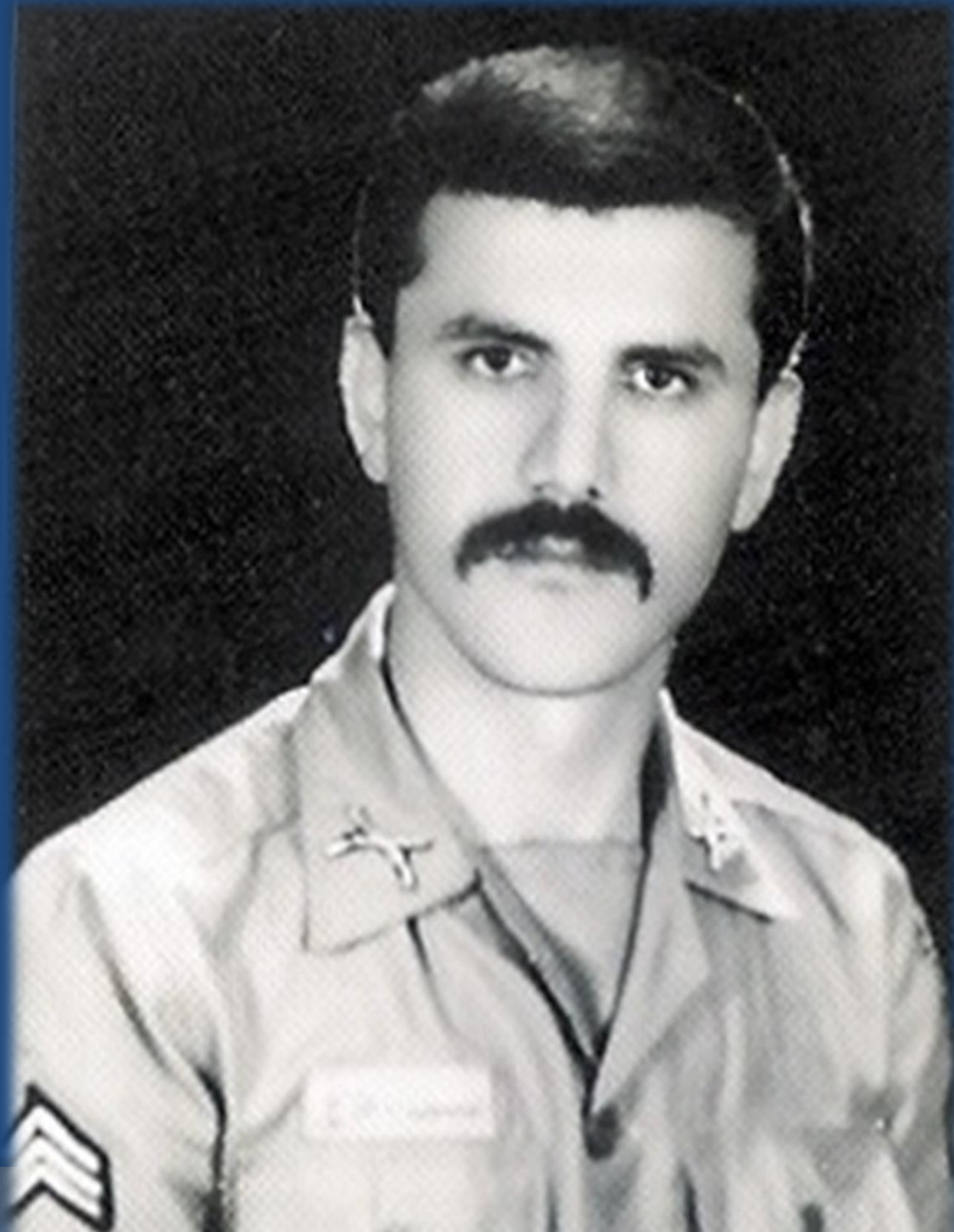


بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

إِنَّ اللَّهَ لَا يُغَيِّرُ مَا بِقَوْمٍ حَتَّىٰ يُغَيِّرَ مَا بِأَنفُسِهِمْ



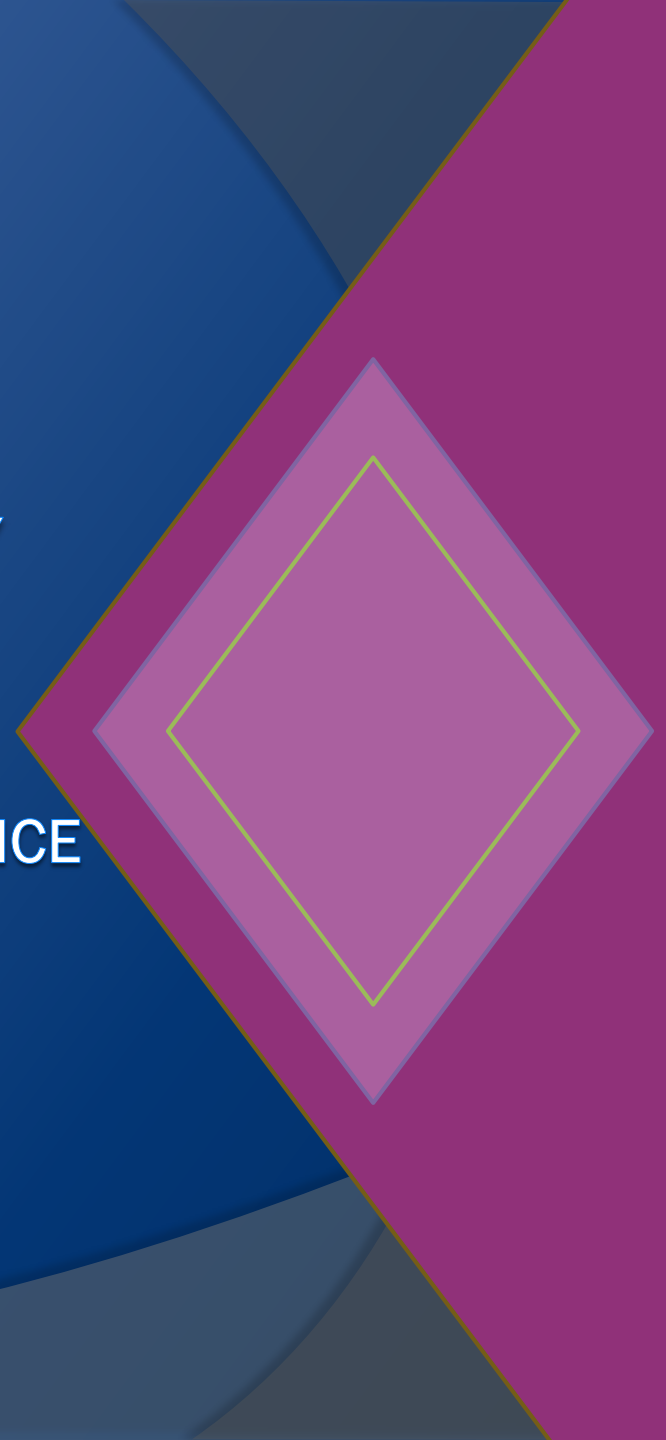




# MALE INFERTILITY

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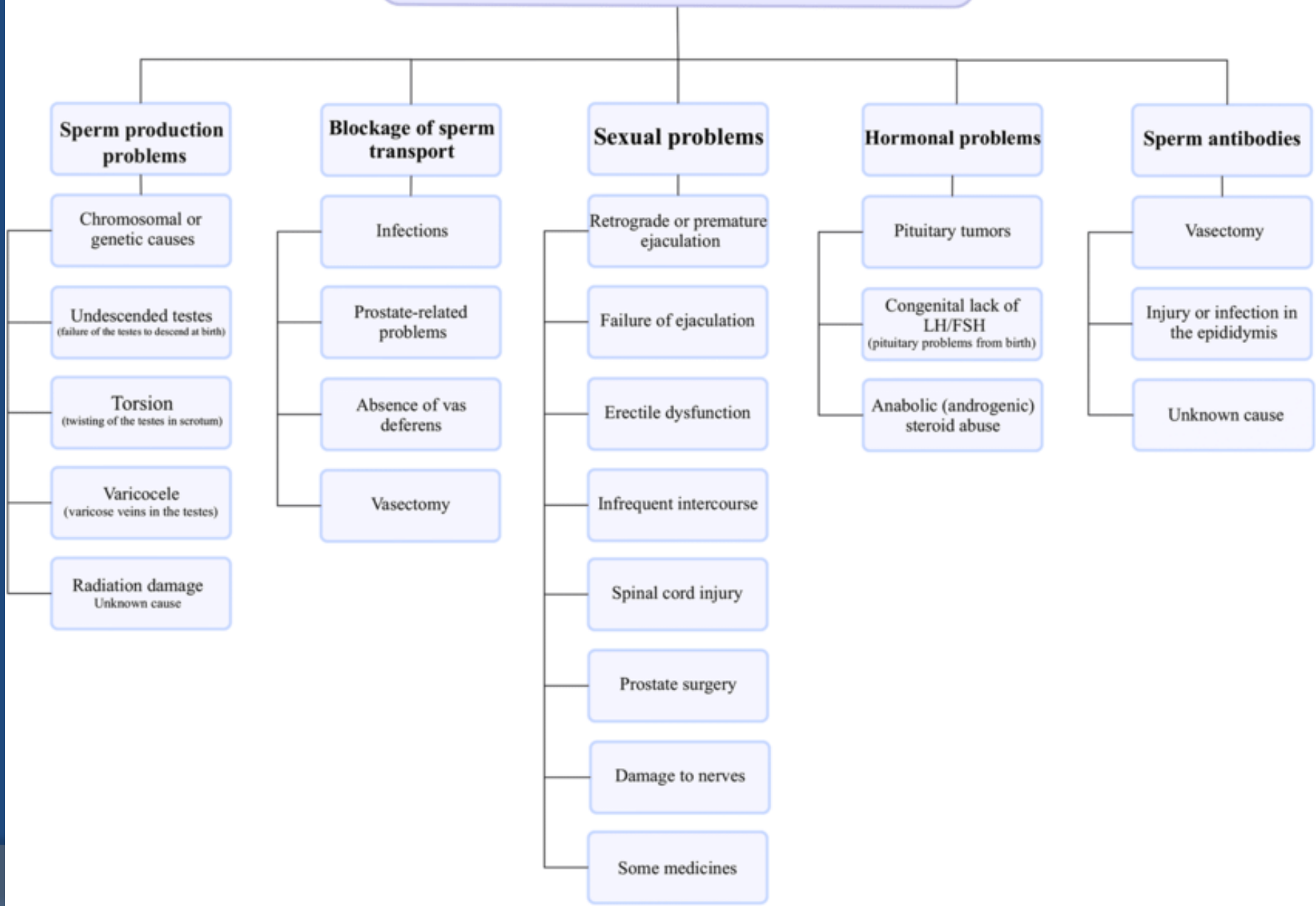
Infertility is

“a disease of the reproductive system

**Defined** by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.”...

(WHO-ICMART glossary<sup>1</sup>).

# Causes of male infertility



# History

- ID (occupation)
- PIHX ( infertility & sexual history)
- PMHX (Medical & Surgical)
- DHX
- Previous treatments
- SHX
- FHX

# Who is at risk for male infertility?

- Past inflammation of the prostate or past genital infections
- Injury to or twisting (torsion) of the testicles
- Early or late puberty
- Exposure of the genitals to high temperatures
- Hernia repair
- Undescended testicles
- medicines for ulcers, psoriasis, depression, and high blood pressure.



# Causes of Male Infertility, CDC

## ● Defective Spermatogenesis

Presence of endocrine disorders such as diabetes mellitus and hyperthyroidism lead to azospermia or the formation of faulty sperms that are not capable to fertilize the ovum. Moreover, testicular disorder such as undescended testis can also affect fertility.

## ● Defective Transport

Obstruction of the seminal vesicles or absence of the seminal ducts may affect the mobility of the sperms, and thus end up in infertility.

## ● Ineffective Delivery

The psychosexual problems like impotence, ejaculatory dysfunction, physical disability, hypospadias, and epispadias can affect fertility of males.

As male fertility can be influenced by a variety of factors, one possible explanation for the declining trend would be that there are **environmental and/or occupational** factors along with **lifestyle** practices that contribute to the deterioration of semen quality.

