# ESHRE 2020 Virtual (5-8 July 2020)

# Questions for the speakers

# PCC01: Andrology: Diagnostics & therapy for 2030 and beyond

## Why sperm EQA is essential? - Jose Antonio Castilla (Spain)

**Q: Is one problem that EQA schemes need EQA to each other, shouldn't there be a single world scheme when we all judge the results the same?**

A: Jose Antonio Castilla. The first thing for an EQAP to fulfill its function is that it has enough participants, and for this, accessibility to the organizers before and after the shipments is important. Ongoing attention to participants is key to ensuring that they receive the materials to be analyzed and they interpret adequately the reports. That is why most of the EQAP in clinical laboratories are organized by National Scientific Societies which are in permanent contact with the participating laboratories.

Like any laboratory activity, the organizers of an EQAP must be rigorous in their procedures. For this they can follow the recommendations of ISO 17043: 2010. Conformity assessment - General requirements for proficiency testing. ISO / CASCO - Committee on conformity assessment. 2010; and ISO 13528: 2015. Statistical methods for use in proficiency testing by interlaboratory comparison. ISO TC 69. 2015; or the WHO 2010 semen analysis manual in relation to EQAP.

If there were only one worldwide EQAP for semen analysis, I believe that logistics would be very difficult and maintaining close contact (feedback) with all participating laboratories would be impossible.

**Q: Do you think we should measure rapid sperm? Or are you saying it is too difficult?**

A: Jose Antonio Castilla: Yes, of course. As Björndahl wrote 10 years ago, this parameter has a huge clinical utility.

But for it to be clinically useful, its determination must be made with precision and accuracy. The EQAP results that I have shown show that this determination is not performed well in many laboratories. That it is difficult to achieve this objective should not mean that it is not done. What we have to do is train to do it correctly. Several authors (Barratt et al., 2011; Sanchez et al., 2018) have shown that after taking training courses, variability between participants is reduced and accuracy is improved.

If it is useful, do it but reliably.

Björndahl L. The usefulness and significance of assessing rapidly progressive spermatozoa. *Asian J Androl*. 2010;12(1):33-35. doi:10.1038/aja.2008.50

Barratt CL, Björndahl L, Menkveld R, Mortimer D. ESHRE special interest group for andrology basic semen analysis course: a continued focus on accuracy, quality, efficiency and clinical relevance. *Hum Reprod*. 2011;26(12):3207-3212. doi:10.1093/humrep/der312

Sanchez A.M., Natali I., Costantino A., Pena-Cotarelo R., Terribile M., Rubino P., Castilla J.A., de Mendoza M.V.H. The impact of ESHRE basic semen analysis course: 6 years of Italian experience. Current Trends in Clinical Embryology 2018;5:115-121

**Q: How to handle EQC if you use CASA? Especially motility evaluation will be a problem.**

A: Jose Antonio Castilla: As established by ISO 15189: 2012. Medical laboratories - requirements for quality and competence, any procedure must be evaluated, and for this, external and internal quality control is essential. As far as I know, there are only some external quality control programs provided by commercial houses for their own equipment, but there is no EQAP that can be applied to different CASA systems.

It will be difficult for CASA to ever reach a sufficient level of reliability until EQAP is developed. Something similar occurs with the determination of sperm DNA fragmentation.

**Q: Do you think it is beneficial to assess total motility instead of rapid motility? to shrink observation bias**

A: Jose Antonio Castilla: Yes, of course. As Björndahl wrote 10 years ago, this parameter has a huge clinical utility.

But for it to be clinically useful, its determination must be made with precision and accuracy. The EQAP results that I have shown show that this determination is not performed well in many laboratories. That it is difficult to achieve this objective should not mean that it is not done. What we have to do is train to do it correctly. Several authors (Barratt et al., 2011; Sanchez et al., 2018) have shown that after taking training courses, variability between participants is reduced and accuracy is improved.

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**Q: Does morphology EQA really need a team to start from shipped sperm sample and stain the slides and examine on their own microscope? I worry that online pictures do not look similar to what we see when we stain.**

A: I totally agree. Material from an EQAP should be analyzed using the same procedures used for patient samples. The example you give is correct, evaluating downloaded images is not very similar to the procedure of staining a sample and evaluating that slide later.

Something similar occurs when the laboratories that use Makler for the concentration with live sperm, analyze the fixed sperm they receive from the EQAP organizers. They will probably get good results in EQAP, but it does not mean that when they do it with live sperm in their patient samples, they do it reliably.

We recommend sending stained and unstained slides as sperm morphology EQAP material.

For all of the above, we recommend that the evaluation of sperm motility be performed routinely on a video screen and not directly on the microscope, since we will perform external quality control with downloaded video and analyze it on screens. In this way, the procedure for analyzing patient samples and EQAP material is the same.

