

Clinical male infertility: Epidemiology and basic evaluation

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It is estimated that one in seven couples have problems conceiving. The incidence of infertility is similar in most countries regardless of their level of development. Over 80% of couples who have “regular” frequency of sexual intercourse (every 2 to 3 days) and who do not use any means of contraception will achieve pregnancies within one year. Approximately 92% of couples can achieve pregnancy within 2 years. Although in many cultures and societies the cause of infertility is assumed to be on the female side, in reality, roughly a third of infertile couples are due to problems with the man, another third due to problems with the woman and another third due to a combination of both male and female factors. Thus, evaluation of male infertility is essential in counseling couples for their fertility options.

Clinical evaluation of male fertility begins with a detailed history and physical examination, which generally will provide valuable information to guide what additional laboratory investigations or imaging studies to complete the evaluation. The two main purposes of male fertility evaluation are: i) to identify any modifiable factors that can improve the fertility status of the man; and ii) to identify any underlying serious conditions, such as testis cancer, osteoporosis, endocrinological and genetic problems that present first as infertility.

Important information to be obtained from the patient’s history includes the duration of infertility, previous history of natural fecundity, or fertility treatment. Important past medical history such as past or current sexually transmitted infection, genital urinary problems, malignancy, congenital, developmental or genetic problems, may point to the cause of infertility. Surgical history such as previous hernia repair, scrotal surgery such as orchiopexy for undescended testes, history of trauma to the pelvis or genital-urinary tract may be associated with an increased risk of infertility. A list of medication used currently or in the past should be obtained. Family history of infertility, endocrinological disorders, malignancy and other genetic conditions such as cystic fibrosis may also suggest the underlying cause of infertility. A detailed sexual history and social history including the use of tobacco and recreational drugs, anabolic steroids or exposure to any other gonadotoxins is also required as part of the evaluation.

A thorough physical examination begins with an evaluation on the general physique of the man, focusing on the proper development of secondary sexual characteristics. Additional signs associated with infertility include gynecomastia (which may indicate endocrinological or hepatic

problems), anosmia (indicating hypogonadotropic hypogonadism) and situs inversus (associated with sperm defects). Genital examination should be performed in a warmed room and should include the evaluation of the phallus for any defects such as hypospadias (downward-shift of urethral opening), anomalies in the development of the scrotal wall and the contents. Testicular size and texture and the bilateral symmetry are important. Testis cancer, which is known to be associated with infertility, may present as a painless hard mass. Bilateral soft and small testes may be associated with hypogonadism. An orchidometer may be helpful to objectively determine the testicular volume. Men with Klinefelter’s syndrome (Chapters 16, 17), one of the most commonly diagnosed genetic cause of infertility, may have hard testis with less than 3 cc in volume. Determination of the presence of vasa deferentia bilaterally, the position and fullness of the epididymis, the presence of inguinal hernia are all important part of the genital examination. Inspection and palpation for varicoceles (abnormal enlargement of veins in the scrotum that drain the testes) in the spermatic cord should be done when the patient is in an upright position. Finally, a digital rectal examination of the prostate may sometimes reveal i) tenderness that may suggest inflammatory or infectious process of the genital tract; ii) a mass which may represent cyst, stone or prostate cancer.

The basic laboratory evaluation includes two semen analyses (at least 1 to 2 months apart) and morning serum hormonal profile. In the absence of any significant findings in the history and physical examination, some investigators believe that if a single semen analysis demonstrated sperm count above 60 million/ml (four times the WHO reference values) with no additional parameters below the WHO reference values (Chapter 12), no additional evaluation is required. It must be emphasized that without a detailed history and a thorough physical examination, semen analysis alone, even if all parameters met the WHO reference values, does not rule out the presence of correctable male-factor infertility. Although semen analysis is the most commonly used laboratory evaluation for male fertility, other than at the extreme ends (extremely low or high parameters), semen analysis results have a weak predictive value on the probability of success of achieving pregnancy with the female partners naturally or with assisted reproductive technologies.

Basic blood tests for male fertility evaluation include a morning total testosterone and follicle-stimulating hormone (FSH). Evaluation of estradiol level, which has a role to negatively suppress the level of gonadotropins, can also be useful. In the presence of hypogonadism (low testosterone level), the levels of leutinizing hormone (LH) and prolactin should be determined. Interpretation of serum hormonal profile should be done in conjunction with the clinical history and physical examination. Men with azoospermia or

severe oligospermia with an FSH level above 10 IU/L is indicative of non-obstructive azoospermia or testicular dysfunction. If the level of FSH is in the low normal range, it may indicate the presence of obstruction in the excurrent ductal system leading to the low level or absence of sperm in semen. FSH levels well below normal (< 1.5 IU/L) are consistent with hypogonadotropic hypogonadism. Determination of inhibin-B level can also provide important information on the fertility status. However, the assay for inhibin-B is costly and is not widely available in most laboratories.

In men with azoospermia or severe oligospermia, genetic evaluation may be indicated. Currently, in azoospermic men with absence of the vas deferens, he and his partner should be evaluated for mutation in the cystic fibrosis transmembrane conductance regular (CFTR) gene. In men with azoospermia or severe oligospermia due to testicular dysfunction, blood test for karyotype and Y-chromosome microdeletion should be done to evaluate chromosomal anomalies. Many of these men with azoospermia or severe oligospermia may still be candidates for advanced assisted reproductive technologies to procreate. Since there are risks that they may pass similar or related genetic problems to their offspring, proper genetic counseling is important for couples who have genetic causes of infertility.

Additional evaluation for male fertility includes imaging studies such as i) trans rectal ultrasound for evaluation of prostatic cysts and ejaculatory duct obstruction; ii) scrotal ultrasound for evaluation of epididymal cysts, testis mass, varicoceles and other scrotal pathology; iii) magnetic resonance imaging for evaluation of pituitary prolactinoma that may lead to hypogonadism. Diagnostic testicular biopsy may occasionally be used to confirm the presence of normal spermatogenesis in men who are azoospermic or severely oligospermic in preparation for subsequent microsurgical reconstruction of the male excurrent ductal system to bypass the obstruction.

The use of various molecular assays to determine sperm chromatin integrity has recently generated a lot of interest among clinicians (Chapter 13). Common techniques such as the comet assay, TUNEL assay, sperm chromatin structure assay (SCSA®) have been applied in human sperm by various investigators. Men with clinical infertility as a group tend to have poorer sperm chromatin integrity than men who have no difficulty achieving natural fecundity. Some studies have demonstrated a correlation on the sperm chromatin integrity with reproductive success while others fail to demonstrate a significant predictive value of these assays on reproductive outcomes. Currently, according to the guidelines published by the American Society of Reproductive Medicine, sperm chromatin integrity assays is not cost effective to be used routinely for all couples being evaluated for infertility. Further studies will be required to fully explore the clinical values of

these assays in predicting success in fertility and the risks of adverse reproductive outcomes.

Suggested reading

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