

MALE INFERTILITY: SEMEN ANALYSIS

FACT #1 THE SEMEN ANALYSIS MUST BE EVALUATED IN CONTEXT

*Information
for Patients*

The semen analysis (SA) is a critical part of the overall male assessment. Some background on interpretation:

1. SA cannot differentiate fertile from infertile couples with one exception – no sperm = sterile. Some men with results ‘in reference range’ can be infertile and some men with results ‘out of range’ are capable of having children.
2. The WHO reference ranges are descriptive of men who fathered children. Importantly, men *below* the *lower end* of the reference range had proven paternity.
3. SA parameters do not follow a bell-shaped (normal) distribution – therefore the concepts of ‘average’ or ‘normal’ do not apply (even though they can be calculated).
4. Very large variances in SA results between tests are expected and completely normal.
5. SA is a ‘bulk’ (i.e. crude) measure– but only *one* sperm ultimately fertilizes the egg.
6. Sperm is the ‘vehicle’ for the genetic information DNA. SA does not evaluate DNA.
7. Sperm concentration is the only important parameter (with few exceptions).

Evolution of World Health Organization (WHO) Semen Reference Range

YEAR/PARAMETER	1980	1987	1992	1999	2010 (5 th ed)			
Volume (mL)	–	≥2	≥2	≥2	≥1.5			
CONCENTRATION (million/mL)	20-200	≥20	≥20	≥20	≥15			
Motility (%)	–	≥40	≥40	≥40	≥39			
Morphology (%)	80.5	≥50	≥30	≥15*	≥4*			

* Strict (Tygerberg/Kruger) Criteria.

FACT #2 SPERM CONCENTRATION = MOST IMPORTANT PARAMETER

CONCENTRATION: the number of sperm in a given volume

Concentration is the single best indicator in the semen analysis of your chances of conception. In fact, the correlation is such that the other parameters can (*almost* always) be ignored. More sperm are better to a point – greater than about 50 million sperm per mL saturates female reproductive tract such that higher counts do not seem to result in a higher pregnancy rate.

General Guidance:

Concentration	Comment	Recommendation
≥ 50	More sperm does not make any improve pregnancy rate	Ongoing attempts at natural conception reasonable; consider ART ^
15-50	Small but measurably lower chance of conception	As above^
<15	Large clinically important reduction chances of natural. NO sperm is a special circumstance have no chance of <i>natural</i> conception*	Strongly consider ART. Concentrations less than about 5 million/mL requires specialized assessment.

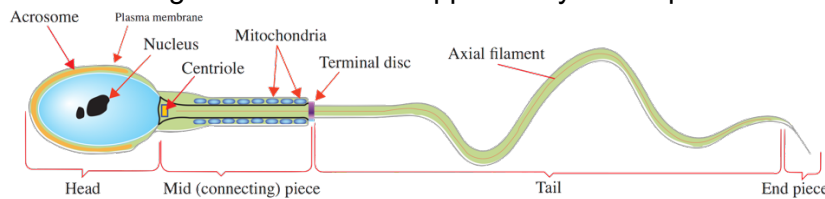
^ Assisted Reproduction (ART) should be considered: e.g. female age, prolonged failure to conceive (2-3 years), other male factor, personal preference; * Surgical retrieval plus IVF may be an option

VOLUME: Minimal to no importance unless very low – less than about 1 mL. Reasons for low volume: failure to abstain from ejaculation for at least 4 days, problems with collection (e.g. spilled, awkward or unnatural), problems with getting it out of the collection cup.

MOTILITY: Minimal to no importance unless zero motility or inflammatory cells (WBC).

MORPHOLOGY: outward appearance or form – ‘looks’ or ‘beauty’

‘Good looking sperm’ – what does this mean? The currently adopted criteria for sperm ‘beauty’ were developed by Dr. Kruger – he worked at Tygerberg Hospital in South Africa hence ‘Kruger’, ‘Tygerberg’, or ‘Strict’ criteria. Shape and proportions for sperm were specified. He noted that couples undergoing intrauterine insemination seemed more likely to have success when more of the sperm fit his criteria. Importantly, he was not looking at conception by intercourse and his findings have not been supported by subsequent studies.



