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MALE INFERTILITY

Infertility

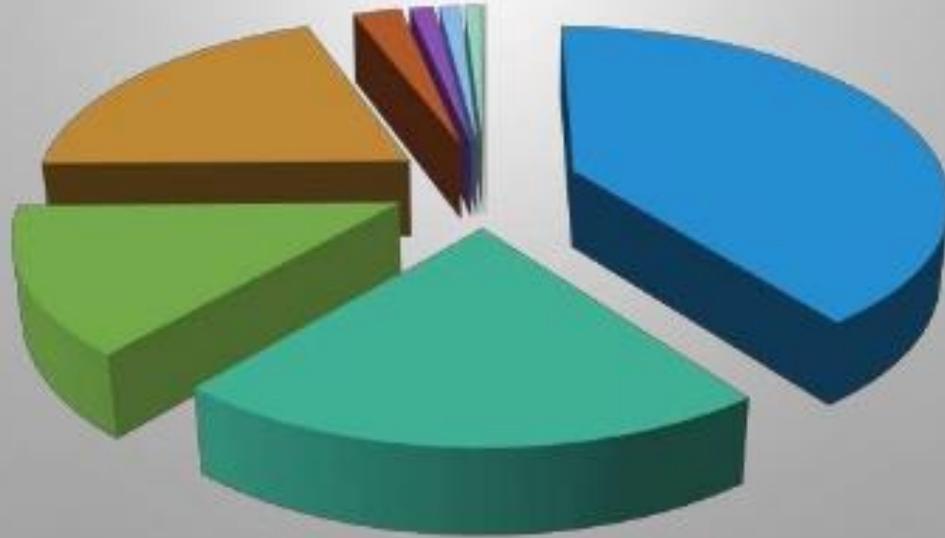
- The inability to conceive following unprotected sexual intercourse
 - 1 year (age < 35) or 6 months (age >35)
 - Affects 15% of reproductive couples
 - 6.1 million couples
 - Men and women equally affected



Causes of Male Infertility

- Hypothalamic pituitary disorders (1-2%)
- Primary gonadal disorders (30-40%)
- Disorders of sperm transport (10-20%)
- Idiopathic (40-50%)

CAUSES



■ Varicocele 42.2%

■ Obstruction 14.3%

■ Immunological 2.6%

■ Endocrinologic 1.1%

■ Genetic 0.1%

■ Idopathic 22.7%

■ Others 20.8%

■ Ejaculatory Dsyfunction 1.3%

■ Infection 0.9%

MANAGEMENT

- History
- Physical Examination
- Semen Analysis
- Endocrine Evaluation
- Urologic Evaluation
- Post Ejaculatory Semen Analysis
- Specialised Tests

HISTORY

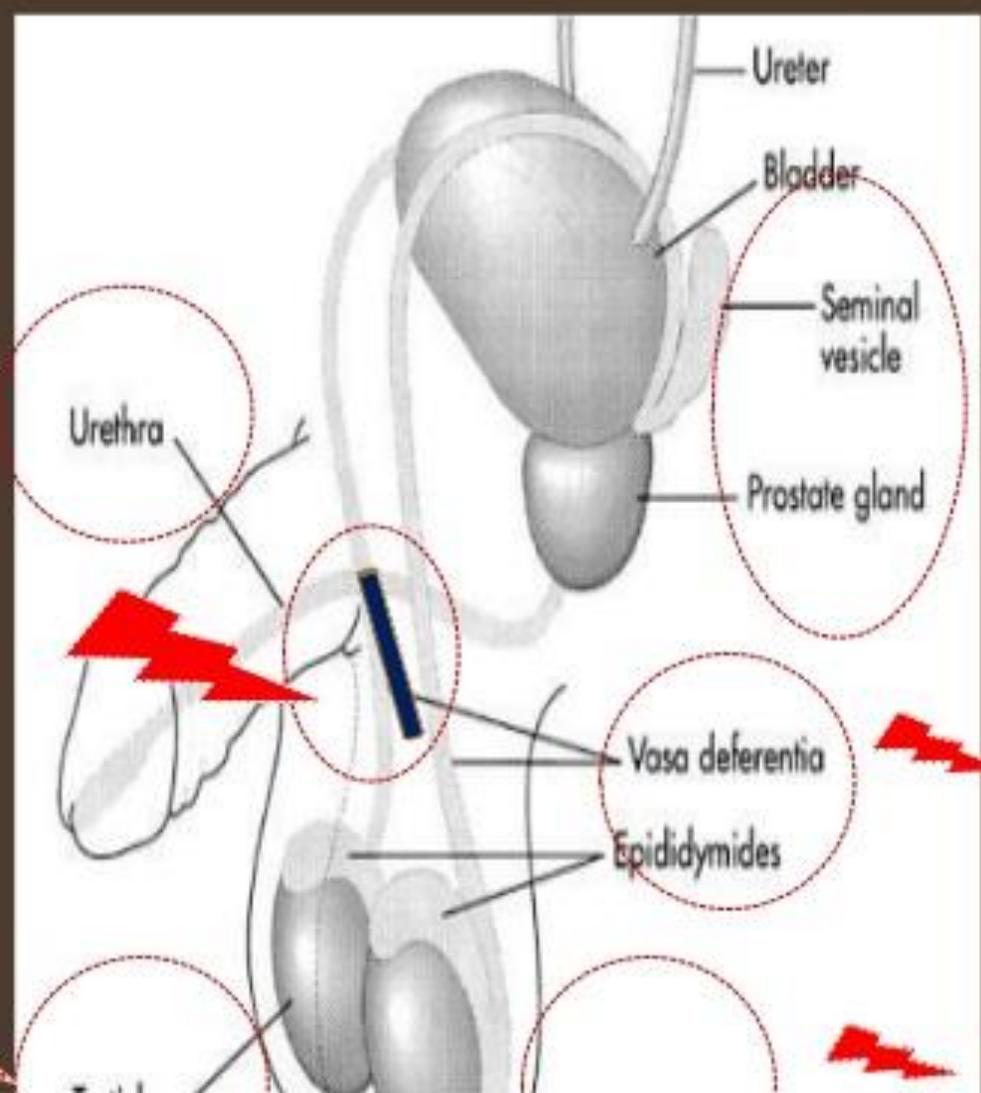


- Duration of infertility & previous fertility.
- Did puberty and virilization proceed normally?
- Have there been changes in libido, potency, or hair loss suggestive of hypogonadism?
- Are there anatomic abnormalities (*e.g.*, hypospadias, microphallus)?
- Are there any voiding difficulties or recent changes in voiding pattern?

- Hypospadias
- Micripenis

Varicocele
(Grade)

- Size/ volume
- Consistency
- Location



Per rectal
examination

- CBAVD/CUAVD
- Epididymal cyst/distension/induration

- Size
- Consistency

Male factor: Evaluation

	Initial evaluation	Further evaluation
Male Factor	<ul style="list-style-type: none">• Semen analysis• Urologic evaluation	<ul style="list-style-type: none">• FSH, LH, and testosterone level• Genetic evaluation• Epididymal sperm aspiration (PESA, MESA)• Testicular biopsy

