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Management of Male Infertility Today

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Introduction

Description of Study Area

Couple infertility has become more frequent during the last two decades, increasing from less than 10% to approximately 15% in recent years. There is evidence suggesting that it is the decrease of male fertility, due to deterioration of sperm quality, which is responsible for this evolution. Happily enough, new techniques have been developed to cope with male subfertility, such as in vitro fertilization (IVF) and intra cytoplasmic sperm injection (ICSI). There is, however, increasing concern over the universal and rather indiscriminate application of these techniques, particularly in cases with unexplained sperm deficiency where Y-chromosome linked genetic defects may eventually be transmitted through ICSI. Also, the exuberant cost per successful delivery[1] and the birth of many low weight offsprings from multiple pregnancies are presently unresolved drawbacks of these methods. Hence the renewed interest in "conventional" andrology, which experiences a true revival.

Definition of Infertility, Subfertility and Sperm deficiency

The majority of couples consulting for infertility are subfertile rather than infertile. Their level of fecundity is decreased, so that the probability of conception per cycle of exposure is less than optimal, and the time period required to conceive is prolonged. By arbitrary definition, a couple is considered infertile when conception has failed to occur after 12 or more months of "exposure to the risk of pregnancy"[2]. Based on statistical and empirical observations it is known that the probability of conception per month of subsequent exposure decreases with the duration of infertility. Several additional factors do define this probability in each individual couple (Table 1), and it is possible to calculate the expected probability of conception in the forthcoming months or years with reasonable accuracy using a computer program (PC-RATE, Fertipro, Lotenhulle, Belgium).

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TABLE I. Different formulae used.

Formula I			
Proportion of infertile and fertile couples (in %) related to the conception rate per cycle (P/C) and duration of "exposure to the risk of pregnancy" (n; number of cycles of trial to conceive).			
(Ia) infertile couples = $(1 - P/C)^n \times 100$			
(Ib) fertile couples = $[1 - (1 - P/C)^n] \times 100$			
Formula II			
(IIa) Probability of conception per cycle (P/C in %) related to the duration of infertility (n in months) in couples consulting for infertility 12 to 48 months duration.			
$P/C = 4 \times 0.97^n$			
(IIb) Probability of spontaneous conception per cycle in couples consulting for infertility of more than 4 years duration (x is the number of years of unsuccesful exposure).			
$P/C = 1.3 - 0.1 \times$			
Formula III			
Probability of conception per cycle (P/C in %) related to duration of infertility (n in months), type of infertility (a), severity of male (bm) and female factor (bf).			
$P/C = 4 \times 0.97^n \times$ (a) × (bm) × (bf)			
Estimated coefficients expressing the relative influence of different factors affecting the spontaneous conception rate of infertile couples:			
(a)	Primary infertility	=	0.9
	Secondary infertility	=	1.35
(bm)	Male factors		
	No antisperm antibodies present		
	Sperm concentration ≥ 20 million/ml	=	1.25
	Sperm concentration 1.9 - 19.9 million/ml	=	0.8
	Sperm concentration 0.1 - 1.9 milliion/ml	=	0.4
	Idiopathic azoospermia	=	0.08
	Significant presence of antisperm antibodies on spermatozoa		
	Sperm concentration ≥ 20 million/ml	=	0.4
	Sperm concentration 1.9 - 19.9 million/ml	=	0.25
	Sperm concentration 0.1 - 1.9 million/ml	=	0.15
(bf)	Female factors		
	No demonstrable abnormality or minimal Endometriosis (AFS I)		
	Age 20-30 years	=	1.25
	Age 30-40 years	=	0.75
	Age > 40 years	=	0.50
	In case of demonstrable pathology		
	Functional ovulatory disturbances	=	1.2
	Cervical factor or Mild endometriosis (AFS II)	=	0.8
	Minor tubal pathology or Moderate endometriosis (AFS III)	=	0.6
	Bilateral tubal occlusion on hysterisapoingography or severe endometriosis (AFS IV)	=	0.3

Several approaches can be taken with regards to the definition of male infertility. We favour the definition that states that the male partner is the probable cause of infertility if a couple is unable to attain conception and there are no demonstrable abnormalities in the female partner (diagnosis "per exclusionem"). Next, the cut-off values of normal as compared to abnormal semen can be defined by statistical methods (such as the receiver operating characteristic curves, MedCalc program, MedCalc Software, Mariakerke, Belgium) applied to the comparison of samples originating from fertile men who did achieve conception within no more than 12 months of "exposure", and infertile men as defined above. Using this method we have obtained cut off values permitting to categorize a particular semen sample as potentially fertile, probably subfertile, and probably infertile (Table 2). In addition we could quantify the power of each sperm characteristic as to its potential to discriminate between these three categories (Table 3). It is the concentration of spermatozoa with rapid linear progression that has the strongest power to discriminate between semen that will be fertile, subfertile or infertile under *in vivo* circumstances, and this variable must be assessed using objective methods and criteria.

