An AUA Best Practice Policy and ASRM Practice Committee Report

Report on Optimal Evaluation of the Infertile Male
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.

ISBN 0-9649702-7-9 (Volume 1) ISBN 09649702-6-0 (4 Volume set)
Introduction

Approximately 15% of couples are unable to conceive after one year of unprotected intercourse. A male factor is solely responsible in about 20% of infertile couples and contributory in another 30-40% (1). If a male infertility factor is present, it is almost always defined by the finding of an abnormal semen analysis, although other male factors may play a role even when the semen analysis is normal.

This review offers recommendations for the optimal diagnostic evaluation of the male partner of an infertile couple.
Male infertility can be due to a variety of conditions. Some of these conditions are identifiable and reversible, such as ductal obstruction and hypogonadotropic hypogonadism. Other conditions are identifiable but not reversible, such as bilateral testicular atrophy secondary to viral orchitis. When identification of the etiology of an abnormal semen analysis is not possible, as is the case in many patients, the condition is termed idiopathic. Rarely, patients with normal semen analyses have sperm that do not function in a manner necessary for fertility.

The purpose of the male evaluation is to identify these conditions when present. Identification and treatment of reversible conditions may improve the male’s fertility and allow for conception through intercourse. Even azoospermic patients may have active sperm production or could have sperm production induced with treatment. Detection of conditions for which there is no treatment will spare couples the distress of attempting ineffective therapies. Detection of certain genetic causes of male infertility allows couples to be informed about the potential to transmit genetic abnormalities that may affect the health of offspring. Thus, an appropriate male evaluation may allow the couple to better understand the basis of their infertility and to obtain genetic counseling when appropriate. If specific corrective treatment is not available, it still may be possible to employ assisted reproductive techniques such as testicular or epididymal sperm retrieval with intracytoplasmic sperm injection (ICSI). Alternatively, such couples may consider therapeutic donor insemination or adoption.

Finally, male infertility may occasionally be the presenting manifestation of an underlying life-threatening condition (2). Failure to identify diseases such as testicular cancer or pituitary tumors may have serious consequences, including, in rare cases, death.

The goals of the evaluation of the infertile male are to identify:
- potentially correctable conditions;
- irreversible conditions that are amenable to assisted reproductive techniques using the sperm of the male partner;
- irreversible conditions that are not amenable to the above, and for which donor insemination or adoption are possible options;
- life- or health-threatening conditions that may underlie the infertility and require medical attention; and
- genetic abnormalities that may affect the health of offspring if assisted reproductive techniques are to be employed.
When to do an evaluation for infertility

A couple attempting to conceive should have an evaluation for infertility if pregnancy fails to occur within one year of regular unprotected intercourse. An evaluation should be done before one year if 1) male infertility risk factors such as a history of bilateral cryptorchidism are known to be present; 2) female infertility risk factors, including advanced female age (over 35 years), are suspected; or 3) the couple questions the male partner’s fertility potential. In addition, men who question their fertility status despite the absence of a current partner should have an evaluation of their fertility potential. The initial screening evaluation of the male partner of an infertile couple should include, at a minimum, a reproductive history and two semen analyses. If possible, the two semen analyses should be separated by a time period of one month. The reproductive history should include 1) coital frequency and timing; 2) duration of infertility and prior fertility; 3) childhood illnesses and developmental history; 4) systemic medical illnesses (e.g., diabetes mellitus and upper respiratory diseases) and prior surgeries; 5) sexual history including sexually transmitted infections; and 6) gonadal toxin exposure including heat. The semen analyses should be conducted as described in the next section, ‘Components of a full evaluation of male infertility.’ While a man may have a history of previous fertility, this does not exclude the possibility that he has acquired a new, or secondary, male infertility factor. Men with secondary infertility should be evaluated in the same way as men who have never initiated a pregnancy (primary infertility).

**Recommendations:** An initial screening evaluation of the male partner of an infertile couple should be done if pregnancy has not occurred within one year of unprotected intercourse. An earlier evaluation may be warranted if a known male or female infertility risk factor exists or if a man questions his fertility potential. The initial evaluation for male factor infertility should include a reproductive history and two properly performed semen analyses.

