



American
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INFERTILITY

Report on Management of Obstructive Azoospermia

An **AUA**
Best Practice Policy
and
ASRM
Practice Committee Report



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How This Document Was Created

This document was written by the Male Infertility Best Practice Policy Committee of the American Urological Association, Inc.[®] (AUA) and the Practice Committee of the American Society for Reproductive Medicine (ASRM). The two organizations agreed to collaborate to prepare documents of importance in the field of male infertility. The Male Infertility Best Practice Policy Committee was created in 1999 by the Board of Directors of the American Urological Association, Inc.[®] The Committee co-chairmen and members were selected by the Practice Parameters, Guidelines and Standards Committee (PPGSC) of the AUA. The membership of the Committee included nine urologists, one reproductive endocrinologist, one family physician and one research andrologist. The mission of the Committee was to develop recommendations, based on expert opinion, for optimal clinical practices in the diagnosis and treatment of male infertility. It was not the intention of the committee to produce a comprehensive treatise on male infertility. This document was submitted for peer review by 125 physicians and researchers from the disciplines of urology, gynecology, reproductive endocrinology, primary care and family medicine, andrology and reproductive laboratory medicine. Modifications were made by the Practice Committee of the ASRM. After the final revisions were made based upon the peer review process and the Practice Committee of the ASRM, the documents were submitted to, and approved by the Board of Directors of the AUA and the Board of Directors of the ASRM. These "Best Practice Policies" are intended to assist urologists, gynecologists, reproductive endocrinologists, primary care practitioners and reproductive researchers. Funding of the Committee was provided by the AUA. Committee members received no remuneration for their work. Each member of the Committee provided a conflict of interest disclosure to the AUA.

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Introduction

Azoospermia, defined as complete absence of sperm from the ejaculate, is present in less than 1% of all men and in 10 to 15 percent of infertile men. Although there are many causes of azoospermia, obstruction of the ductal system is responsible for approximately 40% of cases (1). Obstructive azoospermia may result from epididymal, vasal, or ejaculatory duct pathology. Vasectomy is the most common cause of vasal obstruction. Severe genitourinary infections, iatrogenic injury during scrotal or inguinal surgical procedures and congenital anomalies are other common causes of obstructive azoospermia.

A limited evaluation of both partners is important before reaching a final decision on the management of the couple with infertility due to obstructive azoospermia. Other factors either unrelated or indirectly related to the obstruction may play a role in the decision regarding management. For instance, congenital bilateral absence of the vasa deferentia (CBAVD) is a common cause of obstructive azoospermia and is associated with mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene (2). Genetic testing and counseling should be considered in the management of these couples prior to treatment to allow the couple to make an informed decision as to whether or not to use the husband's sperm. Since female factors may also play a role, the female partner should be offered at least a limited evaluation prior to treatment of the infertile couple with obstructive azoospermia.

This review offers recommendations for management of couples with infertility due to obstructive azoospermia.

Treatment methods for obstructive azoospermia

Men with obstructive azoospermia may father children either by 1) surgical correction of the obstruction, which may produce pregnancy by intercourse and obviate the need for assisted reproductive technology; or 2) retrieval of sperm from the male reproductive system for in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI).

Surgical treatment

Surgical correction may be accomplished by microsurgical reconstruction of the vas and/or epididymis or, in cases of ejaculatory duct obstruction, by transurethral resection of the ejaculatory ducts (TURED). Prior to performing microsurgery in the male, the female partner should be evaluated to determine if female infertility factors are present.

Microsurgical reconstruction of the reproductive tract

Microsurgical reconstruction of the reproductive tract often is successful in patients with obstructive azoospermia. Following vasectomy reversal, for example, return of sperm to the ejaculate occurs in 70-95 percent of patients, and pregnancies are obtained without the need for assisted reproduction in 30-75 percent of couples. A very important factor influencing the likelihood of sperm returning to the semen and of pregnancy after vasectomy reversal is the number of years between vasectomy and attempted reconstruction (3). The length of the obstructive interval and the chance for successful outcome of vasectomy reversal are inversely related. Other factors influencing the success of vasectomy reversal include: the presence or absence of sperm in the intraoperative vas fluid; the gross appearance of the vas fluid; the quality of the sperm in the vas fluid; the length of the vas segment between the epididymis and the vasectomy site; and the presence or absence of a sperm granuloma at the vasectomy site. The likelihood of pregnancy after vasectomy reversal is also heavily influenced by the age of the female partner.

