AZOOSPERMIA

Complete absence of sperm in the ejaculate of a man.

♂ Diagnosis  ♂ Male

Related Diagnoses:
Varicocele | Erectile dysfunction | Obesity | Undescended testes | Anejaculation | Ejaculatory disorders | Retrograde ejaculation | Klinefelter syndrome | Non-obstructive azoospermia | XX male syndrome | Hypogonadism | Benign prostatic hyperplasia | Aspermia | Hypospermia | Obstructive azoospermia | Orchitis | Cryptozoospermia | Idiopathic male infertility | Testicular failure | Y-chromosome deletions | Sertoli cell-only syndrome

About Azoospermia

Azoospermia is defined as the complete absence of spermatozoa upon examination of the semen (including capillary tube centrifugation, strictly confirmed by the absence of spermatozoa issued in urine after ejaculation). The presence of rare spermatozoa (<500,000/ml) in seminal fluid after centrifugation is called cryptozoospermia.

The complete absence of spermatozoa should be confirmed with repeat testing after a long time, because many external factors (e.g., febrile episodes and some therapies) may cause transient azoospermia.

Azoospermia is present in approximately 1% of all men, and in approximately 15% of infertile men.

Azoospermia may result from a lack of spermatozoa production in the testes (secretory or Non-Obstructive Azoospermia, NOA), or from an inability of produced spermatozoa to reach the emitted semen (excretory or Obstructive Azoospermia, OA); however, in clinical practice both components are sometimes present in a single patient (mixed genesis azoospermia).

The initial diagnosis of azoospermia is made when no spermatozoa can be detected on high-powered microscopic examination of centrifuged seminal fluid on at least two occasions.

Classification: The evaluation of a patient with azoospermia is performed to determine the etiology of the patient's condition. The numerous etiologies for azoospermia fall into three principal categories: pre-testicular, testicular, and post-testicular.

1. **pre-testicular azoospermia** affects approximately 2% of men with azoospermia, and is due to a hypothalamic or pituitary abnormality diagnosed with hypogonadotropic hypogonadism;
2. **testicular failure or non-obstructive azoospermia** is estimated to affect from 49% to 93% of azoospermic men. While the term testicular failure would seem to indicate a complete absence of spermatogenesis, men with testicular failure actually have either reduced spermatogenesis (hypospermatogenesis), maturation arrest at an early or late stage of spermatogenesis, or a complete failure of spermatogenesis (noted with Sertoli cell-only syndrome);
3. **post-testicular obstruction or retrograde ejaculation** are estimated to affect from 7% to 51% of azoospermic men. In these cases, spermatogenesis is normal even though the semen lacks spermatozoa.

If none of the above categories cannot be applied, it is possible to use the term “idiopathic azoospermia”.

**Idiopathic azoospermia**, one of the most severe forms of male infertility, affects up to 1% of all adult men in the general population. Idiopathic azoospermia is where there is no known cause of the condition. It may be a
result of multiple risk factors, such as age and weight. For example, a review in 2013 came to the result that oligospermia and azoospermia are significantly associated with being overweight, obese and morbidly obese, but the cause of this is unknown.

**Diagnosis:** The minimum initial evaluation of an azoospermic patient should include a complete medical history, physical examination, and hormone level measurements. Relevant history should investigate prior fertility; childhood illnesses such as orchitis or cryptorchidism; genital trauma or prior pelvic/inguinal surgery; infections; gonadotoxic exposure, such as spinal radiation therapy/chemotherapy and current medical therapy; and a familial history of birth defects, mental retardation, reproductive failure, or cystic fibrosis. Physical examination includes: testis size and consistency; consistency of the epididymides; secondary sex characteristics; presence and consistency of the vasa deferentia; presence of a varicocele; and masses upon digital rectal examination. The initial hormonal evaluation should include measurement of serum testosterone (T) and follicle stimulating hormone (FSH) levels.

