The Office Visit

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KEYWORDS

• Male infertility • Semen analysis • Assisted reproductive technology • Men's health

KEY POINTS

- A comprehensive history and physical examination remains an essential component of the infertility evaluation.
- No single semen analysis parameter is a powerful discriminator of fertility and semen analysis reference ranges are not the minimum values required for conception.
- Endocrine testing is recommended in men with oligospermia, azoospermia, or history and physical examination findings suggestive of hormonal abnormalities.
- A karyotype and Y-chromosome microdeletion assay are indicated in men with a sperm concentration less than or equal to 5 million/mL, nonobstructive azoospermia, or clinical suggestions of an abnormality.
- DNA fragmentation and fluorescent in situ hybridization testing are replacing some of the previously used evaluations of sperm function (eg, postcoital test, sperm penetration assay).

INTRODUCTION

There is nothing more important to life than reproduction. Infertility is not only a challenging and stressful condition for patients and physicians but is also major public health concern that results in rippling psychosocial effects. It is estimated that approximately 7.3 million couples seek infertility care annually in the United States.[1] Infertility is due a male factor alone in approximately 30% of these couples, while combined male and female factors comprise an additional 20%.[2] In a study from the US Center for Disease Control, 7.5% of all sexually experienced men reported seeing a physician for a fertility evaluation, and 18.1% of men evaluated were found to have male-factor infertility.[3] Although the use of assisted reproductive technology (ART) has steadily increased and currently contributes to 1.4% of all births in the United States,[4] the number of male reproductive procedures performed is on the decline.[5] Men from infertile couples often do not seek evaluation.[6] Additionally, couples in which the man has significant semen abnormalities are often immediately directed toward in vitro fertilization (IVF) or other forms of ART, effectively bypassing the male evaluation completely. This trend is quite concerning given numerous recent studies closely linking male fertility with overall male health, cardiovascular fitness, and the development of

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cancer. Moreover, treatable causes of infertility or other medical problems are often discovered during the male evaluation.

There have been dramatic advances in the diagnosis and treatment of male infertility during the past several decades. Since 1992 with the introduction of intracytoplasmic sperm injection (ICSI), which allows for conception with only a single sperm, there has been rapid growth in the understanding of the genetic basis for male infertility. Examples include the elucidation of the relationship between cystic fibrosis mutations and congenital bilateral absence of the vas deferens (CBAVD), as well as the identification of Y-chromosome microdeletions. Similarly, microsurgical techniques for sperm retrieval and reconstruction have resulted in continued success. Considering the latest advances in the evaluation of the subfertile man, the goal of this article is to describe the essential components of the history, physical examination, and laboratory and radiographic studies in the initial office evaluation, and offer our vision of the future in male-infertility evaluation.

THE HISTORY AND PHYSICAL EXAMINATION

History

Couples with normal fertility may be counseled that pregnancy rates by intercourse are approximately 20% to 25% per month, 75% by 6 months, and 90% by 1 year.[7] Ten percent of fertile couples take longer than 1 year to conceive naturally. The accepted definition of infertility by the American Society for Reproductive Medicine is the inability to conceive naturally within 12 months. Despite this definition, a basic fertility workup should be initiated for any couple desiring one, with concurrent assessment of each partner. It is becoming more common that couples delay parenthood until after career development, or they may have questions or anxiety about their fertility status before attempts to conceive. For these reasons, a simple, cost-effective evaluation should be available for attempts at natural conception. This allows for earlier diagnosis and treatment of potential problems as well as alleviation of anxiety, which itself may be therapeutic.

A thorough, careful, and methodical history is necessary for successful diagnosis and treatment of male infertility because of the broad potential causes, including genetic, congenital, medical, surgical, environmental, and even psychosocial sources. The key components of the history and physical examination in the male-infertility workup are summarized in **Table 1**. The most efficient interview is with the couple. Because spermatogenesis lasts, on average, 64 days,[8] careful attention to the patient's history over the previous 2 to 3 months, especially recent fevers, other illnesses, substance abuse, and gonadotoxin exposures. Evaluation should be repeated in 3 months, if necessary. The history should begin with discussion of the duration of the couple's infertility, previous fertility treatments, previous pregnancies, and a detailed reproductive and sexual history, followed by a thorough past general medical and surgical history, social history, family history, and review of systems.[9]

The reproductive and sexual history may begin with a survey of the couple's sexual behavior. Infertility attributable to sexual behavior may be present in up to 5% of couples.[10,11] One of the most commonly reported misconceptions is the frequency and timing of intercourse around ovulation.[12,13] The authors recommend that intercourse should be performed every other day beginning 5 days before expected ovulation until 5 days after. An inquiry into the use of lubricants, which may be spermatotoxic or impair motility, is also advised.[9]

The history should additionally elicit information on past medical and surgical history stemming all the way to childhood. Report of genitourinary anomalies, reconstructive surgery, or pediatric illness associated with prolonged fevers or hospitalization may prove relevant. A history of pubertal mumps orchitis can result in subfertility in 13% of men.[14] In utero or childhood exposure to chemotherapy, radiation, or hormones may result in defects in spermatogenesis.[9,15]

Cryptorchidism can have negative implications for fertility even with appropriate timing of surgical correction. Despite treatment, 13% and 34% of men with unilateral and bilateral cryptorchidism, respectively, will demonstrate azoospermia. If left untreated, these rates are much higher.[16] Surgery for testicular torsion or pediatric hernia repair can similarly affect future paternity. Childhood hernia repairs have been associated with a 26.7% incidence of vasal obstruction.[17]

Clinicians should also inquire into common diseases of adulthood, including diabetes mellitus, sleep apnea, infectious diseases (eg, HIV, gonorrhea, chlamydia), neurologic disorders, and trauma. These illnesses may have implications for fertility and affect emission, ejaculation, or potentially result in obstruction of the male reproductive system.[9]

Pharmacologic or environmental exposures should similarly be addressed. Environmental toxins may include synthetic estrogens associated with pesticide use, organic solvents in paints or inks, ionizing radiation in nuclear power plant