# Smoking

- ⦿ Cigarette smoke contains **>7000** chemicals
- ⦿ tar, nicotine , carbon monoxide, and heavy metals (e.g. cadmium and lead)
- ⦿ The decline in semen quality was found to be more marked in **heavy (>20 cigarettes/day)** and moderate (10–20 cigarettes/day) smokers compared to mild smokers (1–10 cigarettes/day).
- ⦿ oxidative stress, consequently impairing sperm function and ultimately compromising male fertility

# Alcohol

- ⦿ Alcohol intake has a detrimental effect on semen **volume** and sperm **morphology**
- ⦿ Alcohol appears to interfere with the production of GnRH, FSH, LH, and testosterone, as well as impair the functions of Leydig and Sertoli cells.
- ⦿ Reduce alcohol intake to no more than 4 standardized drinks per week

# Recreational drugs

Marijuana, cocaine, anabolic–androgenic steroids, opiates, and methamphetamines are examples of illicit drugs that exert a **negative impact on male fertility**.

- ⊙ The adverse effects of these drugs could impair
  - 1) The HPG axis,
  - 2) Testicular architecture
  - 3) Sperm function



# Obesity

- **Overweight (BMI 25–<30 kg/m<sup>2</sup>) and obese (BMI ≥30 kg/m<sup>2</sup>)** males are associated with a decrease in sperm quality and a greater risk of infertility
- The presence of excess white adipose tissue in obese individuals causes **increased conversion of testosterone to oestrogen**, and affects the **HPG axis** leading to a reduction in gonadotrophin release.
- These effects result in **secondary hypogonadism** and **impaired spermatogenesis**

# Psychological stress

- a) The classical stress response activates the sympathetic nervous system and involves the hypothalamus–pituitary–adrenal axis
- b) Impairment of testosterone secretion forms the main basis underlying the detrimental effects of psychological stress on spermatogenesis

# Advanced paternal age

A meta-analysis of 90 studies involving 93 839 participants reported an age-associated decline in

- 1) semen volume,
- 2) sperm total, and progressive motility,
- 3) normal sperm morphology
- 4) increase in DNA fragmentation.

# Diet

- ④ The **Mediterranean diet**, which is enriched with omega-3 fatty acids, antioxidants, and vitamins, and low in saturated and trans-fatty acids, were found to be inversely associated with low semen quality parameters
- ④ Vegetables and fruits, fish and poultry, cereals and low-fat dairy products were amongst the foods positively associated with sperm quality

# Caffeine

based on the current available data, there is **no firm potential relationship** between caffeine intake and male infertility.

reduce caffeine intake to no more than 250 mg daily (2 cups of coffee)



# Genital heat stress

- Genital heat stress resulting from scrotal hyperthermia is a substantial risk factor for male infertility.
- Prolonged hours of sitting or exposure to radiant heat, varicocele, and cryptorchidism can all lead to testicular heat stress
- Elevated scrotal temperatures lead to spermatogenic arrest, germ cell apoptosis, oxidative stress, and sperm DNA damage

# Environmental pollution

Organic farmers who were asked to provide semen samples were found to have significantly higher sperm concentrations than printers, electricians, or metal workers

# Sleep

Sleep disturbances may possibly have adverse effects on male fertility, as **semen volume was lower** in patients with difficulty in initiating sleep, including those who smoked or were overweight

# GENETIC ASSOCIATIONS

- ⦿ Considering that 10% of the human genome is involved in reproduction,
- ⦿ Genetic abnormalities are thought to account for 15%–30% of male factor infertility
- ⦿ Cystic fibrosis
- ⦿ Klinefelter syndrome
- ⦿ Deletions involving the Y chromosome

# ONCOLOGIC DISEASE

- ⦿ It is well known that cancer and its treatment can impair male fertility
- ⦿ Recent data suggesting that male infertility may serve not only as a biomarker for an individual man's health, but also as a marker of oncologic risk for the affected man's family members



