Is quality assurance in semen analysis still really necessary? A clinician’s viewpoint

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Quality assurance in semen analysis is now a standard procedure in most andrology laboratories. This communication is now questioning its value in any clinical situation and as a consequence asks whether the effort and the expense of such a process is really worthwhile. It concludes that semen analysis needs only to be performed competently without the need for costly and time-consuming forms of quality assurance.

Key words: quality assurance/semen analysis

Introduction

Over the last 25 years, considerable effort has been expended in quality assurance in relation to the analysis of semen. Today it would appear that semen analysis is for the most part carried out satisfactorily all over the world. It would therefore seem that the energy expended in running quality assurance schemes in relation to semen analysis might now be a waste of time. As I was one of the first people to suggest the need for such schemes, it might now be pertinent that I at least put the case for its review.

The first person to suggest that semen analysis should be a routine investigation in the evaluation of every case of infertility was Edward Martin (1902; cited by Jequier, 1991). Martin also demonstrated that there were two major causes of azoospermia and he was also the first to recognize the polymorphism of human sperm.

John MacLeod then elevated semen analysis from being a simple observation into a science. He recognized that not only sperm numbers but sperm motility and morphology were also important in the evaluation of the potential fertility of semen (MacLeod, 1956). He even tried to associate certain sperm shapes with specific clinical entities such as varicocele (MacLeod, 1965).

However, many clinicians and laboratory personnel did not follow MacLeod’s lead in relation to semen analysis. In or around 1980, it became clear, in Britain at least, that many laboratories were not even attempting to examine a number of variables within a semen sample that were important in the determination of fertility. Often only an estimation of the sperm concentration was being performed and no assessment of either motility or morphology was made by a number of pathology laboratories. Thus what information that could be obtained from the examination of semen was not being sought.

In response to this problem, the newly formed British Andrology Society then organized a number of courses for medical laboratory scientists to which clinicians were also welcome. These courses taught the participants the correct ways in which to examine sperm numbers, sperm motility as well as sperm morphology (Jequier and Ukombe, 1983). Many aspects of sperm function and its assessment were also demonstrated. These workshops proved to be very popular and to this day continue to be well attended.

By the early 1980s, however, Mortimer and colleagues were anxious to further advance the understanding of the inter-relationships between the different variables in a semen analysis (Mortimer et al., 1982) and also introduced the concept of quality assurance in relation to the analysis of semen (Mortimer et al., 1986). It is now very clear that careful training in semen analysis, such as that set up by the ESHRE Andrology Special Interest Group that includes both theoretical as well as practical training in semen analysis, is very effective in raising the skills of laboratory personnel in relation to semen analysis (Bjorndahl et al., 2002).

Superimposed upon this training system are quality assurance programmes that assist in the maintenance of skills in relation to semen analysis. These schemes allow for the exchange of samples between laboratories and for the use of videos so that medical laboratory scientists can test their skills in carrying out sperm counts and assessing sperm motility. Stained slides of semen can also be exchanged in order to monitor accuracy in the assessment of sperm morphology.

Today, the question that must be asked is whether this very accurate and highly reproducible assessment of any of the variables in a semen analysis is still relevant to the determination of the potential fertility of a sample of semen—at least from the clinical point of view—or whether such an activity is a waste of time and/or a waste of money.
It is thus now time to consider the use of quality assurance in semen analysis and discuss whether or not it is of any value in the clinical management of infertility.

**Of how much value is a semen analysis in the determination of fertility?**

What the clinician needs for the correct management of infertility in the male is a diagnosis. Infertility is not a diagnosis: it is only a symptom. The analysis of semen only occasionally gives the clinician a diagnosis, as for the most part, the changes that take place in semen are largely non-specific. However, in conditions such as globozoospermia, only a semen analysis can provide a diagnosis but this situation is not common. Thus at best a semen analysis can usually only be a measure of the severity of a condition and will only rarely indicate the pathology that is causing that infertility. As infertility has no other presenting symptom, the main value of a semen analysis is in the identification of the infertility, i.e. it is simply a screening test for infertility in the male.

There are other reasons why a semen analysis is only of limited value in the determination of infertility. Over time it has become clear that the relationship between infertility and sperm numbers, sperm movement and sperm morphology is not a simple one. Low sperm counts may be found among previously fertile men seeking vasectomy for fertility control (Rehan et al., 1975) and pregnancy is known to occur, sometimes with uncanny ease, among men with both very low sperm counts and poor sperm motility (Thomson et al., 1993).

Although the higher the sperm count, the better the pregnancy rate, nevertheless it is thus clear that, apart from the presence of azoospermia, a semen analysis alone is not a very good predictor of either fertility or of infertility: indeed only when the sperm counts are at the extremes can the sperm count predict the occurrence of conceptions or their absence with any accuracy.