A full evaluation by a urologist or other specialist in male reproduction should be done if the initial screening evaluation demonstrates an abnormal male reproductive history or an abnormal semen analysis. Further evaluation of the male partner should also be considered in couples with unexplained infertility and in couples in whom there is a treated female factor and persistent infertility.
The full evaluation for male infertility should include a complete medical and reproductive history, a physical examination by a urologist or other specialist in male reproduction, and at least two semen analyses. Based on the results of the full evaluation, the physician may recommend other procedures and tests to elucidate the etiology of a patient’s infertility. These tests may include additional semen analyses, endocrine evaluation, post-ejaculatory urinalysis, ultrasonography, specialized tests on semen and sperm, and genetic screening.

Required evaluation components for every patient

Medical history
The patient’s medical history is used to identify risk factors and behavior patterns that could have a significant impact on male infertility. The history should include all factors listed above for a reproductive history plus 1) a complete medical and surgical history; 2) medications (prescription and non-prescription) and allergies; 3) review of systems; 4) family reproductive history; and 5) a survey of past infections such as sexually transmitted diseases and respiratory infections.

Physical examination
A general physical examination is an integral part of the evaluation of male infertility. In addition to the general physical examination, particular focus should be given to the genitalia including 1) examination of the penis; including the location of the urethral meatus; 2) palpation of the testes and measurement of their size; 3) presence and consistency of both the vasa and epididymides; 4) presence of a varicocele; 5) secondary sex characteristics including body habitus, hair distribution and breast development; and 6) digital rectal exam. The diagnosis of congenital bilateral absence of the vasa deferentia (CBAVD) is established by physical examination. Scrotal exploration is not needed to make this diagnosis.

Semen analysis
Semen analysis is the cornerstone of the laboratory evaluation of the infertile male and helps to define the severity of the male factor. Methods of semen analysis are discussed in many textbooks, and detailed laboratory protocols have been published by the World Health Organization (WHO) (3). Physicians should provide patients with standard instructions for semen collection. These instructions should include a defined period of abstinence of two to three days. Semen can be collected by masturbation or by intercourse using special semen collection condoms that do not contain substances detrimental to sperm. The specimen may be collected at home or at the laboratory. The specimen should be kept at room or body temperature during transport and examined within one hour of collection. To ensure accurate results, the laboratory should have a quality control program for semen analysis, which conforms to the standards outlined in the Clinical Laboratory Improvement Amendments (CLIA). Information on these standards, which include proficiency testing, can be found at the CLIA web site (4).

The semen analysis provides information on semen volume as well as sperm concentration, motility and morphology. Azoospermia should not be diagnosed until the specimen is centrifuged at maximum speed (preferably 3000g) for 15 minutes, and the pellet is examined. Although the methods for routine measurement of sperm concentration and motility have changed little during the past two decades, sperm morphology assessment has evolved considerably. The current WHO criteria for scoring sperm morphology (3) are similar to the Kruger (Tygerberg) strict criteria, (5, 6) in that relatively few sperm are classified as having normal morphology, even in semen from fertile men. Sperm morphology assessment by strict criteria is used to identify couples who have a poor chance of fertilization with standard in vitro fertilization (IVF) (5) or a better chance of fertilization with ICSI (7). The WHO criteria of 1987 and 1992 (8,9), which classify more sperm in the normal category, are also widely used in the routine semen evaluation.

True reference ranges have not been established for semen parameters. The reference values in Table 1 are based on the clinical literature. Values that fall outside these ranges suggest a male infertility factor and indicate the need for additional clinical and/or laboratory evaluation of the patient. It must be emphasized that the reference values for semen parameters are not the same as the
Table 1 Semen Analysis: Reference Values