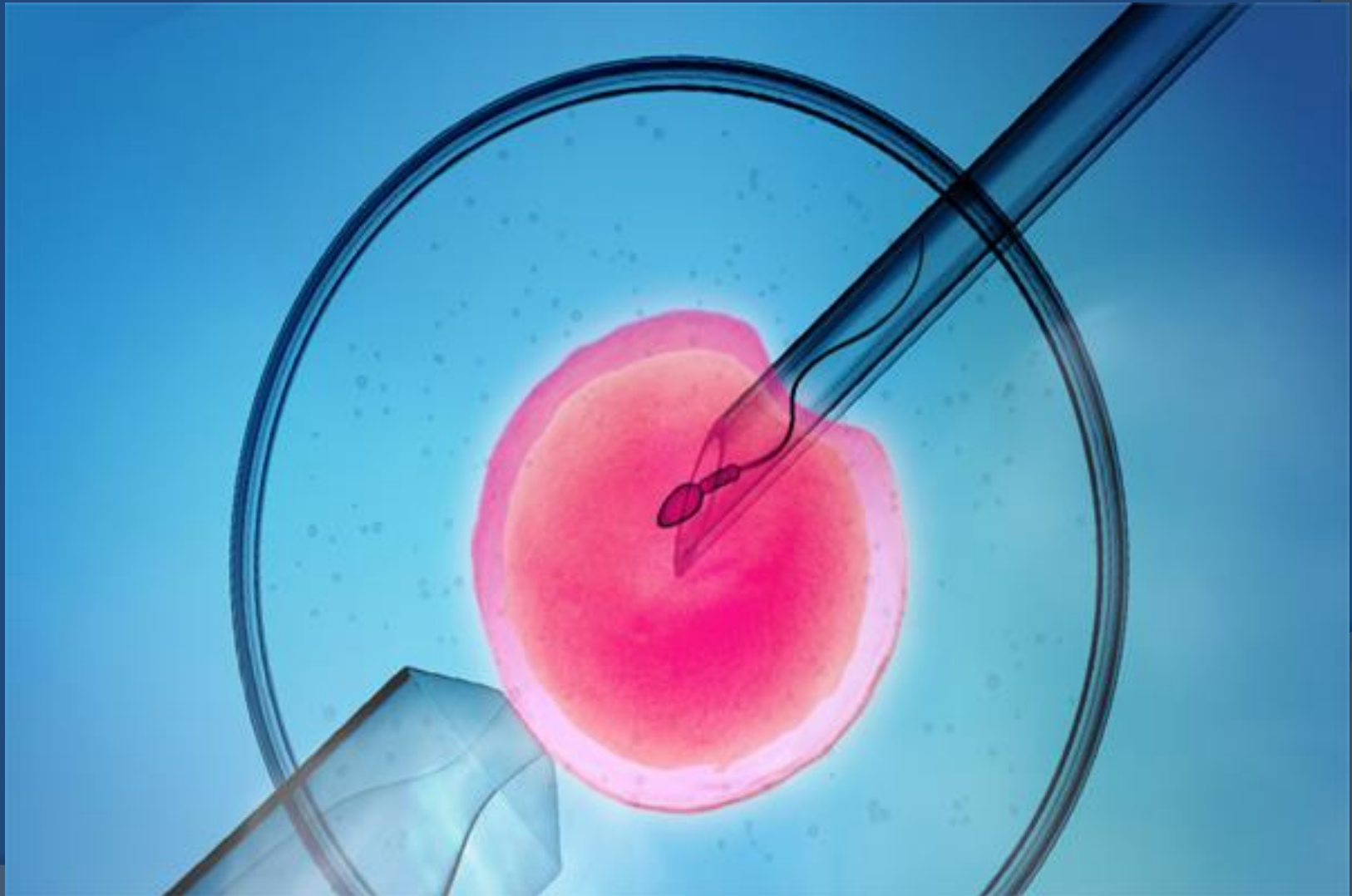
# CARDIOVASCULAR DISEASE

- **Hypertensive men have reduced testosterone levels** compared with normotensive men
- Childless men had an increased risk of death from cardiovascular disease during the study period (an average of 10.2 years) compared with fathers

# Infection

- ① **Chlamydia trachomatis,**
- ① **Mycoplasma genitalium,**
- ① **hepatitis B virus,**
- ① **tuberculosis,**
- ① **Streptococcus faecalis,**
- ① **mumps**

# Treatment



# Coit

Cumulative pregnancy rates for all tracked subjects in one well conducted study were

- ⦿ 38% at one cycle,
- ⦿ 68% at three cycles,
- ⦿ 81% at six cycles, and
- ⦿ 92% at 12 cycles

