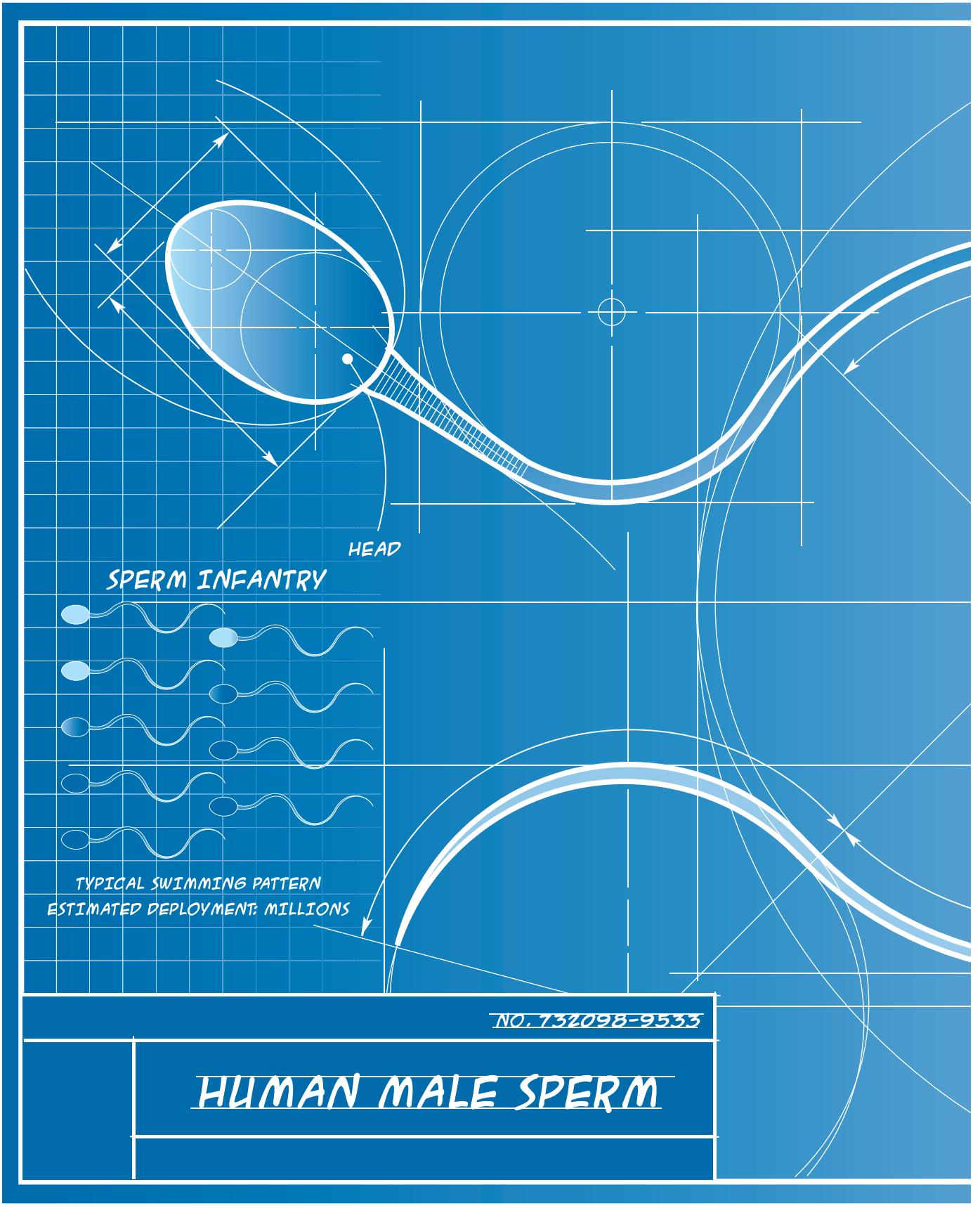
CE 2.6 CONTACT HOURS



Male infertility

a primer for NPs

Abstract: Few NPs are exposed to the topic of male infertility during the course of their training. There are medical and surgical treatment options for many of the most common diagnoses that contribute to decreased fertility in men. Recognizing these etiologies can help patients receive cost-effective treatment.

