Male infertility & semen tests

Fertility Facts
In about half of all infertility the male is an important contributor. Although there are blood tests for reproductive hormones like FSH and testosterone, semen analysis remains the most important test. In recent years there has been more emphasis on the quality of sperm rather than their number – including DNA damage.

REF 3186.20

About 25% of infertility is directly due to the male partner and another 15-25% has some male contribution. How is male infertility diagnosed, what does it mean, and what can be done about it?

Male Reproductive System
Sperm are produced in long, densely packed tubes in the testis called the seminiferous tubules. The ends of each tubule empty into an area called the “rete testis”, and the rete testis leads to the epididymis. The epididymis is a single highly coiled tube in which the sperm undergo their final maturation. The epididymis connects with the vas deferens which transports sperm.

Testis and epididymis
To produce sperm, the testis must be 2-3°C cooler than the core body temperature of 37°C. The male reproductive system is also designed to keep sperm away from cells of the immune system that would otherwise recognise the sperm as “foreign”, and produce antibodies to them. This barrier may be breached if the testis is physically damaged or if sperm leak from the end of the cut vas deferens after a vasectomy.

As well as producing sperm, the testis makes the male sex hormone testosterone. Testosterone levels rise at puberty, inducing development of the genitals, seminal vesicles and prostate, body hair, beard growth and the muscle development associated with male physique.

Sperm and testosterone production are stimulated by two hormones from the pituitary gland at the base of the brain – luteinising hormone (LH) and follicle stimulating hormone (FSH) which are named after their functions in the female (not the male)!

At ejaculation, fluid from the epididymis (about 5% of the total volume), the prostate (30%) and the seminal vesicle (65%) are mixed. Components in the seminal vesicle fluid make the semen coagulate soon after ejaculation. After 20 minutes or so, enzymes in semen make it liquid again.
Male infertility & semen tests continued...

**Male Fertility tests**
**Physical examination**
As part of a physical examination the doctor looks at the size of the testes, the consistency of the testes and for the presence of a varicocoele, the development of the genitals, and hair patterns. The hair patterns are a sign of testosterone production. A varicocoele is the occurrence of “varicose” veins in the blood vessels that supply the testis – which can be felt but usually not seen.

**Hormone tests**
Blood tests can measure FSH and testosterone levels. A high FSH level indicates the pituitary gland is trying to stimulate sperm production but the testes are unable to respond sufficiently. A low testosterone level can reduce sperm production and male sex drive.

**Karyotype**
A karyotype detects chromosome abnormalities that may cause male infertility.

**Y-deletion**
About 10% of men with very few or no sperm have a tiny piece of the Y chromosome missing. This is called a Y chromosome microdeletion. There are three regions on the Y chromosome where deletions commonly occur – the regions are called AZFa, AZFb and AZFc. Knowing which deletion is present can help predict whether there are likely to be sperm in the testis, and hence whether a testicular biopsy is worthwhile.

If a man has a Y microdeletion and there are sperm that can be used for treatment, the fertilisation rate and pregnancy rate using IVF with microinjection (ICSI) are the same as for those for other causes of male infertility. Boys conceived of fathers who have a Y deletion nearly always inherit the same condition and so will be infertile when they grow up.

The Clinic recommends that men with non-obstructive azoospermia or with fewer than 5 million sperm per ml in their ejaculate should consider having a blood test to screen for Y microdeletions. The test is not publicly funded in New Zealand.

**Semen analysis**
A semen analysis measures the volume of the semen, the number of sperm, and the proportion that are moving, known as motility. Motility is further divided into rapid, slow and non-progressive movement. We recommend 1-2 days abstinence before a diagnostic semen analysis and for treatment. The longer the period of abstinence, the more damage sperm accumulate from aging.

Masturbation is the best way to collect semen for a semen analysis, since it is more likely that all of the sample will be collected, especially the sperm-rich first portion.

A semen analysis is not a definitive test, and the ‘normal range’ is very wide.

In addition, sperm number and quality can vary considerably between one sample and the next. Changes in sperm concentration of up to 50% (for instance from 20 million/ml to 30 million/ml the next time) and in motility of 15% (for instance from 30% motility to 45% the next time) are common. Hence, two or three semen analyses, usually one month apart, are often requested to get a representative picture.

