Guidelines

Diagnosis and Treatment of Infertility in Men: AUA/ASRM Guideline

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Guideline Amendment Summary [pdf]
Algorithm associated with this Guideline [pdf]

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SUMMARY

Purpose

Infertility is due in whole or in part to the male in approximately one-half of all infertile couples. Although many couples can achieve a pregnancy with– intrauterine insemination (IUI) and assisted reproductive technologies (ART) (in vitro fertilization [IVF] with or without intracytoplasmic sperm injection [ICSI]), evaluation of the male is important to most appropriately direct therapy. Some male factor conditions are treatable with medical or surgical therapy, and others may require donor sperm or adoption, if appropriate. Some conditions are life threatening, while others have health and genetic implications for the patient and potential offspring. A male evaluation is necessary to adequately design the management of the patient and the couple. Without an adequate male infertility workup, unnecessary costly, time-consuming, and invasive treatment might be pursued for the female partner.

The purpose of this Guideline is to outline the appropriate evaluation and management of the male partner in an infertile couple. Recommendations proceed from obtaining an appropriate history and physical exam (Appendix I), as well as diagnostic testing, where indicated. Medical therapies, surgical techniques, and use of IUI and ART are covered to allow for optimal patient management. Recommendations are based on a strict process of evaluation of published literature as discussed in the Methodology section. This process is based on the PICO question approach (Problem/Patient/Population, Intervention/Indicator, Comparison, and Outcome) as described in the Methodology section. In this Guideline, the term "male" is used to refer to biological or genetic men.

Methodology

The Emergency Care Research Institute (ECRI) Evidence-based Practice Center team searched PubMed®, EMBASE® (Excerpta Medica), and Medline from January 2000 through May 2019. An experienced medical librarian developed an individual search strategy for each individual key question using medical subject headings terms and key words appropriate for each question's PICO framework. When sufficient evidence existed, the body of evidence was assigned a strength rating of A (high), B (moderate), or C (low) for support of Strong, Moderate, or Conditional Recommendations. In the absence of sufficient evidence, additional information is provided as Clinical Principles and Expert Opinions. In 2023, the Male Infertility Guideline was updated through the AUA amendment process in which newly published literature is reviewed and integrated into previously published guidelines. ECRI's medical research librarian conducted literature searches of EMBASE (Excerpta Medica)/Medline and PubMed (PreMedline) from May 30, 2019, through August 30, 2023, yielding 4,093 new abstracts. ECRI's research analysts performed abstract screening and data extraction of 125 eligible study abstracts meeting inclusion criteria. There were 22 studies of interest that were included in the evidence base.

GUIDELINE STATEMENTS

Assessment

1. For initial infertility evaluation, clinicians should initiate concurrent assessment of both male and female partners. (*Expert Opinion*)

2. Clinicians should include a reproductive history during initial evaluation of the male for fertility. (*Clinical Principle*) Clinicians should also include one or more semen analyses (SAs) during initial evaluation of the male. (*Strong Recommendation; Evidence Level: Grade B*)

3. Male reproductive experts should evaluate patients with a complete history and physical examination as well as other directed tests, when indicated by one or more abnormal semen parameters or presumed male infertility. (*Expert Opinion*)

4. In couples with failed assisted reproductive technology cycles or recurrent pregnancy losses (RPL) (two or more), clinicians should evaluate the male partner. (*Moderate Recommendation; Evidence Level: Grade C*)

Lifestyle Factors and Relationships Between Infertility and General Health

5. Clinicians should counsel infertile males or males with abnormal semen parameters on the health risks associated with abnormal sperm production. (*Moderate Recommendation; Evidence Level: Grade B*)

6. For infertile males with specific, identifiable causes of male infertility, clinicians should inform the patient of relevant, associated health conditions. (*Moderate Recommendation; Evidence Level: Grade B*)

7. Clinicians should advise couples with advanced paternal age (≥40) that there is an increased risk of adverse health outcomes for their offspring. (*Expert Opinion*)

8. Clinicians may discuss risk factors (i.e., lifestyle, medication usage, environmental exposures, occupational exposures) associated with male infertility, and counsel the patients that the current data on the majority of risk factors are limited. (*Conditional Recommendation; Evidence Level: Grade C*)

Diagnosis/Assessment/Evaluation

9. Clinicians should use the results from the semen analysis to guide management of the patient. In general, results are of greatest clinical significance when multiple abnormalities are present. (*Expert Opinion*)

10. Clinicians should obtain hormonal evaluation including follicle-stimulating hormone (FSH) and testosterone for infertile males with impaired libido, erectile dysfunction, oligozoospermia or azoospermia, atrophic testes, or evidence of hormonal abnormality on physical evaluation. (*Expert Opinion*)

11. Clinicians should initially evaluate azoospermic males with physical exam, semen volume, semen pH, and serum follicle-stimulating hormone levels to differentiate genital tract obstruction from impaired sperm production. (*Expert Opinion*)

12. Clinicians should recommend karyotype testing for males with primary infertility and azoospermia or sperm concentration <5 million sperm/mL when accompanied by elevated follicle-stimulating hormone, testicular atrophy, or a diagnosis of impaired sperm production. (*Expert Opinion*)

13. Clinicians should recommend Y-chromosome microdeletion analysis for males with primary infertility and azoospermia or sperm concentration ≤1 million sperm/mL when accompanied by elevated follicle-stimulating hormone, testicular atrophy, or a diagnosis of impaired sperm production. (*Moderate Recommendation; Evidence Level: Grade B*)

14. Clinicians should recommend Cystic Fibrosis Transmembrane Conductance Regulator *(CFTR)* mutation carrier testing (including assessment of the 5T allele) in males with vasal agenesis or idiopathic obstructive azoospermia. (*Expert Opinion*)

15. For males who harbor a *CFTR* mutation or have absence of the vas deferens (unilateral or bilateral), clinicians should recommend genetic evaluation of the female partner. (*Expert Opinion*)

16. Clinicians should not recommend sperm deoxyribonucleic acid (DNA) fragmentation analysis in the initial evaluation of the infertile couple. (*Moderate Recommendation; Evidence Level: Grade C*)

17. In males with increased round cells on semen analysis (>1million/mL), clinicians should evaluate the patient further to differentiate white blood cells (pyospermia) from germ cells. (*Expert Opinion*)

18. In patients with pyospermia, clinicians should evaluate the patient for the presence of infection. (*Clinical Principle*)

19. Clinicians should not perform antisperm antibody (ASA) testing in the initial evaluation of male infertility. (*Expert Opinion*)