By Susanne Quallich, ANP-BC, NP-C, CUNP

Primary care practices do not usually perform fertility screenings, with the possible exceptions of gynecology or women's health providers. Male infertility receives even less attention, in part because men do not make primary care or preventive services appointments to the degree that women do.[1] There is also a common misconception that men are needed only "to provide a few sperm" for procedures such as in-vitro fertilization (IVF). The reality is that in one third of infertility cases the male partner is the sole contributor to the infertility, in one third of cases the female partner is the sole cause, and in the remaining one third there are combined male and female factors, or the causes are unexplained.[2] There are many causes for male infertility and contributors to male subfertility (the inability to conceive with a partner spontaneously) that are amenable to medical or surgical management. This represents not only significant cost savings for a couple seeking treatment if high-tech interventions can be avoided, but also the opportunity to restore the option to conceive naturally and privately at home. The male fertility evaluation can help identify lifestyle and other risk factors for the development of subsequent disease, or identification of undiagnosed conditions. The key is to recognize the male patient who may

Key words: male reproductive failure, male subfertility, sexual dysfunction, sperm

Conditions that predispose to male-factor infertility

Pretesticular	Testicular	Posttesticular
• Anabolic steroid use	• Cryptorchidism	• Antisperm antibodies
• Diabetes with anejaculation	• Klinefelter syndrome	• CF
• Idiopathic hypogonadotropic hypogonadism	• Previous chemotherapy or radiation treatment	• ED
• Kallmann syndrome	• Varicocele	• Failed vasectomy reversal
• Obesity		• Inguinal hernia repair
• Pituitary or hypothalamic dysfunction		• Retrograde ejaculation
		• Vasectomy

Key points in a male fertility history

Medical	History of cryptorchidism, epispadias, mumps orchitis, diabetes, hypothyroidism, varicocele, pituitary malfunction, diabetes, chronic obstructive pulmonary disease, sleep apnea, renal insufficiency, hemochromatosis, hepatic insufficiency, previous treatment for malignancy, history of febrile illness in the last 3 to 6 months
Surgical	History of genitourinary surgeries, previous vasectomy; inguinal hernia repair as an infant, small child, or adult
Medication	Dose and duration of use, especially antibiotics; use of supplements and nutraceuticals
Sexual	Pattern of sexual activity as the couple has being trying to conceive, specifically in relation to ovulation; history of STDs; issues with libido, erection, ejaculation; use of lubricants
Social	Previous paternity with same or different partner(s); cigarette smoking, alcohol use, illicit drug use, especially marijuana; recreational activities, such as cycling
Family	Fertility issues, genetic diseases, cancer history, prostate issues, bladder problems
Female partner history	Menstrual cycle length, previous contraception use, previous pregnancies or miscarriages, gynecologic surgeries, use of ovulation predictor kits or basal body temperature monitoring; status of female infertility evaluation

have risk factors or diagnoses that place him at risk for subfertility or infertility, and understand the preliminary evaluation and need for specialist referral.

Presentation

In general, there are no symptoms to male-factor infertility—other than the inability to conceive with a partner. According to the American Society for Reproductive Medicine, couples should seek evaluation after 12 months of unprotected intercourse, but if the female is 35 or older, couples should seek evaluation after 6 months.[2] Many evaluations for male infertility are requested by a provider evaluating a female, although the evaluations can occur simultaneously.

Male infertility can be pretesticular, testicular, or posttesticular (see *Conditions that predispose to male-factor infertility*). Some conditions and issues in the medical or surgical history are likely to predispose males to subfertility or infertility. Rarely, an undiagnosed malignancy, such as a testicular cancer, is the cause of the fertility alteration. If any of these are present or suspected, the man should be asked about his plans for a family. The patient should undergo a fertility evaluation if he is interested in knowing his fertility status (even if unpartnered), regardless of any evaluation that a female partner is undergoing.