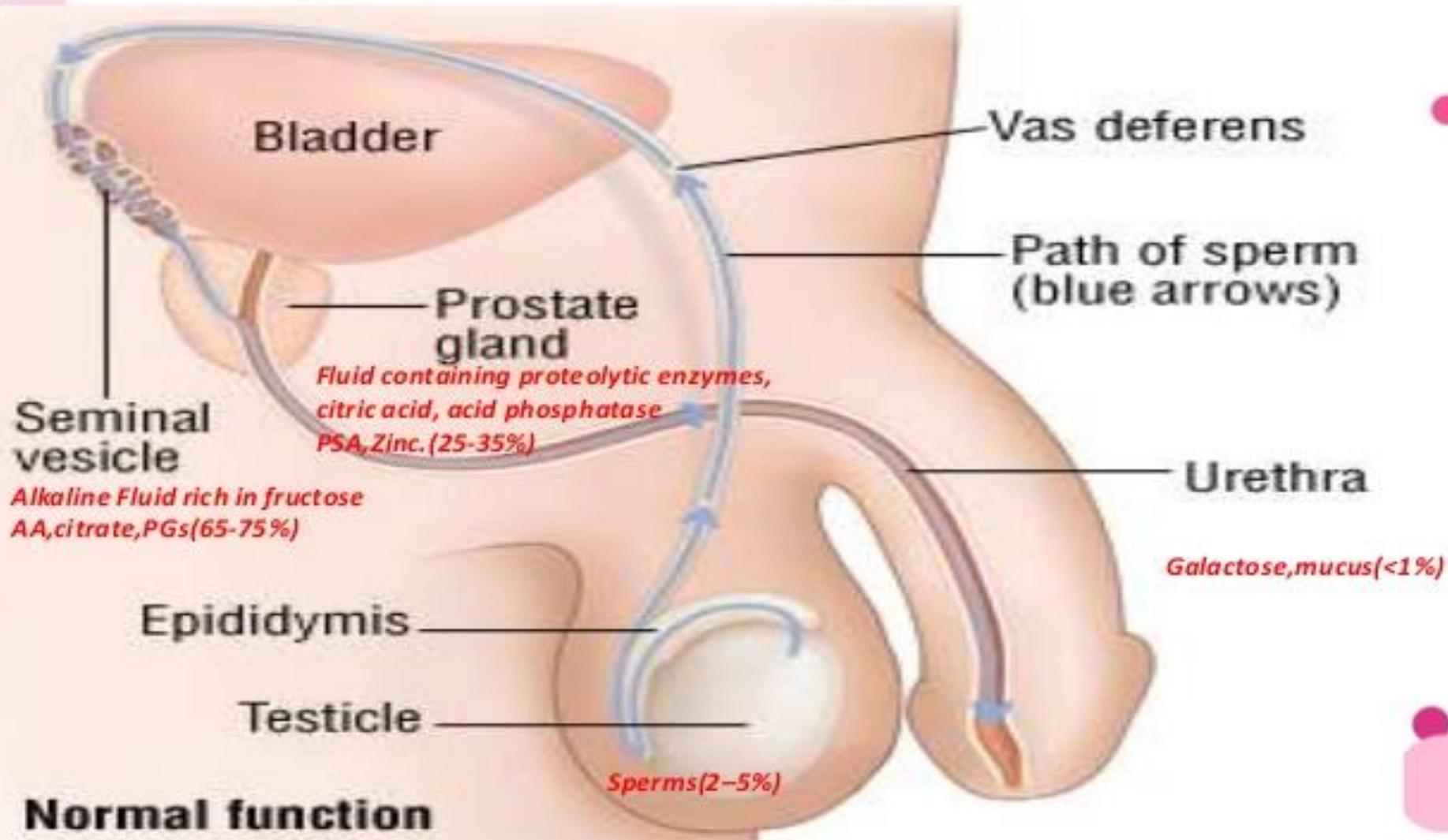
□ Collection:

- After 2-7 d of sexual abstinence
- at the doctor's office
- Masturbation
- If this is not possible:
 - condoms without chemical additives
 - delivered to the laboratory within 1 h
- At least 2 samples collected 1-2 w apart & not more than 3 months apart.
 - {marked variation of sperm production within one individual}
- Any systemic disease during sperm generation time (72 days for spermatogenesis & 14 days for transport through the epididymis & vas): ±negative impact.

Semen Analysis (SA)

- Obtained by masturbation
 - Provides immediate information
 - Quantity
 - Quality
 - Density of the sperm
 - Abstain from coitus 2 to 3 days
 - Collect all the ejaculate
 - Analyze within 1 hour
 - A normal semen analysis excludes male factor 90% of the time
- Morphology
Motility

CONSTITUENTS OF SEMEN



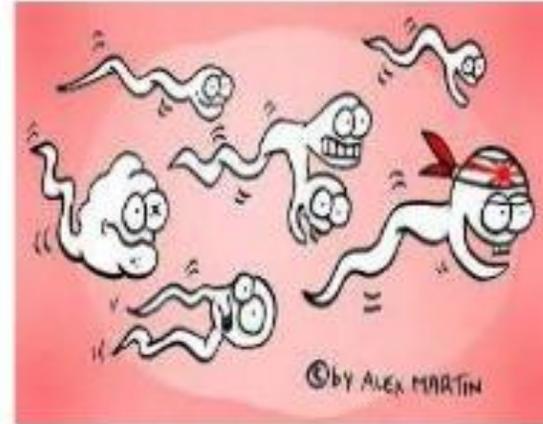
WHO reference values changed

	1980	1987	1992	1999	2010
Volume (mL)	ND	≥2	≥2	≥2	≥1.5
Count (10 ⁶ /mL)	20-200	≥20	≥20	≥20	≥15
Total count (10 ⁶)	ND	≥40	≥40	≥40	≥39
Motility (%)	≥ 60	≥50	≥50	≥50	≥40
Progressive (%)	≥ 2	≥25%	≥25% (a)	≥25% (a)	≥32%
Vitality (%)	ND	≥50	≥75	≥75	≥58
Morphology (%)	80.5	≥50	≥30	(14)*	≥4*
Leukocytes (10 ⁶ /mL)	<4.7	<1.0	<1.0	<1.0	1.0

*Strict criteria (Tygerberg); Esteves et al. *Urology* 2012

Sperm Concentration & Total Sperm Count

- **Azoospermia** : Complete absence of sperm on std microscopic examination in ejaculate.
 - To confirm diagnosis semen is centrifuged & pellet examined
 - Obstructive
 - Non Obstructive- Primary & secondary testicular failure. Candidate for IVF (TESE)
- **Oligospermia** : sperm density < 20 million/ml. Severe when < 5 million/ml
- Total motile sperm count = total sperm count & % of progressively motile sperm

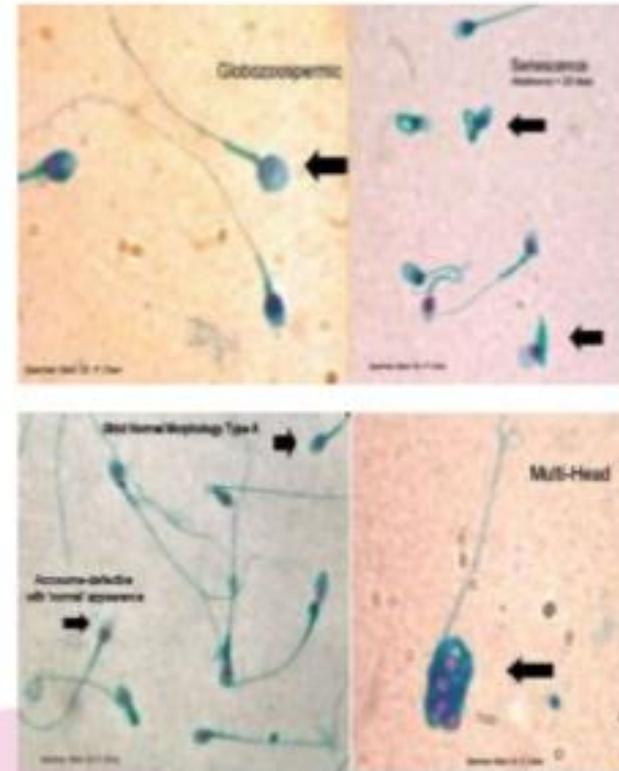


- **Hypospermia:** Semen volume <2 ml
- **Necrozoospermia:**
Nonviable ("dead") sperm
- **Oligoasthenozoospermia:** Motile density is <8 million sperm/ml
- **Polyzoospermia:** Excessively high sperm concentration
- **Pyospermia:** Leukocytes (germ-fighting cells) present in semen
- **Teratozoospermia:** > 40% of sperm seen are abnormally formed

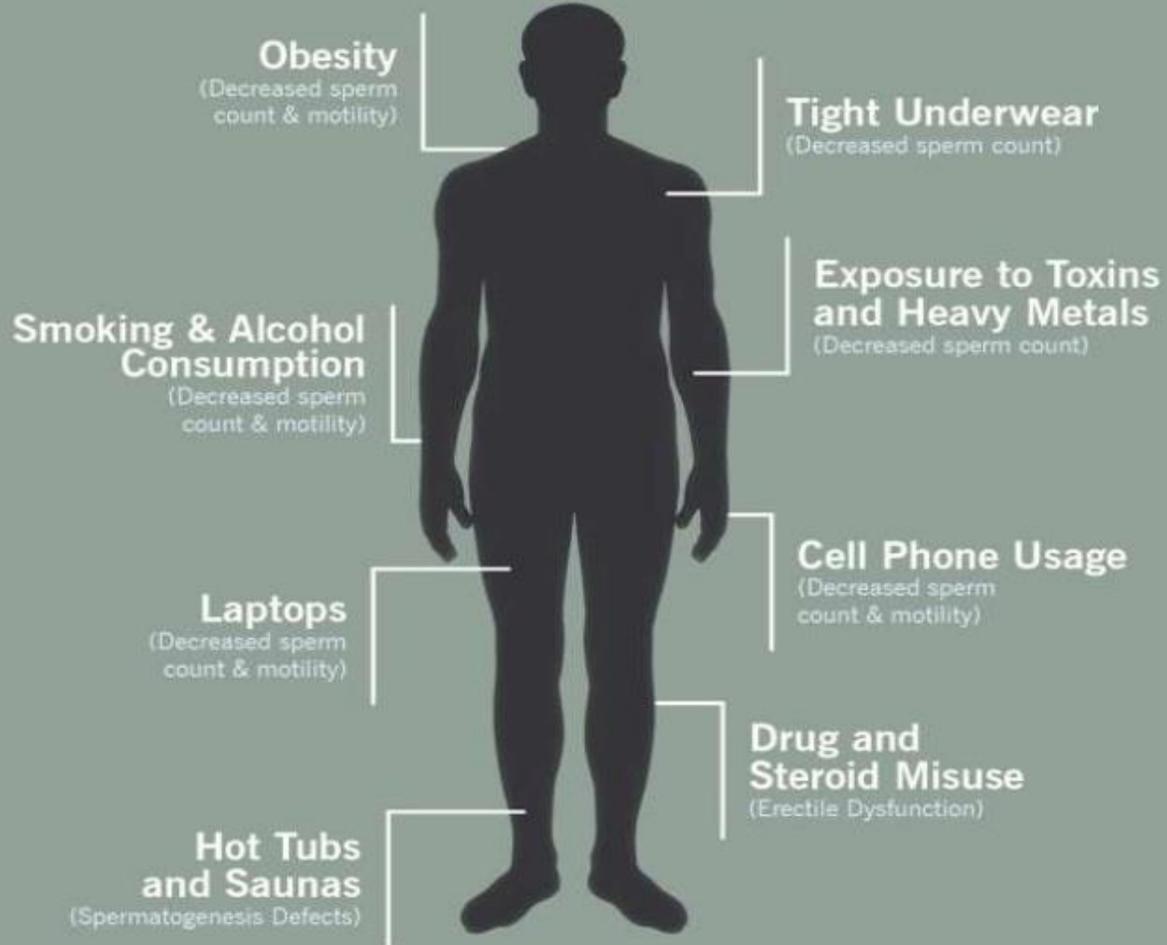
- *Round cells (Immature germ cells+leucocytes)*
- *If > 5 million round cells /ml - analyzed for the presence of leukocytes*
> 1 million leukocytes /ml - indicative of possible infection.