Sperm numbers can rise and fall sharply among otherwise fertile men. At times, sperm numbers may fall by orders of magnitude for a variety of reasons, many of which cannot be identified. Laboratory scientists often fail to appreciate that this situation can occur quite commonly among men attending an infertility clinic: frequently such patients appear in the clinic with a low sperm count that over a period of time reverts to normal. Without a careful history and clinical examination, such changes may be mistaken for male infertility where in fact none exists.

When such differences in sperm concentration between samples from a single individual do occur, is it necessary to achieve such accuracy in the estimation of any sperm concentration? Does it matter whether a sperm count is reported as 1, 2 or $3 \times 10^6$ or even another sample is reported as 50, 75 or $100 \times 10^6$? It will certainly make little difference clinically. Thus if the ‘accuracy’ of a sperm count does little to enhance the clinician’s understanding of its fertility potential, why is it necessary to undertake these time-consuming and relatively costly methods of quality assurance such as those suggested by organizations that include the Andrology Special Interest Group from ESHRE?

It has been known for a long time that reproductive pathology in the female partner reduces the potential fertility of a male with a ‘normal’ sperm count (Arumugam, 1993) while a high sperm count such as that achieved using donated sperm can overcome female problems that could otherwise result in childlessness (Hammond et al., 1986). Thus the male–female interaction in infertility is immensely important to the outcome in relation to pregnancy, and this interaction relationship cannot in any way be incorporated into a semen analysis. Indeed each degree of impairment in male fertility can only be assessed when paired with that of the female (Cooke et al., 1981). If conception can thus be determined not just by the sperm count but by the presence or absence of female problems such as endometriosis or anovulation, how can a very accurate and highly reproducible sperm count either determine the occurrence of conception or influence clinical decision-making?

Time is a very important factor in relation to pregnancy. It is an area about which insufficient attention is often paid and is of course a variable that is difficult to include in any form of quality assurance. However, it is clear that the length of infertility relates inversely to the chances of spontaneous conception (Cooke et al., 1981) and this of course is likely to apply to the duration of an abnormal semen analysis. However, there is no way in which we can apply quality assurance to the ‘trying time’ to pregnancy.

It must also be remembered that semen is not a homogeneous fluid. Mixing of the components that make up semen does not occur until after ejaculation and, in the natural situation, the leading sperm in the ejaculate may enter the cervical mucus and may make little or no contact with the rest of the seminal fluid (Bjorndahl and Kvist, 2003). Thus what we see in a semen pot even a few minutes after ejaculation may not be representative of the sperm that enter the female genital tract. As Björndahl and Kvist also point out, the semen that we examine in the semen pot has also been in contact with light, with high oxygen concentrations and probably many other factors that may compromise sperm function, making assessment of the fertility potential of that sample difficult.

As Eliasson (1971) indicated, the chance of conception and implantation relate to a number of factors that give rise, not to a certainty of either fertility or infertility, but only to a probability of firstly conception and then of implantation and embryo development. Thus semen analysis will not tell you whether or not a couple will achieve a pregnancy: it can only give you a probability of that result—and a very approximate probability at that.

**The fate of the sperm in the female genital tract**

The literature in relation to the fate of the sperm once they enter the female genital tract in the human is very sparse. However, it is clear that of the total number of sperm that enter this tract in a conception cycle, all but one are lost. This phenomenon makes the value of quality assurance in
relation to a complete ejaculate somewhat difficult to understand.

If one examines the fate of the sperm in a human ejaculate and the passage of the sperm through the female genital tract, it becomes clear that the probability of a sperm coming in contact with the oocyte is fairly low. Firstly most of the sperm in an ejaculate remain in the vagina and, at mid-cycle, many of the sperm left behind in this way are rapidly killed by the low pH of the vaginal secretions at the time of ovulation. Those sperm that are going to enter the mucus appear to do so within 15–20 min (Perloff and Steinberger, 1963).

There is little evidence that increased sperm numbers in the ejaculate have much influence on the numbers of sperm entering the cervical mucus (Tredway, 1975). As sperm can be found in the cervical mucus in <2 min after ejaculation, it is likely that these sperm are those that have not been trapped by coagulation. Thus the sperm that do enter the cervical mucus may be there for no other reason than their position in the ejaculate.

Recolonization of the cervical mucus after liquefaction of the ejaculate in the human is thought to be minimal (Tredway, 1975). It has been estimated by Bedford (1971) that, at least in the rabbit, the ejaculate is no longer necessary for fertility 5 min post coitum although this may be longer in the human (Fordney-Settlage, 1981).