The history

A routine history and physical exam is the first step in the male infertility evaluation. However, there are several specific points that must be included to determine the need for specialized testing and evaluation (see *Pertinent topics for the male fertility history*). Previous paternity and any previous pregnancies for the female partner should be discussed; if the couple has been pregnant together in the past, this can be an important clue to potential causes, both male and female.

A careful history of medication and supplement use is vital, and should include any substances that have been ingested in the last 12 to 24 months (see *Selected medications and their effect on male fertility*). Because sperm require approximately 90 days to mature, effects from medications or other substances are not reflected as changes to the semen analysis for at least 3 months. Consequently, these effects last for 3 months after cessation of any substance. The semen sample can be affected by a febrile illness (temperature over 102° F) that occurred 90 days before sample collection, making it critical that the patient is specifically asked about any recent febrile illness.

Physical exam

A full examination of the male patient establishes whether the chronologic age matches the Tanner stage and notes development of secondary sexual characteristics and body habitus (see *Tanner stages in the male*). Evidence of underdevelopment or apparent delayed development can be a clue that both the endocrine status and genetics need to be further evaluated. The examination should be performed in a warm room whenever possible to avoid activation of the cremasteric reflex, and should focus on the genitalia. In general, the patient should be examined for gynecomastia or hirsutism, and should be evaluated for lesions or scarring to the abdomen, groin, penis, or scrotum. The location and size of the opening of the penile meatus and the size, shape, and consistency of the testicles should be noted. Not all the structures that influence male fertility are examined. Relevant structures include the testes, epididymides, spermatic cord, vas deferens, prostate, seminal vesicles, Cowper gland, penis, and scrotum.

Palpation of the scrotal contents is the most informative component of the genital exam. It's important for the NP to understand the internal structures; the scrotum must be carefully and thoroughly palpated and the presence of anticipated scrotal structures confirmed as well as their size and consistency. Examination should confirm that both testes are present in the scrotum, are of normal size, and are roughly symmetrical. Both vas deferens and epididymides should be confirmed as well. Masses may be felt at the surface of the testicle, next to the testes, or adjacent to the epididymis. Epididymal induration on physical exam can indicate a blockage of the vas deferens or ejaculatory duct. Examination may show complete absence of the vas unilaterally or bilaterally or a gap in the length of the vas deferens. A unilateral or bilateral varicocele ("bag of worms") may be noted as well, although in many cases it may not be apparent without having the patient perform a Valsalva maneuver to distend the pampiniform plexus that surrounds the spermatic cord. The physical exam includes a digital rectal exam (DRE) when there are complaints of pain with ejaculation, low-volume ejaculation, or anejaculation. This is to evaluate for possible prostatitis or distended seminal vesicles, although this is an unusual finding on palpation (see *Specific maneuvers for the male infertility exam*).

Lab evaluation and semen analysis

Evaluation of a patient's hormone status is necessary as part of the infertility workup, and can hint at the causes for

Selected medications and their effect on male fertility

Medication	Effect
5-Alpha reductase inhibitors	Impaired erection/ejaculation possible
Alpha antagonists	Retrograde ejaculation
Antibiotics	Gentamicin: decreased spermatogenesis Nitrofurantoin: maturation arrest Erythromycin: decreases motility and sperm density
Calcium channel blockers	Interferes with sperm-oocyte binding
Chemotherapeutic agents	Specific effects vary by type; generally suppress spermatogenesis; may recover sperm production in 4 years or less after final dose. Long-term or permanent sterility is possible, and varies by type of malignancy and treatment
Cimetidine	Impaired sperm transport in epididymis
Cyclosporine	Decreased motility and sperm density
LH-releasing hormone agonists, antiandrogens	Impaired erection/ejaculation, decreased libido, decreased spermatogenesis
Spironolactone	Impaired erection/ejaculation, decreased libido, decreased spermatogenesis
Testosterone, anabolic steroids	Suppresses hypothalamus-pituitary-gonadal (HPG) axis, causes decreased count, motility, morphology
TCAs, SSRIs	Potential decreased testosterone, impaired erection/ejaculation