**History and initial investigations for men with azoospermia:**

**Cryptorchidism:** the bilateral form is almost always associated with azoospermia and irreversible gonadal secretory dysfunction. The age at which surgical intervention is practiced and subsequent gonadal development may sometimes affect the prognosis. In addition, not infrequently, germinal malformations are also associated with atrophy of the epididymis and sometimes with iatrogenic damage to the vas deferens. In unilateral cryptorchidism, azoospermia is less frequent; azoospermia in a patient with unilateral cryptorchidism is likely the result of concurrent secretory dysfunction (dysgenesis) or other pathology of the contralateral testis.

**Reduced volume of ejaculate:** occurs progressively in the post-inflammatory obstruction of the ejaculatory ducts (ED), with a concomitant reduction of seminal fructose and lowering of pH. Ejaculate volume is normally reduced in cases of vas deferens agenesis or in the presence of large seminal cysts (Müllerian or Wolffian). The same phenomenon is present in primary hypogonadism. Partial retrograde ejaculation is present in patients with systemic neuropathy (e.g., juvenile diabetes and multiple sclerosis), and is a possible outcome of endoscopic urological surgery for bladder neck sclerosis.

**Urological symptoms and signs:** the clinician must always pay close attention to symptoms, even prior symptoms that may previously have had no apparent significance, such as episodes of hematospermia, burning urination, urinary frequency, and urethral catheterization after surgery. All of these symptoms should raise the suspicion that the proximal or distal seminal tract may be obstructed. The presence of hypospadias may be associated with urinary abnormalities, hypogonadism, cryptorchidism, and the presence of residues in the Müllerian duct of the prostate (urtricular cysts). These cysts can be responsible for extrinsic compression of the ED.

**Surgery:** Inguinal hernioplasty interventions (often performed during infancy) may have damaged the tubes, and then create a condition of seminal tract obstruction. Resection of the funiculovesicular vessels may result in hypotrophy of the gonad.

**Family history:** Clinicians should be attentive to the concomitant presence of infertility in the patient’s male relatives (as a result of chromosomal abnormalities, genetic conditions, tuberculosis, etc.). Scrotal traumas are often responsible for complete or incomplete epididymis obstruction, as well as trophic changes of the gonad.

**Genetic cause:** Pretesticular azoospermia may be caused by congenital hypopituitarism, Kallmann syndrome, Prader-Willi syndrome and other genetic conditions that lead to GnRH or gonadotropin deficiency. Testicular azoospermia is seen in Klinefelter syndrome (XXY) and the XX male syndrome. The genetic factors most frequently related to male infertility are somatic chromosomal anomalies and Y chromosomal microdeletions within the Yq11 region, where the genes that control spermatogenesis, known as azoospermia factor genes (AZF). The reported incidence of AZF microdeletions in non obstructive azoospermia or severe idiopathic oligospermia varies widely due to the selection criteria used. The incidence of such microdeletions is higher in azoospermic than in oligospermic men and, consequently, the frequency of deletion found in different laboratories may vary from 2 to 10% (or higher), reflecting the composition of the study sample. In view of the genetic risks for the next generation, the importance of careful evaluation of karyotypes and AZF microdeletions in male infertility prior to assisted reproduction by ICSI is evident.

**Prior chemotherapy and radiotherapy:** Drug and radiation treatments for tumors usually cause irreversible damage to spermatogenesis. Even high-dose hormone therapy; antibiotic therapy with tetracyclines, nitrofurans, and sulfasalazine; or other drug therapies often temporarily alter spermatogenesis.
Associated disease

- infection
- congenital anomalies
- hypogonadotropic hypogonadism
- hypopituitarism
- hyperprolactinemia
- Klinefelter syndrome
- Sertoli cell-only syndrome
- orchitis
- testicular cancer
- cystic fibrosis
- ejaculatory duct obstruction
- retrograde ejaculation
- anejaculation
- Kalman syndrome
- Prader Willi syndrome
- cryptorchidism
- mental retardation

Complications

- infertility

Risk factors

- obesity
- overweight
- chemotherapeutic agents
- pesticides
- recreational drugs (marijuana, excessive alcohol)
- heat exposure of the testes
- radiotherapy
- genital trauma
- pelvic/inguinal surgery
- antibiotic therapy

Impact on fertility

The initial evaluation aims at resolving the following issues: confirming azoospermia, differentiating obstructive from non-obstructive etiology, assessing for the presence of reversible factors and evaluating for the presence of genetic abnormalities. The most common reversible factors that need to be ruled out include recent exogenous hormone administration, severe febrile illnesses, chemotherapy/radiation or prolonged antibiotic use.

