

George Kedia

3.1 Definition

Infertility is a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse [1]. Infertility affects both men and women. The components of the evaluation of the men include medical history, physical and ultrasound examination, semen analysis and endocrine and genetic tests.

3.2 Medical History

A detailed history of an infertile men should include family history, developmental history (descensus testis, pubertal/mental development, voice mutation, loss of body hair), systemic diseases (diabetes, renal and liver insufficiency, cancer, hemochromatosis), infections (mumps orchitis, sinopulmonary symptoms, sexually transmitted infection, genitourinary tract infections), surgical procedures (vasectomy, orchiectomy, herniorrhaphy), exogenous factors (medications, cytotoxic chemotherapy, radiation therapy) and lifestyle factors (alcohol, obesity, smoking, drugs, anabolic steroids). A detailed sexual history should also be obtained, including libido, frequency of intercourse and previous fertility assessments of the men and their partner.

G. Kedia
Department of Urology and Urological Oncology, Hannover Medical School, Carl-Neuberg-
Str. 1, Hannover 30625, Germany
e-mail: kedia.george@mh-hannover.de

3.3 Diagnostics

The evaluation of an infertile men should begin with a physical examination that focuses on the secondary sex characteristics including general appearance (constitution type, eunuchoid features, body fat, muscle mass), breasts (gynecomastia), hair (pubic, axillary and facial), skin (sebum production, acne, pallor, skin wrinkling) and external genitalia (size of the penis, testicular volume, epididymis, vas deferens). Absence or partial atresia of the vas deferens, epididymal thickening and cysts, varicocele and scrotal hernia can be detected by inspection and digital or ultrasound examination of the scrotum. Ultrasound examination of the testis should be performed to measure the testicular volume and also to exclude tumours and microcalcifications, especially in men with a history of cryptorchidism. Transrectal ultrasound examination is recommended in men with a low volume of ejaculate (<1.5 mL) to exclude obstruction of the ejaculatory ducts caused by a prostatic cyst (Mullerian cyst) or stenosis of the ejaculatory ducts due to infection or surgery.

The semen analysis, standardised by the WHO [2], is essential for the evaluation of the male partner of an infertile couple. The standard semen analysis consists of the following: measurement of semen volume and pH, microscopy for debris and agglutination, assessment of sperm concentration, motility and morphology, sperm leukocyte count and search for immature germ cells [3]. More specialised semen analysis (e.g. detection of sperm autoantibodies, semen biochemistry) are optional. If the semen analysis and the investigation of the female partner are normal, then specialised tests of sperm function should be performed.

Microbiological investigation is indicated in men with abnormal urine or semen samples, urinary tract infections, male accessory gland infections and sexually transmitted diseases.

The endocrine tests include measurements of follicle-stimulating hormone (FSH), luteinizing hormone (LH), serum testosterone and sex hormone-binding globulin (SHBG). Serum prolactin should be measured in men with a low serum testosterone and normal to low serum LH.

Magnetic resonance imaging (MRI) of the pituitary gland should be performed in infertile men with unexplained hypogonadotropic hypogonadism or high serum prolactin.

In men with oligoasthenoteratozoospermia (OAT) or azoospermia, karyotyping and deletions in the azoospermic factor (AZFa, AZFb, AZFc) region of the Y-chromosome are recommended for diagnosis and for genetic counselling. The infertile men with absence of the vas deferens, low seminal fluid volume and acidic pH should be tested for mutations in the CFTR (cystic fibrosis transmembrane conductance regulator) gene.

Open biopsy of the testis should be performed to exclude tumour in infertile men with risk factors for testicular cancer (male infertility, cryptorchidism, history of a testicular tumour, testicular atrophy). In infertile men with azoospermia or extreme OAT, a normal testicular volume and normal FSH levels, a diagnostic testicular biopsy should be considered to differentiate between testicular insufficiency and obstruction of the male genital tract. Testicular fine-needle aspiration (TEFNA), testicular sperm extraction (TESE) or microsurgical epididymal sperm aspiration

(MESA) is usually performed as part of a therapeutic intervention for assisted reproduction in azoospermic men. The flow chart (Fig. 3.1) demonstrates the pathway from symptoms to diagnosis.