Adapted from http://www.reprotox.org

abnormal sperm production or low counts (see *Endocrine abnormalities seen with infertility*). Initial lab studies should include total testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH). Additional studies such as free testosterone and prolactin may be included depending on the clinical suspicion for an endocrinopathy. An estradiol level may be helpful in determining the effect of obesity on hormone status if the patient has a high body mass index (BMI).[8]

The semen analysis evaluates several parameters that help to narrow the cause of male-factor infertility. The primary values that are evaluated are the volume of the ejaculate, sperm motility, total sperm count, and sperm morphology (shape) (see *WHO semen parameters*). Samples are usually obtained via masturbation into a container that is not toxic to sperm, after abstinence from ejaculation from 2 to 5 days. Coitus interruptus is not a recommended, or reliable, means for sample collection[2] and men should not be advised to collect a sample via intercourse. Ideally sample collection should occur at the lab where the sample will be processed to prevent any delays. It is common practice to require at least two samples, approximately 3 weeks apart, before establishing treatment goals.

If the semen analysis shows a very low count (severe oligospermia) or azoospermia (absence of sperm) and/or the physical exam findings reveal abnormalities in testicular size or the male's secondary sexual development, a karyotype analysis and Y-chromosome microdeletion testing are also indicated, but often these tests may be left to the discretion of the male infertility or andrology specialist.

Patients usually repeat their semen analysis every 3 months after initiating treatment because of the length of time it takes sperm to reach maturity. The semen analysis results can indicate any additional testing that might be useful.

Common causes and treatment of male-factor infertility

Timing. There are couples who do not have a complete understanding of the menstrual cycle, in that they do not take advantage of optimal timing for intercourse. A careful history should include when the couple concentrates their efforts at conception. Ideally, they should count back 7 days from the middle of the woman's cycle (ovulation) and begin intercourse daily or every day.[4] Since sperm can live for up to 5 to 7 days in the female reproductive tract, this approach

Tanner stages in the male

Stage 1	No hair, or fine pigmented; testes 2.5 cm; penis length less than 6 cm
Stage 2	Scant hair to base of symphysis pubis; testicular enlargement (2 to 3 cm diameter), enlarged scrotum; little change to penis
Stage 3	Increased pigmented hair that spreads across symphysis pubis; testes 3.5 cm diameter, scrotal skins thins, darkens, wrinkles; penis lengthens
Stage 4	Hair fills in pubic triangle; scrotum darkens, testes 4 to 4.5 cm diameter; penis to 11 to 17 cm length flaccid, glans increases in size
Stage 5	Hair extends to medial thighs and toward umbilicus; testes 4.5 cm or greater; genitalia fully grown

Adapted from Tanner JM. *Growth at Adolescence.* 2nd ed. Oxford, UK: Blackwell Scientific; 1962.

Specific maneuvers for the male infertility exam

Cremasteric reflex
One or both testicles elevate due to the action for the cremaster muscle in response to downward touching of the scrotum. Reflex is prompted by a cool room or cold temperatures—reflex may be engaged before any contact.

DRE
Gloved, lubricated finger is inserted into anus and swept across surface of prostate; also involves estimation of anal sphincter tone. Normal exam yields symmetrical, nontender, walnut-sized gland that is free from nodules, with a smooth rubbery consistency; seminal vesicles cannot be palpated.

Neurologic exam
Perianal sensation: reflex contraction of external anal sphincter ("anal wink") if neurologically intact, as result of brushing the anus with cotton swab

Bulbocavernosus reflex: contraction of anal sphincter and bulbocavernosus muscles as result of insertion of gloved finger into anus and squeezing glans penis

(*These tests most helpful when evaluating complaints of ejaculatory dysfunction in apparently neurologically intact male. Uncommon to routine evaluation of male infertility.*)

Valsalva maneuver to evaluate for varicocele
Ideally patient is standing in warm room (to avoid activating cremasteric reflex). Asking him to perform the Valsalva maneuver will reverse flow into the pampiniform plexus of the scrotum, and result in distension of the vessels ("bag of worms" if varicocele of sufficient size) that can be noted on exam.

