Male factor

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Fellowship infertility

male reproductive function and the importance of male factors in infertility has advanced significantly over the last two decades.

In the past, the female partner was the primary focus of attention and male factors were regarded as a relatively uncommon cause of infertility.

REGULATION OF TESTICULAR FUNCTION

The testes have two distinct components

the seminiferous tubules (the site of spermatogenesis) and the Leydig cells (the source of testosterone).

the Leydig cells (the source of testosterone).

Spermatogenesis

takes approximately 70 days to complete from the spermatocyte stage.

Another 12–21 days are required for the transport of sperms from the testis through the epididymis to the ejaculatory duct

Hormone Regulation

Normal testicular function requires the actions of both pituitary gonadotropins, FSH ,LH

luteinizing hormone (LH). LH stimulates the Leydig cells in the testicular interstitium to synthesize and secrete testosterone

- **FSH supported** indirectly actions of LH are by, which induces the appearance of LH receptors on testicular Leydig cells
- Synthesis of androgen-binding protein(ABP) in Sertoli cells.

AGING AND MALE REPRODUCTIVE FUNCTION

Although aging has adverse effects on male reproductive function, the impact of age is less obvious than it is in women.

Semen quality and male fertility, as well as androgen production and serum testosterone levels, decrease very gradually as age increases

Aging and Male Fertility

- Semen volume
- sperm motility
- morphologically normal
- but not sperm concentration

Increased paternal age has been associated with an increase in

- numerical and structural chromosomal
- increased DNA fragmentation
- Higher frequency of point mutations
- spontaneous abortion
- birth defects
- Autosomal dominant mutations
- X-linked disease
- schizophrenia
- autism

Androgen Deficiency in the Aging Male

- SHBG concentrations increase gradually with age
- Free testosterone levels decrease more than total testosterone concentrations
- SHBG levels also may rise in association with increased abdominal obesity, further contributing to the decrease in free testosterone

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Hypogonadal men

- total testosterone <300–325 ng/dl
- free testosterone <5 ng/dL
- symptoms of hypogonadism.

Andropause

- Decreased libido
- Erectile dysfunction
- Reduced strength, energy
- Irritability ,lower quality of life, sleep disturbance, depressed, lethargy and changes in cognitive function.
- Physical changes, osteopenia or osteoporosis, decreased muscle mass, increased visceral adipose tissue, testicular atrophy, and gynecomastia, central obesity, increased insulin, metabolic syndrome, diabetes, and increased mortality.

- *Men with symptoms or signs of androgen deficiency measuring the serum total testosterone level, ideally during the morning hours*.

- **Low concentrations (<200 ng/dL) should be confirmed by repeated measurements**.

- *Normal or low serum LH*

- **Suggests a secondary hypogonadism additional evaluation by measurement of serum prolactin, (MRI) to detect any hypothalamic or pituitary mass lesion.**

Treatment

- Suggested that a total testosterone level under 200 ng/dL is evidence of hypogonadism that warrants treatment
- Concentrations between 200 and 400 ng/dL may benefit from treatment.

The potential risks of testosterone treatment

- Prostate or Breast cancer
- Palpable prostate nodule or induration
- Prostate-specific antigen (PSA) greater than 3 ng/mL without further urologic evaluation
- Erythrocytosis (hematocrit >50%)
- Untreated obstructive sleep apnea
- Severe lower urinary tract symptoms (International Prostate Symptom Score >19)
- Class III or IV heart failure.

Androgen therapy must be monitored

- Physical examination (breasts, heart, lungs, prostate)
- Serum PSA
- Complete blood count should be obtained
- Prostate biopsy is recommended when the digital rectal examination or serum PSA is abnormal.
- Within 3 months after therapy begins
- Evaluated for weight gain
- Peripheral edema
- Gynecomastia or breast tenderness, sleep disorders, or prostate enlargement.

• Men with a good clinical response continue treatment but should return for similar monitoring after another 6 months and at least annually thereafter.

• If osteoporosis was one of the indications for treatment, bone mineral density also should be reevaluated approximately 1–2 years after treatment starts.