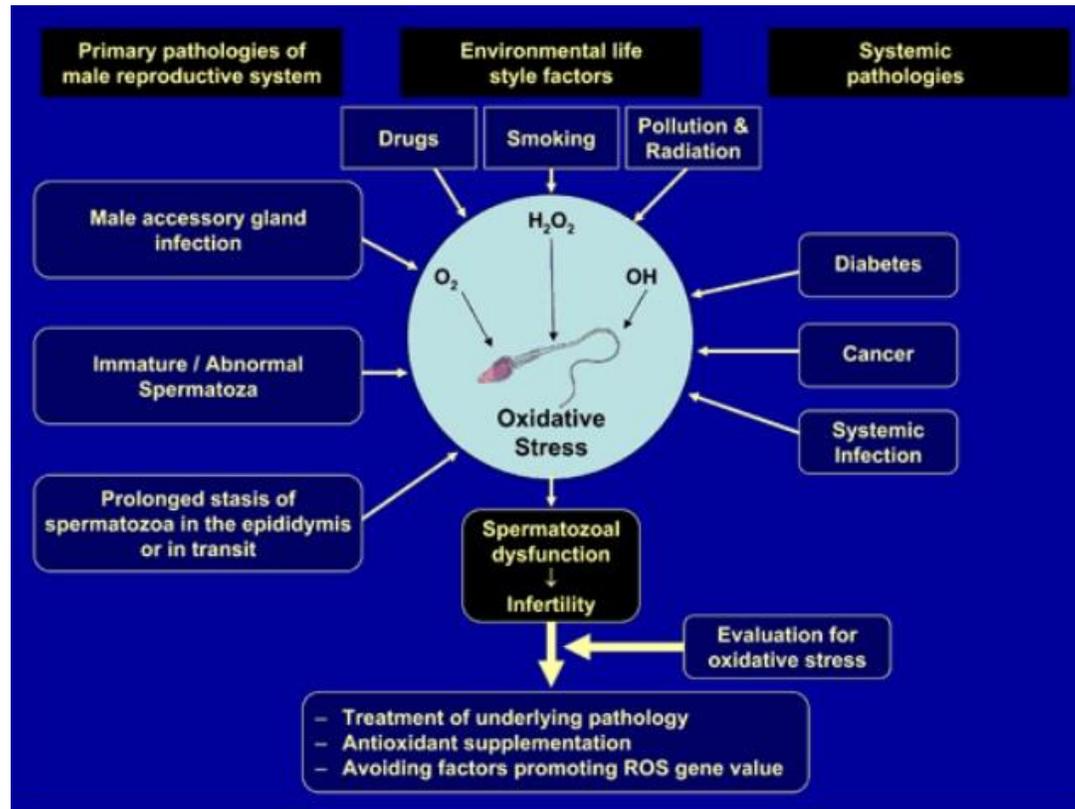
(WHO,2010)

- **Asthenospermia** : Poor sperm motility.
 - Anti sperm antibodies
 - Genital tract infections
 - Partial obstruction of ejaculatory duct
 - Varicocele
 - Vasectomy reversal
 - Prolonged abstinence
- **Globozoospermia** : Round headed sperm without acrosome
- **Hemospermia**: Red blood cells present in semen
- **Hyperspermia**: Semen volume >5.5 ml

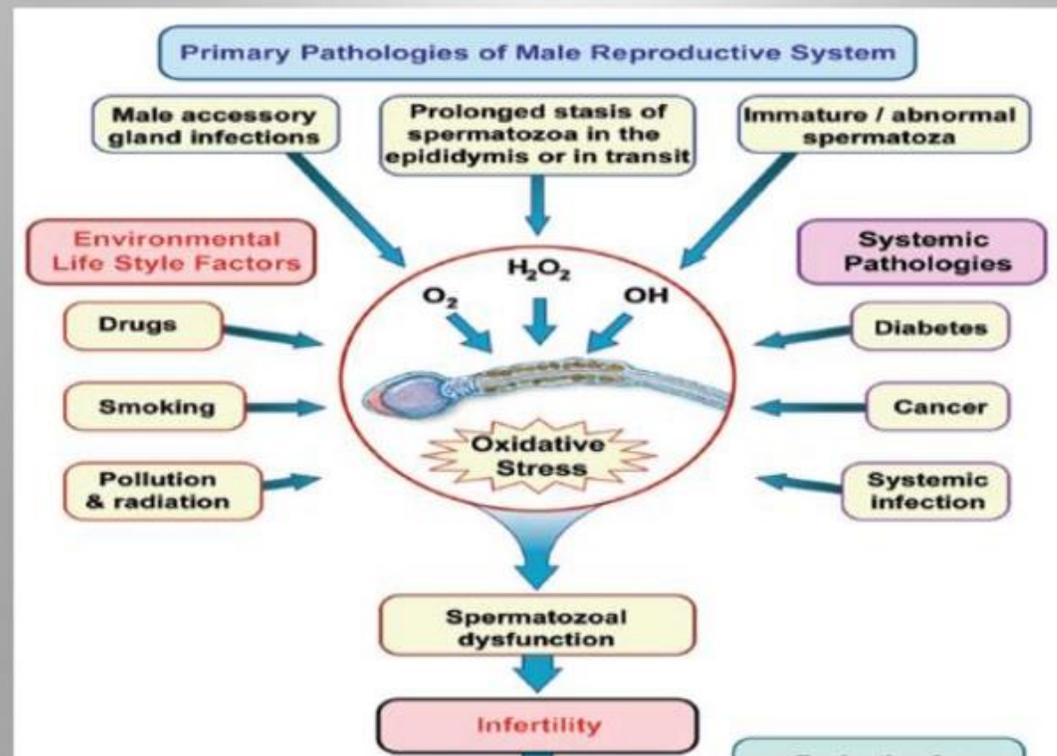


Lifestyle factors



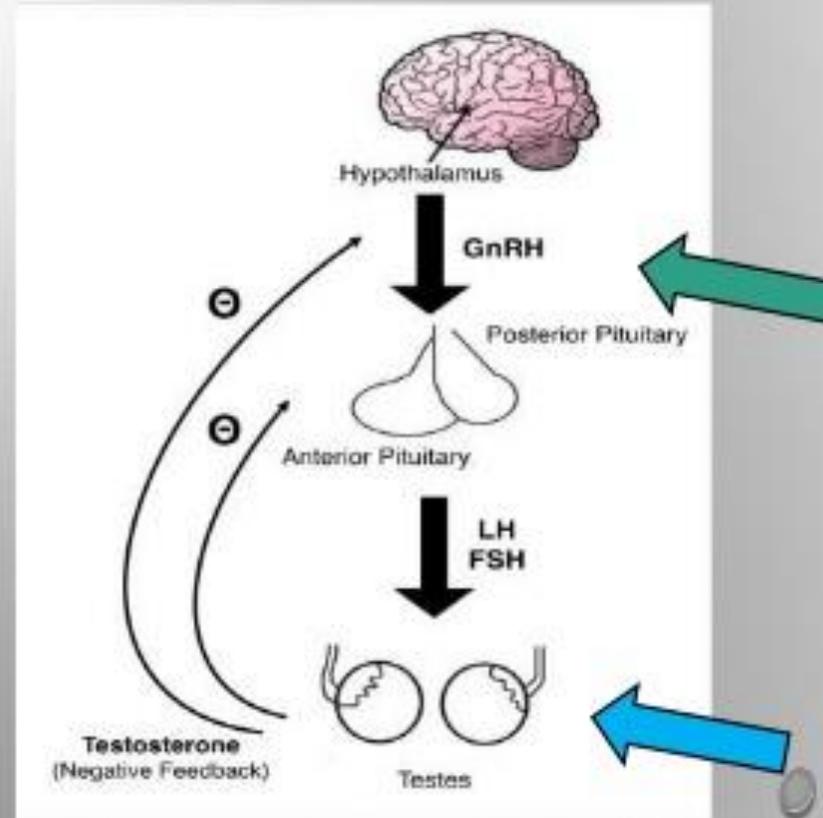


ROS (REACTIVE OXYGEN SPECIES)



