### Male infertility

### **Semen analysis**

A specimen is collected by masturbation into a clean, dry, sterile container or during coitus using special condoms (containing no spermicidal lubricants). The patient should be abstinent for 2-3 days prior to maximize sperm number and quality.

The sample should be processed within 1 hour, and 2-3 samples (at a minimum of 2-3 days apart) should be evaluated because of daily variations in sperm number and quality

Normal ejaculate volume is 1.5-5 mL,

*Semen quality:* Semen is initially a coagulum that liquefies in 5-25 minutes due to prostatic enzymes. At this point, pouring the semen drop by drop should be possible. Semen that is not initially a coagulum is often an indication of an ejaculatory duct obstruction or the absence of seminal vesicles.

*Sperm density :*Normal sperm density is greater than 20 million sperm/mL. The WHO lower reference limit (5th percentile) is 15 million sperm per mL, or 39 million sperm per ejaculate. Oligospermia is defined as fewer than 20 million sperm/mL, severe oligospermia is less than 5 million/mL, and azoospermia is defined as no sperm present

Ph>= 7.2

To verify azoospermia, the semen should be centrifuged and evaluated under a light microscope for the presence of sperm. Patients with azoospermia should have a postejaculatory urine sample analyzed for sperm, should be evaluated for ejaculatory duct obstruction, and should undergo a hormonal evaluation

Motility is described as the percent of sperm present with flagellar motion viewed on a bright-field or phase-contrast microscope. Normal motility is defined as more than 60% of sperm having normal movement, and the WHO 2010 lower reference limit (5th percentile) is 40%. Causes Pyospermia , Antisperm ,antibodies ,Varicocele ,Partial ductal obstruction

Normal sperm have a smooth oval head approximately 3-5 μm long and 2-3 μm wide. More than 60% of sperm should be normal,

A routine part of the initial evaluation is testing of specific serum hormone levels, which usually includes FSH, LH, testosterone, and prolactin

Patients with a high number of immature sperm should be evaluated for excessive exposure to heat or radiation or for infectious processes

Infertility in men can result from deficiencies in sperm formation, concentration, or transportation.

### Pretesticular causes of infertility

Disorders of the hypothalamus lead to hypogonadotropic hypogonadism. If gonadotropin-releasing hormone (GnRH) is not secreted, the pituitary does not release luteinizing hormone (LH) and follicle-stimulating hormone (FSH). Ideally, such patients respond to replacement with exogenous GnRH or human chorionic gonadotropin (hCG), an LH analogue

Prader-Willi syndrome

PWS occurs as the result of absence of expression of paternal genes from chromosome 15. DNA-based methylation testing will detect abnormal parent-specific imprinting within the Prader-Willi critical region on chromosome. Patients have characteristic obesity, developmental delay, small hands and feet, and hypogonadotropic hypogonadism due to a GnRH deficiency.

Laurence-Moon-Biedl syndrome

Patients with this syndrome have retinitis pigmentosa and polydactyly. Infertility is due to hypogonadotropic hypogonadism.

LNMS is most commonly attributed to changes (mutations) in the PNPLA6 gene. The PNPLA6 protein is an enzyme that is thought to drive the growth of nerve and non-nerve cells as they grow and mature. Patients with this syndrome have retinitis pigmentosa and polydactyly. Infertility is due to hypogonadotropic hypogonadism

central nervous system tumors, temporal lobe seizures, and many drugs (eg, dopamine antagonists) may interrupt the hypothalamic-pituitary axis at the hypothalamus

Both pituitary insufficiency and pituitary excess cause infertility. Nonfunctional pituitary tumors may compress the pituitary stalk or the gonadotropic cells, interrupting the proper chain of signals leading to pituitary failure. In contrast, functional pituitary tumors may lead to unregulated gonadotropin release or prolactin excess, interrupting the proper signaling.

Prolactinoma

A prolactin-secreting adenoma is the most common functional pituitary tumor.

infertility due to a prolactinoma may have gynecomastia and galactorrhea.

Bromocriptine and cabergoline are dopamine agonists used to suppress prolactin levels. These are both first-line treatment options for microprolactinoma. Some men respond with an increase in testosterone levels; many also recover normal sperm counts.

Isolated LH deficiency (fertile eunuch)

In these patients, LH levels are decreased while FSH levels are within the reference range. Patients have eunuchoidal body habitus, large testis, and a low ejaculatory volume. The treatment of choice is exogenous hCG.

Isolated FSH deficiency

This is a very rare cause of infertility. Patients present with oligospermia but have LH levels within the reference range. Treatment is with human menopausal gonadotropin (HMG) or exogenous FSH.