CAUSES OF MALE INFERTILITY

- Hypothalamic-pituitary disorders (1–2%), congenital, be acquired, or result from systemic illness
- Primary gonadal disorders (30–40%), both congenital and acquired
- Disorders of sperm transport (10–20%)
- Idiopathic (40–50%)

Hypothalamic-pituitary disorders	• Idiopathic isolated gonadotropin deficiency • Kallmann syndrome • Single gene mutations (e.g., involving the GnRH receptor, FSHβ, LHβ, or transcription factors involved in pituitary development) • Hypothalamic and pituitary tumors (e.g., craniopharyngioma, macroadenoma) • Infiltrative diseases (sarcoidosis, histiocytosis, transfusion siderosis, hemochromatosis) • Hyperprolactinemia • Drugs (GnRH analogs, androgens, estrogens, glucocorticoids, opiates) • Critical illness or injury • Chronic systemic illness or malnutrition • Infections (e.g., meningitis) • Obesity
Primary gonadal disorders	• Klinefelter syndrome • Y chromosome deletions • Single-gene mutations and polymorphisms (e.g., involving the androgen, estrogen, or FSH receptor) • Cryptorchidism • Varicoceles • Infections (e.g., viral orchitis, leprosy, tuberculosis) • Drugs (e.g., alkylating agents, alcohol, antiandrogens, cimetidine) • Radiation • Environmental gonadotoxins (e.g., heat, smoking, metals, organic solvents, pesticides) • Chronic illness (renal insufficiency, cirrhosis, cancer, sickle cell disease, amyloidosis, vasculitis, celiac disease)
Disorders of sperm transport	• Epididymal obstruction or dysfunction • Congenital bilateral absence of the vas deferens (relating to *CFTR* mutations) • Infections causing obstruction of the vas deferens (e.g., gonorrhea, *Chlamydia*, tuberculosis) • Vasectomy • Kartagener syndrome (primary ciliary dyskinesia) • Young syndrome • Ejaculatory dysfunction (e.g., spinal cord disease, autonomic dysfunction)

Hypothalamic-Pituitary Disorders

Kallmann syndrome

Hypothalamic or pituitary tumors

Hyperprolactinemia

chronic systemic illness

Infections

treatment with GnRH analogs (for prostate cancer), androgens, glucocorticoids, Opiates can suppress gonadotropin secretio

Infiltrative diseases

Klinefelter Syndrome

- One of the most common causes of primary testicular failure
- Extra X chromosome (47,XXY) is the most common form,some men with Klinefelter syndrome have a greater or lesser number of X chromosomes 48,XXXY, 46,XY/47,XXY
- They have an increased risk for developing pulmonary diseases, breast cancer, mediastinal germ cell tumors, varicose veins and leg ulcers, systemic lupus erythematosus, and diabetes mellitus.

• longer CAG repeat associated with taller stature, lower bone mineral

density, gynecomastia, and decreased penile length.

• Men with Klinefelter syndrome generally have small, firm testes

• Serum concentrations of FSH and LH are elevated and testosterone levels

are decreased extent.

• Cryptorchidism is more common

Y Chromosome Deletions

- Micro deletions of the long arm of the Y
- Affecting 2–5% of men with severe oligospermia and 8% of men with azoospermia.
- Y chromosome deletions also have been identified in men with cryptorchidism, varicocele

- Because all Y chromosome abnormalities will be transmitted to sons of affected men conceived via ICSI
- Genetic testing and counseling should be offered to affected men before their sperms are used for that purpose.

Cryptorchidism

- **Failure of testicular descent during fetal development, which is an androgen-dependent process.**

- *Consequently, it is common in men with abnormalities of testosterone production, such as Kallmann syndrome, androgen resistance, and defects in testosterone synthesis.*
- *The severity of the semen abnormality relates to the duration of time the testes have been outside of the scrotum.*

- Men having low serum inhibin B levels, increased FSH concentrations, and decreased sperm density after repair of cryptorchidism are at increased risk for infertility.

Varicoceles

• Dilation of the pampiniform plexus of the spermatic
veins in the scrotum.
• They are more prevalent in infertile men (up to 30%)
than in fertile men (10–15%) and are 10 times more
commonly found on the left than on the right
• Although increased testicular temperature, delayed
removal of local toxins, hypoxia, and stasis are viewed as the mechanisms

Other Causes of Primary Gonadal Failure

- Mumps orchitis ,Gonorrhea and chlamydia infections

- **Drugs:adversely affect spermatogenesis or Leydig cell function**

- Doses of radiation (15 rad) can suppress spermatogenesis, and doses above 6Gy generally cause permanent azoospermia

Environmental exposures

•Heat, smoking or heavy use of marijuana, alcohol, or cocaine

• A modest increase in scrotal temperature can adversely affect spermatogenesis, and a febrile illness can result in dramatic, if also transient, decreases in sperm density and motility.