CAUSES

- PRETESTICULAR
- TESTICULAR
- POST-TESTICULAR



Abnormal Semen Analysis

- Azospermia
 - Klinefelter's (1 in 500)
 - Hypogonadotropic-hypogonadism
 - Ductal obstruction (absence of the Vas deferens)
- Oligospermia
 - Anatomic defects
 - Endocrinopathies
 - Genetic factors
 - Exogenous (e.g. heat)
- Abnormal volume
 - Retrograde ejaculation
 - Infection
 - Ejaculatory failure

CAUSES

PRE TESTICULAR	TESTICULAR	POST TESTICULAR
<p>ENDOCRINE:</p> <ul style="list-style-type: none">• Hypogonadotropic hypogonadism• Hypothyroidism• Hyperprolactinaemia• Diabetes <p>COITAL DISORDERS:</p> <ul style="list-style-type: none">• Erectile dysfunction• Ejaculatory failure	<p>GENETIC:</p> <ul style="list-style-type: none">• Klinefelter syndrome• Y chromosome deletion• Immotile cilia syndrome <p>CONGENITAL:</p> <ul style="list-style-type: none">• Cryptorchidism• Infective• Antispermato-genic agents heat, irradiation, drugs, chemotherapy <p>VASCULAR :</p> <ul style="list-style-type: none">TorsionVaricocele <p>IMMUNOLOGICAL</p>	<p>OBSTRUCTIVE:</p> <p>Epididymal congenital infective</p> <p>Vasal Genetic: cystic fibrosis. Acquired: Vasectomy Ejaculatory duct obstruction Accessory gland infection Immunological Idiopathic post vasectomy</p>

EVIDENCE

Obesity

(by imbalance of reproductive hormone levels, reduced SHBG and elevated estrogen levels. Sedentary lifestyle factors)

CAUSE

Sharpe RM, 2002
Hammoud AO, 2008

Anabolic-androgenic steroids

(by interfering with HPG axis, loss of libido and erectile dysfunction secondary to low endogenous testosterone levels)

Gazvani MR, 1997
Menon DK, 2003
de Souza GL, 2011

Heavy alcohol consumption/Tobacco/ smoking
Cannabis/recreational drugs such as cocaine,
amphetamines and opiates

Buffum J, 1982
Vine MF, 1996
Nudell DM, 2002



Disorders of sperm transport

- Epididymal obstruction or dysfunction
- Infections causing obstruction to vas deferens
- Vasectomy
- Kartagener syndrome
- Ejaculatory dysfunction
- Young syndrome

❑ Infectios

❑ Leukospermia,

No symptoms

Culture is negative:

10-day course of

- Erythromycin or
- Trimethoprim-sulfamethoxazole or
- Quinolone.

5. Obstructive azoospermia

□ Diagnosis:

Azoospermia or severe oligospermia +

✓ normal size testis

✓ normal FSH

✓ normal testicular histology.

3. Semen culture

- Indicated:
semen samples contain inflammatory cells
- Results:
usually not diagnostic.
- Precautions
during sample collection to prevent skin contamination.
- The yield of semen culture
may be improved by performing a prostatic
massage before sample collection.

2. Semen biochemistry

- *Rarely useful in clinical practice.*

- **Fructose**

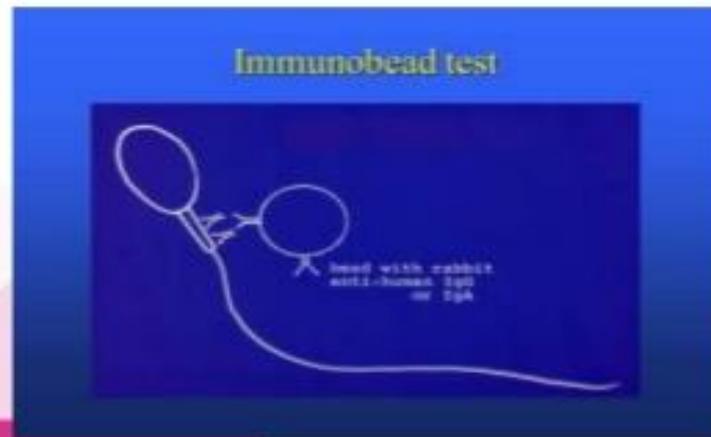
marker of seminal vesicle function.

Low or non-detectable:

- ✓ congenital absence of the vas deferens and seminal vesicles or
- ✓ ejaculatory duct obstruction

ANTI-SPERM ANTIBODIES

- Found in 80% of men who have undergone vasectomy and a/w vasoepididymostomy or vasovasostomy, testicular biopsy, infection, varicocele, cryptorchidism and testicular torsion or trauma.
- **Indication-**
 - Men with semen analyses that show clumping or agglutination of sperm
 - Asthenospermia
- **Mixed antiglobulin reaction test**
- **Immunobead test**



- 
- **Transrectal ultrasonography:** less invasive
indicated in diagnosis severe oligospermia or azoospermia.
 - **Renal ultrasonography:** unilateral or bilateral vasal agenesis.
 - **Trans scrotal ultrasonography:** To confirm physical findings. Detect non palpable varicocele.