Vasopididymostomy is performed for congenital, infectious, postvasectomy or idiopathic epididymal obstruction. Following this type of microsurgery, 20-40 percent of couples achieve pregnancy through inter-

course and without assisted reproductive techniques. Accuracy and delicacy of microsurgical technique affect the outcome of reconstructive procedures on the male reproductive system. The best results are achieved by surgeons with training and on-going experience in microsurgery. In order to maximize successful outcomes, surgeons performing vasectomy reversal should be comfortable with anastomoses involving extremely small luminal diameters and must be competent and comfortable with both vasovasostomy and vasoepididymostomy, because the latter may be unexpectedly necessary in many cases.

In rare cases, obstruction of the male reproductive tract occurs in the inguinal portion of the vas deferens. Obstruction in this location is usually caused by an injury to the vas during inguinal hernia repair and should be considered in azoospermic men who have a history of previous inguinal surgery. Some of these injuries can be corrected by vasovasostomy performed in the inguinal canal, provided that the ends of the vas can be located and approximated without tension.

Sperm retrieval and cryopreservation may be performed at the time of microsurgical reconstruction in order to avoid a second procedure in the event that the microsurgical reconstruction does not reverse a patient's azoospermia.

Transurethral resection of the ejaculatory ducts

The possibility of ejaculatory duct obstruction should not be overlooked in the differential diagnosis of obstructive azoospermia. This condition is uncommon, but can be treated by transurethral resection of the ejaculatory duct at the point where the duct enters the distal prostatic urethra near the veru montanum. Transurethral resection of the ejaculatory duct results in the appearance of sperm in the ejaculate in about one-half to three-fourths of cases. The pregnancy rate achieved by this surgery is about 25 percent.

Sperm retrieval techniques and IVF/ICSI

ICSI

ICSI is an adjunct to standard IVF. ICSI must be used in almost all cases in which sperm are retrieved from the testes or epididymides of a man with obstructive azoospermia, because the sperm retrieval techniques that must be employed to obtain sperm from these men very rarely produce enough motile sperm for intrauterine insemination (IUI) or standard IVF (4; 5). ICSI provides fertilization rates of 45-75 percent per injected oocyte when surgically retrieved epididymal or testicular spermatozoa are used (6; 7; 8; 9; 10; 11; 12). Clinical pregnancy rates reported in the recent literature range from 26-57 percent and delivery rates range from 18- 54 percent (8; 9; 10; 11; 12). At most reproductive centers, it is reasonable to expect clinical pregnancy rates of 30-40% and delivery rates of 25-30% when surgically retrieved epididymal or testicular sperm are used for ICSI.

In reproductive centers managing men with obstructive azoospermia, it is essential for the IVF team to have ICSI capability. Individuals with specific clinical and technical expertise must be available for all of the phases of IVF/ICSI. Sperm retrieval is best performed by a surgeon trained in this procedure, because the possible postoperative complications of sperm retrieval include bleeding and infection that may require surgical intervention.

Sperm retrieval

Common methods of sperm retrieval are listed in Table 1. Less frequently used sperm retrieval methods include vasal sperm aspiration (13) and seminal vesicle sperm aspiration aided by transrectal ultrasonography (14). The choice of sperm retrieval method in men with obstructive azoospermia depends primarily on the experience and preference of both the physician who will perform the retrieval and the IVF laboratory embryologist. There

are not enough data to conclude that either the technique of sperm retrieval (open or percutaneous) or the source of sperm (testicular, epididymal, vasal or seminal vesicular) significantly affects pregnancy rates. Each technique and sperm source usually provides a sufficient number of sperm for ICSI and may provide enough viable sperm for cryopreservation.

Sperm retrieval may be performed prior to or simultaneously with the female partner's egg retrieval. Although there is insufficient evidence to prove that, for successful ICSI, fresh sperm harvested from the testis or epididymis are superior to cryopreserved sperm, most laboratories prefer fresh sperm. For numerous scheduling and financial reasons, however, it is frequently appropriate to harvest sperm prior to oocyte retrieval and cryopreserve them for future use with an expectation of reasonable results.

Risks associated with IVF/ICSI

Any couple considering IVF/ICSI should be apprised of the risks involved in this type of treatment. These include the possibility of ovarian hyperstimulation, the potential complications of oocyte retrieval and the risks and consequences of multiple gestations (15).

IVF carries an incidence of mild ovarian hyperstimulation syndrome in up to 20 percent of patients. Moderate ovarian hyperstimulation occurs in up to 5 percent of women undergoing IVF. Severe ovarian hyperstimulation, which may require hospitalization and may be life threatening, occurs in 1 percent of women undergoing IVF (16).