Disorders of Sperm Transport

- **Even when sperm production is normal, epididymal obstruction or dysfunction can result in infertility.**

- *Congenital or acquired abnormalities of the vas deferens*

- Approximately 1–2% of infertile men and up to 6% of men with obstructive azoospermia Have congenital bilateral absence of the vas deferens (CBAVD)

- Infections(gonorrhea,chlamydia,tuberculosis
- • Vasectomy
- • Primary ciliary dyskinesia (Kartagener syndrome)
- • Young syndrome is another genetic disease

THE MALE INFERTILITY EVALUATION

HISTORY

- Duration of infertility and previous fertility
- Coital frequency and any sexual dysfunction
- Results of any previous evaluation or treatment for infertility
- Childhood illnesses and developmental history
- Previous surgery, its indications and outcome, and systemic medical illness
- Past episodes of or exposures to sexually transmitted infection
- Exposures to environmental toxins, including heat
- Current medications and allergies
- Occupations and use of tobacco, alcohol, and other drugs

Physical Examination

- • Examination of the penis, to include the location of the urethral meatus
- • Palpation of the testes and measurement of their size
- • The presence and consistency of both the vasa and epididymides
- • Presence of any varicocele
- • Secondary sex characteristics, including body habitus, hair distribution, and breast development
- • Digital rectal examination

Semen Analysis

- • The initial evaluation for male factor infertility should include at least one properly performed semen analysis.
- • If abnormal, another semen analysis should be obtained after at least 4 weeks.
- • Semen parameters can vary widely over time, even among fertile men and also exhibit seasonal variations

- Normal semen analysis generally excludes an important male factor when there is no complaint or suspicion of sexual dysfunction.

- Conversely, abnormal semen parameters suggest the need for additional endocrine , urologic, or genetic evaluation

Standard but detailed instructions for semen collection

- Should be provided, abstinence period of 2–3 days.
- Shorter intervals of abstinence decrease the semen volume and sperm density but generally have little or no impact on sperm motility or morphology.
- Longer abstinence intervals increase semen volume and sperm density but also increase the proportion of dead, immotile, or morphologically abnormal sperm.
- Ideally, the semen specimen should be collected by masturbation directly into a clean container.
- Semen sample should be examined within an hour after collection

Normal Reference Values

- Overall, the odds of male infertility increase with the number of major semen parameters (concentration, motility, morphology) in the subfertile range
- 2 to 3 times higher when one is abnormal
- 5 to 7 times higher when two are abnormal,
- 16 times greater when all three are abnormal

Volume	1.5–5.0 mL
pH	>7.2
Viscosity	<3 (scale 0–4)
Sperm concentration	>20 million/mL
Total sperm number	>40 million/ejaculate
Percent motility	>50%
Forward progression	>2 (scale 0–4)
Normal morphology	>50% normal[303] >30% normal[304] >14% normal[305]
Round cells	<5 million/mL

Volume	1.5 (1.4–1.7) mL
Sperm concentration	15 (12–16) million/mL
Total sperm number	39 (33–46) million/ejaculate
Total motility	40 (38–42) %
Progressive motility	32 (31–34) %
Normal morphology	4 (3–4) %
Vitality	58 (55–63) %

Ejaculate Volume and pH

- **The majority of semen volume comes from the seminal vesicles, which share are common embryology with the vasadeferentia.**
- Seminal vesicle secretions are alkaline and contain fructose.
- **When both ejaculatory ducts are completely obstructed, the semen is acidic (containing only prostatic secretions) and contains neither fructose nor sperms**

Sperm Concentration and Total Sperm Count

- The absence of sperms should be documented on at least two separate occasions

- Azoospermia is generally classified

- Obstructive (normal sperm production) infection, iatrogenic injury during scrotal or inguinal surgery, or congenital anomalies(CBAVD); approximately 40% of azoospermic men have an obstruction.

- Non obstructive (decreased or absent spermatogenesis) (primary testicular failure) or endocrinopathies and other conditions that suppress spermatogenesis.

- **Oligospermia is defined traditionally by a sperm density less than 20 million/mL**

- *Severe when the sperm concentration is below 5 million/mL.*

- **Probability of conception increases with increasing sperm concentrations up to approximately 40–50 million/ mL but does not rise further with higher sperm densities.**

Oligospermia

- Oligospermia may be associated with a varicocele hypogonadism, or specific microdeletions in the Y chromosome.