20. For couples with recurrent pregnancy loss, clinicians should evaluate the male partner with karyotype (*Expert Opinion*) and sperm DNA fragmentation. (*Moderate Recommendation; Evidence Level: Grade C*)

21. Clinicians should not routinely perform diagnostic testicular biopsy to differentiate between obstructive azoospermia and non-obstructive azoospermia (NOA). (*Expert Opinion*)

Imaging

22. Clinicians should not routinely perform scrotal ultrasound in the initial evaluation of the infertile male. (*Expert Opinion*)

23. Clinicians should not perform transrectal ultrasonography (TRUS) or pelvic magnetic resonance imaging (MRI) as part of the initial evaluation of the infertile male. Clinicians may recommend TRUS or pelvic MRI in males with semen analysis suggestive of ejaculatory duct obstruction (EDO) (i.e., acidic, azoospermic semen with volume <1.4mL, with normal serum T, palpable vas deferens). (*Expert Opinion*)

24. Clinicians should not routinely perform abdominal imaging for the sole indication of an isolated small or moderate right varicocele. (*Expert Opinion*)

25. Clinicians should recommend renal ultrasonography for patients with vasal agenesis to evaluate for renal abnormalities. (*Expert Opinion*)

Treatment

VARICOCELE REPAIR/VARICOCELECTOMY

26. Clinicians should consider surgical varicocelectomy in males attempting to conceive who have palpable varicocele(s), infertility, and abnormal semen parameters, except for azoospermic males. (*Moderate Recommendation; Evidence Level: Grade B*)

27. Clinicians should not recommend varicocelectomy for males with non-palpable varicoceles detected solely by imaging. (*Strong Recommendation; Evidence Level: Grade C*)

28. For males with clinical varicocele and non-obstructive azoospermia, clinicians should inform couples of the absence of definitive evidence supporting varicocele repair prior to surgical sperm retrieval with assisted reproductive technologies. (*Expert Opinion*)

SPERM RETRIEVAL

29. For males with non-obstructive azoospermia undergoing sperm retrieval, clinicians should perform a microdissection testicular sperm extraction (micro-TESE). (*Moderate Recommendation; Evidence Level: Grade C*)

30. In males undergoing surgical sperm retrieval by a clinician, intracytoplasmic sperm injection may be performed with fresh or cryopreserved sperm. (*Conditional Recommendation; Evidence Level: Grade C*)

31. In males with azoospermia due to obstruction undergoing surgical sperm retrieval, clinicians may extract sperm from either the testis or the epididymis. (*Conditional Recommendation; Evidence Level: Grade C*)

32. Clinicians may consider the utilization of testicular sperm in nonazoospermic males with an elevated sperm DNA Fragmentation Index (DFI). (*Clinical Principle*)

33. For males with aspermia, clinicians may perform surgical sperm extraction or induced ejaculation (sympathomimetics, vibratory stimulation or electroejaculation) depending on the patient's condition and clinician's experience. (*Expert Opinion*)

34. Clinicians may treat infertility associated with retrograde ejaculation (RE) with sympathomimetics (with or without alkalinization and/or urethral catheterization), induced ejaculation, or surgical sperm retrieval. (*Expert Opinion*)

OBSTRUCTIVE AZOOSPERMIA, INCLUDING POST-VASECTOMY INFERTILITY

35. Clinicians should counsel couples desiring conception after vasectomy that surgical reconstruction, surgical sperm retrieval, or both reconstruction and simultaneous sperm retrieval for cryopreservation are viable options. (*Moderate Recommendation; Evidence Level: Grade C*)

36. Clinicians should counsel males with vasal or epididymal obstructive azoospermia that microsurgical reconstruction may be successful in returning sperm to the ejaculate. (*Expert Opinion*)

37. For infertile males with ejaculatory duct obstruction, clinicians may consider transurethral resection of ejaculatory ducts (TURED) and/or surgical sperm extraction. (*Expert Opinion*)

MEDICAL AND NUTRACEUTICAL INTERVENTIONS FOR FERTILITY

38. Clinicians may manage male infertility with assisted reproductive technology. (*Expert Opinion*)

39. Clinicians may advise an infertile couple with a low total motile sperm count on repeated semen analyses that intrauterine insemination success rates may be reduced, and treatment with assisted reproductive technology (in vitro fertilization/intracytoplasmic sperm injection) may be considered. (*Expert Opinion*)

40. In a patient presenting with hypogonadotropic hypogonadism (HH), clinicians should evaluate the patient to determine the etiology of the disorder and treat based on diagnosis. (*Clinical Principle*)

41. Clinicians may use aromatase inhibitors (AIs), human chorionic gonadotropin (hCG), selective estrogen receptor modulators (SERMs), or a combination thereof for infertile males with low serum testosterone. (*Conditional Recommendation; Evidence Level: Grade C*)

42. For the male interested in current or future fertility, clinicians should not prescribe exogenous testosterone therapy. (*Clinical Principle*)

43. For the infertile male with hyperprolactinemia, clinicians should evaluate the patient for the etiology and treat accordingly. (*Expert Opinion*)

44. Clinicians should inform the male with idiopathic infertility that the use of selective estrogen receptor modulators has limited benefits relative to results of assisted reproductive technology. (*Expert Opinion*)

45. Clinicians should counsel patients that the benefits of supplements (e.g., antioxidants, vitamins) are of questionable clinical utility in treating male infertility. Existing data are inadequate to provide recommendation for specific agents to use for this purpose. (*Moderate Recommendation; Evidence Level: Grade B*)

46. For males with idiopathic infertility, clinicians may consider treatment using a follicle-stimulating hormone analogue with the aim of improving sperm concentration, pregnancy rate, and live birth rate. (*Conditional Recommendation; Evidence Level: Grade B*)

47. In patients with non-obstructive azoospermia, clinicians may inform the patient of the limited data supporting pharmacologic manipulation with selective estrogen receptor modulators, aromatase inhibitors, and gonadotropins prior to surgical intervention. (*Conditional Recommendation; Evidence Level: Grade C*)

GONADOTOXIC THERAPIES AND FERTILITY PRESERVATION

48. Clinicians should discuss the effects of gonadotoxic therapies and other cancer treatments on sperm production with patients prior to commencement of therapy. (*Moderate Recommendation: Evidence Level: Grade C*)

49. Clinicians should inform patients undergoing chemotherapy and/or radiation therapy to avoid initiating a pregnancy for a period of at least 12 months after completion of treatment. (*Expert Opinion*)

