Medical and Surgical Management
Male Infertility

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Medical treatment for male infertility generally falls under two categories: specific therapy and empiric therapy. In approaching a patient, it is practical to first seek a clear etiology to which a specific strategy can be applied rather than using medication for all infertile patients. When a cause cannot be identified, several hormonal therapies are available. It is difficult to predict who will respond to empiric hormonal treatment of idiopathic infertility, but this choice may prove valuable in conjunction with advanced assisted reproductive techniques.

Specific therapy

Gonadotropins

Hypogonadotrophic hypogonadism accounts for less than 1% of all cases of male infertility and is discussed in great detail by Layman elsewhere in this issue. Gonadotropin replacement is the rational treatment and is the only clearly accepted and effective management of associated infertility. Normal male fertility requires adequate levels of intratesticular testosterone and follicle-stimulating hormone (FSH); the latter has been shown to initiate and maintain spermatogenesis [1,2]. FSH administered to men who have hypogonadotropic hypogonadism has demonstrated increases in sperm count, motility, morphology, and testicular volume [3]. Thus, it has been postulated that treatment solely with FSH may be adequate, however prolonged.
Treatment classically includes human chorionic gonadotropin (hCG), a leuteinizing hormone (LH) analog; human menopausal gonadotropin (hMG), which mimics LH and FSH; or purified FSH. Recombinant human FSH (rhFSH) and hCG have replaced their purified counterparts as the standard treatment for hormonal replacement because they are less expensive and more pure. Moreover, they have exhibited equal efficacy in increasing sperm counts and improving motility, morphology, and pregnancy outcomes [4,5]. Pulsatile GnRH may be used to imitate normal physiology, as in tertiary hypogonadotropic hypogonadism (Kallman syndrome); however, its use is infrequent because administration of the drug involves a portable minipump, an inconvenient, costly practice.

Typically, initial management consists of hCG (intramuscular, subcutaneous, 3000–6000 IU/wk) administered until adequate serum testosterone levels are detected. Although intratesticular testosterone concentration is not normally measured, it has been shown to increase linearly with the dose of hCG [6]. If sperm are undetected after 6 months, concomitant treatment with hMG (75–150 U two or three times weekly) or FSH (50–150 IU three times per week) ensues [7]. Although it takes on average 6 to 9 months before sperm appear in the ejaculate, therapy may be needed for 1 to 2 years, and some patients may not respond at all. Larger baseline testicular volume [8], prior gonadotropin therapy [5], postpubertal status [5], or the absence of bilateral maldescended testes may positively correlate with the patient’s response [9] and hasten the time to detect sperm in the ejaculate. Treatment with hCG/hMG has also been reported to be effective in a patient who has anabolic steroid-induced azoospermia [10].

Although spermatogenesis is induced in the majority of patients, sperm counts ordinarily do not reach normal levels and may require assisted reproductive techniques. In a study of 24 men who had isolated hypogonadotropic hypogonadism, 92% became fertile after gonadotropin therapy, resulting in 40 pregnancies, 71% of which occurred with sperm concentrations below 20 million/mL [11]. Small study sizes and insufficient formal comparison studies of treatment modalities make it difficult to predict the likelihood of conceiving. Nevertheless, an increase in pregnancies has been established, and, overall, gonadotropins have proven highly effective in inducing fertility [9,12,13].

**Androgens**

Exogenous testosterone therapy is detrimental to sperm production and has a contraceptive effect [14]. Meta-analyses of 10 randomized, controlled studies of testosterone and mesterolone demonstrate no effect on sperm production and no increases in pregnancy rates [15]. The theory of a reflex increase in gonadotropins occurring after sudden cessation of androgens, known as the rebound effect, was thought to initiate spermatogenesis. However, this rationale, and an androgenic direct effect on spermatogenesis,
is unpersuasive given the lack of efficacy in treating idiopathic infertility. Testosterone rebound therapy is not warranted because the patient’s condition may worsen with treatment.