**Q: Can computer assisted semen analysis replace WHO manual method?**

A: When the results obtained by means of the WHO2010 manual method and those obtained by CASA have been compared, differences have been observed that probably do not have any clinical importance in a wide range of values. However, in extreme values (for example in concentration <1 million / mL and greater than 150 million / mL) the differences can be clinically significant, especially in very low concentration values.

Learning to use a CASA is not easy and requires training, in addition to carrying out internal and external quality controls. And we have already mentioned the problem of external quality controls for CASA.

In my opinion, CASA can help and complement the semen analysis performed according to WHO 2010 manual for mobility and concentration, even replacing it in certain samples under proper use. But I see it difficult to completely replace manual analysis due to the aforementioned limitations.

## Declining sperm quality – infertility for all? - Nicolás Garrido Puchalt (Spain)

**Q: In longitudinal studies assessing change in TMSC which confounding factors should be considered in terms of extrinsic factors (lifestyle, diet, occupational hazards etc)?Could they have influenced data in old studies?**

A: Thanks for the question, very good point. In fact, some of the metanalyses published took into account some potential confounders but given its very retrospective nature, it is very complex. Ideally, and being extremely clean, for this, any factor that has been demonstrated to have a strong influence semen quality should have been accounted for, and also a trend over the years' study on this factor could have clarified better the causes.

**Q: How would you account for the decline in the semen parameters and what would you do to reverse this trend. What are the causal factors?**

A: Thanks for this question. The study design (retrospective, observational), only provides weak references to answer this question. These were not studying about causal factors, but to confirm the trend. That said, in order to be reversed, we can only try to attack on modifiable habits or exposures related with sperm quality harm or count decrease, although evidences about the effects are scarce so far.

**Q: What was the average abstinence period for your study?**

A: Thanks for the question, the average abstinence was not estimated for this work. As reported within the paper "Male patients were instructed to maintain 2-7 days of sexual abstinence prior to sample collection" as per routine practice. I checked in our database and was around 4.5.

**Q: You showed nice data on sperm quality decline. What I missed is the connection with the increased incidence of testicular cancer and hypospadia. I think this can support the results. Can you speculate on this?**

A: Good point. Undoubtedly. It seems (I am not the specialist on that), that there is a parallel increase on both cancer and hypospadias that goes with the decrease on sperm quality. This might point to an endocrine disruption related problem (just speculating, as requested).

**Q: Does decline sperm quality mean declining natural fertility? The increase of TMSC <5 mill observed in your clinics could be due that women age in your clinic has increased. Ten years ago these men could get pregnant Younger women**

A: Thanks for the observation, this is a good point. Interestingly, it seems that the change on TMSC is bigger than the change on the average women's age through the years in our clinics, so it seems this can only explain a small percentage only.

**Q: Do you see any evidence of sperm quality is actually improving? Would decreasing smoking rates, general improvement of health in the industrialized world, declining death rates suggest better reproductive health?**

A: Thanks for this. Unfortunately, I am not able to find any report on improvements on the overall/global sperm quality so far. Probably refraining from toxic exposures, known to affect global health status and in some cases

**Q: Do you have any idea of how motility parameters are changing? Particularly, whether cells with particular flagellar beat characteristics are being lost, or if this more indiscriminate?**

A: Well, from our work and the data available, first, motility seems not to be an issue, and second, such detail is not achieved on the literature: there are not, as far as I know, papers evaluating how specific flagellar beat types have evolved through the years.

**Q: Do we have information on what is the more important environmental contribution to sperm quality - damaged already caused in fetal or pre-pubertal development, or (maybe reversible) lifestyle factors in adult men?**

A: This is a very good question, very difficult to answer. On one side, sperm cells or testicular germ cells seem very sensitive to external harm (with the potential to extend the harm to the whole individual of the next generation), but also fetal or pre-pubertal development is. Reversibility seem something that can only be achieved as an adult.

## Male urological assessment - Dolores J. Lamb (U.S.A.)

**Q: Can computer assisted semen analysis replace WHO manual method?**

A: No. The results from CASA do not correlate well with routine semen analysis results and even when are results compared between different units from the same vendor or between vendors, they are not

necessarily comparable. Analysis of poor semen samples can be problematic with over estimation of count and underestimation of motility in samples from men with oligozoospermia. The method can be useful in the research laboratory where accuracy many not be required (a result can be precise without being accurate but if comparing semen samples from a model organism before and after treatment it may not matter). In addition, there is a great deal of information provided by CASA systems regarding sperm motility parameters that are not yet clearly understood (except for hyperactivation) that may have functional information yet to be discovered. However, today in the clinical diagnostic laboratory these characteristics do not impact clinical decision making.