When a semi-computerized method of semen analysis is applied (e.g.,Autosperm,) to objectively assess sperm characteristics, almost 90% correct semen categorization can be obtained[3]. As a result, it has become admissible to define male subinfertility on the basis of objectively assessed sperm characteristics, rather than on the basis of epidemiological or "per exclusion" criteria.

TABLE 2. Values for the conventional characteristics of spermatozoa defining potentially fertile semen, subfertile semen and probable infertile semen.

	Zone I - Zone II	Zone II - Zone III
Concentration (mill/ml)	35	4
Grade (a) motility (%)	28	3
Grade (a) + (b) motility	48	1.4
Grade (a) motile sperm concentration (mill/ml)	15	0.3
Grade (a) + (b) motile sperm concentration (mill/ml)	21	0.6
Morphology (%)	28	6

*Values for the conventional characteristics of spermatozoa defining potentially fertile semen (zone I, values better than the 5th percentile of fertile donor group), subfertile semen (zone II, values below the 5th percentile of the fertile donor group but better than the 5th percentile of the subfertile group who did ultimately attain spontaneous conception), and probable infertile semen (zone III, values below the 5th percentile of the successful subfertile group).

Investigation of the Infertile Male

After systematic investigation of over 8,000 couples, using a strict and comprehensive protocol[4], a critical analysis has been performed to assess whether particular questions or tests were relevant for the final diagnosis and management of the infertile couple. Based on this analysis, a simplified method for the standardized investigation and diagnosis has been developed[2]. This method must be followed for every individual couple, and complementary investigations and techniques may help to sustain or refine the diagnostic classification. In the present review we will highlight some new developments with regards to the diagnosis of particular pathological conditions and their treatment. The general outline of the diagnostic flow chart (Fig. 1) will be followed in doing so.

TABLE 3. Accuracy of sperm parameters assessed by conventional methods or the computer assisted Autosperm(R) technique in differentiating between semen of fertile and subfertile men.

	Criterion Value	Sensitivity[a] (%)	Specificity[a] (%)	Error[b] Rate (%)
Autosperm				
Velocity (um/sec)	22.7	83	82	17.5
Linear Velocity (um/sec)	20.9	84	81	17.5
Angular Velocity (um/sec)	21.0	85	81	17.0
Linearity Index (%)	90.1	45	69	43.0
Angularity Index (%)	90.4	66	71	31.5
Grade (a) (%)	21	89	86	12.5
Grade (b) (%)	24	61	60	39.5
Grade (c) (%)	3	41	90	34.5
Grade (d) (%)	47	88	79	16.5
Grade (a) concentration (10^6 /ml)	9.5	86	95	9.5
Conventional				
ATP - concentration (umol/l)	4.8	79	85	18
Grade (a) concentration (10^6 /ml)	28	77	83	20
Viability (% live)	72	75	75	25
Grade (d) (%)	32	68	80	26
Morphology (% normal)	42	75	72	26.5
Grade (a) + (b) (%)	60	78	68	27
Grade (a) + (b) motile sperm concentration	36	67	79	27
Sperm concentration (10^6/ml)	75	72	65	31.5
Count/ejaculate (10^6/ml)	230	77	58	32.5
Peroxidase Neg-cells per 100 spermatozoa	2.6	60	73	33.5
ATP per 10^6 spermatozoa (pmol)	66	50	80	35
Concentration of peroxidase negative cells (mill/ml)	1.9	50	60	45

(a) Sensitivity is the percentage of true fertile classifications.
Specificity is the percentage of true infertile classifications.
(b) Error rate is the percentage of false fertile plus the percentage of false infertile classifications divided by 2.

Sexual and/or Ejaculatory Inadequacy

This diagnosis is made on the basis of history taking, which must be confirmed by questioning of the female partner. Sometimes the diagnosis is revealed by a negative postcoital test (PCT) in spite of good quality semen.