Corticosteroids

The current use of glucocorticoids in male infertility is in the treatment of antisperm antibodies. Various doses of prednisolone have been considered to suppress the inflammatory response, allowing sperm–oocyte interactions to ensue without interference. An increase in pregnancies after prednisolone treatment for more than 3 months has been reported [16]; however, an inconsistent and incomplete meta-analysis of four of the six randomized, controlled studies available revealed no significant enhancement of fertility [17]. Some authors have recommended glucocorticoid treatment before intracytoplasmic sperm injection (ICSI) as the method of choice for patients who have high antisperm antibody titers, although statistical significance is lacking [18,19]. Taking into account adverse events, such as aseptic necrosis of the hip, steroid treatment is not recommended for men with antisperm antibodies.

Antibiotics

The incidence of genital tract infections among men who have infertility varies between 10% and 20% [20]. Often these infections are asymptomatic and difficult to diagnose. When leukocytospermia, defined as greater than one million white blood cells per milliliter, is present in an asymptomatic infertile male on semen analysis, an evaluation for a genital tract infection is recommended [21]. However, 54% of men who have leukocytospermia have no evidence of infection, positive semen cultures may be found in up to 83% of healthy men, and pathogens such as *Ureaplasma urealyticum*, *Proteus mirabilis*, *Mycoplasma hominis*, *Escherichia coli*, and *Enterococcus* are isolated in the same frequency in men who have leukocytospermia and men who do not [22]. The indigenous flora of the male genitourinary tract, contamination during sample collection, and the sexual activity and predictions of the individual need to be considered [22].

Certain organisms are considered pathogenic and warrant treatment. *Chlamydia trachomatis* has been isolated frequently in asymptomatic men who have unexplained infertility and has been found to bind to and penetrate human sperm [23]. *M hominis* and *U urealyticum* have been associated with nongonococcal urethritis and have been demonstrated to impair human sperm function in vitro [24,25]. *E coli* and *U urealyticum* have been reported to decrease sperm motility [26–28]. Other pathogens include *Neisseria gonorrhoeae*, *Treponema pallidum*, *Mycobacterium tuberculosis*, *Haemophilus ducreyi*, herpes simplex virus I and II, papillomaviruses, and *Trichomonas vaginalis*. Therefore, in men who have overt signs of genitourinary
infections (e.g., cystitis, urethritis, or prostatitis), semen and urine cultures are
performed, and appropriate antibiotic treatment is initiated. In asymptomatic
infertile men who have leukocytospermia or in cases of truly unexplained
infertility, semen cultures can be considered and appropriate antibiotic
treatment instituted depending on the organism isolated.

α-Sympathomimetics and anticholinergics

Ejaculatory dysfunction may take the form of failure of emission or
retrograde ejaculation. Reported causes are spinal-cord injury, diabetes mel-
itus, retroperitoneal surgery, multiple sclerosis, and bladder-neck and pros-
tate surgery. The cause may be psychogenic or idiopathic. Medical therapy
for ejaculatory dysfunction is initiated with α-sympathomimetic medications:
ephedrine, pseudoephedrine, imipramine, and phenylpropanolamine. When
these agents are unsuccessful or contraindicated, ejaculatory dysfunction is
often successfully treated with vibratory simulation or electroejaculation.
Electroejaculation—the application of transrectal electrical current to stimu-
late the pelvic nerves—results in approximately 90% of patients producing
a semen specimen. These specimens are often suboptimal in quality and are
used in conjunction with intrauterine insemination or more advanced assisted
reproductive techniques [29,30].

Empiric therapy

Antiestrogens

Clomiphene citrate, a synthetic antiestrogen, is the most commonly used
drug in the treatment of idiopathic oligospermia. The rationale for its use is
based on the drug’s ability to bind estrogen receptors, causing antiestrogen
and, to a lesser extent, estrogen effects. This removes the negative feedback
inhibition of estrogen at the hypothalamic and pituitary levels, increasing
GnRH, LH, and FSH secretion and stimulating testosterone production
and spermatogenesis. Due to the peripheral conversion of testosterone, es-
trogen levels may increase above normal levels. Therefore, monitoring of
serum testosterone and estradiol is required to make sure levels do not
rise to detrimental levels.