The risk of multiple gestations after ICSI in the United States is 30-35 percent for twin gestations and 5-10 percent for triplets or higher-order gestations (17). Multiple-

Table 1 Common methods of sperm retrieval

Acronym	Method
MESA	Microsurgical epididymal sperm aspiration
PESA	Percutaneous epididymal sperm aspiration
TESE	Testicular sperm extraction
TESA	Percutaneous testicular sperm aspiration

gestation births are associated with increased infant morbidity and mortality rates due primarily to prematurity (18). The neonatal and maternal morbidity induced by multiple gestations accounts for the increased perinatal expense associated with multiple gestations. Whereas the in-hospital costs for delivery of a singleton child are typically less than \$10,000, perinatal care for triplets averages more than \$100,000 (19).

Microsurgical reconstruction versus sperm retrieval with IVF/ICSI

Microsurgical vasovasostomy (20) and vasoepididymostomy (21) have been shown to be more cost-effective than sperm retrieval with IVF/ICSI, which requires intervention in both the male and female. In addition, microsurgical reconstruction, if successful, allows couples to have subsequent children without additional medical treatment. Therefore, in most cases, microsurgical reconstruction is more appropriate as an initial treatment for obstructive azoospermia.

There are situations, however, where sperm retrieval with IVF/ICSI may be the method of choice for couples in which the male has obstructive azoospermia. Financial factors are a legitimate concern in the management of this problem and may dictate the ultimate choice in treatment. If the situation involves a possible vasovasostomy, then the time that has elapsed since the vasectomy should also be taken into account. If the interval from vasal obstruction to repair is long, sperm retrieval with ICSI may be preferable; pregnancy occurs in only 30-40 percent of the female partners of men with obstructive intervals greater than 15 years (3).

Female infertility factors might also favor the selection of IVF/ICSI. The fertility status of the female partner is related to the presence or absence of specific risk factors such as endometriosis or ovulatory dysfunction, and to age. When the female partner has tubal disease or has undergone tubal ligation, sperm retrieval with IVF/ICSI is clearly preferable, because it avoids subjecting both partners to reconstructive microsurgery. The woman's age is important because a woman's fertility progressively decreases after age 35 years and is limited after age 40 years (22). Due to the fact that the average interval until pregnancy after a successful microsurgical vasectomy reversal is 12 months (3), couples may consider sperm

retrieval with ICSI when the female partner is greater than 37 years of age. However, in couples in which the female partner approaches age 40, the success rate of IVF with or without ICSI decreases dramatically as well (17). Older women should be evaluated before any fertility treatment is undertaken. The choice of either sperm retrieval with IVF/ICSI or microsurgical reconstruction should also be influenced by the pregnancy rates achieved with ICSI by the IVF team when epididymal or testicular sperm is used and by the surgeon's results with microsurgical reconstructive procedures.

The final decision concerning microsurgical reconstruction versus sperm retrieval with IVF/ICSI is ideally made by the well-informed couple together with both partners' reproductive specialists.

Recommendations: *Microsurgical reconstruction of the reproductive tract is preferable to sperm retrieval with IVF/ICSI in men with prior vasectomy if the obstructive interval is less than 15 years and no female fertility risk factors are present. If epididymal obstruction is present, the decision to use either microsurgical reconstruction or sperm retrieval with IVF/ICSI should be individualized. Vasoepididymostomy should be performed by an expert in reproductive microsurgery.*

Sperm retrieval/ICSI is preferred to surgical treatment when (1) advanced female age is present, (2) female factors requiring IVF are present (3) the chance for success with sperm retrieval/ICSI exceeds the chance for success with surgical treatment or (4) sperm retrieval/ICSI is preferred by the couple for financial reasons.

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This report is intended to provide medical practitioners with a consensus of principles and strategies for the care of couples with male infertility problems. The report is based on current professional literature, clinical experience and expert opinion. It does not establish a fixed set of rules or define the legal standard of care and it does not pre-empt physician judgment in individual cases. Physician judgment must take into account variations in resources and in patient needs and preferences.

Conformance with this best practice policy cannot ensure a successful result.

Date of publication:
April, 2001

ISBN 0-9709327-0-7 (Volume 3) ISBN 09649702-6-0 (4 Volume set)

This report is part of a series on male infertility. Other titles include: *Report on Optimal Evaluation of the Infertile Male*, *Report on Evaluation of the Azoospermic Male*, and *Report on Varicocele and Infertility*.

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Table 2

Clinical Condition	FSH	LH	Testosterone	Prolactin
Normal spermatogenesis	Normal	Normal	Normal	Normal
Hypogonadotropic hypogonadism	Low	Low	Low	Normal
Abnormal spermatogenesis*	High/Normal	Normal	Normal	Normal
Complete testicular failure/ Hypergonadotropic hypogonadism	High	High	Normal/Low	Normal
Prolactin-secreting pituitary tumor	Normal/Low	Normal/Low	Low	High

* Many men with abnormal spermatogenesis have a normal serum FSH, but a marked elevation of serum FSH is clearly indicative of an abnormality in spermatogenesis.