<table>
<thead>
<tr>
<th>WHO ‘normal range’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Semen volume</td>
</tr>
<tr>
<td>Sperm concentration</td>
</tr>
<tr>
<td>Proportion of sperm motile</td>
</tr>
<tr>
<td>Proportion with rapid plus slow motility</td>
</tr>
<tr>
<td>Proportion of sperm with a normal shape, using strict criteria</td>
</tr>
</tbody>
</table>

**Sperm morphology**
The shape of sperm is also important, but very few have the ‘ideal’ shape using strict criteria. We only suggest measuring strict morphology if it is needed to help decide what treatment to offer.

**Sperm antibodies**
Antibodies to sperm can reduce or stop sperm fertilising an egg, and can reduce sperm movement in the woman’s cervical mucus. We use a screening test called the ‘SpermMar’ test in which sperm with antibodies bind to tiny plastic beads. More than 40% binding is generally considered significant, although lower levels may be important after vasectomy or vasectomy reversal.

**DNA fragmentation**
Sperm differ from most cells in the body because they do not have an efficient DNA repair mechanism, and because every part of their DNA will be needed if they fertilise an egg. There are several tests for DNA fragmentation in sperm – Fertility Associates offers the “Sperm Chromatin Structure Assay” (SCSA) test, which uses computer flow cytometry to measure DNA damage in individual sperm. The test measures thousands of sperm at once so tends to be more accurate than other tests.
Male infertility & semen tests continued…

However, like most fertility tests, a sperm DNA test does not give a black and white answer. The higher the test result, the more sperm DNA damage, and the more likely that the damage may affect your chance of pregnancy. We divide the results into green, orange and red zones in the graph to indicate the likely impact of your SCSA test result.

IVF
While IVF is a treatment, the outcome can sometimes be diagnostic. For instance low or no fertilisation in IVF can sometimes indicate a functional problem with sperm.

Treatments for male infertility
It is rare for the sperm problem to be due to a deficiency of the hormone FSH, but if it is then, drug treatment over several months usually induces enough sperm for pregnancy to occur naturally or for the sperm to be used in fertility treatment.

Sometimes an obstruction of the epididymis giving rise to no sperm in the ejaculate (azoospermia) can be corrected by micro surgery but now most people choose sperm retrieval and IVF/ICSI because it is more successful. If the obstruction is due to vasectomy, a micro-surgical vasectomy reversal is often the best approach but there are many factors to consider and it is best to discuss all issues with a fertility expert first.

Men with non-obstructive azoospermia often have areas in their tubules which produce enough sperm to be harvested by Surgical Sperm Retrieval (SSR) for use in IVF with ICSI.

Some men suffer from retrograde ejaculation of semen into the bladder. The concentration and acidity of the urine can usually be sufficiently controlled by bicarbonate tablets and careful fluid intake to allow sperm to be recovered from the urine, which can then be used for artificial insemination or IVF.

There is increasing evidence that sperm may be damaged by reactive oxygen molecules that cause DNA fragmentation of the sperm. A possible approach is increasing the amount of antioxidants in the diet, and/or taking antioxidant supplements such as Menevit.

Varicoceles are essentially varicose veins within the blood vessels carrying blood away from the testis, and are more common in infertile men (30-40%) than in fertile men (10-15%). In men with impaired semen analysis repair of a varicocele may result in the production of better quality sperm.

Unfortunately at least 75% of male infertility cannot be corrected. In this case, it is a matter of making the best use of the sperm available by choosing an appropriate reproductive technology such as intrauterine insemination, IVF or ICSI.

Lifestyle changes
There is interest in whether antioxidants such as vitamin C, vitamin E, folic acid and zinc can help improve sperm quality, with strongest evidence for antioxidants.

Smoking, heavy use of alcohol and being overweight can reduce fertility. Many infertile men seem to have higher testicular temperatures than fertile men, and while activities which increase testicular temperature further may be unhelpful (eg. hot saunas), there is little evidence to show that actively reducing testicular temperature improves sperm quality.

Because most couples have some chance of becoming pregnant over long periods of time without treatment, you should be very cautious about attributing cause and effect to changes that coincide with people becoming pregnant.