Although clomiphene citrate is widely used, its efficacy has been ques-
tioned since the first study yielded poor results in 1966 [31]. Within the
past 40 years, numerous controlled and uncontrolled studies have demon-
strated conflicting results in sperm counts, morphology, motility, and preg-
nancy rates. These variations may be in part due to differences in subject
parameters, patient selection, sperm counts, and female factors. In a ran-
domized, double-blind, placebo-controlled study of 190 couples by the
World Health Organization [32], clomiphene was found to have no signifi-
cant effect on pregnancy rates or semen characteristics, although multiple
studies suggest the converse [33–35]. In a meta-analysis of 10 controlled studies involving 738 men, antiestrogens demonstrated a positive hormonal effect, whereas no improvement in pregnancy rate was observed in trials with known randomization [36]. Tamoxifen citrate, an alternative antiestrogen, has yielded similar results in treating idiopathic oligospermia [36].

Despite mixed fertility outcomes, studies have verified beneficial effects on LH, FSH, and testosterone levels. Therefore, therapy with clomiphene may be more advantageous in men who have mild oligospermia and low serum gonadotropins or increased estrogen. Therapy is less likely to be efficacious in men who have elevated baseline gonadotropins and in men who have remarkably abnormal semen analyses or testicular biopsies.

More recently, with the advancement of assisted reproduction techniques, the goal may not be to improve male fertility directly but to augment spermatogenesis so that in vitro fertilization is possible. Hussein and colleagues [37] studied the effects of clomiphene citrate on sperm production in 42 patients who had nonobstructive azoospermia. After 3 to 9 months of therapy with dose titration to achieve testosterone levels of 600 to 800 ng/dL, 64.3% of patients demonstrated semen analyses containing sperm. Although the remaining patients revealed negative semen analyses, adequate sperm for intracytoplasmic sperm injection was retrieved in 100% of patients via testicular sperm extraction, supporting the use of clomiphene in azoospermatic men undergoing sperm retrieval [37].

Although they are usually self-limited, common side effects of clomiphene include weight gain, blurred vision, hypertension, gastrointestinal disturbances, and insomnia. Clomiphene may improve erectile dysfunction in men who have secondary hypogonadism, but data are limited [38]. Commonly used are daily dose regimens of 25 mg for 25 days with a 5-day rest period; however, doses of 25 mg administered every other day may reduce receptor down-regulation and further improve sperm counts, concentration, and motility [39]. The dose should be titrated to reflect increased testosterone levels within the normal range.

**Aromatase inhibitors**

Aromatase, a P450 cytochrome enzyme, converts testosterone to estradiol and is discussed in great detail by Carlson and Narula in their article on gynecomastia elsewhere in this issue. Estradiol inhibits gonadotropin secretion and may exert direct effects on intratesticular testosterone production [40]. Consequently, aromatase inhibitors have been used to block the conversion of androgens to estrogen and therefore increase testosterone with the hopes of improving male infertility.

Aromatase inhibitors are steroidal (eg, testolactone) or nonsteroidal (eg, anastrazole), the latter being highly potent and less likely to cause interruption of the adrenal axis beyond aromatase inhibition. Anastrazole was found to be comparable to testolactone in raising testosterone levels and
in improving semen parameters but more effective in lowering serum estradiol and increasing testosterone/estradiol ratio. Only in men who had Klinefelter syndrome was anastrozole not significantly effective [41].

Although aromatase inhibitors normalized testosterone/estradiol ratios in oligospermatic men and improved in semen parameters in early, poorly controlled studies [42–44], a double-blind randomized controlled trials of testolactone in 25 idiopathic oligospermatic men showed significant increases only in free testosterone, FSH, and LH, in addition to decreased levels of sex hormone-binding globulin. Free and total estradiol and total testosterone levels showed no significant change, and no improvement was seen in semen parameters [45].