Adapted from Quallich SA. Male reproductive system. In: Goolsby MJ, Grubbs L, editors. *Advanced Assessment: Interpreting Findings and Formulating Differential Diagnoses.* Philadelphia: F.A. Davis; 2005.

Endocrine abnormalities seen with male infertility

Condition	Testosterone level	LH level	FSH level
Abnormal spermatogenesis	Normal	Normal	Elevated or normal
Hypogonadotropic hypogonadism	Decreased	Decreased	Decreased
Testicular failure	Decreased or normal	Elevated	Elevated

will give a couple the greatest chance for success. In some cases, this very basic educational intervention is all that is required.

Varicocele. A varicocele is the retrograde reflux of venous blood from the internal spermatic vein, which in turn dilates the pampiniform plexus. They are more commonly identified on the left, due to the greater distance between the internal spermatic vein and left renal vein versus the right. The precise etiology of varicoceles remains undetermined, resulting in a lack of specific risk factors. Current estimates place the prevalence in the male population at 15% to 20%, and this number increases to 40% or higher in men presenting for an infertility evaluation, in the context of secondary infertility.[3]

Although most men are asymptomatic, some may report a history of a dull ache, fullness, pain that may or may not radiate to the inguinal area, or pulling to the affected side of the scrotum after prolonged standing, exertion, or sitting. Varicoceles alter the semen analysis, but the manner in which this occurs is also unknown; temperature elevation, venous congestion, and testicular hormone changes are all suggested causes. Treatment of the varicocele has been proposed as a way to prevent future decline in the quality of the semen analysis.[5] Scrotal ultrasound can be helpful in the diagnosis of a varicocele and in eliminating other pathology, but only varicoceles noted on palpation have been implicated in alterations to semen parameters and infertility.[3,6]

Men with fertility concerns can be offered surgical repair of the varicocele or percutaneous embolization. Although both approaches are successful at treating the varicocele, studies vary in reporting the endpoints of pregnancy versus improvements to semen parameters; neither is superior in regards to improving or restoring fertility.[3,5] Semen parameters can be expected to improve in the 6 to 12 months after treatment.

Klinefelter syndrome. Klinefelter syndrome occurs in 1 in 500 to 1 in 1,000 live male births, and so is the most common abnormality of sexual differentiation.[7] It is the most common sex chromosome abnormality seen in infertile men. Presentation varies from a classic eunuchoid appearance that is likely to be identified during the teen years, to males that are appropriately virilized and are diagnosed only due to an evaluation for male infertility. In fact, an infertility evaluation may be the first contact with the healthcare system and physical exam these men have as an adult male. The typical triad of small testes, gynecomastia, and elevated urine gonadotropins is a helpful clinical guide to diagnosis. Patients diagnosed with Klinefelter syndrome may demonstrate increased height, diabetes mellitus, obesity, and decreased intelligence; there is also an increased risk for breast cancer and non-Hodgkin lymphoma.[7]

WHO semen parameters

Semen parameters	Normal values
Morphology (shape)	≥15% normal forms
Motility	≥50%
Sperm count/mL	≥20 million
Volume	2.0 to 5.0 mL

Adapted from Rowe PJ, Comhaire FH, Hargreave TB, Mahmoud AMA. *WHO Manual for the Standardized Investigation, Diagnosis and Management of the Infertile Male.* Cambridge, UK: Cambridge University Press; 2000.

Klinefelter syndrome causes few physical symptoms, although men can describe delayed virilization and late puberty. Physical exam will reveal a lack of development of sexual characteristics, atrophic (less than 2.0 cm) testes, small phallus, likely diminished muscle bulk, and truncal fat distribution that often includes gynecomastia.