Hormonal imbalance or lack of hormonal stimulation is the main reason of non obstructive azoospermia. If we manage to improve this imbalance, there is possibility to conceive child the natural way. In other cases, we have to use techniques of assisted reproduction.

In obstructive azospermia sperm are produced but not ejaculated. In these cases we need to fix the obstruction, or get the sperm itself.

Some genetic abnormalities can be coded in information of sperm's DNA. In these cases we do preimplantation genetic diagnosis which allows studying the DNA of eggs or embryos to select those that carry certain damaging characteristics and then have healthy child.

Prevention

Azoospermia cannot be prevented, but you can eliminate some related risk factors. The best way is to lose weight and keep healthy lifestyle.
Symptoms

Azoospermia is usually detected in the course of an infertility investigation. It is established on the basis of two semen analysis evaluations done at separate occasions (when the seminal specimen after centrifugation shows no sperm under the microscope) and requires a further work-up. Congenital absence of the vas deferens may be detectable on physical examination and can be confirmed by a transrectal ultrasound (TRUS). If confirmed genetic testing for cystic fibrosis is in order. Transrectal ultrasound can also assess azoospermia caused by obstruction, or anomalies related to obstruction of the ejaculatory duct, such as abnormalities within the duct itself, a median cyst of the prostate (indicating a need for cyst aspiration), or an impairment of the seminal vesicles to become enlarged or emptied. Retrograde ejaculation is diagnosed by examining a postejaculatory urine for presence of sperm after making it alkaline and centrifuging it.

Low levels of LH and FSH with low or normal testosterone levels are indicative of pretesticular problems, while high levels of gonadotropins indicate testicular problems. However, often this distinction is not clear and the differentiation between obstructive versus non-obstructive azoospermia may require a testicular biopsy.

Therapies

Self therapy

There is no self-therapy for azoospermia.

Conventional medicine

Pharmacotherapy

Men with azoospermia due to hyperprolactinemia may resume sperm production after treatment of hyperprolactinemia or men whose sperm production is suppressed by exogenous androgens are expected to produce sperm after cessation of androgen intake. In situations where the testes are normal but unstimulated, gonadotropin therapy can be expected to induce sperm production.

Surgical therapy

Iatrogenic damage to the seminal tract is one of the causes of obstructive azoospermia, which can be an indication for reconstruction surgery.

Bone marrow transplantation

Bone marrow-derived mesenchymal stem cells (BMSCs) might offer alternative treatment for the patients with azoospermic infertility after cancer chemotherapy. BMSCs possess the potential to differentiate or transdifferentiate into multi lineage cells, secrete paracrine factors to recruit the resident stem cells to participate in tissue regeneration, or fuse with the local cells in the affected region.

Assisted reproduction

In patients with obstructive azoospermia, if reconstructive surgery fails or is not feasible, microscopic epididymal sperm aspiration (MESA) or testicular sperm extraction (TESE) is the method of choice for recovering spermatozoa. In patients with non-obstructive azoospermia, TESE is usually used for obtaining several spermatozoa as a male therapeutic approach in IVF-ICSI. In the case of genetic-related azoospermia, PGD/PGS of early embryos is strongly recommended.