More recently, efforts have been aimed at treating subsets of infertile men, specifically those who have decreased testosterone/estradiol ratios. Semen parameters and testosterone/estradiol ratios improved in a study of 63 hypergonadotropic hypogonadic infertile men, including those who had Klinefelter syndrome or other chromosomal abnormalities, varicoceles, cryptorchidism, and postchemotherapy patients [46]. A certain minimal amount of estrogen may be necessary for normal male reproductive function; the lower testolactone dose in this study (100–200 mg/d, the current standard dose, as opposed to 1–2 g/d in earlier studies) may have contributed to the positive outcome. The results were substantiated in a larger trial [41]. Controlled studies looking at pregnancy rates using aromatase inhibitors are lacking.

There are no absolute contraindications to the use of aromatase inhibitors, but given that elevations in liver enzymes have been described in 7% to 17.7% of patients, caution should be taken in patients who have hepatic disease, and liver function tests should be monitored. Estrogen deficiency may lead to osteopenia or osteoporosis. Other adverse reactions include increases in blood pressure that could be significant in hypertensive patients, rash, paresthesias, malaise, aches, peripheral edema, glossitis, anorexia, nausea/vomiting, and, rarely, alopecia that has resolved spontaneously.

**Gonadotropins**

Gonadotropins have also been used in the treatment of idiopathic infertility, but randomized controlled trials have observed no significant effect of hCG, hMG, or rhFSH on pregnancy rates or seminal parameters [47,48]. In contrast, many uncontrolled studies with positive outcomes have sparked interest in continued investigations [49,50]. Likewise, the development of rhFSH has prompted reconsideration of FSH treatment [51,52].

FSH may be beneficial in certain subsets of patients, such as those who have normal plasma levels of FSH and inhibin B and a testicular tubular appearance of hypospermatogenesis without maturation disturbances [53,54]. Using cytologic analysis, increased stimulation of spermatogenesis was observed after treatment with FSH 100 IU on alternate days but not at doses
of 50 IU, and significant increases in testicular volume and sperm parameters were detected with doses of 150 IU [55].

FSH may be useful in infertile men who have certain defects in sperm structure, such as those who have apoptotic or immature sperm, because treatment seems to improve the quality of sperm micro-organelles [56,57]. A single, randomized, controlled study by Foresta and colleagues [58] has strengthened this hypothesis. Of 112 men who had idiopathic oligospermia and normal FSH concentrations, rhFSH treatment showed no significant improvement in sperm parameters when no distinction was made between decreased and defective spermatogenesis. After subgroup analysis, subjects who had isolated hypospermatogenesis without spermatogenic arrest showed a significant rise in sperm count. A significant increase in spontaneous pregnancies was observed in this subset of patients, eliminating the need for assisted reproductive techniques. Additionally, several controlled studies have found better quality embryos and implantation rates after pretreatment of infertile men undergoing in vitro fertilization (IVF)/intra-cytoplasmic sperm injection (ICSI) [55,59]. These data suggest that the role of FSH in treating idiopathic oligospermia may be most practical in patients who have hypospermatogenesis or those attempting IVF/ICSI, rather than in all idiopathic oligospermic patients without specific selection criteria. However, the current data are controversial.

Alternative therapy

Approximately 30% of men presenting for infertility evaluation use alternative therapies, of which the majority are antioxidants, such as tocopherol (vitamin E), ascorbic acid (vitamin C), acetylcysteine, or glutathione [60]. The role of dietary supplements in erectile dysfunction and prostate health is discussed by Tamler and Mechanick elsewhere in this issue.

Reactive oxygen species (ROS) are involved in innate sperm function, but observations of increased ROS in semen of infertile men coupled with evidence of cellular damage with overproduction of ROS in spermatozoa have brought about the widespread use of antioxidants [61,62]. A number of small studies have suggested a beneficial role of antioxidants, including improved sperm quality and increasing fertilizing capacity. Treatment with tocopherol improved sperm function (sperm–zona pellucida binding capacity) [63] and IVF rates [64]. Increased sperm count, decreased ROS, and an augmented acrosome reaction were reported in men who had oligospermia after treatment with acetylcysteine and retinol (vitamin A) together with tocopherol and essential fatty acids [65]. Folic acid and zinc supplements have been also shown to increase sperm concentration in subfertile men, whereas seminal and hormonal parameters were unaffected [66,67]. More recently, L-carnitine, a vital component of sperm metabolism and maturation, has been shown to improve semen quality, including sperm concentration and motility; however, the majority of positive outcomes have
resulted from uncontrolled, unblinded studies [68]. Because overall results are encouraging and side effects are minimal, antioxidants continue to be recommended as adjunctive therapy.