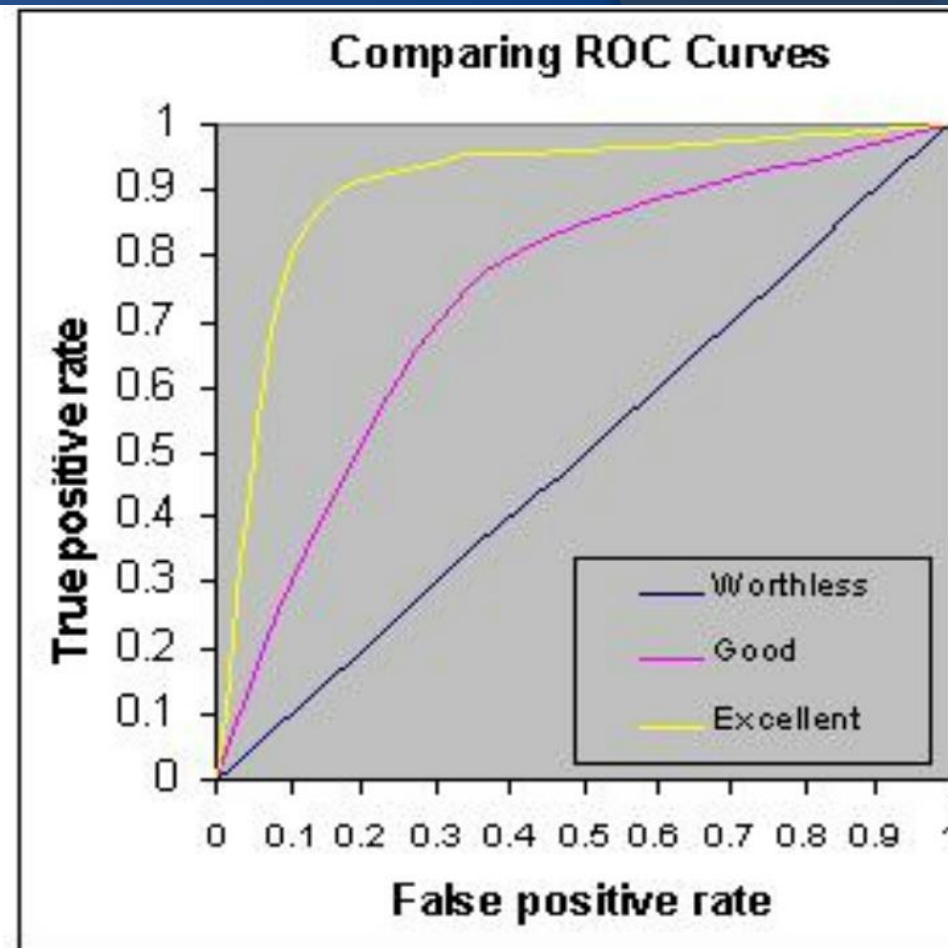
(Gnoth et al, 2003).

# Coit

- Frequency of intercourse, which may be altered in up to half of men being treated for infertility.



Complicating epidemiologic assessment is the fact that the primary assay for male infertility, the semen analysis, is a poor predictor with a low receiver operating characteristic (ROC) curve area for all available parameters (Guzick et al, 2001)



S/A as an predictor

# TUS

● Eshre توصیه می‌کند همه‌ی مردان نابارور از بیضه سونوگرافی شوند.

● AUA, ASRM فقط در موارد زیر توصیه می‌کنند:

- Hx of UDT
- Hx of germ cell tumor
- unexplained abnormalities on testis exam
- body habitus limits PE
- PE is equivocal
- after BX (Hematoma or scar affect the timing for subsequent TESE)

## AUA/ASRM Practice Committee Recommendations (2006) for **hormone assay**

- ⊙ An abnormally low sperm concentration, especially if  $<10$  million/ml.
- ⊙ Impaired sexual function.
- ⊙ Other clinical findings suggestive of endocrinopathy such as marked reduction in testicular size or gynecomastia.

# Karyotype/AZF

1. NOA
2. oligo (<10m/ml)

⦿ 17% of NOA had genetic defects.

# Chromosomal Abnormalities

- Approximately 5% of infertility in males
- The prevalence increases to 15% in the population of azoospermic males (Ferlin A., et al. 2007).

**TABLE 1**

Prevalence and phenotypes of common chromosomal abnormalities associated with male infertility.