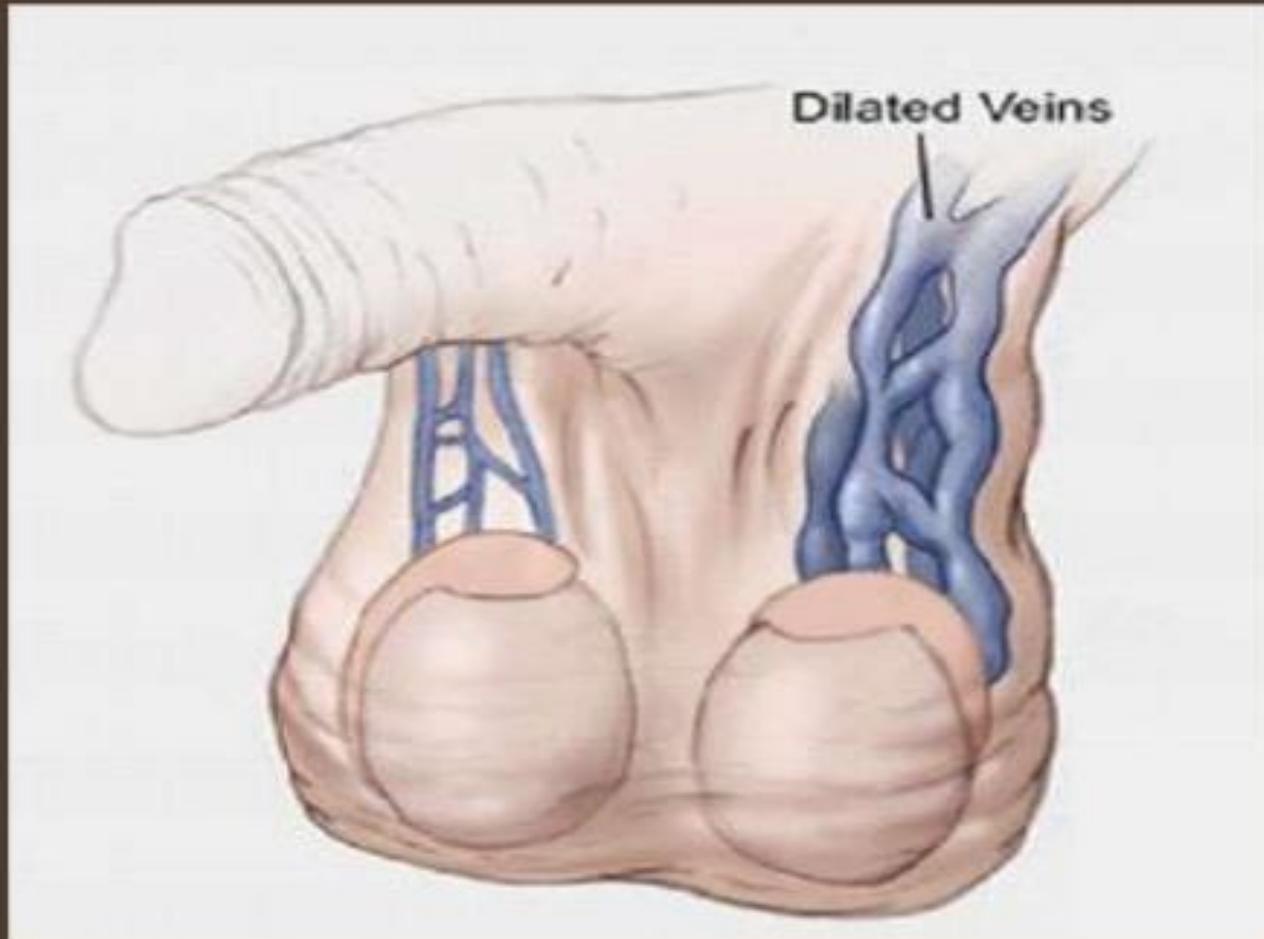
Varicoceles

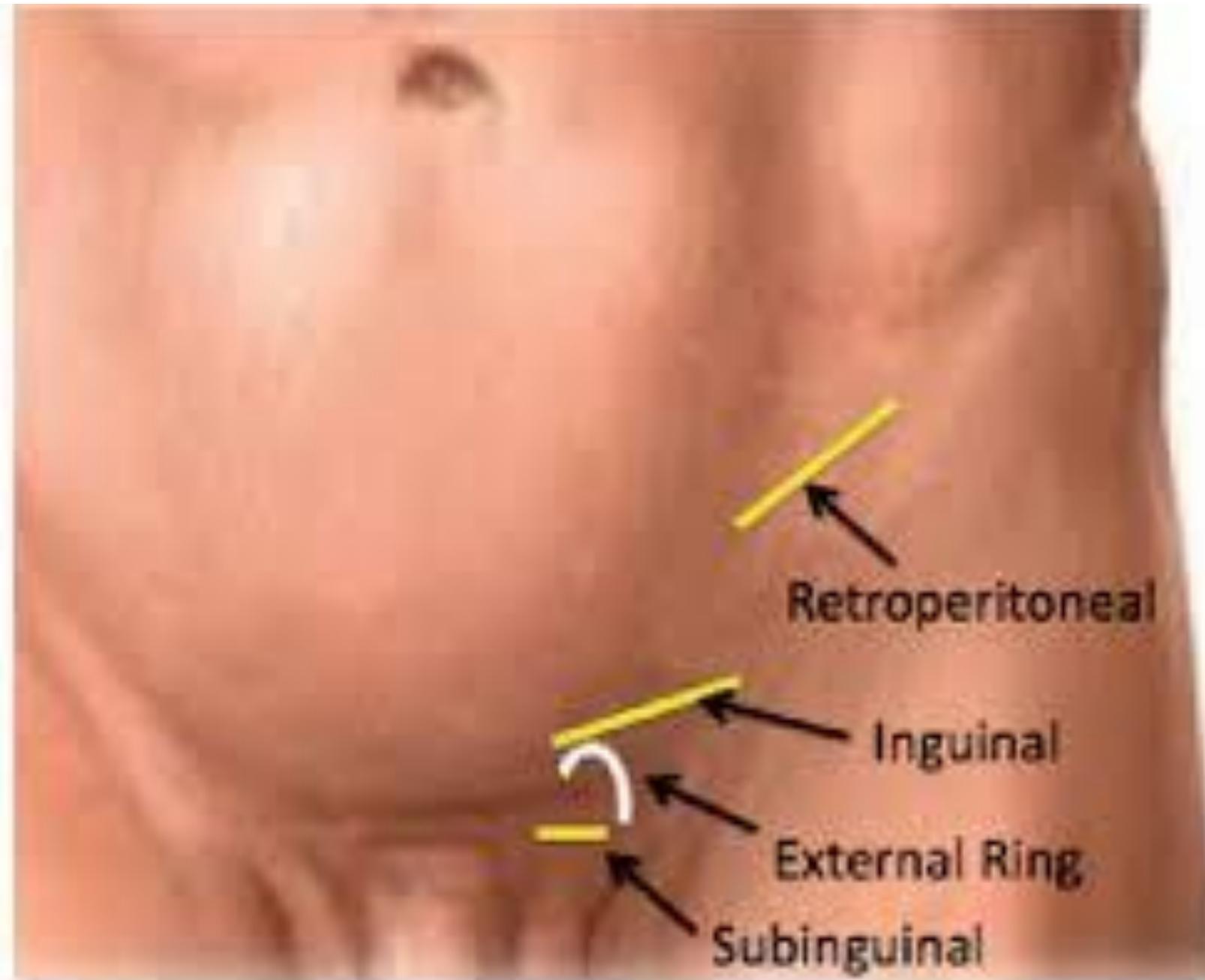
- Dilated veins of the pampiniform plexus
- Predominant left-sided (98%)
- Isolated right-sided varicocele may be caused by a retroperitoneal
 - NEED abdominal imaging
- Varicocele grading:
 - Grade I: palpable only with valsalva
 - Grade II: easily palpable without valsalva
 - Grade III: large, visible through scrotal skin



Grade III: “bag of worms”

VARICOCELE





Retroperitoneal

Inguinal

External Ring

Subinguinal

Genetic evaluation

- **Indication-**

- Azoospermia** *-should we do it for every azoospermic patient?? - NO*

- Normal testis volume

- palpable vasa on physical examination, and strong suspicion for obstruction

- normal serum FSH and normal semen volume- no genetic testing is indicated

- Severe oligospermia**(<5 million /ml).

- Those with suspected congenital obstruction (normal testis volume and FSH)-
no

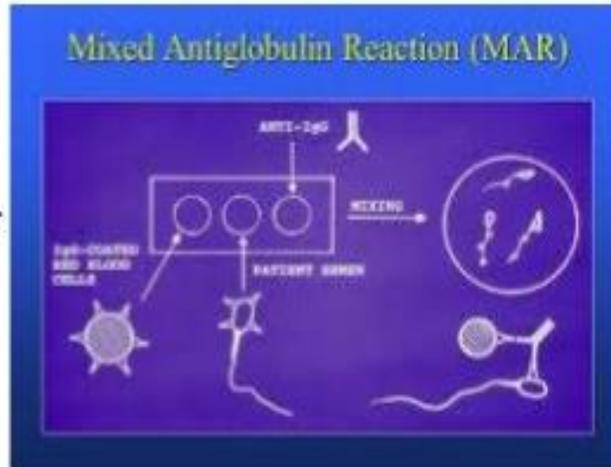
- genetic testing indicated

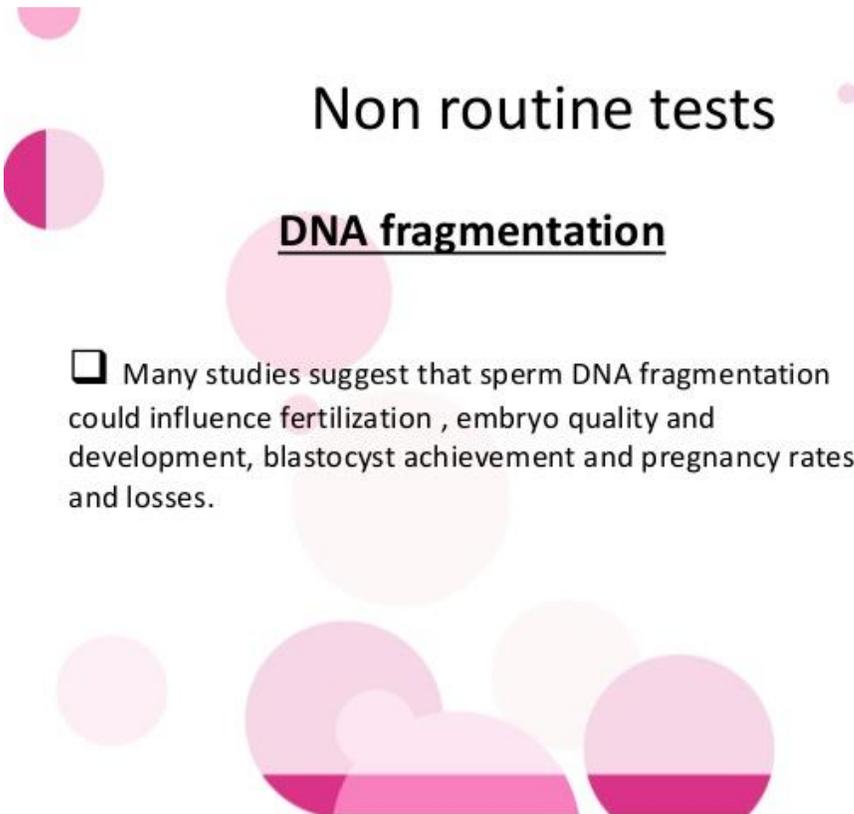
- (FIGO 2016)

- Y chromosome deletions
- Chromosomal anomalies-most common Klinefelter's syndrome(46XXY)
- CFTR gene mutations (CABVD)
- Karyotyping
- Cytogenetic testing /PCR