- Endocrine and genetic evaluation is indicated for men with severe oligospermia

Poor sperm motility

- Asthenospermia suggests:
- Testicular or epididymal dysfunction
- Sperm autoantibodies (predisposing to aggregation)
- Genital tract infections (leukocytes in the semen)
- Partial obstruction of the ejaculatory ducts vasectomy reversal
(reanastomosis)
- Varicoceles, and prolonged abstinence intervals.
- Large numbers of viable non motile sperms suggest (Kartagener syndrome)

When no motile sperms are observed

- **Sperm vitality test can differentiate viable non motile sperms from dead sperms.**
- Eosin Y or trypan blue: sperms with intact membrane function do not take up the stain
- Another method, the hypo-osmotic sperm swelling test, the tails of sperms with normal membrane function swell and coil as fluid is transported across the membrane.
- In men with few or no motile sperms, the hypoosmotic swelling test can be used to identify living non motile sperms for ICSI

Sperm Morphology

- Sperm morphology reflects the quality of spermatogenesis.

- Morphologic abnormalities(terato spermia) are categorized by location, involving the head, neck or tail

- Sperms classified as normal must be normal in all respects.

- Terato spermia has been associated with varicocele and with both primary and secondary testicular failure.

• **severe terato spermia became widely accepted as an indication for ICSI in IVF cycles.**

• However, others have observed no differences in the fertilization, pregnancy, and live birth rates achieved with ICSI and conventional fertilization and argue that isolated terato spermia is not a valid indication for performing ICSI.

Round Cells and Leukocyto spermia

- When the round cell count exceeds 5 million/mL, additional studies should be performed to differentiate leukocytes from immature sperms

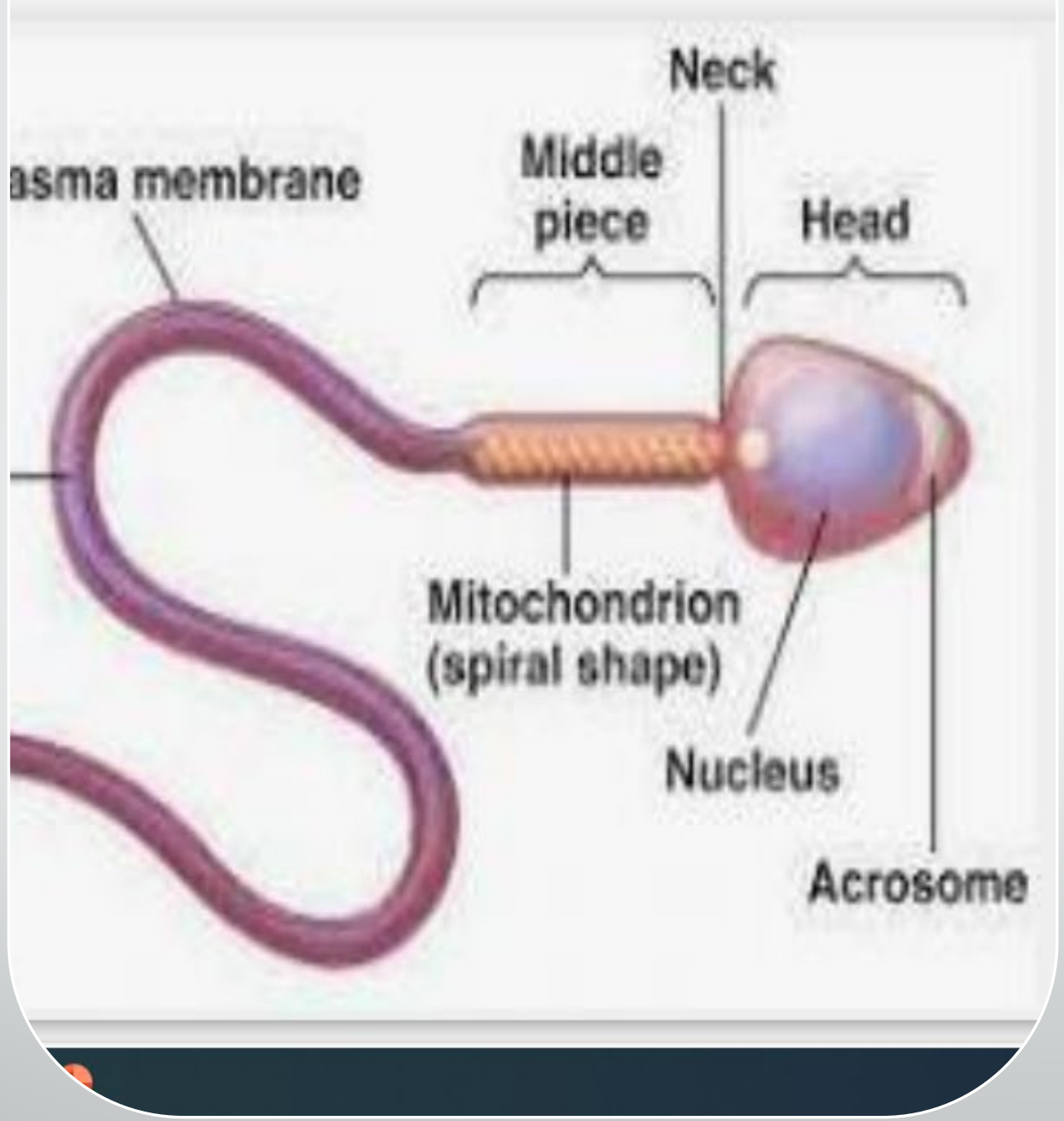
- leukocytospermia (>1 million leukocytes/mL) who may require additional evaluation for genital tract infection or inflammation.