Complete andrological investigation can identify a clear organic cause in about one third of cases. Endocrine (17%), vascular (7%), metabolic (4%) or neurological (5%) factors must be searched for. A relative androgen deficit, with serum LB below median, is commonly found in cases with so-called psychogenic erectile dysfunction, suggesting a moderate hypothalamic deficiency[5].

Cavernosometry, or rather the test-injection of either an alfalytic drug (Fentolamine, Moxisylyte), or a smooth muscle relaxant (Papaverine), or prostaglandin E_1 (Prostin,

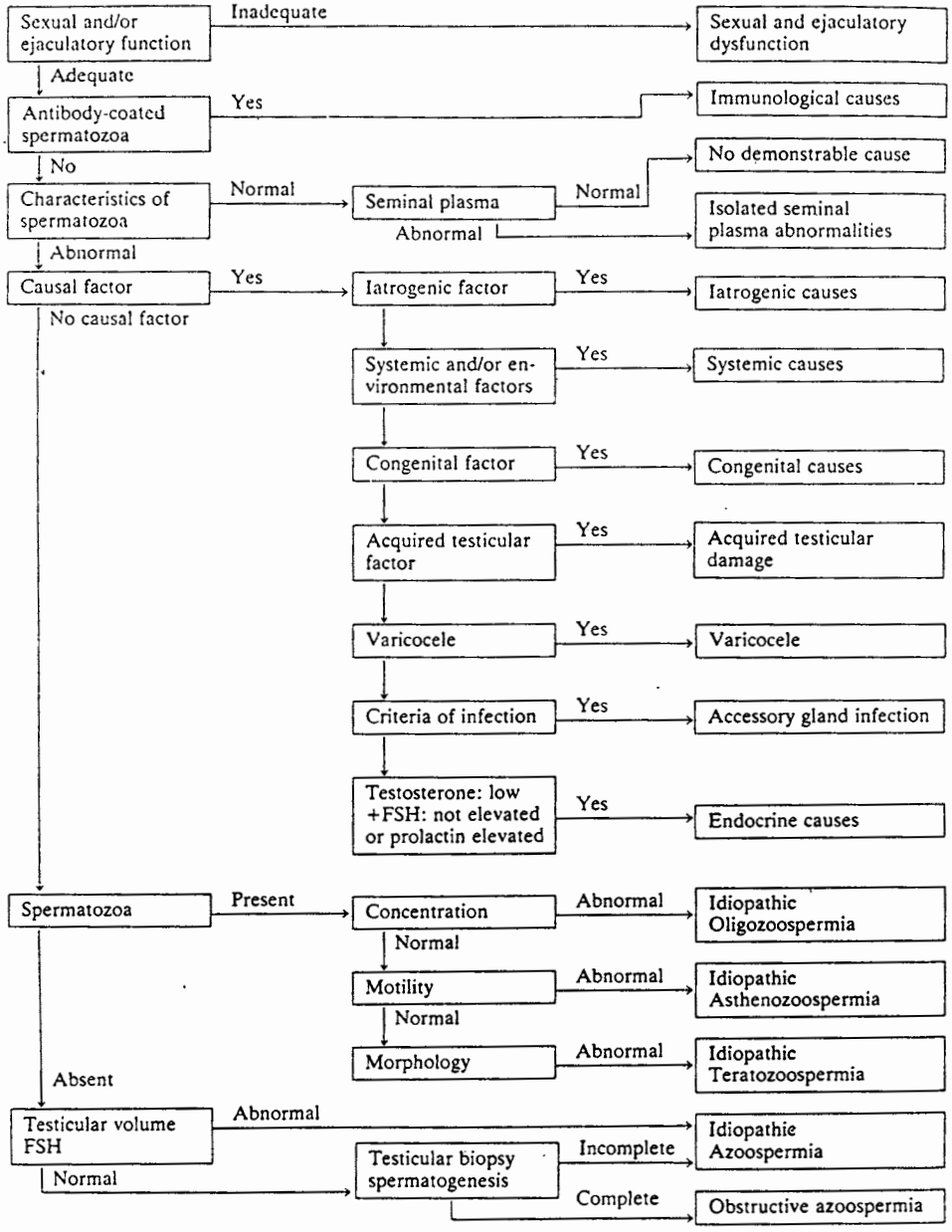

FIGURE 1. Diagnostic flow chart for the male.

Caverject) into the corpora cavernosis and subsequent treatment. This technique must be considered part of the andrological armatorium.