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Non routine tests

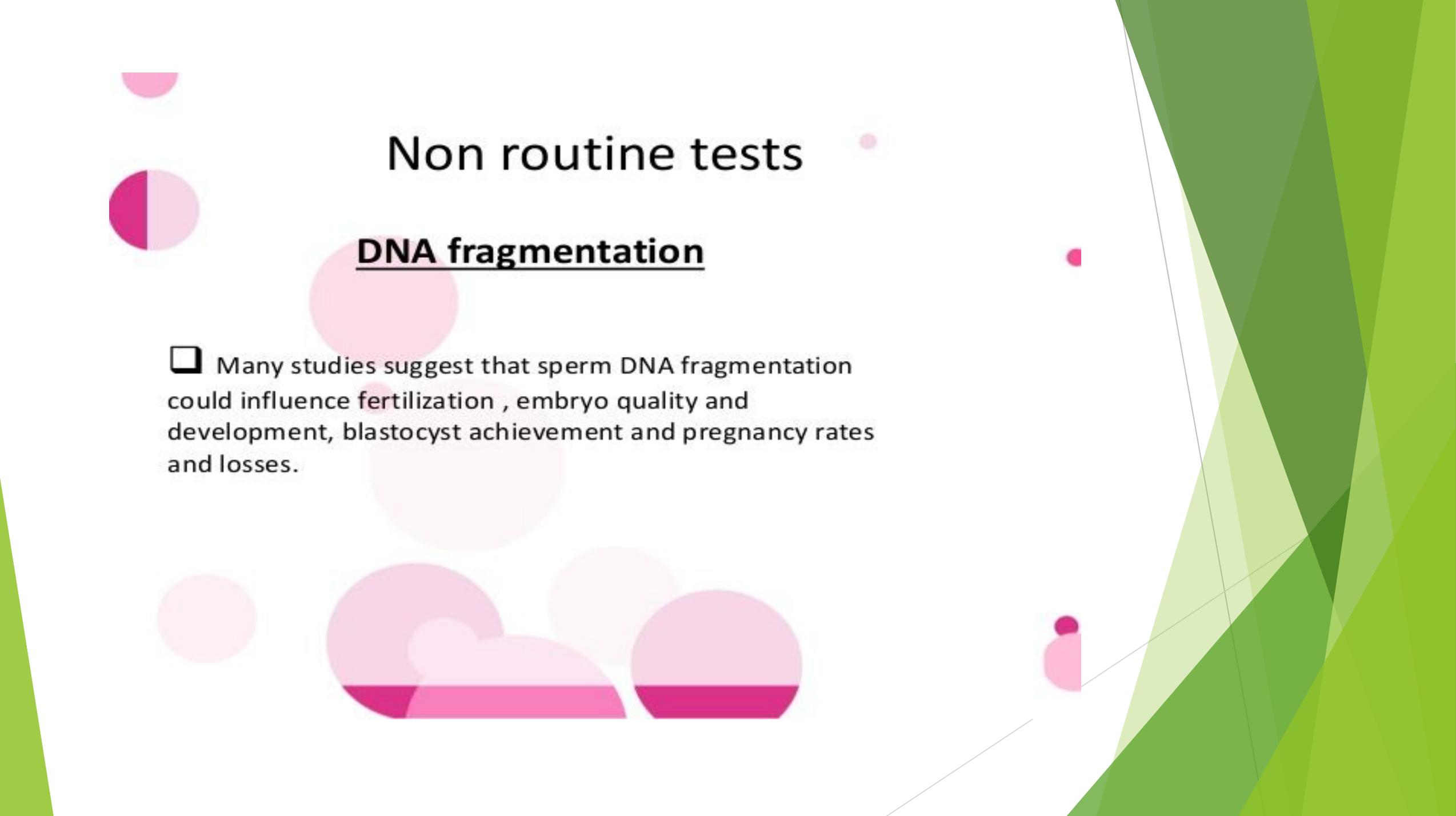
DNA fragmentation

- ❑ Many studies suggest that sperm DNA fragmentation could influence fertilization , embryo quality and development, blastocyst achievement and pregnancy rates and losses.
- 

Diagnostic tests



- Most studies define an upper normal level of the percentage of cells with DNA fragmentation.
- Unit of measurement – DFI (DNA fragmentation Index)
- Samples with assay results above this threshold percentage are considered to have high DNA fragmentation.
- Percentage of spermatozoa with fragmented DNA
 - ≤ 15 – good fertility potential
 - 15-25% - average
 - > 25% - poor fertility potential



Non routine tests

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What is Azoospermia?



Oligozoospermia



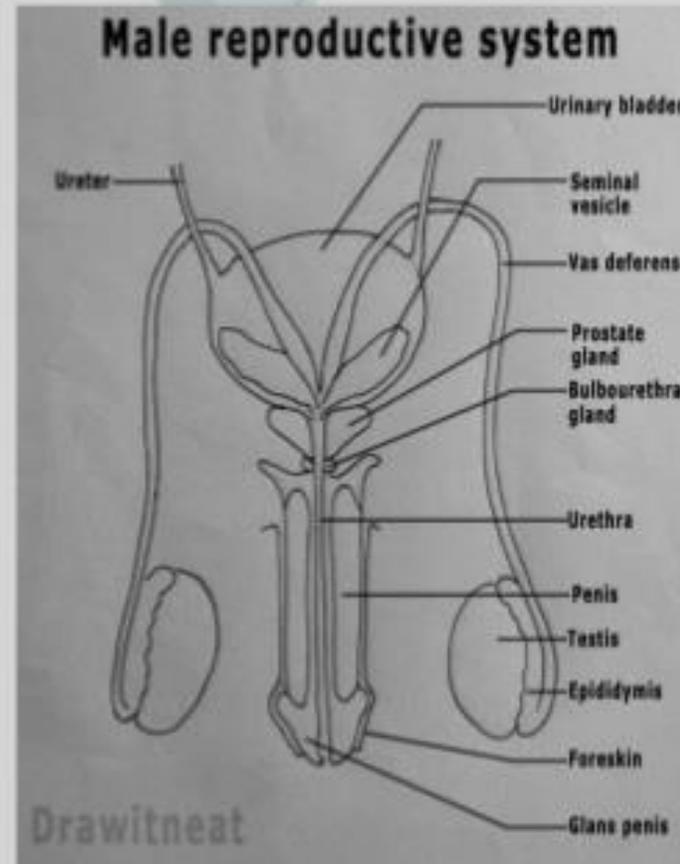
Azoospermia

Investigating azoospermia, by site of abnormality

	Obstructive		Non-obstructive
	<i>Post-testicular</i>	<i>Testicular</i>	<i>Hypothalamic-pituitary</i>
Congenital causes	Vasal aplasia, cystic fibrosis, mullerian cysts	Genetic causes, cryptorchidism, anorchia	Kallman's syndrome, isolated FSH deficiency
Acquired causes	Gonorrhoea, chlamydia, tuberculosis, prostatitis, vasectomy	Radiotherapy, chemotherapy, orchitis, trauma, torsion	Craniopharyngioma, pituitary tumour, pituitary ablation, anabolic steroids
Testicular size	Normal	Small, atrophic	Small, prepubertal
FSH	Normal	Raised	Low
Testosterone	Normal	Low	Low

Semen Analysis

- Volume < 1.5 ml
if Vas palpable
Repeat after 2-3 days abstinence
Ejaculatory Duct Obstruction
(EDO)
- pH < 7.2
Acidic – prostatic secretions
EDO



❑ Ejaculatory duct obstruction

✓ Transurethral resection of the ejaculatory ducts

✓ ICSI

can be combined to use sperm from men who have obstructive azoospermia to fertilize ova of their partners and achieve pregnancy.

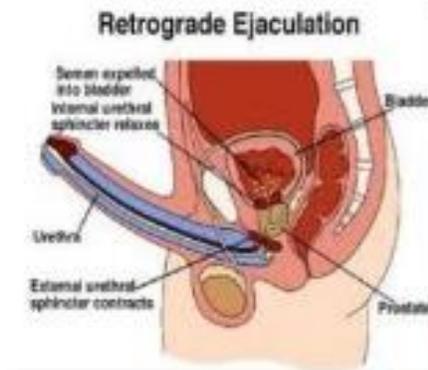
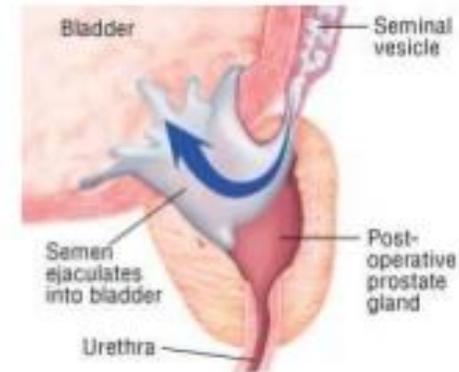
Post-ejaculatory Urinalysis

- **INDICATION**

- A low-volume or absent antegrade ejaculate
- Centrifuging the urine specimen for 10 minutes at 300g, followed by microscopic examination of the pellet at 400 magnification.

