Sperm Antibodies in Males

A relatively uncommon cause of infertility is the presence of sperm antibodies in the male partner. Sometimes it is a lone finding in otherwise normal semen and sometimes it is associated with other abnormalities in the various sperm parameters. While the significance of sperm antibodies has in the past been hotly debated, it is now recognised that sperm antibodies in the male, in a sufficiently strong concentration, can be solely responsible for infertility.

Why do men form antibodies against their own sperm?
The formation of antibodies by the body against any of its own cells is generally considered a pathological condition, often with quite serious consequences. During the first year of life our developing immune systems look at all the cells in the body, recognise them as *self*, and subsequently develop antibodies only against foreign invading cells to protect the body, particularly from viruses. In rare conditions the immune system's memory of what is *self* fails and it produces antibodies against certain types of cells in the body in what are known as *auto-immune diseases.*

With sperm antibodies the situation is slightly different. In early life, when the immune system is being programmed for recognition of *self*, sperm are not present in the male body - they do not appear until puberty. The immune system is however protected from encountering these immunologically foreign cells in the adult male by what is known as the *blood-testis barrier*. In the vast majority of men this provides lifelong protection. This protection can fail if a male suffers serious trauma to the testes or suffers inflammation of the testes, *orchitis*, as a result of a bacterial or viral infection.

When we encounter males with sperm antibodies we enquire as to whether they have ever suffered such trauma or infection. There are few males who, at some stage of their life, have not suffered some degree of testicular trauma, particularly as a sporting accident, so it is difficult to set a degree of severity to try to recall. Sometimes they can remember specific instances or trauma or infection but in a great many cases there is no such history. One situation in which there is a somewhat higher incidence of sperm antibodies is men who have had a vasectomy for a period of time before having it surgically reversed. The length of time of the surgical obstruction seems to govern the likelihood of presence and strength of sperm antibodies. Sometimes the antibodies are relatively weak and do not inhibit fertility but in others they are quite potent and are most likely a major contributor to the infertility.

How do male sperm antibodies cause infertility?
The sperm antibodies are secreted in the fluids of some of the accessory glands which contribute liquid components to ejaculated semen but not in the testis itself. The sperm do not contact the antibodies until after ejaculation and all the components of the semen are mixed - either in the vagina during sexual intercourse or in a bottle after collection of a semen sample. The antibodies then bind to various sites on the sperm surface - sometimes on the tail and sometimes on the sperm head.

Sperm with antibodies bound to their surface have difficulty doing two necessary things. They are unable to swim progressively through the cervical mucus and other fluids in the reproductive tract of the female partner and therefore have difficulty reaching the egg in the fallopian tube. If they make it to the egg the antibodies, particularly if they are attached to the sperm head, prevent the sperm from penetrating the *zona pellucida,* the shell of the egg and binding to the *ooplasm* of the egg. These are necessary stages in fertilisation of the egg and without egg fertilisation there can be no pregnancy.

How are sperm antibodies in men detected?
The effects of the presence of severe sperm antibodies can be seen during the examination of a semen specimen down a microscope. The sperm will be bound together in clumps by the antibodies in a manner known as *agglutination*. The agglutinates may be in a tail-to-tail, head-to-head, or a mixed configuration. Since true agglutination can be difficult to distinguish from simple adhesion to other cells and debris within the semen, confirmatory tests are usually performed.

Older tests using the agglutinating ability of dilutions of the liquid component of the semen against normal sperm have given way to simpler and more direct tests. These tests use forms of *immunobeads* where microscopic latex spheres coated with human antibodies and mixed with the sperm in question and an antibody against human antibodies. If the sperm become coated with the latex spheres then we know that sperm antibodies are present. The percentage of sperm with beads attached give a guide as to the severity of the sperm antibodies.

Your doctor can also perform a test on the female partner which detects the effects of sperm antibodies although it cannot simply differentiate between male and female sperm antibodies. It is known as the *Huhner's* or *post-coital test (PCT)*. The couple is asked to have sexual intercourse in the evening and next morning the doctor aspirates a sample of cervical mucus from the female partner and studies the motility of the sperm in the mucus. In the presence of sperm antibodies the sperm will not be making good forward progress through the mucus.

How can male sperm antibodies be treated?

Steroid therapy has been advocated to reduce the production of the sperm antibodies but, as it also suppresses any other antibody formation, it renders the patient far more susceptible to any infection. For this reason it is not widely used.

In the early 1980's the Queensland Fertility Group adapted a technique which had been advocated for use with artificial insemination with husband's semen to IVF. We found that the approach yielded in vitro fertilisation and subsequent pregnancies in patients with sperm antibodies who in the past had not been able to have any eggs fertilise. It involved having the husband produce his semen sample directly into a bottle containing about 20ml of a simple culture medium called Tyrode solution. It is immediately mixed and the sample immediately washed by centrifugation. This has the effect of diluting the antibodies before they attach to the sperm and antibody binding is further minimised by the washing away of the antibodies. It is imperative that the mixing and washing be done immediately after collection of the specimen.

This approach helps reduce antibody binding to sperm but does not totally prevent it. In cases of very severe sperm antibodies it is sometimes incapable of reducing the binding to a level where fertilisation can occur. For patients with this degree of a problem the assisted fertilisation by microinjection technique of ICSI (intracytoplasmic sperm injection) has come to their rescue. It totally replaces the stage which sperm antibodies inhibit - the penetration of the egg by the sperm. In ICSI a sperm is injected directly into an egg. Once in the egg, it loses its form and the egg becomes fertilised - steps over which the antibodies have no effect. ICSI therefore has become the treatment of choice for severe sperm antibodies. The Fertility Gold Coast Office has an information sheet on the ICSI technique.

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