- Leukocytospermia unrelated to infection or inflammation also may be observed in the semen of men with spinal cord injuries.

Sperm Auto antibodies

- The blood-testis barrier normally isolates sperms from immune recognition
- They may interfere with sperm motility or prevent fertilization

- Risk factors for anti sperm antibodies include
ductal obstruction, previous genital infection,
testicular torsion or trauma, and sterilization
reversal (vasovasostomy vasoepididymostomy).


Neck
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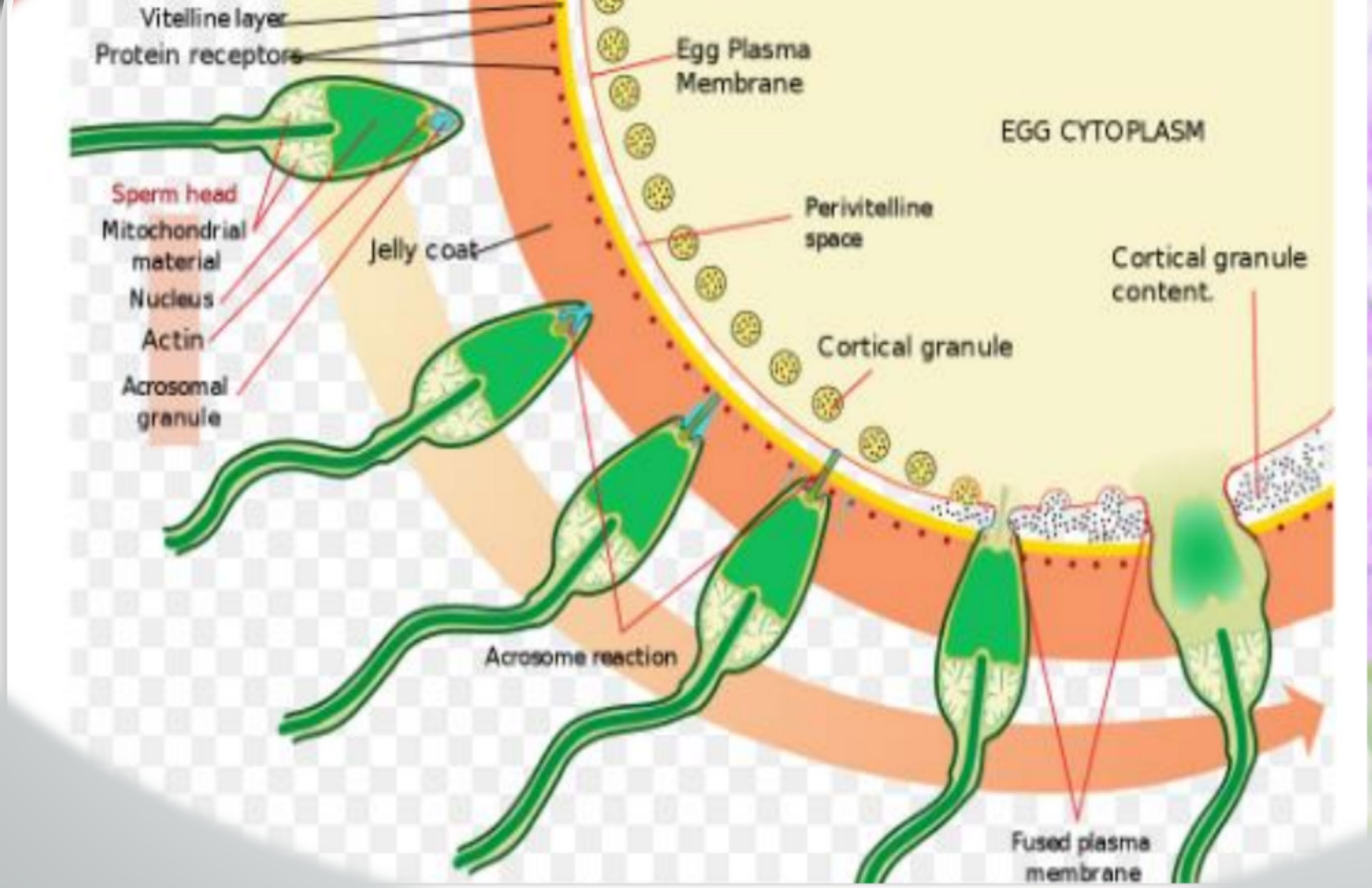
Acrosome


