

# The interpretation of a semen analysis

*A semen analysis is still a cornerstone laboratory evaluation.*

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Infertility is diagnosed in about 15% of couples who, after one year of regular, unprotected intercourse, still have not conceived. A male factor for infertility is diagnosed when an abnormal semen analysis is found. Male factor infertility is solely responsible in ~20% of cases and contributory in ~30 - 40%. Therefore, in at least 50% of cases a male factor for infertility contributes to failure to conceive. A semen analysis is still a cornerstone laboratory evaluation and contributes to defining the severity of a possible single or contributing male factor to a couple's infertility.<sup>1</sup>

The standard work-up of the infertile couple is similar to the basic approach to any medical condition – taking a full medical and reproductive history, performing a physical examination with emphasis on the genitalia, and requesting special investigations, including a semen analysis. There are no short-cuts in the work-up of the male partner of an infertile couple – one cannot reliably interpret a semen analysis without being familiar with the details of the male patient's history and clinical examination. The laboratory must comply with international standards and techniques (e.g. WHO semen analysis guidelines) and should participate in an international quality assurance programme. Unless these prerequisites are met, the reader of the report may have useless information and the patient's money would have been wasted, as most medical aid schemes do not cover expenses for infertility tests. Likewise, anybody who feels unable to interpret a report with confidence should rather refer the patient to a dedicated clinic dealing with male infertility. After a spinal cord injury an individual may not only have neurogenic anejaculation, but also the concomitant erectile dysfunction and impaired spermatogenesis related to thermal dysregulation of the testes, stasis of spermatozoa, and chronic genital tract infections, which may be best dealt with at such a clinic.

A semen analysis laboratory should have the following in place:

- Good laboratory practice (GLP)
- GLP refers to control systems in place in the laboratory that will ensure the consistency

and reliability of results.<sup>1</sup> More information can be found at [www.who.int/prequal/info\\_general/.../GLP/glp-handbook.pdf](http://www.who.int/prequal/info_general/.../GLP/glp-handbook.pdf).<sup>2</sup>

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- Quality control (QC)

QC of a semen analysis requires precision of techniques to be determined by estimates of intra- and inter-technician variability of seminal parameters (e.g. concentration, motility, vitality and morphology) at regular intervals (internal QC programme). Participation in an external quality assurance (QA) programme is essential and allows for the evaluation of the analytical performance of the laboratory compared with the results of other laboratories (i.e. accuracy is tested).<sup>1</sup> For example, the Andrology Laboratory at Steve Biko Academic Hospital (SBAH) is a member of the European Society of Human Reproduction and Embryology (ESHRE)'s international QA programme. The laboratory is one of a number of international reference laboratories, and the only one in Africa where all four of the parameters are measured.

## Standard instructions for semen collection

Semen is collected after a standardised period of abstinence, usually 3 days (2 - 4 days), and the period must be indicated on the laboratory report. The time of collection

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and when the semen was liquefied must be reported, as a delay of longer than an hour may adversely affect sperm motility.<sup>3</sup> The standardisation is essential to minimise fluctuations in semen quality, especially sperm count and sperm motility, due to short/long abstinence. Instructions to the patient must be concise – he has to abstain from any form of sexual activity for the requested period.

Samples are collected through masturbation or, in selected cases, a non-spermicidal condom may be used with assistance from the spouse. No lubricants such as soap or K-Y jelly should be allowed, as these impair motility. The sample should be collected into a wide-mouthed, non-spermicidal plastic container in a special private room. The bottles must be clearly marked for identification. While some laboratories may allow home collection, the transport conditions and delay to the laboratory may adversely affect semen quality and contribute to artefacts. Furthermore, if the complete ejaculate was not collected during ejaculation, a sticker is available to indicate this to the technologist. As patients may bring a specimen from home rather than providing one at the laboratory, the technologist should check the paper bin for discarded empty containers.

**There are no short-cuts in the work-up of the male partner of an infertile couple – one cannot reliably interpret a semen analysis without being familiar with the details of the male patient's history and clinical examination.**

The following parameters are considered to be the minimum necessary for the interpretation of a semen analysis. Please note that for a diagnosis the physician needs at least 2 - 3 ejaculates assessed over at least 2 - 3 months, evaluated within one hour of collection.

### Artefactual causes of abnormal semen parameters

Always first exclude the following artificial causes of abnormal parameters (i.e. a high index of suspicion!):

- Home collection – a liquefied ejaculate, with no 'fog' on the inside of the container, should raise this possibility. It may be accompanied by poor sperm motility.
- Incomplete collection of ejaculate – low volume, low pH, normal numbers but poor motility = only first part of ejaculate. Watery appearance, high pH, low count = only second part.
- Incorrect abstinence – <2 days = low volume, count, ?impaired motility; >5 days = high volume, higher count, poor motility.
- Impaired motility – use of a lubricant, especially if string-like material with agglutinates of sperm is observed under the microscope.

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#### pH and volume

The physical examination of the ejaculate includes measuring of the semen volume, assessment of viscosity, general visual appearance and odour. A small volume is from the bulbourethral glands, epididymides and prostate (first part) and the major volume contribution is from the seminal vesicles (second part). Precise measurement of volume is essential to calculate the total number of spermatozoa and non-sperm cells in the ejaculate. Low volume is associated with ejaculatory duct obstruction, congenital bilateral absence of the vas deferens (CBAVD), retrograde ejaculation or androgen deficiency. An ejaculate volume of >6 ml occurs in cases of male accessory gland infection.<sup>3</sup>

pH is measured with pH paper (range 6 - 8) and should be between 7.2 and 8.0.<sup>4</sup> A very low pH indicates acidic prostatic fluid ejaculate, such as in cases of CBAVD.