50. Clinicians should encourage males to bank sperm, preferably multiple specimens when possible, prior to commencement of gonadotoxic therapy or other cancer treatment that may affect fertility in males. (*Expert Opinion*)

51. Clinicians may inform patients that a semen analysis should be performed at least 12 months (and preferably 24 months) after completion of gonadotoxic therapies. (*Conditional Recommendation; Evidence Level: Grade C*)

52. Clinicians should inform patients undergoing a retroperitoneal lymph node dissection (RPLND) of the risk of aspermia or retrograde ejaculation. (*Clinical Principle*)

53. Clinicians should obtain a post-orgasmic urinalysis for males with aspermia after retroperitoneal lymph node dissection and reduced volume ejaculate who are interested in fertility. (*Clinical Principle*)

54. Clinicians should inform males seeking paternity who are persistently azoospermic after gonadotoxic therapies that microdissection testicular sperm extraction is a treatment option. (*Strong Recommendation; Evidence Level: Grade B*)

INTRODUCTION

The Diagnosis and Treatment of the Male Factor Couple

Approximately 15% of couples experience infertility, which is defined as the inability to conceive a pregnancy within 12 months when the female partner is <35 years old and within 6 months when the female partner is >35 years old. A male factor is solely responsible in about 20% of infertile couples and contributory in another 30% to 40%.[1] Despite these estimates, the true prevalence of male infertility is not clearly defined due to multiple factors including variations in definitions of infertility, differences in sources of data, and the populations studied.[2] Male factor infertility may be explained by an abnormal SA or by other sperm function defects, in the setting of a normal SA as well as functional m defects. This document offers guidance for the optimal diagnostic evaluation and management of the male partner o. 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 HH. Other conditions are identifiable and treatable but not reversible, such as bilateral testicular atrophy secondary to viral orchitis. Identification of the etiology of an abnormal SA is not possible in approximately 30% of males in which case this condition is termed idiopathic male infertility.[3] When the reason for infertility is not clear with a normal SA and partner evaluation the infertility is termed unexplained, which is found in up to approximately 25% of couples.[3] In some instances, patients with normal SAs have sperm that do not function in a manner necessary for fertility.

The overall goal of the male evaluation is to identify conditions that may affect management or health of the patient or their offspring. Identification and treatment of reversible conditions may improve the male's fertility and allow for conception through intercourse or through techniques, such as IUI or IVF, when those approaches would otherwise not be possible. Even azoospermic patients may have some degree of active sperm production within the testes or could have sperm production induced with treatment. Identification of conditions for which there is no treatment will spare couples the distress of attempting ineffective therapies and allow them to consider options, such as donor sperm or adoption, if appropriate. Male infertility is associated with other comorbidities including increased mortality, while advanced paternal age is associated with some adverse outcomes in offspring. In addition, male infertility may occasionally be the presenting manifestation of an underlying life-threatening condition.[4] Failure to identify diseases such as testicular cancer or pituitary tumors may have serious consequences, including, in rare cases, death. 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 and seek genetic counseling when appropriate. Thus, an appropriate male evaluation may allow the couple to better understand the basis and implications of their infertility.

In summary, the specific goals of the evaluation of the infertile male are to identify the following:

- potentially correctable conditions;
- irreversible conditions that are amenable to IUI and ART 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 or associated medical comorbidities that require medical attention; and
- genetic abnormalities or lifestyle and age factors that may affect the health of the male patient or of offspring particularly if ART are to be employed.

Definitions of Infertility and Treatment Success

A wide variety of professional and international health organizations have defined infertility in general and male infertility, specifically. Since the condition of infertility reflects the outcome of a couple's attempt to achieve a pregnancy, the most common definition of infertility is "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse".[5] The condition of infertility is categorized as a disease by the World Health Organization (WHO), the American Medical Association (AMA), and the American Society for Reproductive Medicine (ASRM).[6] Evaluation for infertility is also guided by female age and other factors, such as an abnormal male reproductive history (e.g., history of cryptorchidism, chemotherapy, pelvic/retroperitoneal surgery, other conditions that have been associated with male infertility). When such factors are present, male evaluation is indicated regardless of prior attempts to conceive. Infertility should be evaluated after 6 months of attempted conception when the female partner is 35 years of age or older.

Male infertility is typically diagnosed by one or more factors that may include abnormal semen quality or sperm functional parameters; anatomical, endocrine, genetic, functional, or immunological abnormalities of the male reproductive system (including chronic illness); or sexual conditions (e.g., erectile dysfunction) incompatible with the ability to deposit semen in the vagina. Primary male infertility refers to males who have never initiated a clinical pregnancy and meets the criteria of being classified as infertile, whereas secondary infertility refers to a couple where the male is unable to initiate a clinical pregnancy, but who had previously initiated a clinical pregnancy (with the same or different sexual partner). Some conditions may be more common in primary or secondary infertility. Evaluation of males with secondary infertility should include a focus on conditions or exposures that have developed or occurred after initiation of the earlier pregnancy(ies).

Assessment of tests and treatments for the male is challenging due to inconsistent endpoints and the observation tha many of these endpoints are dependent upon and measured from the female partner. Ideally, the endpoint for fertilit, trials should be "live birth (defined as any delivery of a live infant after 20 weeks of gestation) or cumulative live birth, defined as the live birth per women over a defined time period (or number of treatment cycles.)" This definition was

provided by the modified Consolidated Standards of Reporting Trials for Fertility, Improving the Reporting of Clinical Trials of Infertility Treatments.[7] However, due to the variety of confounding variables present in the female, it is difficult to control for many of the most important variables and still include sufficient male subjects in a clinical trial for pregnancy or birth to be a viable outcome measure.

To address this challenge, the majority of clinical trials addressing male fertility and infertility utilize surrogate outcome metrics, the most common being the SA. However, the high variability of SA parameters make them difficult to use in the determination of interventions for male reproduction.[5] Other outcome metrics with similar challenges include other types of sperm tests and ART outcomes such as fertilization, implantation, and pregnancy loss rates. All attempts to measure some aspect of sperm function lessens the confounder effect of a maternal outcome, yet all are also subject to their own limitations. Common terms used in semen analysis can be found in **Table 1**.