On at least two occasions:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejaculate volume</td>
<td>1.5-5.0 ml</td>
</tr>
<tr>
<td>pH</td>
<td>&gt;7.2</td>
</tr>
<tr>
<td>Sperm concentration</td>
<td>&gt;20 million/ml</td>
</tr>
<tr>
<td>Total sperm number</td>
<td>&gt;40 million/ejaculate</td>
</tr>
<tr>
<td>Percent motility</td>
<td>&gt;50%</td>
</tr>
<tr>
<td>Forward progression</td>
<td>&gt;2 (scale 0-4)</td>
</tr>
<tr>
<td>Normal morphology</td>
<td>&gt;50% normal*</td>
</tr>
<tr>
<td></td>
<td>&gt;30% normal**</td>
</tr>
<tr>
<td></td>
<td>&gt;14% normal***</td>
</tr>
</tbody>
</table>

And:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm agglutination</td>
<td>&lt; 2 (Scale 0-3)</td>
</tr>
<tr>
<td>Viscosity</td>
<td>&lt;3 (Scale 0-4)</td>
</tr>
</tbody>
</table>


Minimum values needed for conception, and that men with semen variables outside the reference ranges may be fertile. Conversely, patients with values within the reference range may still be infertile.

Recommendations: The minimum full evaluation for male infertility for every patient should include a complete medical history, physical examination by a urologist or other specialist in male reproduction and at least two semen analyses. Additional procedures and tests, used to elucidate problems discovered by the full evaluation, may be suggested later as well.

Other procedures and tests for assessing male fertility

Endocrine evaluation

Hormonal abnormalities of the hypothalamic-pituitary-testicular axis are well-recognized, though not common causes of male infertility. Endocrine disorders are extremely uncommon in men with normal semen parameters.

An endocrine evaluation should be performed if there is: 1) an abnormal semen analysis, especially if the sperm concentration is less than 10 million/ml; 2) impaired sexual function; or 3) other clinical findings suggestive of a specific endocrinopathy. Some experts believe that all infertile males should have an endocrine evaluation, but there is no consensus of opinion on this controversy. The minimum initial hormonal evaluation should consist of measurements of serum follicle-stimulating-hormone (FSH) and serum testosterone levels. If the testosterone level is low, a repeat measurement of total and free testosterone, as well as determination of serum luteinizing hormone (LH) and prolactin levels should be obtained. Although serum gonadotropin levels are variable because they are secreted in a pulsatile manner, a single measurement is usually sufficient to determine a patient’s clinical endocrine status. The relationship of testosterone, LH, FSH and prolactin helps to identify the clinical condition (see Table 2). 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.

Recommendation: An initial endocrine evaluation should include at least a serum testosterone and FSH. It should be performed if there is: 1) an abnormally low sperm concentration, especially if less than 10 million/ml; 2) impaired sexual function; or 3) other clinical findings suggestive of a specific endocrinopathy.
Table 2

<table>
<thead>
<tr>
<th>Clinical Condition</th>
<th>FSH</th>
<th>LH</th>
<th>Testosterone</th>
<th>Prolactin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal spermatogenesis</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Hypogonadotropic hypogonadism</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Abnormal spermatogenesis*</td>
<td>High/Normal</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Complete testicular failure/</td>
<td>High</td>
<td>High</td>
<td>Normal/Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Hypergonadotropic hypogonadism</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prolactin-secreting pituitary tumor</td>
<td>Normal/Low</td>
<td>Normal/Low</td>
<td>Low</td>
<td>High</td>
</tr>
</tbody>
</table>

* 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.

**Post-ejaculatory urinalysis**

Low-volume or absent ejaculate suggests retrograde ejaculation, lack of emission, ejaculatory duct obstruction, hypogonadism or CBAVD. In order to diagnose possible retrograde ejaculation, the physician should perform a post-ejaculatory urinalysis for any man whose ejaculate volume is less than 1.0 ml, and who has not been diagnosed with hypogonadism or CBAVD. It is also important to assure that improper or incomplete collection, or a very short abstinence period (less than 1 day) is not the cause of the low-volume ejaculate.

The post-ejaculatory urinalysis is performed by centrifuging the specimen for 10 minutes at a minimum of 300g, and microscopically inspecting the pellet at 400x magnification. The presence of any sperm in a post-ejaculatory urinalysis of a patient with azoospermia or aspermia is suggestive of the diagnosis of retrograde ejaculation. Significant numbers of sperm must be found in the urine of patients with low ejaculate volume oligospermia in order to suggest the diagnosis of retrograde ejaculation. Expert consensus on the definition of significant numbers of sperm in the urine does not exist.