Surgical management of male infertility

The surgical management of male infertility provides many options to the couple with male factor infertility. Problems amenable to surgery include varicoceles, obstruction, or sperm retrieval for IVF with intracytoplasmic sperm extraction.

Testicular dysfunction

Varicoceles

Varicoceles are found in 35% to 40% of men who have primary infertility and in 75% to 80% of men who have secondary infertility but are found in only 15% of the general population [69,70]. The association with infertility has been recognized for more than 50 years [71]. Varicocele causes a duration-dependent decline in semen parameters and testosterone production [72,73].

Venous dilation is thought to impair the counter-current heat exchange mechanism in the scrotum [74].Pooling of venous blood is likely to cause the increased intratesticular temperature and the progressive, duration-dependent decline in testis function observed in patients who have varicoceles [75,76]. Repair of a varicocele can prevent further testicular damage, improve sperm production, and improve testosterone production [72]. Ligation of a varicocele may help prevent infertility and low testosterone levels after repair [77,78]. Several investigators have sought to determine preoperative characteristics of a varicocele that would predict response to varicocelectomy [79,80]. Patients who had larger varicoceles were found to have greater improvements in semen analysis parameters after the procedure than men who had smaller varicoceles [81]. Semen analysis parameters improved in men who had clinically nonpalpable varicoceles detected by ultrasound, and a cutoff of a venous diameter of 3 mm or reversal of flow have been suggested as operating criteria [82–85].

We use the microsurgical, subinguinal approach to repair varicoceles [86]. We believe that this approach with optical magnification minimizes complications and produces the best results by ligating all of the internal spermatic and cremasteric veins that contribute to the formation of varicoceles. The testicular artery is identified, preventing damage to this structure. Also, cremasteric arteries and lymphatic channels are preserved, which prevents the formation of hydroceles [87]. Use of the operating microscope results in a hydrocele rate of approximately 1% compared with up to a 30% rate of hydrocele formation 6 months postoperatively after conventional inguinal and laparoscopic approaches [88,89]. Recurrences are not uncommon and are seen in up to 15% to 25% of men using nonmicrosurgical approaches.
but in less than 1% of men using microsurgical approaches [89]. Loupes under 2.5× do not provide enough power to reliably identify the testicular artery or lymphatics. Other methods of varicocele surgery include the conventional inguinal, the retroperitoneal, and the laparoscopic approaches.

Radiologic embolization represents another option to correct varicoceles. In this procedure, the testicular veins are accessed percutaneously, and an alcohol-based sclerosant or coils are used to embolize the veins. Two large investigations demonstrated resolution of varicoceles in 83% of men. Significant improvement after embolization was noted for sperm density, motility, and morphology [90,91].

Surgical ligation of varicoceles reduces intratesticular temperature to the normal range [92] and improves semen parameters and Leydig cell function of the testis.

Several studies have demonstrated improvements in semen parameters, testosterone production, and pregnancy outcomes. Semen parameters improve in 60% to 80% of men after repair [70,85,93]. Bilateral repair in men who have a large unilateral and small contralateral varicocele and repair in younger men may have a greater beneficial effect on sperm parameters and androgen production than repair in older men [94–97].

Obstruction

Although varicoceles cause testicular dysfunction that is associated with infertility, most obstructive causes of male infertility are caused intentionally. Vasectomy is performed on more than 500,000 men per year in the United States to affect “permanent” contraception [98]. Due to a variety of factors, most commonly divorce and remarriage, 3% to 8% of vasectomized men request reversal [99,100]. Injury to the vas is also a common cause of obstruction, most often the result of childhood hernia repair, orchiopexy, or hydrocelectomy [101].