Androgen supplementation can make use of intramuscular injections of testosterone esters (such as testosterone-oenantate, Testoviron depot$^{(R)}$, shering) or of the oral intake of testosterone derivatives (such as testosterone undecanoate, andriol$^{(R)}$ organon). The latter has the distinct advantage not to cause supra-physiological testosterone concentrations in blood, and its formulation avoids the "first passage" through the liver.

Hyperprolactinaemia is another, but rare cause of erectile dysfunction, and it can effectively treated by depaminergic medication.

Immunological Cause

The most efficient way to diagnose immunological infertility is by the SpermMar test for IgG and/or IgA (Fertipro, Belgium), which is more specific and sensitive than the Immonobead test[6]. The presence of antiserum antibodies is related to a history of urogenital infection, and palpable abnormalities of the epididymis[7], and causes severe subfertility. The conception rate after intra uterine insemination (IUI) of spermatozoa which are filtered by means of discontinuous Percoll gradient (Prewash, FertoPro, Belgium) out of an ejaculate collected in *e.g.* Earle's balanced salts medium with 3% albumin added, gives a 8.6% success rate, which is significantly higher than the treatment independent pregnancy rate of 1.7% per cycle. One third of couples with male immunological infertility obtain a pregnancy within 12 cycles of IUI treatment, and this result is at least as good as treatment of the man with coricosteroids. In addition, unsuccessful cases with IUI do not benefit from coricosteroids[8]. Considering the health hazards of high-dose coricotherapy this treatment must be considered obsolete for immunological infertility.

In case of failed IUI, conventional IVF can be applied with a 18.4% success rate per attempt[7], but intra cytoplasmic sperm injection (ICS) may be preferable in cases with severe oligo-, asthono- or teratozoospermia and seems to yield higher success rates.

Isolated Abnormalities of Seminal Plasma

This diagnosis is given when characteristics of the spermatozoa are normal, but seminal plasma is abnormal in volume or consistency, or when there are too many white blood cells (WBC's) but no infection of the accessory sex glands. It is a result of the PCT that will determine the management of this condition. In case the PCT is normal, the seminal abnormalities are not relevant and do not explain the couples infertility. If, in contrast, the PCT is normal then intra-cervical or, preferably, intra-uterine insemination of Percoll selected spermatozoa is indicated. In the latter cases IUI treatment is highly successful with up to 80% pregnancies within the first 2 or 3 cycles.

No Demonstrable Cause

The diagnosis of "no demonstrable cause" in the male requires the sexual and ejaculatory function to be adequate, and normal characteristics of spermatozoa and seminal

plasma. Again, a PCT may be indicated. If the latter is abnormal the diagnosis of cervical hostility of the female partner is probable, and IUI may be indicated. If the PCT is normal IUI will not solve the infertility problem, and should not be applied[9].

Congenital Causes

Klinefelter syndrome and other numeric abnormalities of the sex chromosomes result in irreversible sterility, and artificial insemination with donor semen is the only alternative, if ethically acceptable for the couple. There is an increasing number of patients with severe oligozoospermia or azoospermia in whom so-called point-lesions are detected in the Y-chromosome[10]. In fact, these men suffer from a congenital cause, and such couples should not be treated by ICSI since their sons will also suffer from infertility. There should however, not be problems with their daughters. Hence, preimplantation sex determination may be indicated in case ICSI would be applied.

The ***immotile cilia syndrome*** is characterized by extreme asthenozoospermia due to structural abnormalities of the sperm flagellum. Commonly, similar structural abnormalities are present in cilia of the respiratory tract, and these patients may suffer from chronic bronchial infections, or bronchiectasis, or Carthagner's syndrome. ICSI may result in pregnancy, but the offspring may also suffer from the same condition. In the author's opinion it is ethically unacceptable, therefore, implement ICSI in case of immotile cilia syndrome, as long as we are unable to identify the genetic defect and screen both partners for it.

Similarly, ICSI can be applied using either epididymal or testicular spermatozoa of men with **congenital absence of the deferential ducts** which is usually combined with absence of the seminal vesicles. It has been proven that this condition is caused by genetic defects identical to those causing mucoviscidosis and cystic fibrosis. In these cases ICSI treatment is only acceptable after genetic testing of both partners for the defect in order to ascertain that the offspring can not be homozygotous with full-blown mucoviscidosis. Considering the high prevalence of the genetics defect(s) for mucoviscidosis, namely one in every 23 subjects in Belgium, it would be a serious professional mistake not to perform genetic testing in these couples. Alternatively, preimplantation gentic evaluation of embroyos created by IFV may be considered.