Find more about related issues

Diagnoses
Varicocele
An abnormal enlargement of the pampiniform venous plexus in the scrotum.
Learn more at: www.fertilitypedia.org/therapy/diag/varicocele

Erectile dysfunction
The inability (that lasts more than 6 months) to develop or maintain an erection of the penis during sexual activity.
Learn more at: www.fertilitypedia.org/therapy/diag/erectile-dysfunction

Obesity
A disease of excess body fat that can have a negative effect on health, leading to reduced life expectancy and other health problems.
Learn more at: www.fertilitypedia.org/therapy/diag/obesity

Undescended testes
In the case of cryptorchidism one or both testes are absent from the scrotum. It is the most common etiologic factor of azoospermia in the adult.
Learn more at: www.fertilitypedia.org/therapy/diag/undescended-testes

Anejaculation
The pathological inability to ejaculate in males, with (orgasmic) or without (anorgasmic) orgasm.
Learn more at: www.fertilitypedia.org/therapy/diag/anejaculation

Ejaculatory disorders
A class of sexual disorders defined as the subjective lack of normal ejaculation.
Learn more at: www.fertilitypedia.org/therapy/diag/ejaculatory-disorders

Retrograde ejaculation
The semen, which would normally be ejaculated via the urethra, is redirected to the urinary bladder.
Learn more at: www.fertilitypedia.org/therapy/diag/retrograde-ejaculation

Klinefelter syndrome
The set of symptoms that result from two or more X chromosome in males.
Learn more at: www.fertilitypedia.org/therapy/diag/klinefelter-syndrome

Non-obstructive azoospermia
Complete absence of sperm in the ejaculate due to testicular failure.
Learn more at: www.fertilitypedia.org/therapy/diag/non-obstructive-azoospermia

XX male syndrome
The male sex chromosomal disorder characterized by a spectrum of clinical presentations, ranging from ambiguous to normal male genitalia.
Learn more at: www.fertilitypedia.org/therapy/diag/xx-male-syndrome

Hypogonadism
A medical term which describes a diminished functional activity of the gonads – the testes and ovaries.
Learn more at: www.fertilitypedia.org/therapy/diag/hypogonadism

Benign prostatic hyperplasia
A noncancerous increase in size of the prostate.
Learn more at: www.fertilitypedia.org/therapy/diag/benign-prostatic-hyperplasia

Aspermia
Male diagnosis connected with male infertility characterised by the complete absence of semen.
Learn more at: www.fertilitypedia.org/therapy/diag/aspermia
Hypospermia
A condition in which a man has an unusually low ejaculate (or semen) volume.
Learn more at: www.fertilitypedia.org/therapy/diag/hypospermia

Obstructive azoospermia
Absence of sperm in the ejaculate despite normal spermatogenesis, caused by an obstruction of the genital tract.
Learn more at: www.fertilitypedia.org/therapy/diag/obstructive-azoospermia

Orchitis
An inflammation of the testes, involving swelling and heavy pains.
Learn more at: www.fertilitypedia.org/therapy/diag/orchitis

Cryptozoospermia
Male infertility diagnosis characterized by extremely low concentration of sperm in semen.
Learn more at: www.fertilitypedia.org/therapy/diag/cryptozoospermia

Idiopathic male infertility
A condition in which fertility impairment occurs spontaneously or due to an unknown cause.
Learn more at: www.fertilitypedia.org/therapy/diag/idiopathic-male-infertility

Testicular failure
The inability of the testicles to produce sperm or testosterone.
Learn more at: www.fertilitypedia.org/therapy/diag/testicular-failure

Y-chromosome deletions
A family of genetic disorders caused by missing gene(s) in the Y chromosome.
Learn more at: www.fertilitypedia.org/therapy/diag/y-chromosome-deletions

Sertoli cell-only syndrome
The absence of any developmental stage of sperm cell in the testes.
Learn more at: www.fertilitypedia.org/therapy/diag/sertoli-cell-only-syndrome

Organs

Bulbourethral gland
Bulbourethral gland is one of two small exocrine glands in the reproductive system of male.
Learn more at: www.fertilitypedia.org/edu/ Organs/bulbourethral-gland

Epididymis
The epididymis is a tube that connects a testicle to a vas deferens in the male reproductive system.
Learn more at: www.fertilitypedia.org/edu/ Organs/epididymis