Vitelline layer
Protein receptors
Egg Plasma Membrane
EGG CYTOPLASM
Sperm head
Mitochondrial material
Nucleus
Actin
Acrosomal granule
Jelly coat
Perivitelline space
Cortical granule content
Cortical granule
Acrosome reaction
Fused plasma membrane

Endocrine Evaluation

- Abnormal semen analysis (particularly a sper concentration <10 million/mL)

- Sexual dysfunction (decreased libido, impotence)

- Other clinical symptoms or findings that suggest a specific endocrinopathy

A basic endocrine evaluation infertile male:

- Serum FSH and total testosterone

- When the total testosterone level is low (<300 ng/dL) Should be repeated to confirm the finding, serum free testosterone, LH, and prolactin should be obtained

• In men with hypo gonadotropic hypo gonadism generally all three hormone levels are distinctly low.

• Testicular failure high levels of FSH and LH and a low or normal testosterone concentration.

• Men with a prolactin-secreting pituitary tumor generally have normal or low gonadotropin concentrations, a low serum testosterone, and an elevated prolactin level

• In those with hypo gonadotropic hypo gonadism, with or without hyper prolactinemia, MRI of the hypo thalamic pituitary region is indicated to exclude a mass lesion.

In infertile men with

- Severe oligospermia (<5 million/mL)
- Low testosterone levels (<300 ng/dL)
- Normal gonadotropin concentrations,
- Evaluation might be expanded to
- Serum estradiol and calculation of the testosterone (ng/dL)/estradiol (pg/mL) ratio, because those with low values (<10) may benefit from treatment with an aromatase inhibitor.

Testis biopsy

• Performed for diagnostic purposes in azoospermic men,those with elevated serum FSH levels do not require a diagnostic biopsy because a high FSH concentration is diagnostic for abnormal spermatogenesis.

• In contrast, diagnostic biopsy is indicated for azoospermic men with normal testicular size, at least one palpable vas deferens and a normal serum FSH level, because the normal FSH does not guarantee that spermatogenesis is normal.

Genetic Evaluation

- Genetic abnormalities may cause infertility
- (1)mutations within the CFTR gene, which are highly associated with CBAVD

- (2)chromosomal anomalies resulting in testicular dysfunction (Klinefelter syndrome;47,XXY)

- (3) Y chromosome microdeletions

MEDICAL TREATMENT FOR MALE INFERTILITY

Hypogonadotropic Hypogonadism

- Men with hypogonadotropic hypogonadism

represent one group in which medical

treatment can be successful, after its cause has been defined.

Post pubertal hypogonadotropic hypogonadism

• Uncommon but may arise hypothalamic or pituitary tumor or an inflammatory process(sarcoidosis, hemochromatosis, autoimmune hypophysitis),
pituitary tumors, specifically prolactinomas, are the most common cause.

• Hypogonadotropic hypogonadism due to hyperprolactinemia is generally uncommon in infertile men (approximately 1%) but is amenable to treatment with dopamine agonists when it is identified.