#### Count

Sperm concentration refers to sperm numbers/ml and total sperm number refers

to the total number of sperm in the entire ejaculate (volume x sperm count/ml).<sup>3</sup> Sperm count of <20 million/ml (oligozoospermia) could be due to incomplete sample collection, varying abstinence time and many other external factors, e.g. fever, drugs or occupational exposure.<sup>1</sup> If no spermatozoa are observed (azoospermia), the sediment of the centrifuged sample may still contain sperm (cryptozoospermia).<sup>3</sup> Both may be secondary to testicular failure or obstruction inside the testis, epididymis, vas deferens or ejaculatory duct.

#### Motility

The proportion of rapid progressive sperm at 37°C is an important functional property of sperm in relation to fertility and fertilisation success.<sup>1</sup> The chances of pregnancy are increased with high sperm motility and a low number of immotile sperm.<sup>3,5</sup> Decreased motility may be a result of collection problems, abstinence, temperature and time of assessment (within 1 hour of collection). It may also be because of infection, with inflammation of the male accessory glands, antisperm antibodies and men with ciliary dyskinesia (immotile cilia syndrome or Kartagener's syndrome).<sup>1</sup>

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### Vitality (supravital)

Supravital staining differentiates between live and dead sperm and is assessed when sperm motility is <50%. A large proportion of vital, but immotile, sperm may indicate structural defects in the sperm tail,<sup>6</sup> or Kartagener's syndrome. A high percentage of immotile, non-viable (dead) sperm may indicate epididymal pathology.<sup>3</sup> Anti-sperm antibodies could also be present if the immotile sperm are dead.<sup>1</sup>

### Morphology

Pleomorphic human sperm is well known and the assessment of sperm morphology may be subject to observer bias, especially if the technologist is not well trained. Careful and consistent training within a QC programme will allow for accurate and reliable morphological assessments. For the morphological evaluation of sperm, the whole sperm should be considered. The assessment relates to four regions of the sperm, i.e. head, neck/midpiece, tail defects and cytoplasmic droplets. Defective spermatogenesis and some epididymal pathologies are associated with an increase in abnormal sperm. Depending on the type of abnormality, sperm usually have lower

fertilising potential and may also have abnormal DNA.<sup>5</sup>

### Antisperm antibodies (mixed agglutination reaction)

For the mixed agglutination reaction (MAR) test to be considered clinically significant, at least 50% of the motile spermatozoa need to be coated with antibodies.<sup>6</sup> Sperm stimulates an immune response when exposed to the systemic immune defence system, such as testicular trauma, post-vasectomy, or inflammatory reactions in the male or female genital tract. Antisperm antibodies are almost exclusively IgG and IgA, with the latter clinically more important.<sup>3</sup> Depending on the nature and location of the sperm antigen and the levels of antibodies different effects may be seen, as agglutination of sperm with impaired motility and cytotoxicity with low viability are all effects that may adversely affect sperm quality.

**No lubricants such as soap or K-Y jelly should be allowed, as these impair motility.**

### Other markers

The secretion of zinc by the prostate is androgen dependent and a level of <2.4 µmol/ejaculate indicates a low contribution of the fluid to the ejaculate, incomplete collection of the ejaculate, prostatic inflammation or androgen insufficiency.<sup>1</sup>

Fructose is also an androgen-dependent secretion emanating mainly from the seminal vesicles, with a small contribution from the epithelial cell of the secretory epithelium in the ampulla of the vas deferens. Seminal fructose is used as a marker of the seminal vesicles and <13.0 µmol/ejaculate

is abnormal. This is seen in hypogonadal men after a short abstinence time and where ejaculation or emission of fluid is impaired, such as in neuromuscular diseases, after surgery, in cases of drug use, and in obstruction in the ejaculatory ducts, or with inflammation in the vesicles or prostate that may hinder emission.

Seminal plasma contains a neutral alpha-glucosidase-isoenzyme that originates from the epididymis and is an indicator of the amount of excretion from the cauda epididymis emitted at ejaculation. Values below 20 mU/ejaculate show disturbed emission of fluid through the wolffian ducts, which may be caused by obstructions or neuromuscular impairment.<sup>1</sup>

### Conclusion

Adverse trends in male reproductive health have become evident over the past 50 years, of which declining semen quality is one. Andersson *et al.* suggested that 'we may have reached a crucial "tipping point" where the subsequent subfertility may affect populations.<sup>7</sup> It therefore remains crucial that the interpretation should contribute to defining the male factor of infertility.

References available at [www.cmej.org.za](http://www.cmej.org.za)

## IN A NUTSHELL

- Infertility seems to be on the increase.
- A male factor may be partially or solely responsible in at least 50% of couples.
- Stick to the rule of medicine, i.e. history, examination, special investigations.
- Give detailed instructions for semen collection.
- The laboratory must comply with good laboratory practice and quality control with international bodies.
- Always first exclude artefactual causes of abnormal semen parameters.