- *In men with azoospermia or aspermia, the presence of any sperm in the post-ejaculatory urinalysis suggests retrograde ejaculation.*
- *In men with low ejaculate volume and oligozoospermia, "significant numbers" of sperm must be observed to support the diagnosis of retrograde ejaculation.*

(FIGO,2016)



HORMONAL PROFILE

Increased FSH	Increased LH	Low testosterone	Testicular failure
Increased FSH	Normal LH	Normal testosterone	<u>Failure of Spermatogenesis</u>
Decreased FSH	Decreased LH	Low testosterone	<u>Hypogonadotropic hypogonadism</u>

Endocrine Evaluation

• **Indications:**

- Abnormal semen parameters, particularly sperm concentration is <10mill/ml
- Sexual dysfunction
- Specific endocrinopathy

• **Tests :**

- Sr. FSH
- Total testosterone
- Sr. Free Testosterone
- LH
- PRL, TSH
- Serum estradiol

Disorder	FSH	LH	Free Ts
Hypogonadotropic hypogonadism	low	low	low
Abnormal spermatogenesis	N/high	N	N
Testicular Failure	High	High	N/low

Hormonal profile	Interpretation
Elevated FSH \pm LH Normal or low testosterone	Primary testicular failure
Low FSH, LH Low testosterone	Hypogonadotropic hypogonadism
Normal FSH, LH, testosterone	Normal or primary testicular failure



Genetic evaluation

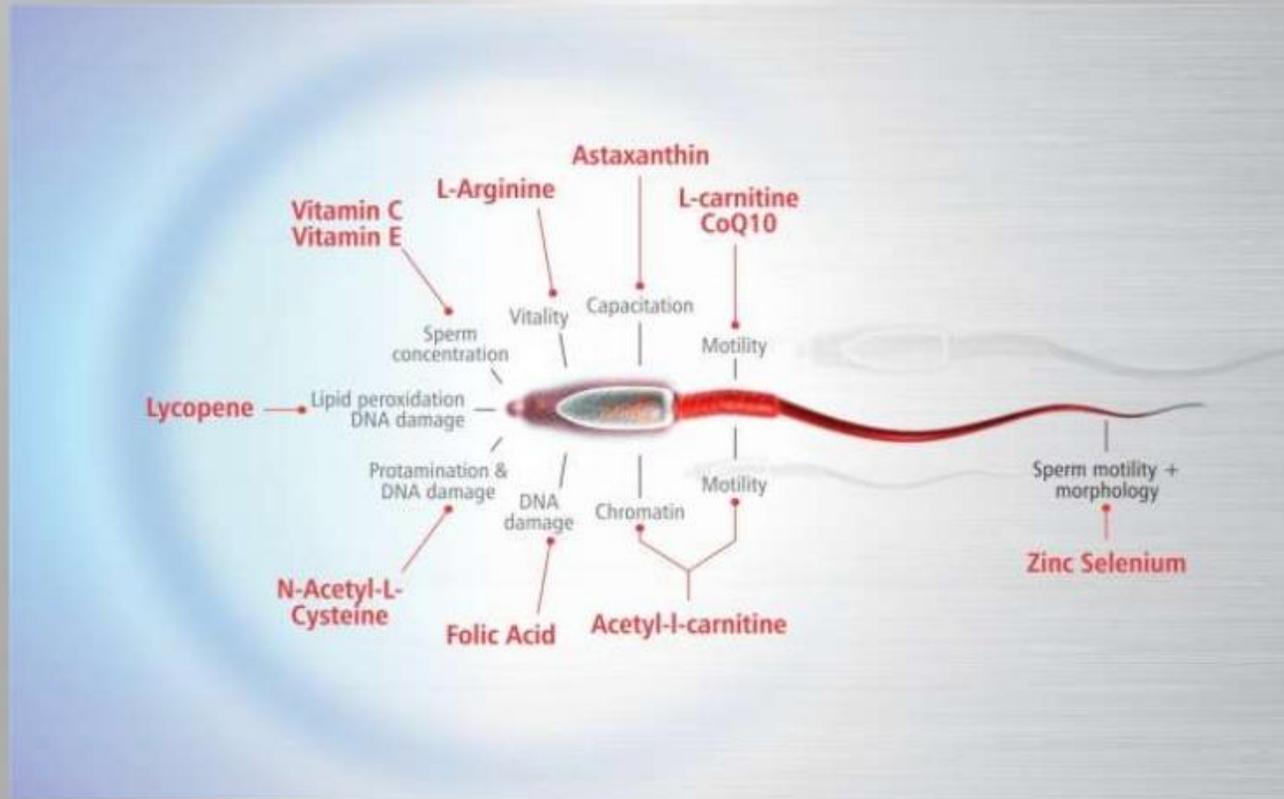
- 1) Mutations within cystic fibrosis transmembrane conductance regulator (CTFR gene)
- 2) Chromosomal anomalies resulting testicular dysfunction - klinefelter syndrome
- 3) Y chromosome deletions associated with abnormalities of spermatogeneis.

III. TREATMENT OF UNCERTAIN EFFICACY

Causes of male factor infertility for which treatment is potentially useful

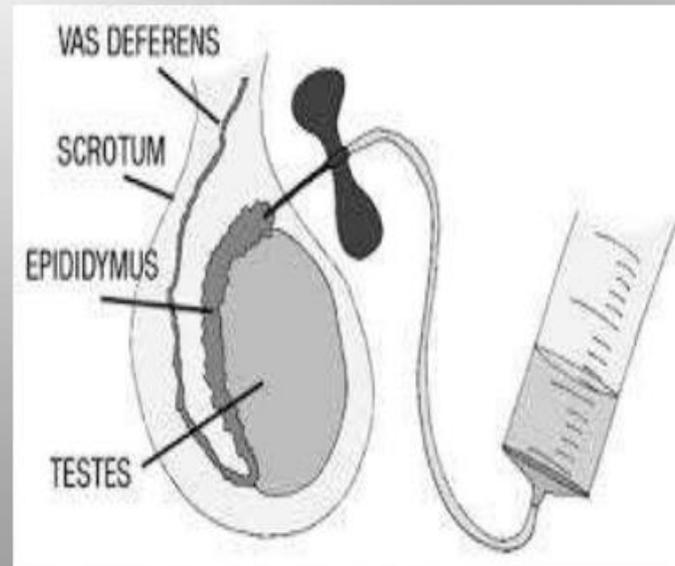
Etiology	General aspects of treatment
Infections	Antibiotics
Sperm autoimmunity	High-dose glucocorticoids; assisted reproductive techniques - intracytoplasmic sperm injection (ICSI)
Sexual dysfunction	Appropriate therapy
Retrograde ejaculation	Intrauterine insemination (IUI) with washed spermatozoa or assisted reproductive techniques
Varicocele	High ligation or embolization of spermatic veins
Obstructive azoospermia	Microsurgical end-to-end anastomoses (epididymal ducts to epididymal ducts or to vas); microsurgical epididymal sperm aspiration and in vitro fertilization/ICSI

NEUTRACEUTICAL



Assisted Reproductive Technology

- ICSI
- PESA
- TESA
- MICRO TESA
- DONOR INSEMINATION



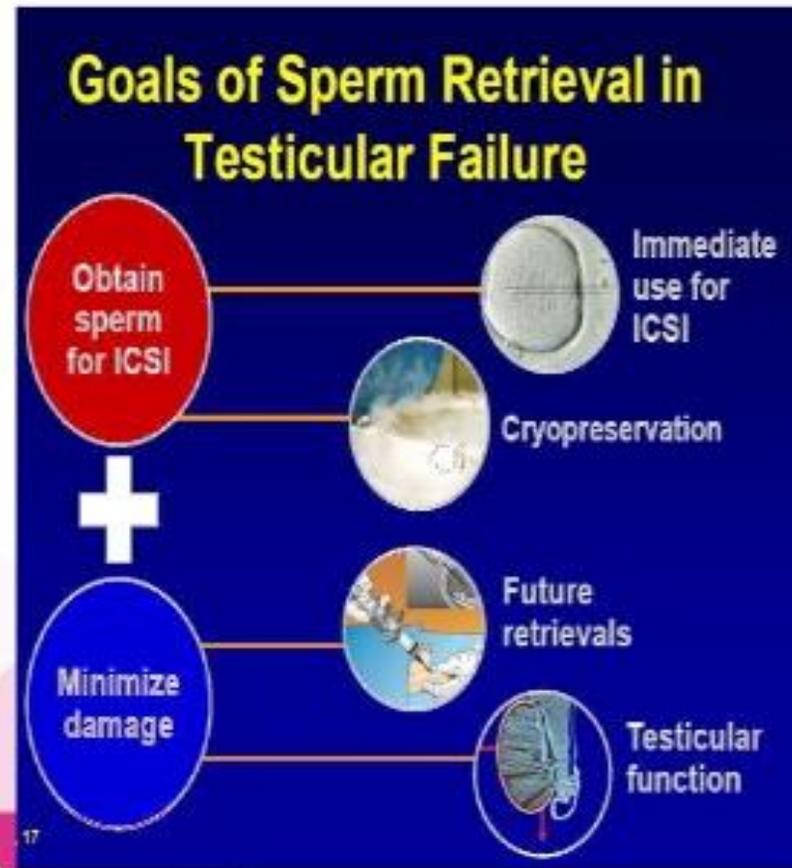
Sperm Retrieval Techniques

1. NON OBSTRUCTIVE AZOOSPERMIA:

- TESE – Testicular sperm extraction
- Micro-TESE – Microdissection testicular sperm extraction