Genetic abnormality	Phenotype	Prevalence, %
Chromosomal abnormalities	Azoospermia to normozoospermia	5 (total infertile population); 15 (azoospermic)
Klinefelter syndrome	Azoospermia to severe oligozoospermia	5 (severe oligozoospermia); 10 (azoospermic)
Robertsonian translocation	Azoospermia to normozoospermia	0.8 (total infertile population); 1.6 (oligozoospermic); 0.09 (azoospermic)
Y chromosome microdeletions	Azoospermia to oligozoospermia	10–15 (azoospermic); 5–10 (oligozoospermic)
AZF <sub>a</sub> deletion	Azoospermia, Sertoli cell-only syndrome	0.5–1.0 (2)
AZF <sub>b</sub> deletion	Azoospermia, spermatogenic arrest	0.5–1.0 (2)
AZF <sub>c</sub> deletion	Severe oligozoospermia to nonobstructive azoospermia	6–12
Partial AZF-c deletions	From azoospermia to normozoospermia	3–5 (2)

*Note:* Prevalence listed refers to listed phenotype unless noted otherwise.

*O'Flynn O'Brien. Genetic causes of MF infertility. Fertil Steril 2010.*

- ⦿ **Antisperm Antibody Tests**
- ⦿ **Magnetic Resonance Imaging**
- ⦿ **Testicular biopsy**

# Intra-uterine Insemination (IUI)

healthy sperms that have been collected and concentrated are placed directly in the uterus around the time of ovulation

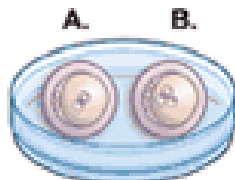
# *In-Vitro Fertilization (IVF)*

multiple mature eggs from a woman are retrieved, and fertilized with a man's sperm outside the womb and inside a laboratory. Then, the fertilized embryos are implanted in the uterus after three to five days of fertilization.



**A****Fertilization**

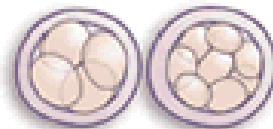
Fertilization



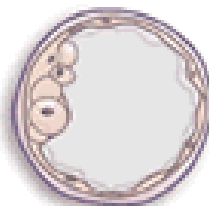
Fertilization  
A: Normal  
B: Abnormal

CCP  
©2005**B****Cleavage  
& Blastocyst  
Formation**

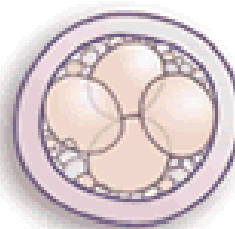
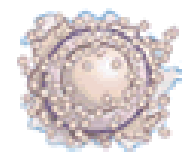
2 Cells:  
(ROS: 2-Cell Block)



4 & 8 Cells: (ROS:  
Low Blastomere Number)



Blastocyst:  
(ROS: Low Blastocyst Rate)

**C****Embryo  
Fragmentation****D****IVM**

GV Oocyte



M1 Oocyte



MII Oocyte

**E****Cryopreservation  
Thawing**

Sperm



Oocyte



2 Pronuclear Stage Embryo



Cleavage Stage Embryo



Blastocyst



Ovarian Cortical Strips

# **Zygote Intra-fallopian Transfer (ZIFT) and Gamete Intrafallopian Transfer**

In ZIFT, the fertilized egg is directly transferred into the fallopian tube; whereas, in GIFT a mixture of sperms and eggs is placed in the fallopian tube and fertilization occurs there.

# Intracytoplasmic Sperm Injection (ICSI)

In ICSI, a single healthy sperm is injected directly into a mature egg.

ICSI is used when there is a problem with the quality of the semen, or there are few sperms, or prior IVF cycles have failed.

Diagnostic group	Treatment choices
Ovulations disorder	Clomiphene citrate (6 cycles) Gonadotrophins (3 cycles) Metformin + clomiphene (3 cycles) Laparoscopic ovarian diathermy IVF (3 cycles)
Tubal disease	Tubal surgery IVF (3 cycles)
Endometriosis	Laparoscopic ablation for stages I and II Surgery for stages III and IV Clomiphene citrate and IUI (6 cycles) Gonadotrophins and IUI (3 cycles) IVF cycles (3 cycles)
Male infertility	IUI, partner (6 cycles) Donor insemination (6 cycles) IVF and ICSI (3 cycles)
Unexplained infertility	Clomiphene citrate and IUI (6 cycles) Gonadotrophins and IUI (3 cycles) IVF (3 cycles)

- ⦿ **Donor Eggs and Sperms**
- ⦿ **Gestational Carrier**



با تشکر