The most common congenital cause is **testicular maldescent.** There is evidence that the prevalence of this disease may be increased during recent decades, which has been suggested to relate to prenatal exposure of the male foetus to environmental estrogen-like substances (xeno or pseudo estrogens) which have been accumulated by the mother[11]. Sperm deficiency in cases with a history of bilateral cryptorchidism usually is extremely poor[4], and also unilateral testicular maldescent is commonly associated with severe subfertility and very low treament-independent conception rate (1.0% per cycle). After treatment of coincidental pathology, such as varicocele, one third of couples attain spontaneous conception. In some cases, where serum FSH is not elevated, hormonal stimulation with the anti-estrogen Tamoxiphen may increase sperm concentration. In our clinical experience intra uterine insemination had a per cycle pregnancy rate of 6.1% and this is not different from that of conventional IVF (8.7% per attempt). The lat-

ter is significantly lower than the overall success rate of IVF for male infertility (27.9%), indicating deficient fusogenic capacity of the spermatozoa. In contrast ICSI treatment is highly successful (40% pregnancies per attempt), because it overcomes the defictive gamete fusion[7].

Acquired Testicular Damage and Iatrogenic Causes

The former condition may result from testicular torsion or (mumps) orchitis, and it should be prevented by early treatment and vaccination against parotitis infectiosa, respectively. More commonly nowadays is the irreversible destruction of spermatogenesis by chemotherapy for leukemia, or Hodgkin's disease, or for (testicular) cancer. Also radiation therapy will irreversibly arrest spermatogenesis. It is the rule that all men who must undergo this treatment must have their semen frozen before initiation of treatment for "fertility insurance". Commonly the concentration and quality of spermatozoa are rather poor in these very ill patients, and the recovery of vital spermatozoa after freezing and thawing may be low. Nevertheless, the semen must be cryopreserved, since only very few (vital) spermatozoa are needed for sucessful ICSI.

Other iatrogenic causes of sperm deficiency are the intake of hormonal substances, namely estrogens, progestagens, anabolic steroids, andragens, or high doses of coricosteroids. Certain pharmaca exert a direct toxic effect on spermatogenesis, among which Sulfasalazine is the best known. In general, spermatogenesis will recover after the medication has been stopped.

Systemic Causes

Any period of elevated body temperature by fever will suppress spermatogenesis, and it may take up to six months before semen quality normalises. Nothing can be done to accelerate the recovery of sperm quality.

If sperm quality does not recover, another causal factor must be involved, or idiopathic testicular failure should be diagnosed. Systemic diseases of the liver, kidneys, endocrine organs or of the metabolism can reduce sperm quality. This also occurs during any disease which affects the general physical condition e.g. malignant diseases, chronic intestinal inflammatory disease, neurological disease, etc. Sometimes a moderate increase of sperms concentration can be attained with anti-estrogen treatment, but commonly used techniques of assisted reproduction (IUI, IVF, ICSI) may be required to attain pregnancy. It is mandatory to assess the life expectancy of these patients before deciding to implement assisted reproduction techniques.

Varicocele

Varicocele is present in approximately 8% of all young men, and is detected in one third of patients with subfertile semen. Although there is still some dispute about the exact mechanism of testicular malfunction in varicocele, it certainly is the reflux of spermatic venous blood that is the basic pathogenic factor. The latter causes Sertoli cell dysfunction[12,13,14,], and decreased sperm concentration related with the grade of severity

of the varicocele, as well as astheno- and teratozoospermia which is unrelated to the degree of distention of the pampiniform plexus[15]. Hence, it is mandatory to carefully search for spermatic venous reflux, even in the absence of palpable distention of the intrascrotal venous plexus in the so called subclinical varicocele. Tele or contact thermography of the scrotum is the most effective way to detect reflux which causes hyperthermia of the overlying skin (Fig. 2, Varicoscreen)[16].

FIGURE 2. Contact thermography of the scrotum (varicscreen).