Hypothalamus
A region of the forebrain that regulates body temperature, some metabolic processes and governs the autonomic nervous system.
Learn more at: www.fertilitypedia.org/edu/ Organs/hypothalamus

Pituitary gland
An endocrine gland, about the size of a pea, whose secretions control the other endocrine glands and influence growth, metabolism, and maturation.
Learn more at: www.fertilitypedia.org/edu/ Organs/pituitary-gland

Prostate
A walnut-sized structure that is located below the urinary bladder in front of the rectum.
Learn more at: www.fertilitypedia.org/edu/ Organs/prostate
Seminal vesicles
One of two simple tubular glands responsible for the production of about 60 percent of the fluid that ultimately becomes semen. Learn more at: www.fertilitypedia.org/edu/organs/seminal-vesicles

Testes
Male gonads which produce both sperm and androgens, such as testosterone, and are active throughout the reproductive lifespan of the male. Learn more at: www.fertilitypedia.org/edu/organs/testes

Reproductive cells

Leydig cell
The cell found in interstitial tissue of testicles responsible for production of androgens - male hormones. Learn more at: www.fertilitypedia.org/edu/reproductive-cells/leydig-cell

Sertoli cells
The cell in seminiferous epithelium responsible for nutrition and development of germ (sperm) cells. Learn more at: www.fertilitypedia.org/edu/reproductive-cells/sertoli-cells

Spermatogonium
An undifferentiated male germ cell with self-renewing capacity representing the first stage of spermatogenesis. Learn more at: www.fertilitypedia.org/edu/reproductive-cells/spermatogonium

Biological control

Follicle-stimulating hormone
FSH is a hormone secreted by the anterior pituitary gland. It regulates the development, growth, pubertal matur and reproductive functions of the body. Learn more at: www.fertilitypedia.org/edu/biological-control/follicle-stimulating-hormone

Gonadotropin-releasing hormone
A releasing hormone responsible for the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) from the anterior pituitary. Learn more at: www.fertilitypedia.org/edu/biological-control/gonadotropin-releasing-hormone

Progesterone
Steroid hormone, secreted by the ovaries, whose function is to prepare the uterus for the implantation of a fertilized ovum and to maintain pregnancy. Learn more at: www.fertilitypedia.org/edu/biological-control/progesterone

Reproductive functions

Fertilization
The fusion of an ovum with a sperm to initiate the development of a new individual organism. Learn more at: www.fertilitypedia.org/edu/reproductive-functions/fertilization

Spermatogenesis
Process in which spermatozoa are produced from male primordial germ cells in testicles by way of mitosis and meiosis. Learn more at: www.fertilitypedia.org/edu/reproductive-functions/spermatogenesis

Risk factors

Abdominal surgery
Surgical procedures that involve opening the abdomen. Learn more at: www.fertilitypedia.org/edu/therapy/abdominal-surgery
Advanced paternal age
Age that may lead to the accumulation of de novo mutations, male infertility and increased genetic risks on the offspring.
Learn more at: www.fertilitypedia.org/therapy/rd/advanced-paternal-age

Alcohol drinking
A pattern of drinking that results in harm to one's health, interpersonal relationships, or ability to work.
Learn more at: www.fertilitypedia.org/therapy/rd/alcohol-drinking

Drug use
A patterned use of a drug in which the user consumes the substance in amounts or with methods which are harmful to themselves or others.
Learn more at: www.fertilitypedia.org/therapy/rd/drug-use-1

Groin surgery
A surgery, which is performed in inguinal part of the body.
Learn more at: www.fertilitypedia.org/therapy/rd/groin-surgery

Mumps
An infection that primarily affects the parotid glands, caused by the mumps virus which can impair male fertility.
Learn more at: www.fertilitypedia.org/therapy/rd/mumps

Obesity
A medical condition of excess body fat that can have a negative effect on health, leading to reduced life expectancy and other health problems.
Learn more at: www.fertilitypedia.org/therapy/rd/obesity

Prenatal testicular maldevelopment
A congenital condition characterized by the disruption of fetal testicular development.
Learn more at: www.fertilitypedia.org/therapy/rd/prenatal-testicular-maldevelopment