Microsurgical techniques have vastly improved the success rate of surgery to repair vasal or epididymal obstruction. Reversal of vasal obstruction, most likely secondary to vasectomy or an iatrogenic injury, can usually be accomplished by a vasovasostomy. In cases of congenital anomalies or secondary epididymal obstruction, a vas-to-epididymis anastomosis is required. Vasovasostomy is successful in up to 99% of cases, whereas vaso-epididymostomy has a success rate of up to 90% [89,102–106].

Vasovasostomy

Microsurgical vasovasostomy, initially described by Owen and Silber in 1975, resulted in significantly improved outcomes compared with older techniques [105,107]. A modified microsurgical, single-layered anastomosis is statistically equivalent to a two-layer technique [102]. Patency and pregnancy rates vary directly with the obstructive interval. Although the overall patency rate was 86% and the pregnancy rate was 51.6%, the results for men with obstruction for less than 3 years were 97% patency with a 76%
pregnancy rate [102]. Others have reported similarly good results with a microsurgical approach to vasectomy reversal [103,108]. The gold standard for vasovasostomy is the microsurgical multilayer sutured technique, which had a success rate of up to 99.5% in a large series [103].

The identification of prognostic features of the vesal fluids helps to guide the surgeon in choosing the type of reconstruction to perform. The best results are achieved when sperm are found in the testicular end of the vas, but high rates of return of sperm to the ejaculate are also achieved with clear watery fluid present or if many sperm heads are found in the fluid [89].

The layers of the anastomosis include a mucosa-to-mucosa layer of six 10-0 nylon sutures, a muscular layer of six 9-0 nylon sutures at the region of the gaps, six additional 9-0 nylon sutures in the serosa between each muscular layer suture, and approximation of the vesal sheath with six 7-0 nylon sutures [103]. This achieves a water-tight anastomosis and prevents the formation of sperm granulomas. The importance of placing these sutures is magnified by the realization that there is no constituent of vesal fluid that promotes the sealing of the anastomotic site internally.

**Vasoepididymostomy**

Vasovasostomy is not always a feasible option to restore vesal patency. If epididymal obstruction is present, whether primary or secondary to chronic vesal obstruction, a vasoepididymostomy, one of the most technically challenging procedures in all of microsurgery, is required proximal to the obstruction to restore continuity for sperm transport. In the situation of epididymal obstruction, the decision to perform a vasovasotomy or vasoepididymostomy is made intraoperatively and is based on the microscopic examination of the proximal ves fluid and the time of obstruction [109,110].

We recently reported results comparing the four main techniques of vasoepididymostomy [104]. Success and pregnancy rates were not significantly different between groups. All conceptions in the groups where intussusception was used were through intercourse; none required assisted reproductive techniques. Among men who had return of sperm to the ejaculate, the intussusception groups had lower rates of disappearance of sperm from the ejaculate after 12 months ($P < .04$). The newer intussusception techniques offer comparable outcomes in terms of return of sperm to the ejaculate and pregnancy rates compared with the older techniques. The late shutdown rates of sperm in the ejaculate are lower. We also use fewer sutures with these techniques, which eases the performance of this challenging anastomosis.

**Sperm retrieval techniques**

Many cases of testicular dysfunction are not correctable by medical or surgical means. Reconstruction of the vesal and epididymal systems is also not always possible. In such situations, sperm retrieval for IVF is undertaken. Sperm retrieval with assisted reproduction is an also an
appropriate option for men who have poor sperm production, in selected cases of obstruction with female factors, or when only one pregnancy is desired.

A variety of genetic and acquired disorders may cause a man who has obstructive azoospermia to be unreconstructable. For example, in congenital bilateral absence of the vas deferens, patients have mutations in the cystic fibrosis transmembrane conductance regulator gene. This results in defects in the sperm transport system from the mid-epididymis to the seminal vesicles, and most of these men are not candidates for reconstruction [111,112].