Doppler ultrasonography may be used as a complementary diagnostic method, but it has a higher false positive rate, whereas technecium scanning or scrotal echography are not sensitive enough to detect subclinical reflux. Surgical treatment of varicocele has become obsolete in view of the availability of transcatheter embolisation using a tissue adhesive, which is less invasive. Being performed under local anaesthesia and on an outpatient basis, this treatment has no complications such as testicular atrophy or hydrocele. The technical success of trearment with complete interruption of spermatic venous reflux can be controlled during the catheterization, and must be confirmed by contact thermography performed a few months after treatment. Between 40 and 60% of couples will attain natural conception within 12 months after treatment, and this is significatly higher than the treatment independent pregnancy rate[14,17]. The success rate depends on 3 major elements being: testicular volume, grade of severity of the varicocele, and serum FSH concetration, and it can be predicted with reasonable accuracy (Fig. 3). Patients with small or subclinical varicocele and total testicular volume of less than 28 ml have a very low natural conception rate after treatment, and should rather be offered assisted reproduction. However, the pregnancy rate after treatment of small or

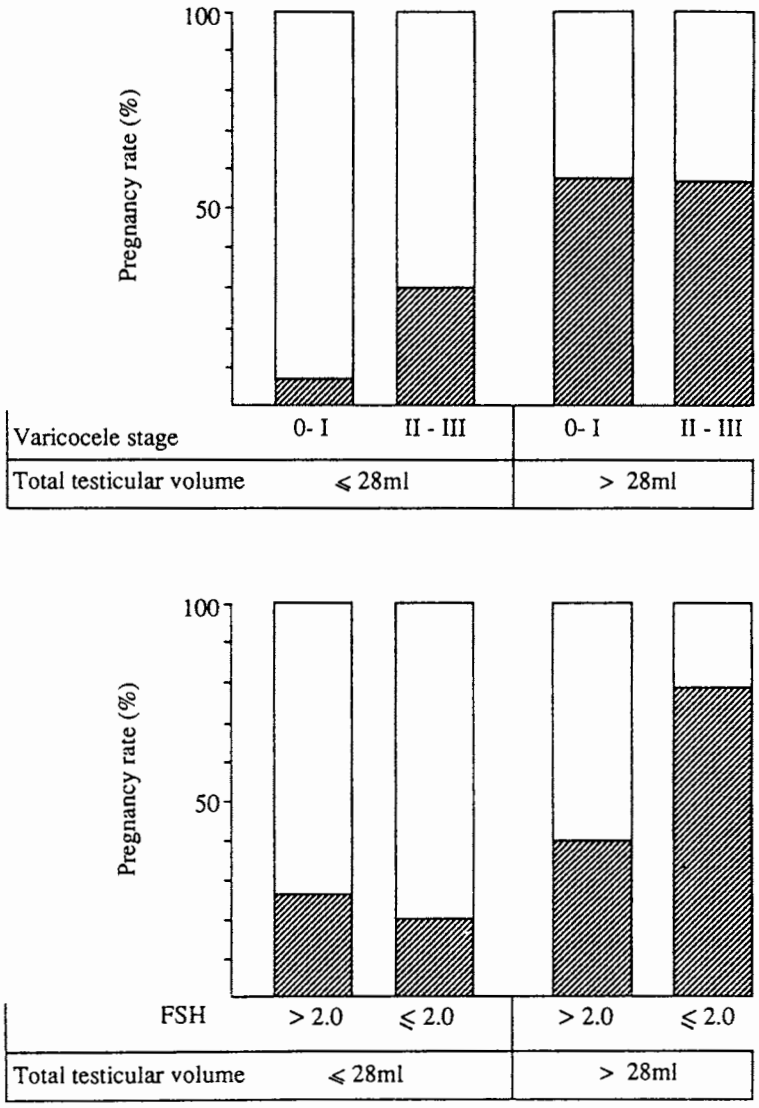

FIGURE 3.

Top panel

Overall pregnancy rate after varicocele treatment by embolization in patients with small or normal testicular volume as related to the clinical stage of varicocele.

Bottom panel

Overall pregnancy rate after varicocele treatment by embolization in patients with small or normal testicular volume as related to the serum concentration of follicle stimulating hormone (FSH in ng/ml) (adapted from Comhaire & Kunnen, 1985[14].

large varicoceles is identical if total testicular volume is at least 30ml, in which case it is the pre-treatment FSH concentration that defines the probability of subsequent success.