Table 1: Common Terms in Semen Analysis*

Term	Definition
Aspermia	Complete absence of semen in ejaculate, indicating the absence of seminal fluid production or blockage in the reproductive tract.
Azoospermia	Absence of spermatozoa in the semen, typically resulting from a blockage in the reproductive tract (obstructive azoospermia) or dysfunction in sperm production (non-obstructive azoospermia).
Oligozoospermia	Low sperm concentration in the semen.
Asthenozoospermia	Reduced sperm motility, where a significant portion of spermatozoa display sluggish or abnormal movement, impacting fertility.
Teratozoospermia	Abnormal sperm morphology, characterized by a high percentage of spermatozoa with morphological defects, potentially affecting fertility.
Normozoospermia	Normal semen parameters including sperm concentration, motility, morphology, and volume, indicating optimal fertility potential.
Retrograde Ejaculation	Condition where semen flows backward into the bladder instead of exiting through the urethra during ejaculation, leading to reduced fertility.
*** This table provides concise definitions for common terms used in semen analysis, facilitating understanding for researchers, clinicians, and individuals seeking information about male fertility assessment.[8,9]**	

Epidemiology

Most couples achieve a pregnancy in the first 3 to 6 months of attempted conception, with 75% of couples achieving a pregnancy after 6 months of trying.[10-13] In general, after one year of attempting to conceive, approximately 85% of couples will have achieved a pregnancy. After two full years of attempting to conceive, this statistic is increased to over 90% of couples.

Age of the female partner is the single most important factor when predicting the chances of conception for a couple. Fertility decreases by almost 50% in women in their late 30's compared to women in their 20's. In women under 35 years of age, infertility is considered present after 12 months of attempting to conceive. This duration is shortened to 6 months in women 35 years of age or older.[14,15]

The etiologic causes of infertility include both female and male factors. For women, these factors include ovulatory dysfunction, tubal factor, endometriosis, and uterine factors. For the woman, ovarian reserve is helpful in predicting her response to medications, but this is not an absolute predictor of fertility. In up to 60% of couples, a male factor is found as part of the etiology of the infertility.[16] In addition, approximately 25% of couples will have unexplained infertility.

RPL is a disease that is distinct from infertility and is defined as two or more failed pregnancies.[6] The workup of RPL yields an etiology in only approximately 50% of couples as most pregnancy losses are related to abnormalities within the fetus itself. The risk of pregnancy loss after two losses is at least 25% depending on the age of the woman. After three consecutive losses, this risk increases to almost 50%. Etiologic causes of recurrent pregnancy losses include genetic causes (e.g., chromosomal translocations), anatomic abnormalities of the female uterus (e.g., septum, submucosal fibroids, adhesions), infections, hematologic and immunologic disorders of the female partner, female partner endocrine issue , thyroid and diabetes), and male factor issues.[17-19] In general, for males, the common identified etiologic issues include karyotypic abnormalities and sperm DNA fragmentation.

Methodology

PANEL FORMATION

The Male Infertility Panel was created in 2017 by the American Urological Association Education and Research, Inc. (AUAER) and ASRM. The AUA Practice Guidelines Committee (PGC) selected the Panel Chairs, who in turn appointed the additional panel members based on specific expertise in this area. The Panel included specialties from urology, andrology, endocrinology, and obstetrics & gynecology. There was also a patient advocate representative from RESOLVE: The National Infertility Association. The Male Infertility Amendment Panel was created in 2023 by the AUA to review new literature and provide updates herein. The Panel received no remuneration for their work.

SEARCHES AND ARTICLE SELECTION

The Emergency Care Research Institute (ECRI) Evidence-based Practice Center team searched PubMed®, Embase®, and Medline from January 2000 through May 2019. An experienced medical librarian developed an individual search strategy for each individual key question using medical subject headings terms and key words appropriate for each question's PICO framework. Search strategies were reviewed by one of the project methodologists. The evidence review team also reviewed relevant systematic reviews and references provided by the Panel to identify articles that may have been missed by the database searches. In 2023, the Male Infertility Guideline was updated through the AUA amendment process in which newly published literature is reviewed and integrated into previously published guidelines. ECRI's medical research librarian conducted literature searches of EMBASE (Excerpta Medica)/Medline and PubMed (PreMedline) from May 30, 2019, through August 30, 2023, yielding 4,093 new abstracts. ECRI's research analysts performed abstract screening and data extraction of 125 eligible study abstracts meeting inclusion criteria.

DATA ABSTRACTIONS

Study selection was based on predefined eligibility criteria for the patient populations, interventions, outcomes, and study designs of interest. Two reviewers independently screened abstracts and full text for inclusion. Conflicts between reviewers regarding eligibility of a given study were resolved through consensus.

Reviewers extracted information on study characteristics, participants, interventions, and outcomes. One reviewer completed data abstraction for each included study.

Members of the AUA Male Infertility Guideline Amendment Panel met with ECRI research analysts in July 2023 to review the recommendation statements from the 2020 Guideline. The Panel identified clinical recommendations for which they asked ECRI to perform an updated search to assess newly retrieved abstracts to inform possible updating of the recommendations. ECRI research analysts mapped the clinical recommendations of interest to the key questions in the systematic review to which they pertained.

RISK OF BIAS ASSESSMENT

One reviewer independently assessed risk of bias (ROB) for individual studies. The Cochrane Collaboration's tool was used for assessing the risk of bias of randomized controlled trials (RCTs).[20] For non-randomized studies of treatment interventions, the reviewers used appropriate items from the Cochrane Risk of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI). For diagnostic studies, reviewers used the quality assessment tool for diagnostic accuracy studies (QUADAS -2).[21] Single-arm studies were assessed by the following domains: prospective or retrospective design, consecutive/non-consecutive enrollment, incomplete outcome data, selective outcome reporting, and any other potential sources of bias. For systematic reviews, ROB was assigned based on the study authors' quality assessment of the individual studies included in the review. If such an assessment was not provided, ECRI analysts assigned a ROB rating based on the author description of the selected literature base and the designs of the included studies. The evidence review team graded strength of evidence on outcomes by adapting the AUA's three predefined levels of strength of evidence.

DETERMINATION OF EVIDENCE STRENGTH

The AUA employs a 3-tiered strength of evidence system to underpin evidence-based guideline statements. Table 2 summarizes the GRADE categories, definitions, and how these categories translate to the AUA strength of evidence categories. In short, high certainty by GRADE translates to AUA A-category strength of evidence, moderate to B, and both low and very low to C.