**Recommendation:** A post-ejaculatory urinalysis should be performed in patients with ejaculate volumes of less than 1 ml, except in patients with bilateral vasal agenesis or clinical signs of hypogonadism.

**Ultrasoundography**

Transrectal ultrasonography Normal seminal vesicles are less than 1.5 cm in anteroposterior diameter (10). The finding of dilated seminal vesicles, dilated ejaculatory ducts and/or midline prostatic cystic structures on transrectal ultrasonography (TRUS) is suggestive of, but not diagnostic of, complete or partial ejaculatory duct obstruction (11). Patients with complete ejaculatory duct obstruction produce low-volume, fructose negative, acidic, azoospermic ejaculates. Patients with CBAVD may also have these findings because they often have absent or atrophic seminal vesicles. Patients with partial ejaculatory duct obstruction often, but not always, present with semen having low volume, oligoasthenospermia and poor forward progression. Some experts routinely recommend TRUS in oligospermic patients with low volume ejaculates, palpable vasa and normal testicular size.

Scrotal ultrasonography Most scrotal pathology is palpable on physical examination. This includes varicoceles, spermatoceles, absence of the vasa, epididymal induration and testicular masses. Scrotal ultrasonography may identify non-palpable varicoceles, but these have not been shown to be clinically significant. Scrotal ultrasonography may be useful to clarify ambiguous findings on examination, such as may occur in patients with testes that are in the upper scrotum, small scrotal sacs or other anatomy that makes physical examination of the scrotum difficult.

**Recommendation:** Scrotal ultrasonography is indicated in those patients in whom physical examination of the un...
Specialized clinical tests on semen and sperm

In some cases, semen analyses have failed to accurately predict a man’s fertility. Therefore, there has been a search for other tests to improve the evaluation of the infertile male. Generally, these specialized clinical tests should be reserved only for those cases in which identification of the cause of male infertility will direct treatment.

Quantitation of leukocytes in semen

An elevated number of white blood cells in the semen has been associated with deficiencies in sperm function and motility. Under wet mount microscopy, both leukocytes and immature germ cells appear similar and are properly termed “round cells.” Many laboratories improperly report all round cells as “white blood cells.” The clinician must make sure that the two types of cells are differentiated. A variety of assays are available to differentiate leukocytes from immature germ cells. These include traditional cytologic staining and immunohistochemical techniques (12). Those patients with true pyospermia (greater than 1 million leukocytes per ml) should be evaluated for a genital tract infection or inflammation.

Tests for antisperm antibodies

Pregnancy rates may be reduced by antisperm antibodies (ASA) in the semen (13). Risk factors for ASA include ductal obstruction, prior genital infection, testicular trauma and prior vasovasostomy or vasectomy. ASA testing should be considered when there is isolated asthenospermia with normal sperm concentration, sperm agglutination or an abnormal postcoital test. Many physicians recommend ASA testing for couples with unexplained infertility. ASA found on the surface of sperm by direct testing are more significant than ASA found in the serum or seminal plasma by indirect testing. ASA testing is not needed if sperm are to be used for ICSI.

Sperm viability tests

Sperm viability can be assessed by mixing fresh semen with a supravital dye such as eosin or trypan blue, or by the use of the hypooosmotic swelling (HOS) test (3). These assays determine whether non-motile but viable sperm, as determined by the HOS test, may be used successfully for ICSI.