Coincidental pathology in the female (e.g. endometriosis, ovulatory disturbances), or the male (e.g. immunological factor, accessory gland infection) causes significant reduction of the pregnancy rate after varicocele treatment. Several studies indicate that varicocele treatment improves the success of subsequent IVF in cases with failed IVF attemp(s) and poor fertilization[18]. This seems to be related to improved chromatin condensation and acrosome as well as membrane structure proven by electron microscopy[19]. It has also been documented that varicocele treatment normalises both Sertoli and Leydig cell functions, provided it is applied before irrepairable damage has occurred. Hence, and because testicular damage has a progressive course, varicocele must be detected in adolescence, and treated by transcatheter embolisation which has an excellent cost/benfit ratio and will prevent fertility problems latter in life.

Male Accessory Gland Infection

Both acute and chronic infection of the genital tract and accessory sex glands (MAGI) cause male subfertility, and the disease is diagnosed in approximately 10% of patients . Infection is commonly caused by trivial urinary infectants such as *E. coli, Proteus* or *Kliebsiella* species, or *Enterococci,* but may result from (recurrent) sexually transmitted disease caused by *Gonococci* or *Chlamydia.* Infection has a direct deleterious effect on sperm quality through the influence of reactive oxygen species (mostly hydrogen peroxide)[20,21], generated by WBC's and which alter the lipid composition of the sperm membrane. Infection also exerts an indirect effect through functional deficiency of the epididymis and the prostate. The latter causes defictive sperm maturation and membrane instability, reducing the natural fertility of spermatozoa, though it may not be relevant for their *in vitro* fertilizing potential.

The diagnosis of MAGI is based on a combination of data from history taking, physical examination, analysis of urine and prostatic fluid, and semen analysis. Echography of the pelvic organs and scrotal contents sometimes gives complementary information [22]. But it is advanced semen analysis that is the most important element for the diagnosis. Sperm quality and the reducing capacity of semen are impaired[23], there is an excess of reactive oxygen species, the number of peroxidase positive WBC's (assessed by the LeukoScreen staining method, FertiPro, Belgium) is elevated, and biochemical markers of the function of the accessory glands are decreased. In particular the concentration of citric acid and activity of gamma glutamyl transferase are diminished due to prostatic dysfunction, and the reduced activity of neutral alpha-glucosidase (Epi-Screen method, FertiPro, Belgium) indicates impaired epididymae secretion.

We have recently shown that an elevated concentration of inflammatory cytokine interleukin-6 (measured with an Eliza kit, Eurogenetics, Belgium) in seminal plasma is an excellent marker of MAGI[24]. Evidently, sperm culture must also be performed on every semen sample, and prescriptions for semen collection must be give to render the interpretation of its result reliable[15].

Treatment of MAGI uses either a third generation (Fluorinated) quinolone (Perfloxacine, Ofloxacine, Ciprofloxacine or Norfloxacine), which must be given during at least 10 days, and will then eradicate bacteria, except enterococci and, in some cases, chlamydia. The latter need to be eliminated by Doxycyclin (200 mg per day for at least 14 days), whereas enterococci are the most difficult to eradicate since the prostatic penetration of semi-synthetic penicillin derivatives on macroslides is rather poor. In general, improvement of semen quality after MAGI treatment is limited. Assisted reproduction techniques, particularly IUI and sometimes IVF-ICSI may be necessary. Therefore, it is of the utmost importance to prevent MAGI by avoiding sexually transmitted diseases and by correctly treating trivial acute cysto-urethritis with antibiotics as mentioned above.

Endocrine Causes

The combination of a low testosterone concentration with FSH not being elevated indicates an endocrine cause of infertility. Hyperprolactinaemia almost never elicits severe sperm deficiency, except if it is caused by a pituitary tumour and accompanied by hypogonadotropic hypoandrogenism. Treatment of hypoandrogenism must first attempt to increase the testosterone production by giving the pure antioestrogen Tamoxiphen. If testosterone can be normalised, Tamoxiphen (20 mg/day) must be continued during 6 to 12 months, or even longer. If the testosterone concentration does not normalise, treatment with gonadotropins is indicated. Human Chorionic gonadotropin (hCG, Pregnyl, Organon) is complemented with human Menopausal Gonadotropin (Humegon, Organon) or urine extracted pure FSH (Metrodin, Serono) in a dose of 3 times per week 150 IU. In the near future hCG and Metrodin will probably be replaced by human FSH obtained by recobinant DNA technology. Treatment of endcrine infertility is highly successful with more than 80% of couples attaining conception.

Until now there is no proof that pulsatile LHRH treatment is superior to gondotropin treatment in case of endocrine infertility.