The categorization of evidence strength is conceptually distinct from the quality of individual studies. Evidence strength refers to the body of evidence available for a particular question and includes not only the quality of individual studies consideration of study design; consistency of findings across studies; adequacy of sample sizes; and generalizability of populations, settings, and interventions for the purposes of the Guideline. The AUA categorizes body of evidence strength as Grade A (well-conducted and highly-generalizable RCTs or exceptionally strong observational studies with consistent

findings), Grade B (RCTs with some weaknesses of procedure or generalizability or moderately strong observational studies with consistent findings), or Grade C (RCTs with serious deficiencies of procedure or generalizability or extremely small sample sizes or observational studies that are inconsistent, have small sample sizes, or have other problems that potentially confound interpretation of data). By definition, Grade A evidence has a high level of certainty, Grade B evidence has a moderate level of certainty, and Grade C evidence has a low level of certainty.[22]

Table 2: Strength of Evidence Definitions

AUA Strength of Evidence Category	GRADE Certainty Rating	Definition
A	High	• Very confident that the true effect lies close to that of the estimate of the effect
B	Moderate	• Moderately confident in the effect estimate • The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
C	Low	• Confidence in the effect estimate is limited • The true effect may be substantially different from the estimate of the effect
	Very Low	• Very little confidence in the effect estimate • The true effect is likely to be substantially different from the estimate of effect

AUA NOMENCLATURE: LINKING STATEMENT TYPE TO EVIDENCE STRENGTH

The AUA nomenclature system explicitly links statement type to body of evidence strength, level of certainty, magnitude of benefit or risk/burdens, and the Panel's judgment regarding the balance between benefits and risks/burdens (Table 3). ***Strong Recommendations*** are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is substantial. ***Moderate Recommendations*** are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is moderate. ***Conditional Recommendations*** are non-directive statements used when the evidence indicates there is no apparent net benefit or harm or when the balance between benefits and risks/burden is unclear. All three statement types may be supported by any body of evidence strength grade. Body of evidence strength Grade A in support of a Strong or Moderate Recommendation indicates the statement can be applied to most patients in most circumstances and that future research is *unlikely to change confidence*. Body of evidence strength Grade B in support of a Strong or Moderate Recommendation indicates the statement can be applied to most patients in most circumstances, but better evidence *could change confidence*. Body of evidence strength Grade C in support of a Strong or Moderate Recommendation indicates the statement can be applied to most patients in most circumstances, but better evidence is *likely to change confidence*. Conditional Recommendations can also be supported by any evidence strength. When body of evidence strength is Grade A, the statement indicates benefits and risks/burdens appear balanced, the best action depends on patient circumstances, and future research is *unlikely to change confidence*. When body of evidence strength Grade B is used, benefits and risks/burdens appear balanced, the best action also depends on individual patient circumstances, and better evidence *could change confidence*. When body of evidence strength Grade C is used, there is uncertainty regarding the balance between benefits and risks/burdens, alternative strategies may be equally reasonable, and better evidence is *likely to change confidence*.

Where gaps in the evidence existed, Clinical Principles or Expert Opinions are provided via consensus of the Panel. A Clinical Principle is a statement about a component of clinical care widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature. Expert Opinion refers to a statement based on members' clinical training, experience, knowledge, and judgment for which there may or may not be evidence in the medical literature.

Table 3: AUA Nomenclature Linking Statement Type to Level of Certainty, Magnitude of Benefit or Risk/Burden, and Body of Evidence Strength

Evidence Grade	Evidence Strength A (High Certainty)	Evidence Strength B (Moderate Certainty)	Evidence Strength C (Low Certainty)
Strong Recommendation (Net benefit or harm substantial)	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is substantial -Applies to most patients in most circumstances and future research is unlikely to change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is substantial -Applies to most patients in most circumstances but better evidence could change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) appears substantial -Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)
Moderate Recommendation (Net benefit or harm moderate)	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is moderate -Applies to most patients in most circumstances and future research is unlikely to change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) is moderate -Applies to most patients in most circumstances but better evidence could change confidence	-Benefits > Risks/Burdens (or vice versa) -Net benefit (or net harm) appears moderate -Applies to most patients in most circumstances but better evidence is likely to change confidence
Conditional Recommendation (Net benefit or harm comparable to other options)	-Benefits=Risks/Burdens -Best action depends on individual patient circumstances -Future Research is unlikely to change confidence	-Benefits= Risks/Burdens -Best action appears to depend on individual patient circumstances -Better evidence could change confidence	-Balance between Benefits & Risks/Burdens unclear -Net benefit (or net harm) comparable to other options -Alternative strategies may be equally reasonable -Better evidence likely to change confidence
Clinical Principle	a statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature		
Expert Opinion	a statement, achieved by consensus of the Panel, that is based on members' clinical training, experience, knowledge, and judgment for which there may or may not be evidence in the medical literature		

PEER REVIEW AND DOCUMENT APPROVAL

An integral part of the Guideline development process at the AUA is external peer review. The AUA conducted a thorough peer review process to ensure that the document was reviewed by experts in the diagnosis and treatment of male infertility. In addition to reviewers from the AUA PGC, Science and Quality Council (SQC), and Board of Directors (BOD), the document was reviewed by representatives from ASRM, as well as external content experts. Additionally, a call for reviewers was placed on the AUA website from January 8-15, 2020 to allow any further interested parties to request a copy of the document for review. The Guideline was also sent to the Urology Care Foundation to open the document further to the patient perspective. The draft Guideline document was distributed to 114 peer reviewers. All peer review comments were blinded and sent to the Panel for review. In total, 49 reviewers provided comments, including 24 external reviewers. At the end of the peer review process, a total of 997 comments were received. Following comment discussion, the Panel revised the draft as needed. Once finalized, the Guideline was submitted for approval to the AUA PGC, SQC, and BOD for final approval. The document was also approved by the ASRM CEO Ricardo Azziz, MD, MPH, MBA, on behalf of the Board and advised by the Practice Committee.

In 2024, as a part of the amendment process, the AUA conducted a thorough peer review process. A call for peer reviewers was posted on March 5th, 2024 and the draft Guideline document was distributed to 111 peer reviewers, 51 of which submitted comments. The Amendment Panel reviewed and discussed all submitted comments and revised the draft a needed. Once finalized, the Guideline was submitted for approval to the PGC and SQC as well as representatives from ASRM. It was then submitted to AUA BODs for final approval.