• Increased testosterone levels and potency are observed within approximately 3–6 months after normal prolactin levels are achieved, changes in semen quality generally take longer.

Congenital Hypogonadotropic hypogonadism treated

- HCG (to stimulate Leydig cell testosterone production)
- Exogenous testosterone; either can induce secondary sexual development, but neither can initiate and support normal spermatogenesis.

- Men with congenital hypogonadotropic hypogonadism and those with postpubertal onset who do not respond to treatment with hCG alone, normal spermatogenesis can be induced by combined treatment with hCG and hMG or pure FSH (75–150 IU three times weekly)

- Men with severe oligospermia (<5 million sperms/mL)
- Low serum testosterone levels (<300 ng/dL)
- Abnormally low serum testosterone (ng/dL)/estradiol (pg/mL) ratio (<10)
- May benefit from medical treatment with aromatase inhibitor.

Hypergonadotropic Hypogonadism

- There is no evidence that any form of medical treatment can improve semen quality and fertility in infertile men with hypergonadotropic hypogonadism

- For men with complete spermatogenic failure, the only treatment options are insemination with donor sperms and adoption.

Retrograde Ejaculation

- Imipramine 25 mg twice daily or 50 mg at bedtime,
- Pseudoephedrine 60 mg
- Ephedrine 25–50 mg four times daily,
- Phenylpropanolamine 50–75 mg twice daily), directed at control of the internal sphincter. for best results,
- Urine pH and osmolality (300–380 mOsm/L) must be carefully controlled by alkalinizing the urine (sodium bicarbonate 650 mg four times daily, beginning 1–2 days before collection) and managing fluid

Leukocyto spermia

• Leukocytospermia has been associated with other abnormal semen parameters, and antibiotic treatment (doxycycline, erythromycin, trimethoprimsulfamethoxazole, or a quinolone) clearly is indicated for men with symptomatic genital tract infections.

• However, antibiotic treatment does not improve semen parameters in men with asymptomatic leukocyto spermia and often fails even to decrease the numbers of leukocytes to normal levels

Idiopathic Male Infertility

- Unfortunately, no medical treatment has proven reliably effective for improving semen parameters or fertility in men with idiopathic subfertility.

- There is no substantial evidence that androgen therapy is an effective treatment for idiopathic male infertility.

• Exogenous FSH may improve semen quality in a subset of men with idiopathic oligospermia in whom testicular biopsy reveals maturation arrest and serum FSH and inhibin B levels are normal.

• Empiric treatment (3–6 months) with either clomiphene citrate (25 mg daily) or tamoxifen (20 mg daily) commonly is offered to stimulate increased gonadotropin secretion and spermatogenesis in men with idiopathic subfertility.

INTRAUTERINE INSEMINATION

- Treatment for men with severe hypospadias,retrograde ejaculation, neurologic impotence, and sexual dysfunction,oligospermia asthenospermia, low ejaculate volumes, sperm autoantibodies, and cervical factors

- Donor sperms is effective treatment for severe and uncorrectable male factor infertility, inherited genetic disorders in the male partner

- Best results are achieved when the number of total motile sperms exceeds a threshold of approximately 10 milion

- Combining the yield from two ejaculates obtained approximately 4 hours apart may increase the numbers of sperms available from oligospermic men.
- Success rates with IUI are highest when 14% or more of the sperms have normal morphology, intermediate with values between 4% and 14%, and generally quite poor when fewer than 4% of sperms are normal.

Sperm Preparation

- Washing sperm the greatest numbers of sperms, but the final specimen also contains dead and abnormal sperms and other cellular debris.
- Swim-up cleaner specimen, devoid of dead sperms and other cellular debris, but also yields significantly lower numbers of sperms
- Density gradient centrifugation select a population of sperms with normal morphology
- The best choice among them may vary with the quality of the semen sample

SURGICAL TREATMENT FOR MALE INFERTILITY

- Obstructive azoospermia
- Varicocele
- Vasovasostomy and Vaso epididymostomy about approximately 2–6% of vasectomized men later seek reversal of their sterilization procedure.

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Transurethral Resection of the Ejaculatory Ducts

- Ejaculatory duct obstruction is a cause of infertility in 1–5% of infertile men
- Low ejaculate volumes combined with low or normal sperm concentration and low or absent motility.
- The condition also may present as hemospermia and painfulI
- Semen volume in approximately two-thirds
- Returns sperms to the ejaculate in about half of azoospermic men.

