Editorial

Ruth Lathi a colleague once told me that she did not believe in male factor infertility in most cases. Sure, a male with azospermia or no moving sperm, or 100 thousand sperm was not conceiving due to male factor. However, she did not understand why a male with 2 ml of ejaculate containing 10 million sperm per ml, with 30 percent motility did not conceive a pregnancy with his partner over a year of regular intercourse. She believed in those cases the woman must also have a factor preventing pregnancy. At the time I thought her theory was interesting, but hard to demonstrate. About five years later, I consulted a couple who presented with infertility. They had previously conceived through in-vitro fertilization at a clinic in the Boston Massachusetts area, due to a diagnosis of male factor infertility. They desired a second child. The woman’s tests were normal. The male had semen analyses similar to the one I cited in the previous paragraph. The male had 1.3 ml of ejaculate 12 million sperm per ml, 30 percent motility and 2% strict morphology, similar to the semen analyses he had had over the last seven years. Before initiating care the couple disappeared and I thought they had returned to the clinic at which they had previously conceived. About a year later the male contacted me. He stated that he and his wife had divorced, which was why they did not return for care. In the interim he had a new girlfriend. Within two months she stated she was pregnant. They terminated the pregnancy. A couple months later he had a second girlfriend and within a few months she also was pregnant. They wondered if he could really be getting them pregnant, since doctors had always told him that the reason he had failed to conceive spontaneously with his ex-wife was due to male factor infertility. At this point Ruth’s theory seemed to have some legitimacy; likely his ex-wife also had a factor limiting conception. Sperm research is complicated by the heterogeneity in the populations studied, difficulties in defining normal sperm parameters and unforeseen issues not diagnosed by the parameters measured in a semen analysis. In 2010 the World Health organization (WHO) performed its most recent classification of normal sperm (1). Parameters were obtained from a fertile population. Ninety-fifth percentiles were used to define normal. Clearly, there are drawbacks to defining normal in a fertile population and applying those numbers to an infertile population. Those two populations are not the same. It may take more sperm to have conception in an infertile population than in a fertile population. This may be due to concomitant female factors which are undiagnosed or just a decreased fecundity in the infertile population. When comparing the 1999 WHO semen analysis norms which were based on an infertile population and the 2010 norms were based on a fertile population, the 1999 norms were more predictive of success at intra uterine insemination (IUI) in an infertile population (2). Suggesting that fertile and infertile populations differ for semen parameters which best predict pregnancy. A recent study evaluated sperm which was abnormal when using the 2010 WHO norms to an infertile population. This group was divided into couples previously diagnosed with male factor infertility and those who had recently had a normal semen analysis but who never the less had an abnormal semen analysis at the time of insemination. The group previously diagnosed with male factor had much poorer pregnancy rates (5%) that the group not diagnosed with male factor (17%). This occurred even though at IUI the sperm in the group previously diagnosed with male factor infertility was on average better than the group who only had poor sperm at that insemination (3). Again suggesting that the female component of a couple with male factor infertility, may have an issue limiting conception, or that semen analysis are poor measures of sperm...
fertilizing capability in couples with male factor infertility. The role of Deoxyribonucleic acid (DNA) sperm fragmentation of the sperm remains controversial (4). It is unknown if rates differ in the fertile and infertile populations. Why rates differ with different assay used and how well the results of DNA fragmentation testing predict success at conception. Therefore, its role in semen testing remains undetermined, and unevaluated in the semen analysis. If it does play a role one would expect levels of DNA fragmentation to differ in the sperm of the fertile and infertile couples, however studies are needed to confirm. Future studies are required to determine at exactly what values of sperm parameters, pregnancy rates decrease in an infertile population. The ninety-fifth percentile of results may not reflect fertilization potential. Never the less, values related to conception potential should differ in a fertile an infertile population particularly, because the infertile population has a combination of male and female factors limiting conception. Heterogeneity in the infertile population has likely contributed to the fact that studies examining total motile sperm counts and relationship to pregnancy at IUI has demonstrated extremely variable results. Different studies have found lower pregnancy rates when total motile sperm counts were less than 0.5 million, five million, ten million and twenty million (5-8) clearly, normal for semen analysis need to be population specific, based on large number of patients and should be based on each treatment modality used. It is unknown if different levels of sperm parameters are needed for clomiphene IUI or gonadotropin IUI. Importantly, these results should come from an infertile population.
References