The World Health Organization adopted the Strict criteria in 1999 for the 4th edition of the Semen Analysis Reference Ranges. “Low morphology” (aka teratospermia) is a common reason for consultation and a major source of anxiety for men and their partners. When it is the only parameter ‘out of range’ this is called **isolated teratospermia**. Common reactions include: “All my sperm are abnormal!”, “Is my baby is going to look abnormal?” and “That’s why we can’t get pregnant”. As a result, patients are often very skeptical when they are told:

FACT #3: THE MORPHOLOGY OF SPERM IS NON-INFORMATIVE

‘Sperm shape is a puzzling parameter, as the semen of a typical *fertile* male is composed in large part of funny looking sperm [according to Dr. Kruger]. For the last 3 decades the trend in assessing sperm has been to become even stricter in calling its shape normal in an elusive quest to link the reproductive potential of a man to his best looking swimmers. Yet ... the stricter a technician is in calling sperm shape normal, the worse the predictive value of the test. It is a counterintuitive finding that calls into question the usefulness of sperm morphology in the first place.” Dr. Niederberger 2011 (Infertility expert for the Journal of Urology). A large body of literature and expert consensus supports Dr. Neiderberger’s view – that **sperm morphology doesn’t matter** (see references below for a few).

It bears emphasizing again that morphology can be disregarded as an indicator of chances of becoming pregnant, carrying a pregnancy to term, how your children will look and what their genetic endowment will be. Furthermore, using ‘better looking sperm’ does not seem to predict success with intrauterine insemination (IUI) or in-vitro fertilization (IVF) (references 2 and 3). It is entirely possible that most if not all of us were conceived from ‘wonky’ looking sperm. It should come as no surprise that you can’t judge a book by its cover.

References for Semen Analysis & Teratospermia

1. General references: Nallella et al, Fertil Steril 85:629-34, 2006 AND Grober E, Crain D et al 2007 AUA Abstract #93804 AND Morbeck D, Leonard A et al Fertil Steril 2011; 96: 1350-1354
2. Morphology and IUI: Hotaling J, Smith J et al 2010 AUA Abstract #1920 AND Borges E, et al 2011 AUA Abstract #2275
3. Morphology and IVF: Keegan B, Barton S Fertil Steril 2007; 88: 1583-1588 AND Dayal M, Gindoff P Fertil Steril 2010; 93: 666-668

Appendix Morphology: The evidence for lack of correlation with conception.

Figures 1 and 2: Effect of Sperm Morphology on Pregnancy Success via Intrauterine Insemination: A Systematic Review and Meta-Analysis. Kohn et al. J Urology 2017 199:812-822