Nonobstructive azoospermia describes the situation whereby genetic or environmental factors result in severe depression in spermatogenesis to the point that no sperm are present in the ejaculate. Successful sperm retrieval is possible in the majority these cases [113]. Spermatogenesis in many of these patients is a patchy process, and a technique that exposes and explores the entire testis is critical to optimize success rates for sperm retrieval in these challenging patients.

One subgroup of men who have nonobstructive azoospermia is men who have Klinefelter’s syndrome, with an abnormal karyotype of 47 XXY. Before the advent of ICSI, men who had Klinefelter’s syndrome were considered sterile. Today, a technique of sperm retrieval with ICSI is the preferred treatment modality in those desiring paternity; with this technique, sperm can be retrieved in over 70% of cases [114,115].

Testicular biopsy

The success of different biopsy methods varies with the cause of infertility. In cases of vasal or epididymal obstruction, various percutaneous techniques are highly successful in terms of retrieving sperm. In cases of primary testicular dysfunction with very low sperm production, open biopsies are the preferred techniques. Of 14 patients who had primary testicular failure as proven by histopathology, only in one case (7.1%) were spermatozoa recovered by multiple aspirations, whereas in nine cases (64.3%) spermatozoa were recovered by open biopsy [116].

Percutaneous aspiration successfully retrieves sperm in cases of unreconstructable obstruction [116] and is substantially less painful than open biopsy techniques and has a faster recovery time. It has a far lower success rate in men who have nonobstructive azoospermia, in whom open biopsy yields much better results [117,118]. Some groups have reported better success rates of sperm retrieval using a percutaneous technique in men who have nonobstructive azoospermia. A recent large series from Jordan found a 53.6% success rate in 84 men [119]. In a series of 291 men, 63 men had successful percutaneous retrievals using a 21-gauge butterfly needle [120]. The remaining 228 men required an open biopsy in this series.

Open biopsy in cases of nonobstructive azoospermia is the preferred means of attempting sperm retrieval. Reports with a multiple biopsy
Fig. 1. Algorithm for the treatment of male infertility.
approach reveal successful sperm retrieval in 40% to 50% of cases among men who have nonobstructive azoospermia [118].

**Microsurgical sperm retrieval techniques**

The technique of microsurgical epididymal sperm aspiration is used to obtain sperm in men who have an intact epididymis. This technique is most commonly used in men who have congenital bilateral absence of the vas deferens or after a long obstructive interval after vasectomy with the desire for only one additional pregnancy. Using this technique, sperm can be aspirated that are suitable for use with ICSI [121,122]. Due to chronic obstruction, the sperm retrieved from these men is often of poor quality and does not fertilize the ovum readily, making ICSI a must.

In men who have nonobstructive azoospermia, the microdissection testicular sperm extraction technique provides the highest yield in terms of sperm retrieval while preserving as much testicular parenchyma as possible [123]. The histology of the testis can often predict the likelihood of successful sperm retrieval; however, even in the worst cases, sperm may be found over 40% of the time [124]. Postchemotherapy, sperm were found in 9 of 20 retrieval attempts in men who had azoospermia [125].

Microsurgical testicular sperm extraction is the most successful technique to retrieve sperm in men who have nonobstructive azoospermia, and it results in the least damage to the testis. Postoperative scarring is substantially lower with this technique compared with open biopsy [126]. The disadvantages of any microsurgical technique are the need for experience and the acquisition of microsurgical skills [127]. These techniques require general anesthesia. In cases of nonobstructive azoospermia, the microsurgical testicular sperm extraction is the procedure of choice for sperm retrieval because it offers the highest success rates with relatively low complications.

**Summary**

Infertility is a couples’ problem, and both partners must be properly evaluated so that the most appropriate therapy can be tailored to the man and the woman. In the vast majority of cases, male infertility is treatable. Whether by medical therapy or surgical means, we can treat the male partner to affect a natural pregnancy or a pregnancy via assisted reproductive techniques. Fig. 1 presents an algorithm that can be used to decide the most appropriate therapy for the male partner of the infertile couple. This is used for guidance, and the specific goals and desires of the individual couple are of paramount importance when deciding on specific therapies.
References