Routine hormone analysis will usually demonstrate hypogonadism, with an elevated FSH and elevated LH. Karyotype analysis will show 47, XXY or a mosaic pattern such as 46, XY/47, XXY.

Fertility treatment is limited; the hypogonadism can be easily addressed with testosterone, if the individual couple cannot pursue expensive assisted reproductive options. Testosterone will not be prescribed if the couple is considering assisted reproduction. Since the advent of the microsurgical testicular sperm extraction (microTESE) procedure, men

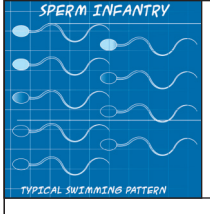
Methods for assisted reproduction

Method	Description	Cost
IUI: also called artificial insemination	Processed semen sample is inserted directly through cervix. Sample is ejaculated.	$$
IVF:	Egg and sperm are allowed to fertilize in the lab, due to low number of sperm. Sperm can be either ejaculated or retrieved via needle or open testicular biopsy; eggs are retrieved.	$$$$
IVF + ICSI:	Egg is manually fertilized with a single sperm, due to extreme low number of sperm available. Sperm can be either ejaculated or retrieved via needle or open testicular biopsy; eggs are retrieved.	$$$$$

Note: There are many variations of the IVF procedure, based on the maturity of embryo and timing of implantation in the woman. This chart is meant only to provide a basis for the concepts in the article.

with Klinefelter syndrome have the potential to father genetic offspring via microTESE and IVF with intracytoplasmic sperm injection (ICSI), although this tends to be quite expensive, regardless of the center in which it is performed (see *Methods for assisted reproduction*).

Endocrinopathy. Men with hypogonadism not due to a genetic cause (such as Klinefelter syndrome) can see improvement to their semen analysis if treated with hormone therapy. Their response depends on the specific cause for the low testosterone and decreased sperm production. Reversible endocrinopathies that directly contribute to male infertility are unusual, at about 1.7% of male infertility patients.[8] Before treatment, there can be complaints of changes in sexual function, fatigue, weight gain, loss of muscle mass, and some loss of secondary sexual characteristics, although the hypogonadism may be more subtle and these symptoms may not be present. Physical exam may reveal regression of secondary sexual characteristics, possible softer, smaller testes but no change to penis or prostate size.



Obesity is a contributor to subfertility, due to the aromatization of testosterone to estradiol in fatty tissue.

Obesity is frequently a contributor to subfertility, due to the aromatization of testosterone to estradiol in fatty tissue. This decreases the level of testosterone available for virilization functions, and results in a decline to sperm production as well. Physical exam may be notable for evidence of feminization (such as gynecomastia) or regression of secondary sexual characteristics (a Tanner stage that is not consistent with chronologic age). Lab evaluation will determine the effect that increased BMI may have disrupted the patient's hormonal balance and contributed to alterations to the semen analysis.

Men with both obesity-related hypogonadism and hypogonadism not due to a genetic etiology are commonly treated with clomiphene citrate, a synthetic nonsteroidal antiestrogen. This medication works to block feedback inhibition and increases FSH and LH, resulting in an increase in both testosterone production and sperm production by the testes. Its use for treatment of male infertility, while widely recognized, is off-label. Clinical trials of the use of clomiphene citrate have suffered from a mixed response in terms of results and improved pregnancy rates.[8] Clomiphene citrate does not improve semen parameters if the man has a normal testosterone level.

Other medications may have a role in medical treatment of male infertility with a patient who has low testosterone. These include gonadotropins, other aromatase inhibitors, oxytocin, other antiestrogens, and gonadotropin-releasing hormone agonists.

Ejaculatory and sexual dysfunction. Difficulty with sexual function can be a primary contributor to failure to conceive, but it can also be the result of the stress associated with the evaluation or pressure to have intercourse according to a monthly schedule. Although a full discussion of erectile dysfunction (ED) and general male sexual dysfunction is beyond the scope of this article, there is a role for phosphodiesterase type-5(PDE-5) inhibitors in the treatment of ED seen as a result of the stress associated with an infertility diagnosis, be it male factor, female factor, or combined infertility. Intracavernosal alprostadil can also be used, such as in males with type 1 diabetes mellitus, but intraurethral alprostadil (MUSE, AstraZeneca) is not recommended, as it may have an effect on the ejaculate.