GUIDELINE STATEMENTS

Assessment

GUIDELINE STATEMENT 1

For initial infertility evaluation, clinicians should initiate concurrent assessment of both male and female partners. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 2

Clinicians should include a reproductive history during initial evaluation of the male for fertility. (***Clinical Principle***)
Clinicians should also include one or more semen analyses during initial evaluation of the male. (***Strong Recommendation; Evidence Level: Grade B***)

Discussion

GUIDELINE STATEMENT 3

Male reproductive experts should evaluate patients with a complete history and physical examination as well as other directed tests, when indicated by one or more abnormal semen parameters or presumed male infertility. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 4

In couples with failed assisted reproductive technology cycles or recurrent pregnancy losses (two or more), clinicians should evaluate the male partner. (***Moderate Recommendation; Evidence Level: Grade C***)

Discussion

Lifestyle Factors and Relationships Between Infertility and General Health

GUIDELINE STATEMENT 5

Clinicians should counsel infertile males or males with abnormal semen parameters on the health risks associated with abnormal sperm production. (***Moderate Recommendation; Evidence Level: Grade B***)

Discussion

GUIDELINE STATEMENT 6

For infertile males with specific, identifiable causes of male infertility, clinicians should inform the patient of relevant, associated health conditions. (***Moderate Recommendation; Evidence Level: Grade B***)

Discussion

GUIDELINE STATEMENT 7

Clinicians should advise couples with advanced paternal age (≥40) that there is an increased risk of adverse health outcomes for their offspring. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 8

Clinicians may discuss risk factors (i.e., lifestyle, medication usage, environmental exposures, occupational exposures) associated with male infertility, and counsel the patients that the current data on the majority of risk factors are limited. (***Conditional Recommendation; Evidence Level: Grade C***)

Discussion

Diagnosis and Evaluation

GUIDELINE STATEMENT 9

Clinicians should use the results from the semen analysis to guide management of the patient. In general, results are of greatest clinical significance when multiple abnormalities are present. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 10

Clinicians should obtain hormonal evaluation including follicle-stimulating hormone and testosterone for infertile males with impaired libido, erectile dysfunction, oligozoospermia or azoospermia, atrophic testes, or evidence of hormonal abnormality on physical evaluation. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 11

Clinicians should initially evaluate azoospermic males with physical exam, semen volume, semen pH, and serum follicle-stimulating hormone levels to differentiate genital tract obstruction from impaired sperm production. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 12

Clinicians should recommend karyotype testing for males with primary infertility and azoospermia or sperm concentration <5 million sperm/mL when accompanied by elevated follicle-stimulating hormone, testicular atrophy, or a diagnosis of impaired sperm production. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 13

Clinicians should recommend Y-chromosome microdeletion analysis for males with primary infertility and azoospermia or sperm concentration ≤1 million sperm/mL when accompanied by elevated follicle-stimulating hormone, testicular atrophy, or a diagnosis of impaired sperm production. (***Moderate Recommendation; Evidence Level: Grade B***)

Discussion

GUIDELINE STATEMENT 14

Clinicians should recommend Cystic Fibrosis Transmembrane Conductance Regulator ***(CFTR)*** mutation carrier testing (including assessment of the 5-thymidine [5T] allele) in males with vasal agenesis or idiopathic obstructive azoospermia. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 15

For males who harbor a ***CFTR*** mutation or have absence of the vas deferens (unilateral or bilateral), clinicians should recommend genetic evaluation of the female partner. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 16

Clinicians should not recommend sperm DNA fragmentation analysis in the initial evaluation of the infertile couple. (***Moderate Recommendation; Evidence Level: Grade C***)

Discussion

GUIDELINE STATEMENT 17

In males with increased round cells on semen analysis (>1 million/mL), clinicians should evaluate the patient further to differentiate white blood cells (pyospermia) from germ cells. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 18

In patients with pyospermia, clinicians should evaluate the patient for the presence of infection. (***Clinical Principle***)

Discussion

GUIDELINE STATEMENT 19

Clinicians should not perform antisperm antibody (ASA) testing in the initial evaluation of male infertility. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 20

For couples with recurrent pregnancy loss (RPL), clinicians should evaluate the male partner with karyotype (***Expert Opinion***) and sperm DNA fragmentation. (***Moderate Recommendation; Evidence Level: Grade C***)

Discussion

GUIDELINE STATEMENT 21

Clinicians should not routinely perform diagnostic testicular biopsy to differentiate between obstructive azoospermia non-obstructive azoospermia (NOA). (***Expert Opinion***)

Discussion

Imaging

GUIDELINE STATEMENT 22

Clinicians should not routinely perform scrotal ultrasound in the initial evaluation of the infertile male. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 23

Clinicians should not perform transrectal ultrasonography (TRUS) or pelvic MRI as part of the initial evaluation of the infertile male. Clinicians may recommend TRUS or pelvic MRI in males with SA suggestive of ejaculatory duct obstruction (EDO) (i.e., acidic, azoospermic semen with volume <1.4 mL, with normal serum T, palpable vas deferens). (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 24

Clinicians should not routinely perform abdominal imaging for the sole indication of an isolated small or moderate right varicocele. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 25

Clinicians should recommend renal ultrasonography for patients with vasal agenesis to evaluate for renal abnormalities. (***Expert Opinion***)

Discussion

Treatment

VARICOCELE REPAIR/VARICOCELECTOMY

GUIDELINE STATEMENT 26

Clinicians should consider surgical varicocelectomy in males attempting to conceive who have palpable varicocele(s), infertility, and abnormal semen parameters, except for azoospermic males. (***Moderate Recommendation; Evidence Level: Grade B***)

Discussion

GUIDELINE STATEMENT 27

Clinicians should not recommend varicocelectomy for males with non-palpable varicoceles detected solely by imaging. (***Strong Recommendation; Evidence Level: Grade C***)

Discussion

GUIDELINE STATEMENT 28

For males with clinical varicocele and non-obstructive azoospermia (NOA), clinicians should inform couples of the absence of definitive evidence supporting varicocele repair prior to surgical sperm retrieval with assisted reproductive technologies. (***Expert Opinion***)

Discussion

SPERM RETRIEVAL

GUIDELINE STATEMENT 29

For males with non-obstructive azoospermia undergoing sperm retrieval, clinicians should perform a microdissection testicular sperm extraction. (***Moderate Recommendation; Evidence Level: Grade C***)

Discussion

GUIDELINE STATEMENT 30

In males undergoing surgical sperm retrieval by a clinician, intracytoplasmic sperm injection may be performed with fresh or cryopreserved sperm. (***Conditional Recommendation; Evidence Level: Grade C***)

Discussion

GUIDELINE STATEMENT 31

In males with azoospermia due to obstruction undergoing surgical sperm retrieval, clinicians may extract sperm from either the testis or the epididymis. (***Conditional Recommendation; Evidence Level: Grade C***)