Thalassemia

Patients with thalassemia have ineffective erythropoiesis and require multiple blood transfusions. Excess iron from multiple transfusions may be deposited in the pituitary gland and the testis, causing parenchymal damage and both pituitary and testicular insufficiency. Treatment is with exogenous gonadotropins and iron-chelating therapy

Cushing disease

Increased cortisol levels cause a negative feedback on the hypothalamus, decreasing GnRH release.

Excess cortisol may be produced by adrenal hyperplasia, adenomas, carcinoma, or lung tumors. High cortisol levels may also be seen with exogenous steroid use, such as that administered to patients with ulcerative colitis, asthma, arthritis, or organ transplant. For example, high cortisol levels are seen in patients with Cushing syndrome, which causes negative feedback on the pituitary to decrease LH release.

### **Primary testicular causes of infertility**

 Classic Klinefelter syndrome has a 47, XXY karyotype and is caused by a nondisjunction during the first meiotic division. Infertility is caused by primary testicular failure, and most patients are azoospermic. Hormonal analysis reveals increased gonadotropin levels, while 60% have decreased testosterone levels. exogenous testosterone may also suppress any underlying sperm production

Noonan syndrome (46, XY) turner syn.

Leydig cell function is impaired, and most patients are infertile due to primary testicular failure.

Androgen receptor dysfunction

Because cells respond inadequately to androgen stimulation, spermatogenesis is impaired. This results in negative feedback stimulation of the hypothalamic-pituitary axis, causing an increased release of gonadotropins and testosterone.

Down syndrome

These patients have mild testicular dysfunction with varying degrees of reduction in germ cell number. LH and FSH levels are usually elevated.

Varicoceles are generally asymptomatic, and most men with varicoceles do not have infertility or testicular atrophy. However, varicoceles may lead to impaired testicular spermatogenesis and steroidogenesis, potentially due to an increased intratesticular temperature, reflux of toxic metabolites, and/or germ cell hypoxia; this appears to be progressive over time. Varicoceles lead to an increased incidence of sperm immaturity, apoptosis, and necrosis

Surgery is the treatement.  Ther are many ways but all involve blocking the blood flow in the pampiniform plexus veins.

The testes are at risk for both thermal and physical trauma because of their exposed position

The agents most often associated with infertility are the alkylating agents such as cyclophosphamide. For example, treatment for Hodgkin lymphoma has been estimated to lead to infertility

 viral orchitis, such as that caused by the mumps virus, echovirus, or group B arbovirus. The virus may either directly damage the seminiferous tubules or indirectly cause ischemic damage . After recovery, the testicle may return to normal or may atrophy.

Excessive use of alcohol, cigarettes, caffeine, or marijuana

Antisperm antibodies

Antisperm antibodies bind to sperm, impair motility, and lead to clumping, impairing movement through the female reproductive tract and interaction with the oocyte

Ejaculation issues: Diabetic neuropathy ,Bladder neck surgery, Retroperitoneal lymph node dissection ,Multiple sclerosis ,Spinal cord injury, alpha-antagonists

Treatments:

### **Endocrinopathies**

A number of patients with hypogonadotropic hypogonadism respond to gonadotropin-releasing hormone (GnRH) therapy or gonadotropin replacement. Pulsatile GnRH therapy can be used in those with intact pituitary function. Gonadotropin replacement can be effective in patients with hypothalamic and pituitary dysfunction.

Human chorionic gonadotropin (hCG) is a luteinizing hormone (LH) analogue that may be used alone or in combination with human menopausal gonadotropin (hMG) for Leydig cell stimulation.

Aromatase inhibitors (eg, anastrozole) block the conversion of testosterone to estrogen, thus increasing the serum testosterone concentration.They are especially useful in improving semen parameters in patients. Anastrozole 1 mg/day, Letrozole 2.5 mg/day.

Clomiphene citrate is a weak estrogen-receptor antagonist that works by blocking the negative feedback inhibition of estrogen on the anterior pituitary, thus increasing the release of FSH and LH. Clomiphene citrate is effective in improving the semen parameters in patients with hypogonadotropic hypogonadism.[53]Tamoxifen is another estrogen-receptor antagonist that, in combination with clomiphene, can increase sperm concentration, sperm motility, and pregnancy rates in males with idiopathic infertility.

Patients with congenital adrenal hyperplasia (CAH) may respond to therapy with glucocorticoids.

Treatment of hyperprolactinemia is with dopamine antagonists, such as bromocriptine or cabergoline.
Cabergoline (0.5-1 mg twice weekly) , bromocriptine (2.5-5.0 mg twice weekly)

Imipramine and alpha-sympathomimetics, such as pseudoephedrine, may help close the bladder neck to assist in antegrade ejaculation

hyperviscosity may benefit from a precoital saline douche or semen processing with chymotrypsin

8 mg of zinc, 100 mg of vitamin C, 12 mg of vitamin E, and 400 µg of folic acid; this was taken once a day, along with 200 mg of selenium every other day after lunch