Difficulties with ejaculation and climax can result with the use of psychotherapeutic agents that block dopamine production. This in turn blunts the hypothalamic-pituitary axis and can decrease libido. Other psychotherapeutic agents can decrease vasodilation and the quality of erections, or lead to ED, anejaculation, and decreased libido. These groups of

drugs include tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and monoamine oxidase inhibitors. It is reasonable to consider alternative regimens, but if patients are stable on a regimen, it may be less disruptive to offer a PDE-5 inhibitor to improve erectile function.

Congenital bilateral absence of the vas deferens. Congenital bilateral absence of the vas deferens is seen with cystic fibrosis (CF) and its multiple variants. Because some of the less profound variants do not result in respiratory conditions, this is again an instance in which the male fertility evaluation can be the first contact with the healthcare system and physical exam these men have as an adult male. These are generally healthy men who may report a history of chronic bronchitis as a child or adolescent that required hospitalization, recurrent respiratory infections as a child and adolescent, asthma or an asthma-like condition, or no childhood symptoms. It is possible that a family history of infertility or persistent respiratory illnesses may be described.

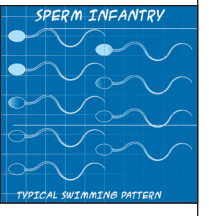
Physical exam is likely to demonstrate some malformation of the epididymis, and may show complete absence of the vas deferens unilaterally or bilaterally, a thready-feeling vas deferens, or a palpable gap in the vas deferens. In more severe variants (that do not result in respiratory compromise), the vas deferens, seminal vesicles, and ejaculatory ducts will be atrophic or absent. Testosterone levels, spermatogenesis, and testes size and consistency are all normal. There will be appropriate secondary sexual characteristics and Tanner stage. Usually examination and history are sufficient to confirm the suspicion of a CF variant. Karyotype analysis is commonly ordered, as is a CF mutation panel to confirm the diagnosis.

If a CF variant is confirmed, the female partner must also be tested for CF, and the couple should be referred for a medical genetics consultation. These couples traditionally proceed to very successful IVF cycles, as there is not a problem with sperm production itself.

Anejaculation after a spinal cord injury. Spinal cord injuries (SCIs) occur most frequently in men between the ages 16 and 45, which corresponds with the peak years of reproduction and family building. The level of a SCI helps to indicate what manner of sexual function is preserved, although most men with SCI do not retain the ability to ejaculate. Injuries below T9 do not preserve erectile function, whereas those above T9 often preserve reflex erections that are usually unreliable for sexual activity.

This difficulty with ejaculatory function presents the most significant challenge to paternity for men with SCI; 5% to 15% of men with SCI preserve their native ability to ejaculate.[9] The situation is further complicated by declines in overall semen quality, decreased motility, decreased ability to penetrate cervical mucus, and decreased fertilizing capability. However, these men can still enjoy biological paternity through the use of either penile vibratory stimulation (PVS) or electroejaculation, which in turn often allow for the possibly for intrauterine insemination (IUI). If semen quality is adequate, couples can be taught to use the PVS procedure for home insemination. IVF is always an option as well, although it is less cost-effective.[10]

Men concerned about preserving their fertility should stop exposure to anything that may potentially alter their sperm.



Fertility preservation

Many men are concerned about preserving their fertility. The best advice is that if they are trying to conceive with their partner, they should stop exposure to anything that may potentially alter the number, function, or shape of their sperm. This includes smoking cessation, stopping illicit drug use, and restricting exposure to environmental or occupational toxins. Varicocele repair can also be seen as prophylactic, if there is a desire for additional pregnancies, as it can help prevent future declines to the semen analysis.[5] Some men find the prospect and process of an infertility evaluation stressful, to the point that erectile quality may suffer. A PDE-5 medication is often successful at addressing this. If the level of stress is significant, referral to a therapist, or specialized sex therapist, can be helpful.