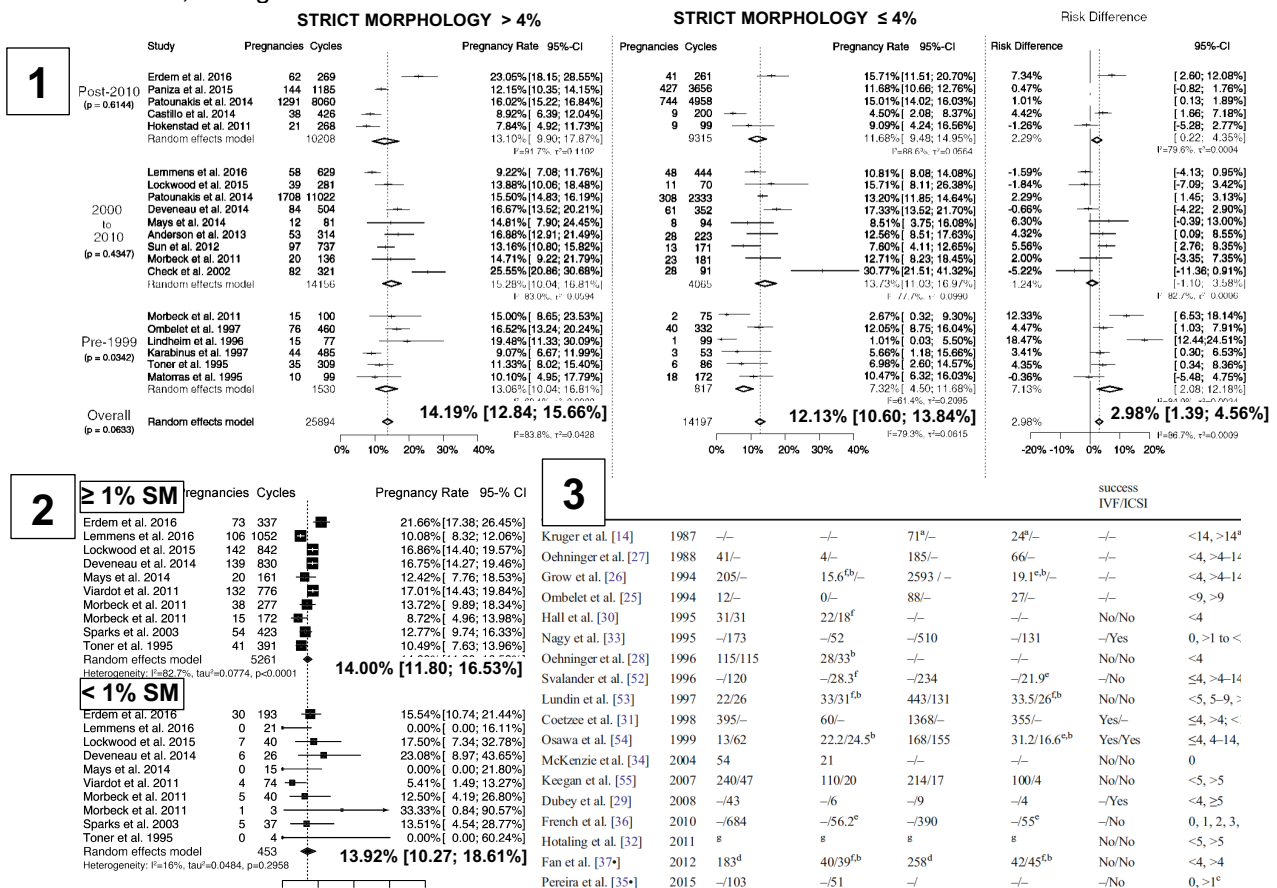
Notes to Reader:

- This report reviewed all of the methodologically sound studies on the effect of sperm morphology on success with intrauterine insemination (IUI). IUI is not far removed from conception with intercourse and the comparative data for the effect of morphology on conception with intercourse is similar (not shown).
- This presentation is called a 'Forest plot' (google if you want more info).
 - There are 3 columns (>4%, ≤4% and Risk difference).
 - In each column, the Individual studies are listed on the left and grouped by date of publication.
 - The size of the squares in (2) are proportional to the number of patients. The horizontal lines provide a 95% 'confidence interval' – if this line overlaps the vertical line that indicates the average, it means the study does *not* show a difference from the average of all the studies.
- The final row labelled "Overall" specifies the per cycle chance of conception per cycle of IUI.
 - Note that for Morphology >4%, this is 14.19% and for morphology ≤4% this is 12.13%. The absolute difference in in conception when morphology is used as a measure of fertility is 1.39%
- The second table looks at those studies in which morphology could be ascertained to be ≥1% normal or <1% (that is, 0% normal morphology). You can see that the per cycle pregnancy rate is no worse with 0% normal.
- The summary statement from this study is that morphology does not predict success of pregnancy with insemination.**

Figure 3: Role of Abnormal Sperm Morphology in Predicting Pregnancy Outcomes. Curr Urol Rep 2016 17: 67. Similar data as Figures 1 and 2 but in evaluated the relationship when **IVF (+/- ICSI)** were used

- One can see that the majority of studies show 'No' correlation between morphology (using various 'cut points' as criteria: <14% vs. ≥14%, <4% vs. >4%, etc.).

Not shown: Men with a complete absence of normal sperm morphology exhibit high rates of success without assisted reproduction. Asian Journal of Andology 2017 19; 39-42. This did not demonstrate any relationship between morphology and **natural conception (intercourse)**. The failure to conceive was, however, strongly associated with low sperm concentration.



This information is not intended to be used as a substitute for professional medical advice, diagnosis, or treatment. You should not rely entirely on this information for your health care needs. Ask your own doctor or health care provider any specific medical questions that you have.