Sexually transmitted diseases
Illnesses that have a significant probability of transmission between humans by means of human sexual behavior and that may impact fertility.
Learn more at: www.fertilitypedia.org/therapy/rd/sexually-transmitted-diseases

Testicular or scrotal injury
Damage of the testicles or scrotum which may be temporary or permanent.
Learn more at: www.fertilitypedia.org/therapy/rd/testicular-or-scrotal-injury

Vasectomy
A surgical procedure for male sterilization or permanent contraception.
Learn more at: www.fertilitypedia.org/therapy/rd/vasectomy

Symptoms

Absence of sperm in ejaculate
The medical condition of a man whose semen contains no sperm.
Learn more at: www.fertilitypedia.org/edu/symptoms/absence-of-sperm-in-ejaculate

Gynecomastia
A disorder of the endocrine system in which there is a non-cancerous swelling of the breast tissue in boys or men.
Learn more at: www.fertilitypedia.org/edu/symptoms/gynecomastia
Inability to have or maintain an erection
The inability to develop or maintain an erection of the penis during sexual activity in humans.
Learn more at: www.fertilitypedia.org/edu/symptoms/inability-to-have-or-maintain-an-erection

Infertility
The failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.
Learn more at: www.fertilitypedia.org/edu/symptoms/infertility

Low facial and body hair growth
Decrease of facial and body hair in males.
Learn more at: www.fertilitypedia.org/edu/symptoms/low-facial-and-body-hair-growth

Lowered libido
The absence of sexual appetite.
Learn more at: www.fertilitypedia.org/edu/symptoms/lowered-libido

Overweight
Body weight that's greater than what is considered healthy for a certain height.
Learn more at: www.fertilitypedia.org/edu/symptoms/overweight

Small penis
An adult penis with an erect length of less than 7 cm or 2.76 inches.
Learn more at: www.fertilitypedia.org/edu/symptoms/small-penis

Small testes
Abnormally small testicular volume.
Learn more at: www.fertilitypedia.org/edu/symptoms/small-testes

Therapies

Egg donation
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research.
Learn more at: www.fertilitypedia.org/edu/therapies/egg-donation

ICSI
A micromanipulative fertilization technique in which a single sperm is injected directly into an egg.
Learn more at: www.fertilitypedia.org/edu/therapies/icsi

MESA
A microsurgical procedure to harvest sperm from the single epididymal tubule (epididymis), used in the case of obstructive azoospermia.
Learn more at: www.fertilitypedia.org/edu/therapies/mesa

Micro TESE
Microsurgical method used to identify areas of sperm production within the testes with the aid of optical magnification.
Learn more at: www.fertilitypedia.org/edu/therapies/micro-tese

PESA
Sperm aspiration procedure in which a needle is inserted into the epididymis in order to retrieve sperm.
Learn more at: www.fertilitypedia.org/edu/therapies/pesa

Preimplantation genetic diagnosis
Technology that allows couples with a family history of monogenic disorders, x-linked diseases and chromosomal abnormality have a healthy baby.
Learn more at: www.fertilitypedia.org/edu/therapies/preimplantation-genetic-diagnosis
Preimplantation genetic screening
The term PGS is used to denote procedures that do not look for a specific disease but to identify embryos at risk of de-novo occurring aneuploidies
Learn more at: www.fertilitypedia.org/edu/therapies/preimplantation-genetic-screening

Sperm donation
The procedure in which a man (sperm donor) provides his sperm for fertility treatment.
Learn more at: www.fertilitypedia.org/edu/therapies/sperm-donation

Standard IVF
A process in which an egg is fertilised by sperm outside the body: in vitro. Own or donated gametes may be used.
Learn more at: www.fertilitypedia.org/edu/therapies/standard-ivf

TESE
Removal of a small portion of testicular tissue in order to extract a few viable sperm.
Learn more at: www.fertilitypedia.org/edu/therapies/tese

Semen analysis
Azoospermia and multiple white blood cells in a semen sample.

Sources
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