Men can also be proactive in terms of fertility by ingesting a supplement that contains antioxidants, although their use remains empiric,[11] some trials have shown improvements to sperm function. Evidence that other supplements, such as l-carnitine, improve sperm count or pregnancy rates remains lacking, and advertised "fertility" formulations can be quite costly.[11]

As medical technology continues to progress, survival rates after a cancer diagnosis continue to climb. For the male patient, this represents the potential for a return to a normal life after treatment, which often includes a desire for paternity. Male patients who need to undergo chemotherapy or radiation should be offered the opportunity for cryopreservation of their sperm, as insurance in the event that they do not recover their capacity for spermatogenesis. Additional resources regarding sperm cryopreservation can be found at http://www.ASRM.org.

Conclusions

NPs have a unique opportunity to identify men who are potentially at risk for alterations to their fertility, and play a role in dispelling misconceptions regarding a diagnosis of a fertility problem. Failure to conceive or a diagnosis of infertility should not be seen as an automatic indication for expensive reproductive technologies. Practitioners should feel comfortable addressing basic reproductive health questions, and referring men to a male infertility specialist or an andrologist for additional evaluation if the male has additional concerns. There are multiple options for medically and/or surgically improving male fertility. If preliminary evaluation yields results, such as hormone abnormalities, that could indicate potential fertility issues, these men should be referred. Patients should also be encouraged to seek the opinion of a male infertility specialist or andrologist before committing to a particular treatment option recommended as a result of a female fertility evaluation. NP

REFERENCES

1. Jimbo M. Organizing preventive healthcare in men. In: Heidelbaugh JJ (ed). *Clinical Men's Health: Evidence in Practice.* Saunders: Philadelphia; 2008.
2. American Society of Reproductive Medicine. Frequently asked questions about infertility. http://www.reproductivefacts.org/detail.aspx?id=876&terms=(+%40Publish_To+Both+Sites+or+%40Publish_To+Patient+Site+Only+)+and+frequently+asked.
3. American Society for Reproductive Medicine and American Urological Association. Report on optimal evaluation of the infertile male (joint guidelines, revised 2010) http://www.auanet.org/guidelines/.
4. Wilcox AJ, Weinberg CR, Baird DD. Timing of sexual intercourse in relation to ovulation. Effects on the probability of conception, survival of the pregnancy, and sex of the baby. *N Eng J Med.* 1995;333(23):1517-1521.
5. Marmar JL, Agarwal A, Pabakaran S. et al. Reassessing the value of varicocelectomy as a treatment for male subfertility with a new meta-analysis. *Fertil Steril.* 2007;88(3):639-648.
6. Agarwal A, Deepinder F, Cocuzza M, et al. Efficacy of varicocelectomy in improving semen parameters: new meta-analytical approach. *Urology.* 2007;70(3):532-538.
7. Oates RD. The genetic basis of male reproductive failure. *Urol Clin North Am.* 2008;35(2):257-270, ix.
8. Kim HH, Schlegel PN. Endocrine manipulation in male infertility. *Urol Clin North Am.* 2008;35(2):303-318.
9. Biering-Sørensen F, Sønksen J. Sexual function in spinal cord lesioned men. *Spinal Cord.* 2001;39:455-470.
10. Brackett NL, Lynne CM, Attia GR, et al. Treatment of infertility in men with spinal cord injury: medical progress and ethical considerations. *Topics in Spinal Cord Injury Rehabilitation.* 2008;13(4):120-133.
11. Patel SR, Sigman, M. Antioxidant therapy in male infertility. *Urol Clin North Am.* 2008;35(2):319-330, x.

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Susanne Quallich is a Certified Urology Nurse Practitioner in the Division of Sexual and Reproductive Medicine, Department of Urology, University of Michigan Health System, Ann Arbor, Mich.

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