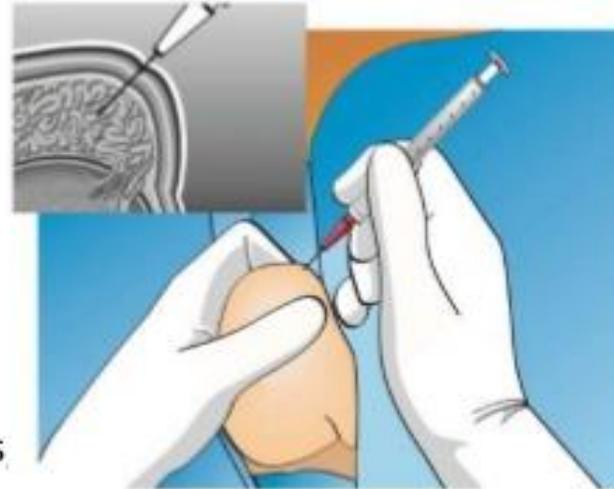
2. OBSTRUCTIVE AZOOSPERMIA :

- MESA – Microsurgical Epididymal Sperm Aspiration
- PESA – Percutaneous epididymal sperm aspiration



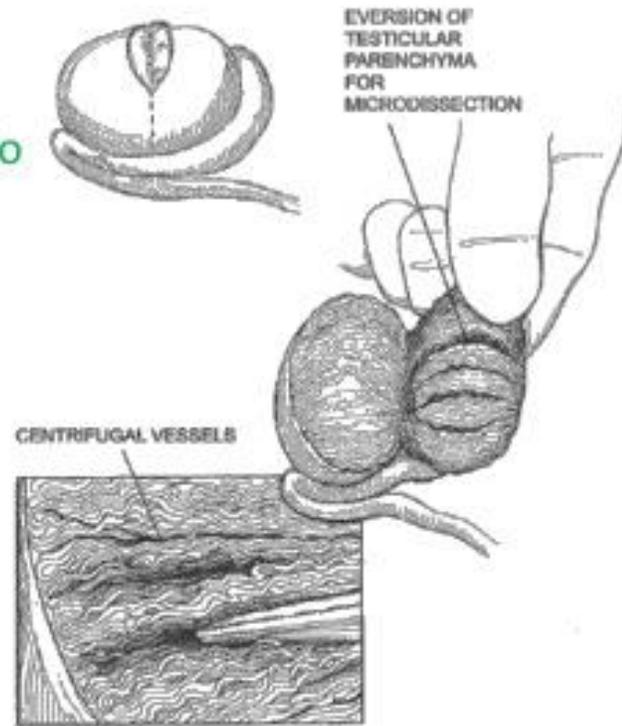
PESA (Percutaneous Epididymal Sperm Aspiration)

- ❑ Blind procedure
- ❑ Local anesthesia
- ❑ Multiple blind passages with a 21- to 23- gauge needle through the epididymis
- ❑ **Advantage** of avoiding a skin incision.
- ❑ **Disadvantage**- significant damage to the epididymis making future attempts at conception difficult.



Micro-testicular Sperm Extraction(m-TESE)

- As proposed by Schlegel in 1999.
- Thorough exploration with a microscope done to see largest tubules in the testis which are associated with more spermatozoa.
- On testicular biopsy, hypospermatogenesis, maturation arrest, or Sertoli cell-only pattern (germinal cell aplasia).
- **Genetic causes-** Klinefelter syndrome (KS) and XX-male syndrome.
- **Acquired-** Testicular failure secondary to cryptorchidism or systemic chemotherapy.
- Better retrieval results than conventional .



- **TESA (Testicular sperm aspiration)**

- Blind procedure
- Immobilization of the testicle. by grasping it with the epididymis and cord between fingers while pulling the scrotum skin taut.
- In the superior pole of the testis -21-gauge butterfly needle is used.



SURGICAL MANAGEMENT

1. Vasovasostomy & vasoepididymostomy- In vasectomized men .
2. Transurethral resection of the ejaculatory ducts- in men with Ejaculatory duct obstruction .
3. Varicocele repair
4. Orchiopexy – In cryptorchidism

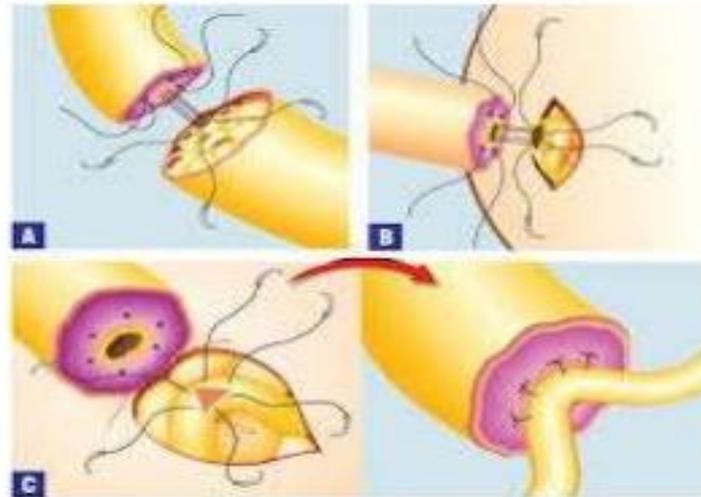


Figure 2 - Microsurgical vasoepididymostomy Techniques: (A) illustration of the end-to-end, (B) end-to-side, and (C) transposition end-to-side anastomoses.

ARTIFICIAL INSEMINATION



- **Indications :**

- Oligospermia,
- Asthenospermia,
- Premature or retrograde ejaculation,
- Sperm autoantibodies & cervical factors,
- Unexplained infertility
- Sex selection in genetic & chromosomal anomalies
- Hypospadias
- HIV positive

Donor Sperm



- **INDICATIONS :**

1. Azoospermia
2. Immunological factors not correctable
3. Genetic disease in husband

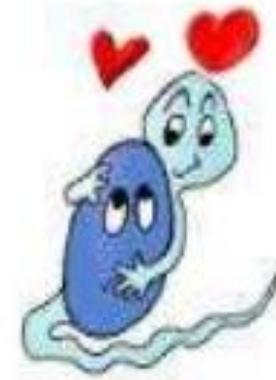
- **GUIDELINES (ASRM,2013)**

- Legal age** ideally less than 40 years of age.
- Screening for risk factors** for, and clinical evidence of, communicable disease agents or diseases.
- Prospective donors then undergo a **physical examination with Extensive screening** for visible physical abnormalities, as well as testing for sexually transmitted diseases.
- Routine blood analysis** includes documentation of the donor's blood type.
- Psychological evaluation and counseling** by a MHP.

Are males going to become extinct?

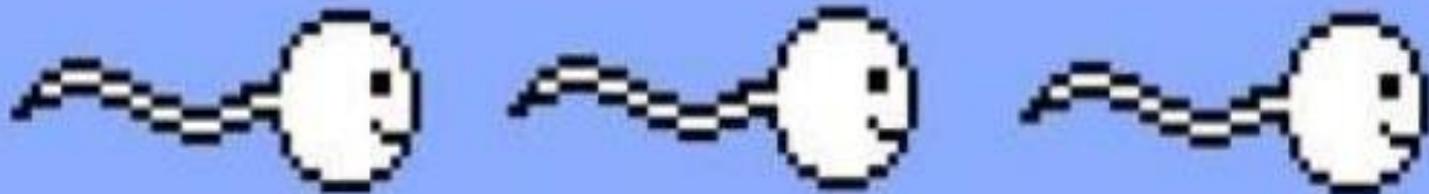


INTRACYTOPLASMIC SPERM INJECTION(ICSI)



- *Unprecedented successful development of ART which has revolutionized the management of severe male infertility (Van Steirteghen 1992)*
- **WHAT IS ICSI??**
- Is an in vitro fertilisation procedure in which single sperm is injected directly into an egg.
- **INDICATIONS**
- Total motile sperm count-<1 million.
- Severe teratozoospermia with less than 4% normal forms.
- Previous failed fertilisation in IVF.
- Presence of OA or NOA(ICSI combined with sperm retrieval)
- (AICOG 2016)

Whenever you feel worthless,
REMEMBER



you were once
the **quickest sperm cell.**

Thank You