Discussion

GUIDELINE STATEMENT 32

Clinicians may consider the utilization of testicular sperm in nonazoospermic males with an elevated sperm DNA Fragmentation Index. (***Clinical Principle***)

Discussion

GUIDELINE STATEMENT 33

For males with aspermia, clinicians may perform surgical sperm extraction or induced ejaculation (sympathomimetics, vibratory stimulation or electroejaculation) depending on the patient's condition and clinician's experience. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 34

Clinicians may treat infertility associated with retrograde ejaculation with sympathomimetics (with or without alkalinization and/or urethral catheterization), induced ejaculation, or surgical sperm retrieval. (***Expert Opinion***)

Discussion

OBSTRUCTIVE AZOOSPERMIA, INCLUDING POST-VASECTOMY INFERTILITY

GUIDELINE STATEMENT 35

Clinicians should counsel couples desiring conception after vasectomy that surgical reconstruction, surgical sperm retrieval, or both reconstruction and simultaneous sperm retrieval for cryopreservation are viable options. (***Moderate Recommendation; Evidence Level: Grade C***)

Discussion

GUIDELINE STATEMENT 36

Clinicians should counsel males with vasal or epididymal obstructive azoospermia that microsurgical reconstruction may be successful in returning sperm to the ejaculate. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 37

For infertile males with ejaculatory duct obstruction, clinicians may consider transurethral resection of ejaculatory ducts (TURED) and/or surgical sperm extraction. (***Expert Opinion***)

Discussion

MEDICAL AND NUTRACEUTICAL INTERVENTIONS FOR FERTILITY

GUIDELINE STATEMENT 38

Clinicians may manage male infertility with assisted reproductive technologies. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 39

Clinicians may advise an infertile couple with a low total motile sperm count on repeated semen analyses that intrauterine insemination success rates may be reduced, and treatment with assisted reproductive technologies (in vitro fertilization with intracytoplasmic sperm injection) may be considered. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 40

In a patient presenting with hypogonadotropic hypogonadism, clinicians should evaluate the patient to determine the etiology of the disorder and treat based on diagnosis. (***Clinical Principle***)

Discussion

GUIDELINE STATEMENT 41

Clinicians may use aromatase inhibitors, human chorionic gonadotropin, selective estrogen receptor modulators, or a combination thereof for infertile males with low serum testosterone. (***Conditional Recommendation; Evidence Leve Grade C***)

Discussion

GUIDELINE STATEMENT 42

For the male interested in current or future fertility, clinicians should not prescribe exogenous testosterone therapy. (***Clinical Principle***)

Discussion

GUIDELINE STATEMENT 43

For the infertile male with hyperprolactinemia, clinicians should evaluate the patient for the etiology and treat accordingly. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 44

Clinicians should inform the male with idiopathic infertility that the use of selective estrogen receptor modulators has limited benefits relative to results of assisted reproductive technologies. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 45

Clinicians should counsel patients that the benefits of supplements (e.g., antioxidants, vitamins) are of questionable clinical utility in treating male infertility. Existing data are inadequate to provide recommendation for specific agents to use for this purpose. (***Moderate Recommendation; Evidence Level: Grade B***)

Discussion

GUIDELINE STATEMENT 46

For males with idiopathic infertility, clinicians may consider treatment using a follicle-stimulating hormone analogue with the aim of improving sperm concentration, pregnancy rate, and live birth rate. (***Conditional Recommendation; Evidence Level: Grade B***)

Discussion

GUIDELINE STATEMENT 47

In patients with non-obstructive azoospermia, clinicians may inform the patient of the limited data supporting pharmacologic manipulation with selective estrogen receptor modulators, aromatase inhibitors, and gonadotropins prior to surgical intervention. (***Conditional Recommendation; Evidence Level: Grade C***)

Discussion

GONADOTOXIC THERAPIES AND FERTILITY PRESERVATION

GUIDELINE STATEMENT 48

Clinicians should discuss the effects of gonadotoxic therapies and other cancer treatments on sperm production with patients prior to commencement of therapy. (***Moderate Recommendation: Evidence Level: Grade C***)

Discussion

GUIDELINE STATEMENT 49

Clinicians should inform patients undergoing chemotherapy and/or radiation therapy to avoid initiating a pregnancy for a period of at least 12 months after completion of treatment. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 50

Clinicians should encourage males to bank sperm, preferably multiple specimens when possible, prior to commencement of gonadotoxic therapy or other cancer treatment that may affect fertility in males. (***Expert Opinion***)

Discussion

GUIDELINE STATEMENT 51

Clinicians may inform patients that a semen analysis should be performed at least 12 months (and preferably 24 months) after completion of gonadotoxic therapies. (***Conditional Recommendation; Evidence Level: Grade C***)

Discussion

GUIDELINE STATEMENT 52

Clinicians should inform patients undergoing a retroperitoneal lymph node dissection of the risk of aspermia or retrograde ejaculation. (***Clinical Principle***)

Discussion

GUIDELINE STATEMENT 53

Clinicians should obtain a post-orgasmic urinalysis for males with aspermia after retroperitoneal lymph node dissection and reduced volume ejaculate who are interested in fertility. (***Clinical Principle***)

Discussion

GUIDELINE STATEMENT 54

Clinicians should inform males seeking paternity who are persistently azoospermic after gonadotoxic therapies that microdissection testicular sperm extraction is a treatment option. (***Strong Recommendation; Evidence Level: Grade B***)

Discussion

FUTURE DIRECTIONS

Newer research techniques, such as next generation sequencing (whole exome and whole genome sequencing) and "-omic" technologies have been applied to better identify underlying defects that may explain infertility in males. As the mechanisms of action of these genetic, genomic, epigenetic, transcriptomic, proteomic, metabolomic defects are defined, we will have further defined the etiologies of the majority of causes of male infertility. For example, damaging mutations and copy number variants (microdeletions and microduplications) may affect reproductive system development[336-340] and

function[341-343] as well as fetal, childhood, adolescent and/or adult development and/or function of other organ systems in the body. Indeed, GeneCards[344] lists >3,600 gene defects associated with human male infertility and another 3,200+ genes associated with genitourinary birth defects causing abnormal male reproductive development and function. This knowledge will improve clinical diagnosis and treatment.

The potential impact of these genetic findings is in the area of genetic and genomic-based spermiogenesis defects causing teratozoospermia and/or asthenozoospermia (multiple abnormalities of the sperm flagella and primary ciliary dyskinesia). Today, this knowledge is used clinically to counsel patients about their chances for successful ART.[345, 346] As many of these "infertility" genes are expressed in select other tissues or even broadly throughout the body, infertility may be the "canary in the coal mine" that portends an increased likelihood of other comorbidities. Given the wide range of types of genes required for fertility,[347-349] it is not surprising that male infertility is associated with other health conditions, such as mortality, malignancies, immune dysfunction, and other non-reproductive disorders.