Tests of sperm-cervical mucus interaction

The post-coital test is the microscopic examination of the cervical mucus, performed shortly before expected ovulation and within hours after intercourse, to identify the presence of motile sperm in the mucus. It is the traditional method for identifying cervical factors that contribute to infertility. Examination of the cervical mucus may reveal gross evidence of cervicitis that deserves treatment. However, abnormal cervical mucus or abnormal sperm/cervical mucus interaction is rarely the sole or principal cause of infertility. Furthermore, controversies exist regarding technique, timing and interpretation of this test. Results of the post-coital test are subjective and exhibit considerable intra- and inter-observer variation. Although its utility and predictive value have been seriously questioned (14), some practitioners still consider it a useful diagnostic test (15) because it may help to identify ineffective coital technique or a cervical factor not otherwise suspected on the basis of history and physical examination. Contemporary treatments for otherwise unexplained infertility, such as superovulation and intrauterine insemination or in vitro fertilization, effectively negate any unrecognized cervical factors. Routine postcoital testing is unnecessary. The test may be reserved for patients in whom results will influence treatment strategy.

Zona free hamster oocyte test

Removal of the zona pellucida from hamster oocytes allows human sperm to fuse with hamster ova. This test is often termed a sperm penetration assay (SPA). This test should also be reserved for patients in whom results will influence treatment strategy. For penetration to occur, sperm must undergo capacitation, the acrosome reaction, fusion with the oolemma and incorporation into the ooplasm. Many versions of the SPA have been used clinically (3,16), and the value of the test results depends, in part, on the experience of the laboratory performing the assay.
Computer-aided sperm analysis

Computer-aided sperm analysis (CASA) requires sophisticated instruments for quantitative assessment of sperm from a microscopic image or from videotape. In principle, CASA can be used to objectively measure sperm numbers, motility and morphology. CASA instruments are most useful clinically for assessing sperm motility and motion parameters, such as velocity or speed and head movement, which some believe may be important factors in determining sperm fertility potential.

**Recommendation:** Specialized tests on semen are not required for diagnosis of male infertility. They may be useful in a small number of patients for identifying a male factor contributing to unexplained infertility, or for selecting therapy, such as assisted reproductive technology.

Less commonly used specialized tests

In addition to the zona-free hamster oocyte tests, numerous tests of sperm function have been employed in research studies. The acrosome reaction of human sperm can be detected using specialized staining techniques. Rates of spontaneous acrosome reactions and acrosome reactions induced by agents such as calcium ionophore and progesterone have been measured. Samples from infertile men tend to demonstrate higher spontaneous acrosome reaction levels and lower levels in the presence of inducers (17). In addition, sperm function can be evaluated using human zona pellucida binding tests. In some cases, these tests have detected a probable cause for low fertilization rates or failed IVF (18). A number of biochemical tests of sperm function have been studied. These include measurements of sperm creatine kinase (19) and reactive oxygen species (ROS). ROS appear to be generated by both seminal leukocytes and sperm cells, and can interfere with sperm function by peroxidation of sperm lipid membranes and creation of toxic fatty acid peroxides (20).

**Recommendation:** Less commonly used specialized tests on semen are important investigative tools, but are not necessary for the routine evaluation of men with infertility.

Genetic screening

Genetic abnormalities may cause infertility by affecting sperm production or sperm transport. The three most common genetic factors known to be related to male infertility are: 1) cystic fibrosis gene mutations associated with congenital absence of the vas deferens; 2) chromosomal abnormalities resulting in impaired testicular function; and 3) Y-chromosome microdeletions associated with isolated spermatogenic impairment.

Azoospermia and severe oligospermia may be associated with genetic abnormalities. Men with non-obstructive azoospermia and severe oligospermia should be informed that they might have chromosomal abnormalities or Y-chromosome microdeletions. In addition, men with azoospermia due to CBAVD should be informed that they probably have an abnormality of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Genetic counseling should be provided whenever a genetic abnormality is detected.

Cystic fibrosis gene mutations

There is a strong association between CBAVD and mutations of the CFTR gene, which is located on chromosome 7 (21). Almost all male patients with clinical cystic fibrosis exhibit CBAVD. Conversely, approximately two-thirds of men with CBAVD have documented mutations of the CFTR gene. Failure to detect a CFTR abnormality in men with CBAVD does not rule out the presence of a mutation currently unidentifiable by routine testing methods. It should be assumed that a man with CBAVD harbors an abnormality in the CFTR gene. Therefore, it is important to test his partner prior to performing a treatment that utilizes his sperm, because of the risk that his partner may be a CF carrier.

