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MALE FACTOR INFERTILITY

Male factor is the primary cause of infertility in approximately 20% of infertile couples and is an important contributing factor in another 20-40% of infertile couples.

The high prevalence of male factor infertility requires that all infertile men be evaluated, even if they have previously fathered a pregnancy. A focused medical history centered on factors that may have adverse influence on male reproductive function can be quite informative. When the evaluation is directed by a gynecologist and there is no history of the male genital abnormality, trauma, surgery, or sexual dysfunction, the physical examination reasonably may be deferred, pending the results of the initial semen analysis. An abnormal reproductive history or semen analysis requires additional evaluation, most often performed by an urologist or other male reproductive specialist, to identify causes that may be correctable. The causes of male infertility are many and include a wide variety of conditions involving abnormalities of sperm production or function.

The semen analysis is the cornerstone of the male infertility evaluation. The test is highly informative, non-invasive, relatively inexpensive, has almost no risk, and therefore should be among the first steps in the evaluation of the infertile couple. At least two semen samples, collected at least 2-3 weeks apart, should be evaluated. The normal reference values for semen parameters are published by the World Health Organization (WHO). The best available evidence suggests abnormal values are a sperm concentration less than 15 million/mL, progressive motility less than 32%, and morphology (shape of the sperm) less than 5% normal as judged by "strict" (also known as "Kruger") criteria. The likelihood of male factor infertility increases with the number of abnormal parameters, 2- to 3-fold when one parameter is abnormal, 5- to 7-fold when two are abnormal, and 16-fold when all three are abnormal. A wide assortment of tests have been proposed for the evaluation of sperm function (e.g., sperm penetration assay, human zona binding assay, acrosome reactivity, reactive oxygen species), but none have proven validity or clinical utility. Currently, a semen analysis with strict sperm morphology represents the best predictor of sperm function. Although no threshold value excludes the possibility of pregnancy, consistent evidence of a very low morphology (count of normally shaped sperm), (< 4% normal) is widely accepted as an indication for IVF with intracytoplasmic sperm injection (ICSI).

Formal urologic evaluation is indicated for men having grossly abnormal semen parameters. Physical examination may reveal evidence for testicular failure or ductal obstruction. Additional evaluation with trans-rectal and trans-scrotal ultrasonography, vasography, vesiculography generally will identify and confirm potentially correctable causes (e.g., varicocele, ductal obstruction). Men with no sperm having normal testes on exam, at least one palpable vas deferens, and a normal serum FSH may require testicular biopsy for diagnosis and to obtain sperm that also may be cryopreserved for later ICSI.

Endocrinologic evaluation is indicated for men having significant low sperm count, (<10 million sperm/mL), sexual dysfunction or other clinical symptoms or findings suggesting a hormonal problem. A basic evaluation (Serum TSH, Prolactin) will detect the majority of clinically significant problems. Men having a low total testosterone level (<300 ng/dL) merit more extensive evaluation. Together, these tests effectively differentiate men having testicular failure (high FSH, low testosterone) from those having hypogonadotropic hypogonadism (low FSH, and testosterone, normal or high prolactin) in whom magnetic imaging of the hypothalamic-pituitary region is indicated to exclude a mass in the brain.

Genetic evaluation should be offered to men with severely abnormal semen parameters because the results may have important implications for offspring that may be conceived with ICSI. All men with congenital absence of the vas deferens (CBAVD) are at risk for transmitting cystic fibrosis to their offspring. Men with very low sperm counts (<10 million/ml) are candidates for a karyotype because the prevalence of chromosomal abnormalities (e.g., 47, XXY, translocations, inversions) is significant (5-15%) when the sperm count is low. Men with abnormal sperm counts may harbor microdeletions to the Y chromosome (7% prevalence) that their sons will inherit this. Finally, infertile men often exhibit increased levels of sperm DNA damage. However, because current methods of DNA testing do not predict treatment outcomes reliably and there is no proven treatment for the abnormality, such tests currently have very limited clinical utility.