Primary Idiopathic Testicular Failure

This diagnosis includes cases with otherwise unexplained oligo-,astheno-or teratozoospermia, or azoospermia. In general terms, these are either due to a genetic defect or its impaired function of the Sertoli cells which create the "milieu interne" for optimal development of the haploid spermatogenic cells. The latter depends on many endocrine, paracrine and autocrine factors, and can be disrupted by all kinds of congenital, systemic or environmental factors.

The detection of genetic defects requires up-to-date techniques of molecular biology, such as polymerase chain reaction (PCR) and fluorescent in-situ hybridization (FISH) on either peripheral WBC's or testicular cells obtained by biopsy or transcutaneous puncture, or on decondensed spermatozoa and shed spermatogenic cells if these are available in the ejaculate[10]. Sertoli cell function can be assessed by measuring the concentration of transferrin in semen[25], and of the dynamic response of inhibin in peripheral blood after stimulation with pure FSH[26].

There is increasing circumstantial sperm deficiency results from either prenatal or post-natal exposure to excess amounts of man-made, so called xeno or pseudo estrogens. The latter all bare some resemblance to the prototype substance didthylstilbestrol (DES), and include pesticides such as DDT and its many derivatives; industrial products such as poly chlorinated biphenys (PCB's); and non-chlorinated products such as surfactants and antioxidants including nonyl phenol. Also, some pharmaceuticals such as clomiphene citrate (mostly its Zu-isomere) may exert an unfavourable role on the male fetus. They are supposed to suppress the regression of embryonal gonadocytes which can develop into testicular cancer later in life, to decrease the division of Sertoli cells during foetal life resulting in oligozoospermia, or to impair spermatogenesis in adult life[11]. In latter cases, idiopathic oligozoospermia will favourably respond to treatment with a specific anti-estrogen namely Tamoxiphen. In fact, this treatment has a cumulative success rate of approximately 30% of couples attaining pregnancy within 6 months of medication.

Assisted reproduction technology can be applied if medical treatment does not improve sperm quality or in cases with severe astheno-teratozospermia, and will involve IUI, IVF or ICSI depending on the severity of the sperm functional impairment. ICSI must be avoided when a genetic defect may be present. Certain functional tests of the spermatozoa, such as the hamster oocyte fusion test, the evaluation of the acrosome reaction and acrosin activity (gelatin lysis test), may help to select the best treatment. Also, careful analysis of sperm morphology by means of the WHO recommended crireria[27], may direct the optimal treatment approach[28].

Obstructive Azoospermia

Idiopathic obstructive azoospermia must be suspected when testicular volume is normal, serum FSH is not elevated, and there is no detectable cause among the aforementioned diseases to explain the absence of spermatozoa in the ejaculate. In these cases measurement of the alpha-glucosidase activity in seminal plasma, but also the measurement of transferrin and of its soluble receptor, which are markers of the Sertoli cell and spermatogenic epithelium, respectively, can help to establish the cause and the exact localisation of the defect[25]. Some patients with small testicular volume and elevated FSH may present focal areas of complete spermatogenesis, with spermatozoa or elongated spermatids in the fine-needle aspirate of the testis. Since testicular spermatozoa can successfully be used for ICSI, it is recommended to carefully examine all cases with idiopathic azoospermia in view of such treatment. However, it should be warned against the transfer of Y-chromosome link genetic defects to male offspring in some of these cases.

Conclusion

The development of new and truly revolutionary techniques have profoundly changed the management of couples and, indeed, male infertility. However, techniques such as ICSI and intracytoplasmic insemination of testicular spermatozoa, have raised exceptionally serious ethical problems with regards to the possible transfer of genetic defects.

At the other hand, there is an epidemic-like increase in the prevalence of male subfertility which is probably due to environmental pollution. During the forthcoming years, all our efforts should be focused on improving the causal diagnosis and treatment elucidating the mechanisms of deficient spermatogenesis, and on preventing male infertility.

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تدبـــير العـقـــم عنـــد الرجـــل

فرانك هـ : كومهير
المستشفى الجامعي ـ قسم الباطنة
(وحدة الغدد الصماء وأمراض الاستقلاب) ـ قنت ـ بلجيكا

المستخلص : يستعرض هذا المقال آخر ماتم التوصل إليه من طرق ووسائل في تشخيص وتدبير العقم عند الرجل من خلال تجارب الكاتب في مقر عمله في بلجيكا .