Male fertility and infertility

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Abstract

Male factor infertility accounts for 30–50% of infertility cases. Over the past two decades, there have been several papers published describing declining numbers and quality of sperms. An increasing incidence of urogenital abnormalities in the new born and rising incidences of testicular cancer from many different countries have stimulated public interest and concern about male infertility. In this review different aetiological factors in male infertility are considered with an attempt to provide an up-to-date account on the investigations and management of male infertility.

Keywords male infertility; semen analysis; spermatazoa; testicular factors; intracytoplasmic sperm injection; donor insemination

Introduction

The true incidence of male infertility is unknown due to great variability in the prevalence of infertility. However in 30–50% of sub-fertile couples the male partner has suboptimal semen quality, either because of low sperm count, poorly motile sperm or sperm with abnormal size and shape (morphology). In more than 50% of male infertility cases, the aetiology remains unknown and the infertility is classified as idiopathic. Male infertility evaluation must go far beyond a simple semen analysis which has to be complemented with a comprehensive history and physical examination as well as relevant endocrine, genetic and other investigations.

The testis comprises of two distinct components, the seminiferous tubules (the site of spermatogenesis) and the Leydig cells (the source of testosterone). The process of spermatogenesis is directed by genes located on the Y chromosome and takes approximately 70 days to complete from the spermatocyte stage. Another 12–21 days are required for the transport of sperm from the testis through the epididymis to the ejaculatory duct. During passage through the epididymis, sperm mature further to develop the capacity for sustained motility. The long time required for sperm development and transit implies that the results of a semen analysis reflect conditions existing many weeks earlier. Semen includes secretions contributed by the prostate, the seminal vesicles, and the distal vas deferens (Figure 1).

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Causes of male infertility

This can be classified as shown in Table 1.

Evaluation of male infertility

The diagnosis of male infertility involves taking a thorough medical history, physical examination followed by laboratory tests such as semen analysis.

The medical history should include the following:

- Developmental history – testicular descent, age of puberty, change in the shaving
- Frequency and loss of body hair
- Infection history – Mumps, sexually transmitted diseases, prostatitis
- Surgical repair – Hernia repair, vasectomy
- Drugs/Environmental – Smoking, alcohol, anabolic steroids, chemotherapy, toxic chemicals and radiation
- Sexual history – Libido, frequency of intercourse and previous fertility assessment
- Chronic medical illness

Physical examination (Table 2): examination of the urogenital system is always recommended to preclude the possibility of testicular cancer and also to look for symptoms of sexually transmitted infection.

Testicular ultrasound (Figure 2)

Testicular ultrasound is frequently utilised in order to assess the scrotal contents for testicular volume and morphology. This non invasive test substantially detects more pathological conditions compared to clinical examination. Additionally, this may give indirect evidence of the presence of possible reversible pathology in the form of obstructive azoospermia. Further imaging in the form of transrectal ultrasound and Magnetic Resonance Imaging (MRI) is then often able to categorise the level of obstruction and facilitate treatment planning.

Semen analysis: The semen analysis should be performed according to the World Health Organization (WHO, 2010) laboratory manual for examination and processing of human semen (Tables 3 and 4). The sample should be collected after 2–7 days of sexual abstinence, preferably at the fertility clinic by masturbation. A study in 2006 by Castilla et al. showed a large biological variation in semen quality when five healthy young volunteers assessed by WHO recommended methods over a one and a half year period. If first analysis is abnormal, biologically, the optimal time for the second sample is at least three months after the initial sample because the cycle of spermatozoa formation takes about three months to complete. However, this delay may cause anxiety and the timing of the second sample and should take into consideration the preferences of the man. If azoospermia or severe oligozoospermia is reported in the initial semen analysis, a repeat test should be undertaken within two to four weeks.

Less than 1% of men are truly sterile and do not produce any spermatozoa (i.e. are consistently azoospermic).

Hormone analysis: if repeat semen analysis demonstrate severe oligozoospermia (<5 million spermatozoa/ml) or azoospermia, then basal serum follicle-stimulating hormone (FSH), luteinising