Varicocele Repair

- The prevalence of varicoceles is approximately 10–15% in the normal male population and about 25–40% in infertile men.
- Varicocele repair is considered primarily for men with palpable varicoceles and abnormal semen
- Adolescent males with unilateral or bilateral varicoceles associated with decreased testicular size

• The best candidates for varicocele repair are young men with large varicoceles and infertility of relatively short duration.

• Poor prognosis :

• Atrophic testes, elevated FSH levels, and severe oligospermia or azoospermia indicate severe epithelial damage

Orchiopexy

- Even in adult men with bilateral cryptorchidism, orchiopexy can result in spermatogenesis and fertility it preserves testicular hormone production.

Vibratory Stimulation and Electroejaculation

- Include men with spinal cord injuries
- Demyelinating neuropathies
- Diabetes and those who have had retroperitoneal lymph node dissections.

Epididymal Sperm Aspiration:

the small quantities of sperms obtained are sometimes inadequate to allow cryopreservation, and pregnancy rates achieved have generally been lower than with the open technique.

Testicular Sperm Extraction and Aspiration

- In men with nonobstructive azoospermia and those in whom epididymal sperm aspiration techniques fail or are inapplicable, sperms may be retrieved directly from the testis

GENETIC RISKS ASSOCIATED WITH ICSI

- karyotyping and Y chromosome deletion analysis should be offered to all men with severe male factor infertility who are candidates for IVF with ICSI

The principal indication for ICSI is male factor infertility

- Severe oligospermia (<5 million sperm/mL)
- Asthenospermia (<5% progressive motility)
- Teratospermia (<4% normal forms by strict criteria)
- Using surgically retrieved sperm
- Treatment includes PGD
- couples with previous failed or poor fertilization with conventional IVF

Table 2. Summary of recommendations by professional society guidelines on indications for SDF testing

Guidelines	AUA/ASRM	EAU	ESHRE	EAA	SIAMS	DGGG, OEGGG, and SGGG
UMI	No specific recommendation	SDF testing strongly recommended	NA	No specific recommendation	No specific recommendation	No specific recommendation
IMI	No specific recommendation	No specific recommendation	NA	SDF testing recommended in infertile men with OAT for decision regarding ART, no specific mention of IMI	No specific recommendation	No specific recommendation
RPL	Moderate recommendation for SDF testing	Strong recommendation for SDF testing	SDF testing recommended	No specific recommendation	Assessing sperm DNA is useful in RPL	No specific recommendation
Risk factors & exposures	No specific recommendation	Risk factors for elevated SDF are listed, but no specific recommendation for testing is made	NA	No specific recommendation	SDF testing beneficial in: DM, MAGI, antineoplastic treatments, exposure to toxicants	No specific recommendation
Varicocele	No specific recommendation	No specific recommendation for testing, but VR may be considered in men with elevated SDF with otherwise UMI	NA	No specific recommendation	SDF testing beneficial for varicocele patients, benefit of VR on SDF is discussed	No specific recommendation
ART planning	No specific recommendation	Strong recommendation for SDF testing in couples with RPL from ART	NA	SDF testing recommended when ART is considered (low quality evidence)	No specific recommendation	SDF testing not recommended routinely for IVF/ICSI (strong consensus)
Sperm cryopreservation	No specific recommendation	No specific recommendation	NA	No specific recommendation	No specific recommendation	No specific recommendation

ART: assisted reproductive technologies, AUA/ASRM: American Urological Association/American Society for Reproductive Medicine, DGGG, OEGGG, and SGGG: Guideline of the German Society of Gynecology and Obstetrics, the Austrian Society of Gynecology and Obstetrics, and the Swiss Society of Gynecology and Obstetrics, DM: diabetes mellitus, EAA: European Academy of Andrology, EAU: European Association of Urology, ESHRE: European Society of Human Reproduction and Embryology, ICSI: intracytoplasmic sperm injection, IMI: idiopathic male infertility, IVF: *in vitro* fertilization, MAGI: male accessory gland infections, NA: not applicable, OAT: oligo-astheno-teratozoospermia, RPL: recurrent pregnancy loss, SDF: sperm DNA fragmentation, SIAMS: Italian Society of Andrology and Sexual Medicine, UMI: unexplained male infertility, VR: varicocele repair.

Thank You For Your Attention