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European Association of Urology

Guidelines

European Association of Urology Guidelines on Male Infertility: The 2012 Update

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Abstract

Context: New data regarding the diagnosis and treatment of male infertility have emerged and led to an update of the European Association of Urology (EAU) guidelines for Male Infertility.
Objective: To review the new EAU guidelines for Male Infertility.
Evidence acquisition: A comprehensive work-up of the literature obtained from Medline, the Cochrane Central Register of Systematic Reviews, and reference lists in publications and review articles was developed and screened by a group of urologists and andrologists appointed by the EAU Guidelines Committee. Previous recommendations based on the older literature on this subject were taken into account. Levels of evidence and grade of guideline recommendations were added, modified from the Oxford Centre for Evidence-based Medicine Levels of Evidence.
Evidence summary: These EAU guidelines are a short comprehensive overview of the updated guidelines of male infertility as recently published by the EAU (http://www.uroweb.org/guidelines/online-guidelines/), and they are also available in the National Guideline Clearinghouse (http://www.guideline.gov/).

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1. Definition

"Infertility is the inability of a sexually active, non-contracepting couple to achieve pregnancy in one year" (World Health Organisation [WHO], 2000) [1].

2. Epidemiology and aetiology

About 15% of couples do not achieve pregnancy within 1 yr; almost 50% of them do so spontaneously in the second year of unprotected intercourse, and another 14% in the third year. Ultimately, <5% remain childless [2]. No cause of infertility can be found using routine diagnostic work-up in 10–15% of couples. A male contribution to infertility is found in 45–50% of the remaining cases [1]. In infertile couples, there is often a coincidence of male and female factors. Table 1 summarises the main factors associated with male infertility. In 30–45%, the cause of the abnormal semen parameters is not identified (idiopathic male infertility) [3,4].

Table 1 – Male infertility causes and associated factors and percentage of distribution in 10 469 patients [3]

Diagnosis	Unselected patients (n = 12 945) (%)	Azoospermic patients (n = 1446) (%)
All	100	11.2
Infertility of known (possible) cause	42.6	42.6
Maldescended testes	8.4	17.2
Varicocele	14.8	10.9
Autoantibodies against sperm	3.9	–
Testicular tumour	1.2	2.8
Others	5.0	1.2
Idiopathic infertility	30.0	13.3
Hypogonadism	10.1	16.4
Klinefelter syndrome (47, XXY)	2.6	13.7
XX male	0.1	0.6
Primary hypogonadism of unknown cause	2.3	0.8
Secondary (hypogonadotropic) hypogonadism	1.6	1.9
Kallmann syndrome	0.3	0.5
Idiopathic hypogonadotrophic hypogonadism	0.4	0.4
Residual after pituitary surgery	<0.1	0.3
Others	0.8	0.8
Late-onset hypogonadism	2.2	–
Constitutional delay of puberty	1.4	–
General/systemic disease	2.2	0.5
Cryopreservation due to malignant disease	7.5	12.5
Testicular tumour	5.0	4.3
Lymphoma	1.5	4.6
Leukaemia	0.7	2.2
Sarcoma	0.6	0.9
Disturbance of erection/ejaculation	2.4	–
Obstruction	2.2	10.3
Vasectomy	0.9	5.3
Cystic fibrosis (CBAVD)	0.5	3.1
Others	0.8	1.9
Gynecomastia	1.5	0.2
Y-chromosomal deletion	0.3	1.6*
Other chromosomal aberrations	0.2	1.3

CBAVD = congenital bilateral absence of vas deferens.
* This frequency refers to all azoospermic men (also including "nonidiopathic" cases).

3. Prognostic factors

The following main factors influence the prognosis in infertility:

- Age and fertility status of the female partner
- Duration of infertility
- Primary or secondary infertility
- Results of semen analysis.

Female age and associated decline in ovarian reserve is the most important single variable influencing outcome in both spontaneous and assisted reproduction [2]. Compared with a 25-yr-old woman, the fertility potential is reduced to 50% at 35 yr, to 25% by 38 yr, and <5% at >40 yr [5].

4. Medical history and physical examination

Investigation of the male partner should include a full medical history and physical examination according to the standardised scheme published by WHO [1], so that any factor associated with male infertility can be diagnosed and treated if possible.

5. Investigations

5.1. Semen analysis

Semen analysis should follow the WHO guidelines, Laboratory Manual for the Examination and Processing of Human Semen [6]. Semen analysis may show a decreased number of spermatozoa (oligozoospermia), decreased motility (asthenozoospermia), and many abnormal forms on morphologic examination (teratozoospermia). These abnormalities usually come together and are described as the OAT syndrome (oligo-astheno-teratozoospermia). Seminal volume and pH can hint about conditions such as agenesis of seminal vesicles and vasa deferentia. Semen analysis in general is a poor predictor of pregnancy. Sperm DNA integrity assessment, by means of sperm chromatin structure assay, seems to be a valuable indicator of spontaneous pregnancy [7].

5.2. Hormonal investigation

Hypogonadotrophic hypogonadism is a rare primary cause of male infertility. Hormonal screening can be limited to determination of follicle-stimulating hormone (FSH), luteinising hormone (LH), and testosterone levels, and it should be performed in all infertile men and in conditions with an increased risk of hypogonadism. In azoospermia, it is important to distinguish between obstructive and nonobstructive causes. A criterion with reasonable predictive value for obstruction is a normal FSH level with bilaterally normal testicular volume. However, 29% of men with normal FSH appear to have defective spermatogenesis (spermatogenic arrest) [8].

5.3. Microbiologic assessment

Indications for microbiologic assessment include abnormal urine samples, urinary tract infections, prostatitis, epididymitis, male accessory gland infection (MAGI), and sexually transmitted diseases [9]. In general, microbiologic assessment plays a minor role in diagnosing male infertility. Also, the clinical implications of detecting white blood cells in semen samples are as yet undetermined. However, in combination with a small ejaculate volume, this may point to a (partial) obstruction of the ejaculatory ducts caused by (chronic) infection of the prostate or seminal vesicles [9].

5.4. Ultrasonography

Scrotal ultrasound is mandatory for the assessment of testicular size; finding signs of obstruction, such as dilatation of the rete testis, enlarged epididymis with cystic lesions, absence of the vas deferens; and assessment of blood reflux in men with varicocele [10]. Scrotal ultrasound may also detect testicular microlithiasis (TM) in infertile men, which might indicate testicular carcinoma in situ (CIS).