The impact of certain lifestyles and behaviors remains relatively unknown. For example, vaping and cannabis use are highly prevalent among young adults, but the precise short- and long-term effects of these agents on reproductive health remain unclear.[350-353] While obesity and metabolic syndrome can impair male fertility via numerous pathophysiological mechanisms, the ability to restore reproductive potential through weight loss and enhanced metabolic health remains understudied. The emergence of the agonists of glucagon-like peptide-1 receptors (GLP-1 AR) class of drugs are proving to be highly efficacious in treating obesity and type 2 diabetes; the effect of these therapies on reproductive health remains to be determined.

Therapeutic advances for male infertility (except for surgical approaches for obstructive azoospermia and NOA) remain relatively stagnant. However, in the laboratory, novel methods are under development to effectively use spermatogonial stem cells to rejuvenate spermatogenesis after gonadotoxin exposures (such as chemotherapy),[354] although potential contamination of spermatogonial stem cells with malignant cells, which must be eliminated before autotransplantation, remain a concern.

Approaches using organ cultures and in vitro systems for spermatogenesis offer additional promise for the treatment of some forms of spermatogenic failure. Qualitative but not quantitative spermatogenesis has been achieved in vitro culminating in live offspring in rodents. With knowledge of the delicate microenvironment needed for completion of spermatogenesis in vitro, researchers are moving closer to achieving this goal, while still maintaining the genetic, genomic, and epigenomic integrity of the sperm.[355]

Finally, gene therapy approaches targeting the process of spermatogenesis, are advantageous because of the continuous production of sperm throughout the adult lifespan. However, whether germline gene therapy in humans should occur is an ethical question. Questions about whether germline genome editing should be done even for genetic disorders and technical considerations remain problematic.[356] Genome editing can result in off-target effects and mosaicism.

In closing, the genomic revolution has placed us at the forefront of vastly improving our diagnostic abilities to define precise etiologies, co-morbidities, and eventually (perhaps) develop medically-based treatments for infertile males to improve not only their fertility potential, but also their overall health. Translation of the newer advances discussed above will be slower but will eventually move from the laboratory to the clinical arena to provide more therapeutic options for males. The future looks promising for improving the health and fertility of the infertile male through precision medicine and the application of advanced technologies.

Tools & Resources

Urology Care FOUNDATION® PATIENT EDUCATION

Male Infertility Web Article

APPENDICES

Appendix I: Male Reproductive Health Physical Examination

The goal of the physical examination is to identify potential etiologies of reproductive impairments, health ailments, or factors that can be optimized to improve health or reproductive success.

General	• Body habitus as overweight obesity is associated with impaired spermatogenesis. • Virilization to assess pubertal development/androgen status • Gynecomastia may be a marker for endocrine disorders
Abdominal exam	• Examination of any scars from prior surgical procedures that may involve the pelvis or impact the urogenital system.
Phallus	• Meatal location as hypospadias/epispadias may make semen deposition in the vagina challenging • Penile plaque as Peyronie's disease may make vaginal intercourse difficult • Penile lesions/ulcers/discharge may be a sign of sexually transmitted infection
Scrotum/Testes	• Examination for prior scars suggesting prior scrotal surgery/trauma • Location as scrotal position of the testes is important for normal function • Size/consistency/contours as a majority of the testis is devoted to spermatogenesis. The exam may also reveal masses consistent with a testicular cancer
Epididymides	• Shape/consistency as normal development should be identified to determine atresia that could be identified by the presence of a *CFTR* mutation. Induration/dilation could suggest obstruction. Epididymal cysts or spermatoceles may also lead to obstruction.
Vas Deferens	• Shape/consistency as normal development and contour should be confirmed to rule out agenesis as may be seen in the presence of a *CFTR* mutation or aberrant Wolffian duct embryogenesis • The presence/location of any vasectomy defect or granuloma should also be assessed
Digital Rectal Examination	• Midline prostatic cysts or dilated seminal vesicles may assist in the diagnosis of EDO

ABBREVIATIONS

ABVD	Adriamycin, Bleomycin, Vinblastine, and Dacarbazine
ACOG	American College of Obstetricians and Gynecologists
AMA	American Medical Association
ASCO	American Society of Clinical Oncology
ASRM	American Society for Reproductive Medicine

AUA	American Urological Association
AUAER	American Urological Association Education and Research, Inc.
ASA	Antisperm Antibody
AIs	Aromatase Inhibitors
ART	Assisted Reproductive Technology
AZF	Azoospermia Factor
BOD	Board of Directors
BPA	Bisphenol A
CVD	Cardiovascular Disease
CCI	Charlson Comorbidity Index
CBAVD	Congenital Bilateral Absence of the Vas Deferens
CF	Cystic Fibrosis
CFTR	Cystic Fibrosis Transmembrane Conductance Regulator
DNA	Deoxyribonucleic acid
DFI	DNA Fragmentation Index
DEHP	Di-2-ethylhexyl phthalate
EDO	Ejaculatory Duct Obstruction
ECRI	Emergency Care Research Institute
FOE	Failure of Emission
FSH	Follicle-Stimulating Hormone
hCG	Human Chorionic Gonadotropin
HH	Hypogonadotropic Hypogonadism
IB	Immunobead
IVF	In Vitro Fertilization
ICSI	Intracytoplasmic Sperm Injection
IUI	Intrauterine Insemination
LRL	Lower Reference Limits
LH	Luteinizing Hormone
micro-TESE	Microdissection-Testicular Sperm Extraction
MRI	Magnetic Resonance Imaging
NOA	Non-Obstructive Azoospermia
OR	Odds Ratio

PGC	Practice Guidelines Committee
RCTs	Randomized Controlled Trials
RPL	Recurrent Pregnancy Loss
RR	Relative Risk
RE	Retrograde Ejaculation
RPLND	Retroperitoneal Lymph Node Dissection
ROB	Risk of Bias
SQC	Science and Quality Council
SERMs	Selective Estrogen Receptor Modulators
SA	Semen Analysis
SRR	Sperm Retrieval Rates
TL	Telomere
TESE	Testicular Sperm Extraction
TRUS	Transrectal Ultrasonography
TURED	Transurethral Resection of Ejaculatory Ducts
WHO	World Health Organization

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