In addition, azoospermia in men with congenital bilateral obstruction of the epididymides or with unilateral vasal agenesis may be associated with CFTR gene abnormalities. Therefore, genetic testing for CFTR gene abnormalities should be considered in these two patient populations.

**Karyotypic chromosomal abnormalities**

Chromosomal abnormalities that can be observed on karyotypes of peripheral leukocytes are present in about 7% of infertile men. The frequency of karyotypic abnormalities is inversely proportional to sperm count, with a prevalence of 10-15% in azoospermic men, approximately 5% in oligospermic men and less than 1% in normospermic men. Sex chromosomal aneuploidy...
(Klinefelter’s syndrome) accounts for about two-thirds of the chromosomal abnormalities observed in infertile men (22). Structural abnormalities of the autosomal chromosomes, such as inversions and translocations, are also observed at a higher frequency in infertile men than in the general population. When the male has gross karyotypic abnormalities, the couple is at increased risk for miscarriages and for having children with chromosomal and congenital defects. Karyotyping should be offered to men who have non-obstructive azoospermia or severe oligospermia prior to performing ICSI with their sperm.

Y-chromosome microdeletions

Microdeletions of sections of the Y chromosome may be found in 10-15 percent of men with azoospermia or severe oligospermia (23). These microdeletions are too small to be detected by standard karyotyping, but can be found by using the polymerase chain reaction to analyze sequence tagged sites that have been mapped along the entire length of the Y chromosome. Most deletions causing azoospermia or oligospermia occur in non-overlapping regions of the long arm of the Y chromosome (Yq11). These regions have been designated as AZFa (proximal), AZFb (central) and AZFc (distal). It appears that these regions, and possibly other regions of the Y chromosome, contain multiple genes necessary for spermatogenesis. The DAZ (deleted in azoospermia) gene, for example, which encodes a transcription factor usually present in men with normal fertility, is located in the AZFc region.

The specific location of the deletion along the Y chromosome may significantly affect spermatogenesis. If the deleted region of the Y chromosome is in the AZFc region, many patients will have sperm production that is sufficient to produce sperm in the ejaculate, albeit with severe oligospermia. Other patients with AZFc region deletions will be azoospermic but still may have sperm production, which is sufficient to allow sperm extraction by testis biopsy. However, the presence of a deletion involving the entire AZFb region appears to predict a very poor prognosis for sperm retrieval (24). Poor sperm retrieval may also result for men with deletions involving the AZFa region (25).

Sons of individuals with such a microdeletion would inherit the microdeletion and consequently may be infertile (26). Although a microdeletion of the Y chromosome is not thought to be associated with other health problems, few data exist on the phenotypes of the sons of fathers with such genetic abnormalities. It is important to note that a negative Y-chromosome microdeletion assay does not necessarily rule out a genetic abnormality, because there may be other, presently unknown, gene sequences on the Y or other chromosomes that might also be necessary for normal spermatogenesis. Conversely, it has been shown that some Y-chromosome microdeletions may be found in fertile or subfertile males who have fathered children (23,27). Y-chromosome analysis should be offered to men who have nonobstructive azoospermia or severe oligospermia prior to performing ICSI with their sperm.

Recommendations:

Genetic testing for CFTR mutations in the female partner should be offered before proceeding with treatments that utilize the sperm of men with CBAVD.

Men with non-obstructive azoospermia and severe oligospermia (less than 5-10 million sperm/ml) should be informed of the potential genetic abnormalities associated with azoospermia or severe oligospermia.

Karyotyping and Y-chromosome analysis should be offered to the male who has nonobstructive azoospermia or severe oligospermia prior to performing ICSI. Genetic counseling may be offered whenever a genetic abnormality is suspected in either the male or female partner and should be provided whenever a genetic abnormality is detected.
References

4. CLIA website: www.hcfa.gov/medicaid/clia/clia-home.htm
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 0-9649702-7-9 (Volume 1) ISBN 09649702-6-0 (4 Volume set)

This report is part of a series on male infertility. Other titles include: Report on Evaluation of the Azoospermic Male,

These reports can be viewed online at http://www.auanet.org

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