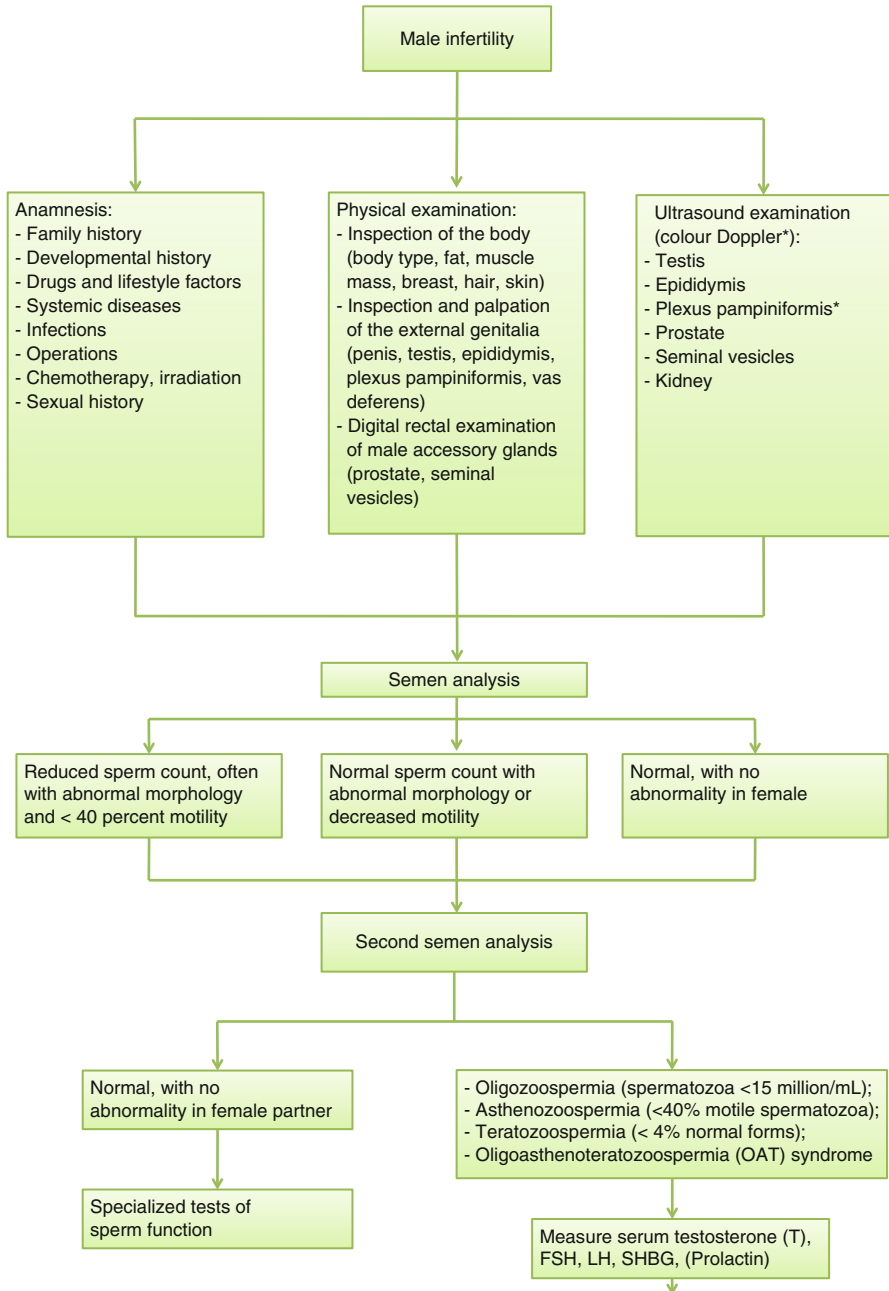


Fig. 3.1 Flow chart demonstrating the pathway from symptoms to diagnosis

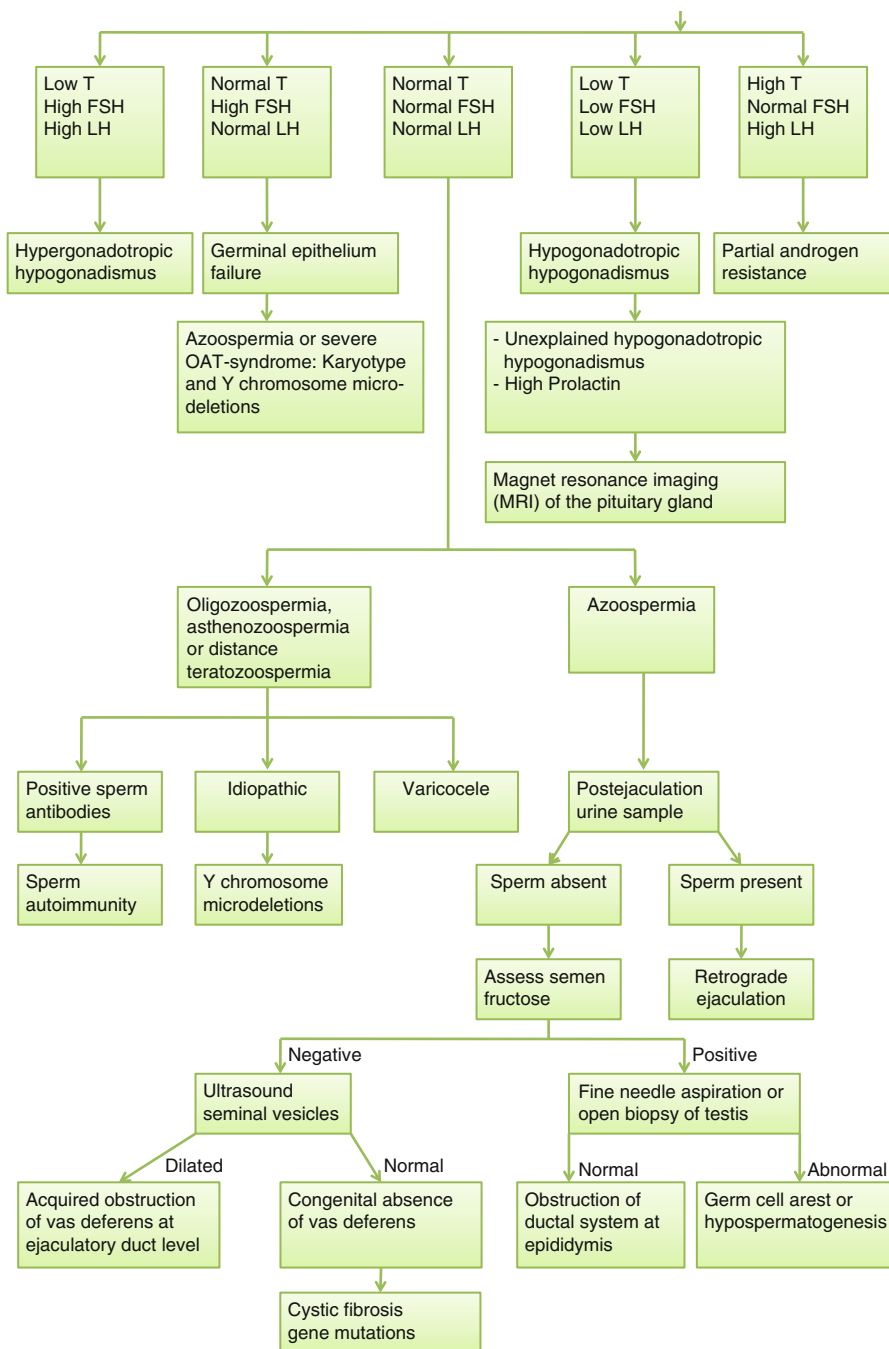


Fig. 3.1 (continued)

3.4 Differential Diagnosis

Reasons for male infertility

Differential diagnosis	Incidence	Diagnostics
Hypothalamic-pituitary disorders Kallmann's syndrome Idiopathic hypogonadotrophic hypogonadismus Multiorgan genetic disorders (e.g. Prader-Willi syndrome, Bardet-Biedl syndrome, familial cerebral ataxia) Malignant CNS tumours Pituitary adenoma Empty sella Hyperprolactinaemia Surgery, trauma Granulomatous illness Hemochromatosis Drugs, anabolic steroids Irradiation Vascular disorders (infarction, aneurysm) Obesity Nutritional deficiencies	++++	Medical/clinical history Clinical examination Semen analysis Hormone and genetic tests Magnet resonance imaging
Primary gonadal disorders Anorchia Testicular dysgenesis/cryptorchidism Klinifelter's syndrome Y chromosome microdeletions Androgen insensitivity syndromes 5-alpha-reductase deficiency Myotonic dystrophy Noonan's syndrome Testicular trauma, torsion Tumour, infection Varicocele Drugs, anabolic steroids Cytotoxic therapy, irradiation Systemic diseases (e.g. renal failure, liver cirrhosis, sickle cell disease) Surgery (orchietomy, herniorrhaphy)	++++	Medical/clinical history Clinical examination Semen analysis Hormone and genetic tests
Disorders of sperm transport Surgery (e.g. vasectomy) Congenital bilateral absence of the vas deferens/cystic fibrosis Infection Young's syndrome	++++	Medical/clinical history Clinical examination Semen analysis Genetic test (CFTR-Gen)

References

1. Zegers-Hochschild F, Adamson GD, de Mouzon J, et al. The International Committee for Monitoring Assisted Reproductive Technology (ICMART) and the World Health Organization (WHO) revised glossary on ART terminology. *Hum Reprod.* 2009;24(11):2683–7.
2. World Health Organization Department of Reproductive Health and Research. WHO laboratory manual for the examination and processing of human semen. 5th ed. Geneva: WHO; 2010.
3. Cooper TG, Noonan E, von Eckardstein S, et al. World Health Organization reference values for human semen characteristics. *Hum Reprod Update.* 2010;16(3):231–45.