when the strict morphology was less than 10% compared to over 70% when the strict morphology score was greater than 10%. (Kruger T, Hum Reprod 1995;Suppl 10:50).

Despite these results, we know from experience that some men with very poor sperm morphology will still fertilize eggs well and some men with normal sperm morphology fertilize eggs very poorly at IVF (and by inference with other treatments as well). A more specific test can help to confirm which men need treatments like IVF immediately and which men can reasonably try treatments like insemination first. Our goal is to avoid futile non-IVF treatments and failed fertilization at IVF.

We use the **Acrosome Reaction Test (AR Test)** to assist us in assessing sperm fertilizing ability. Sperm contain a "cap" that contains enzymes and binding sites for attachment to the egg. The sperm must release its acrosomal cap (called the "acrosome reaction") in order to bind and penetrate the shell around the egg (zona pellucida). The **Acrosome Reaction Test** involves staining the sperm acrosomal cap and then stimulating the sperm to release their caps. Men whose sperm does not undergo the AR in this test have very poor fertilization rates at IVF.

In a study performed before ICSI (intracytoplasmic sperm injection) was available, researchers showed the relationship between fertilization rate and the percentage of sperm which undergo the AR (Calvo LJ, Sherins RJ et al., Hum Reprod, 1994;9:1880-6). In that study, the fertilization rate was 13% when <5% of the sperm underwent the AR; whereas, the fertilization rate was normal if more than 8% of the sperm demonstrated the AR in this test. Very importantly, the fertilization rate was measured using human sperm and eggs at IVF. In other words, the researchers were able to study the correlation between AR test results and fertilization in the laboratory. This study can never be repeated because at the time of the study, there were no reliable treatments for male infertility with IVF. Now we have ICSI which very reliably allows fertilization by poor quality sperm. As such, if there is any question of abnormal sperm function, the IVF lab recommends and performs ICSI precluding the ability to do more studies of this nature.

Further, despite other abnormalities seen with the semen analysis, if the AR test was normal (> 8%) then the IVF fertilization rate was normal. Consequently, men who have a normal AR test should be able to attempt pregnancy without IVF & ICSI.

**Thus, the AR test significantly helps us decide who can delay IVF and who needs IVF/ICSI immediately (assuming there is no correctable cause of the poor sperm function).**

The AR test does not add much information in certain circumstances. If a man had good fertilization in a prior IVF cycle, then the AR test is unnecessary because its purpose is to predict egg fertilization. Likewise, poor or failed fertilization in a prior IVF cycle suggests the need for ICSI regardless of ANY other testing. Men with extremely poor semen quality (various abnormalities) are best treated directly with IVF/ICSI and do not need additional testing. An exception to these situations is that sperm quality may change over time, thus if the last sperm test or IVF cycle was over a year ago, the AR test and other sperm tests may be of value.

**IMPORTANT NOTE:** Despite serious sperm abnormalities, some pregnancies still occur under the direst of circumstances – "miracle babies". These surprise pregnancies remind us that we cannot be absolute in our impressions or recommendations. Also, fertility is a couple's problem and one cannot make a recommendation for treating the male without considering the female contribution to fertility.

QUESTION 3: *Does the man have sperm that will result in a viable embryo and live-born child?* is an intriguing question with important implications. "DNA fragmentation" (sperm DNA fragmentation tests, sperm chromatin structure assays) tests may shed light on this issue but are still in early stages of development and their results are still questionable.