Many of the sperm also drain out of the vagina after coitus in the phenomenon also known as ‘flowback’. What percentage of the ejaculate enters the cervical mucus is unclear but it is probably small. Of those sperm entering the cervical mucus, a proportion may become eliminated by their passage into the folds of the cervical epithelium and by their entry into the cervical glands (Kenemans and Hafez, 1984). Many sperm also loose or change their motility on entering the cervical mucus (Katz et al., 1982). There is thus little evidence for a ‘cervical reservoir’ of sperm, at least in the human (Tredway, 1975).

The numbers of sperm that traverse the uterine cavity in the human and reach the utero-tubal junctions in the human is unknown but probably only a few thousand sperm enter each Fallopian tube (Mortimer and Templeton, 1982). Those sperm that do succeed in entering the Fallopian tubes will therefore only make up a very small percentage of the total numbers seen in the whole ejaculate or more importantly in a semen sample pot.

Due to the relatively vast surface area of the heaped-up epithelium of the Fallopian tubes (certainly vast in relation to the size of a spermatozoon), only a relatively small number of sperm will be able to access the oocyte. Not only must the sperm traverse the corona but they must also be able to exhibit hyperactivated movement and must not have undergone the acrosome reaction until they are close to the zona pellucida. It is thus also possible that human fertilization may depend frequently upon a sperm:oocyte ratio that may be as low 1:1.

If only a few sperm are going to find themselves in contact with a freshly ovulated oocyte within the Fallopian tube, it is therefore not surprising that a semen analysis that purports to have an overview of the whole ejaculate will not be a very good indicator of fertility. Also if only a very small number of sperm from an ejaculate that initially contained many millions of sperm are going to meet up with an oocyte at mid-cycle, what is the value of an analysis of a semen sample in which the numbers of sperm will be several orders of magnitude greater than those arriving in the Fallopian tubes—even though the reproducibility of that estimation of sperm numbers is very acceptable?

Would careful testing of the ejaculate using sperm function tests be of any greater value? This would be unlikely as the question of sperm numbers is again a problem. There are also sperm that may have normal function but that fail to enter the cervical mucus, also simply due to their position in the ejaculate. Likewise sperm with all the features deemed to be acceptable for fertility may also exhibit abnormal function, and thus even if they reach the oocyte they may be unable to achieve fertilization. It would seem that sperm function tests give rise to the same problems as those that occur with routine semen analysis.

However, will the abandonment of quality assurance in semen analysis lead to a return to the poor quality investigations that we saw 20–30 years ago? I think not, as the need for semen analysis, if only by the IVF clinics, is now so huge that this investigation is no longer a one-off investigation of infertility. If a semen analysis is viewed as nothing more than a screening test, then these quality assurance schemes need not apply to semen analysis. From the clinical point of view, one needs to perform semen analysis to a reasonable standard. It is the job of the clinician and not the scientist to determine the standards needed in the performance of a semen analysis.

Although these statements concerning semen analysis may apply to the clinical scene, this does not mean that quality assurance in semen analysis is not required in other situations. Quality assurance would almost certainly be needed in research and in particular in toxicological studies. It is simply difficult to understand how the emphasis on accurate sperm counting can apply to the clinical situation.

Conclusions

There is no doubt that a semen analysis is a useful investigation in the identification as well as the evaluation of male infertility. However, only when the variables within a semen sample are at the extremes can it be used to make a reasonably accurate prognosis for subsequent fertility.

There is no suggestion in this paper that semen analysis as an investigation should be abandoned. What I am suggesting, however, that there should be far less attention paid to the semen and its analysis and far more attention paid to the patient, to his story and to his clinical examination. Only when we begin to understand the causation of his infertility can we begin to understand its pathophysiology. The obsession that so many scientists have with the semen analysis does little to facilitate any change in this attitude.

It must be remembered that few diagnoses in the whole of andrology can be made from a sample of semen and thus
a semen analysis whether accurately or inaccurately performed is diagnostically of little help to the clinician. That in a conception cycle the whole of the ejaculate except for one sperm is lost, makes it difficult for a clinician to understand why such an ‘accurate’ semen analysis is so necessary.

That careful quality control of semen analysis is needed for research, and in particular toxicological research, is undeniable. However, the argument that without quality control the analysis of semen would revert to the standards of the past is not impressive, as the identification of the infertile male is still very important in clinical andrology.

That so much emphasis is placed on the very accurate estimation of the variables that need to be examined during the course of a semen analysis in relation to clinical andrology must be reconsidered. That money is spent on carrying out quality assurance schemes (the cost of which will frequently be passed on to the patient) in order to achieve such a relatively poor discriminant of potential fertility should be reviewed.

References


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