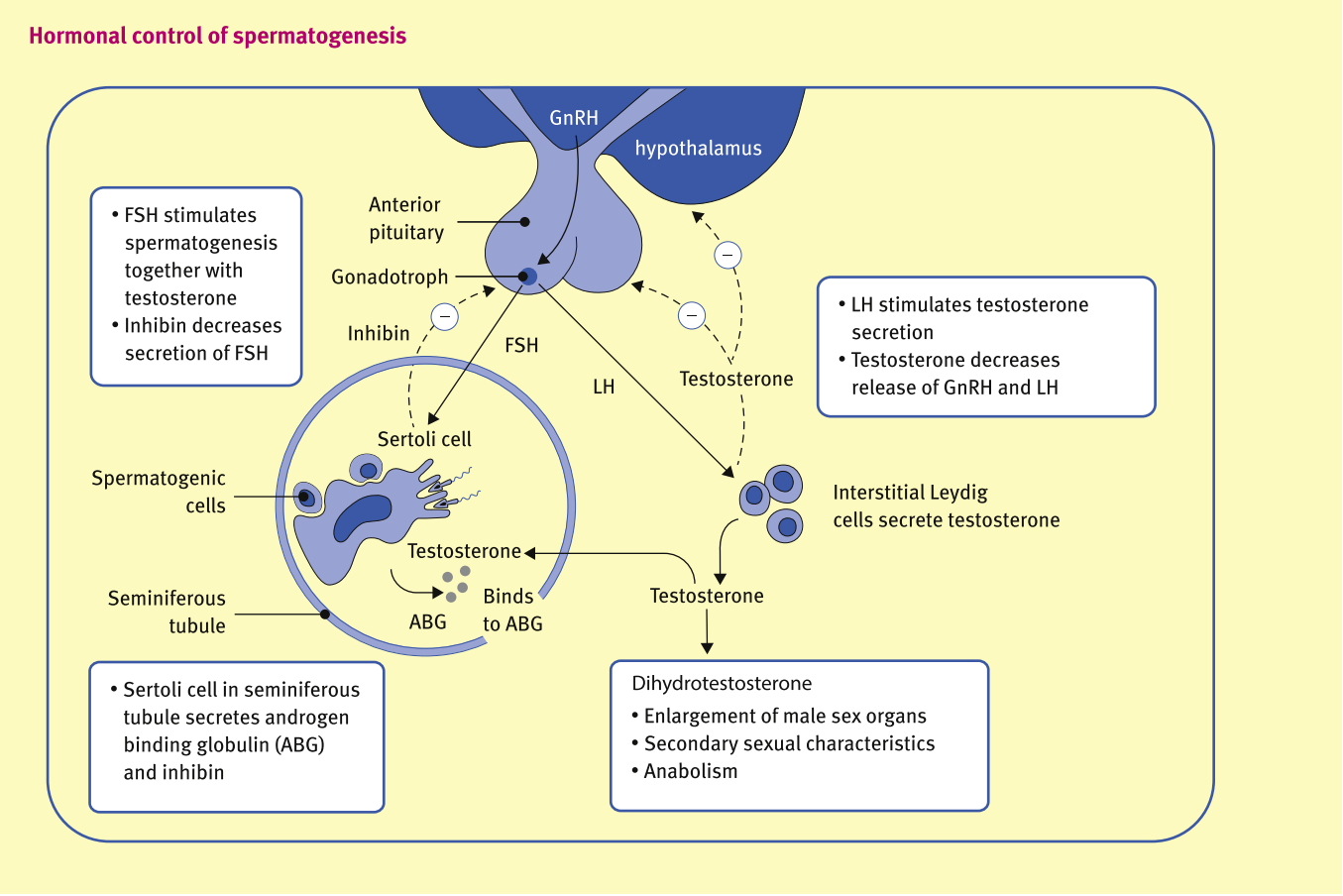

Figure 1

hormone (LH), and testosterone will be valuable. If serum concentrations of FSH, LH, and testosterone are normal and the man has azoospermia, a post-ejaculatory urine sample will provide evidence about retrograde ejaculation if sperm are seen in the urine. If spermatozoa are not present in the post-ejaculatory urine, the man has obstructive azoospermia or impaired spermatogenesis. Low serum FSH, LH and testosterone warrants gonadotrophin treatment (secondary hypogonadism). High serum FSH, LH and low testosterone indicate primary hypogonadism (Testicular failure). Men with low sperm counts and low LH (and FSH) who are well-androgenised should be suspected of anabolic steroid abuse (exogenous testosterone suppresses intratesticular testosterone production, which is an absolute prerequisite for normal spermatogenesis.) The serum testosterone can be low, normal, or high depending upon the specific substance taken. Sperm production recovers in most men when they stop using anabolic steroids, however, this process can take months to years. Prolactin should be measured in men who complain of reduced libido and have low serum testosterone. Low serum inhibin B may be a more sensitive indicator of primary testicular dysfunction than high FSH.

Genetic testing: if an ejaculate contains less than 5 million sperm/ml, then tests for cystic fibrosis carrier status, karyotype and a Y chromosome micro deletion is recommended. The blood tests for screening for cystic fibrosis analyses the most common mutation seen in a selected population group. The values vary depending on the ethnic origin of the patient. In patients with Congenital bilateral absence of Vas Deferens (CBAVD), non classical cystic fibrosis mutation might be present that is not detected by routine screening. Therefore it is prudent to offer both partner screening to establish the carrier status.

Cytogenetic abnormalities have been observed in 10–15% of azoospermic men and in ~5% of men with oligospermia. Additionally, inversions and translocations of autosomes are observed at a higher frequency among infertile men than in the general population. Y microdeletions have a frequency of ~2–10% or higher among infertile men, depending on the population studied. Three regions of Yq (AZFa, AZFb and AZFc) have been shown to be deleted. Deletions of AZFc are the most common (~60%).

Sperm function test

There are specific sperm function tests and these include measuring the ability of sperm to:

- enter and make progression in mid-cycle cervical mucus (sperm mucus penetration tests)
- hyperactivate following capacitation
- bind to the zona pellucida
- undergo the acrosome reaction
- penetrate zona-free hamster eggs.

DNA fragmentation and fluorescent in situ hybridization testing are replacing some of the previously used evaluations of sperm function. However, both the American Society for