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7/9/2022

urology

INFERTILITY

Dr. Fayez zedan

Male Reproductive Function

- The testes are 4 to 5 cm long, 3 cm wide, and 2.5 cm deep and have a volume of 20 mL. Within the capsule, the testis is divided into compartments separated by septa of the testis .
 - Within each septum are individual seminiferous tubules, as well as interstitial tissue. Interstitial tissue contains leydig cells ,responsible for testosterone production.
 - The seminiferous tubules , where spermatogenesis occurs contain Sertoli cells and the developing germ cells(spermatogonia
- 1y
2y → spermatocytes , spermatides , spermatozoa). the combined length of tubules in the testis is approximately 250 meters.

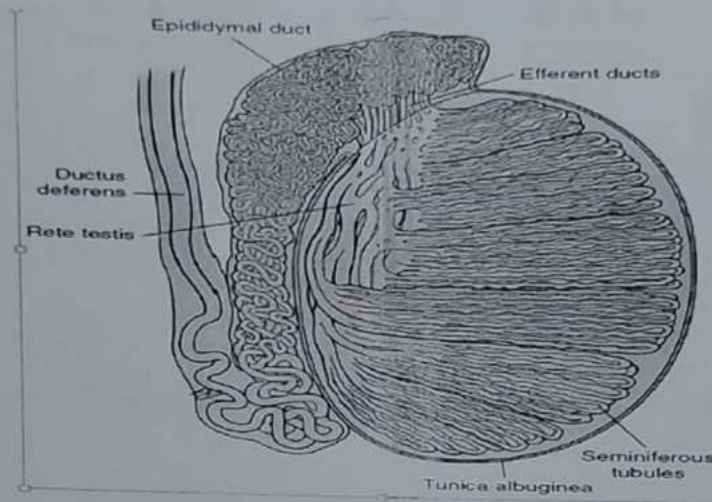
early
round
late spermatides

Efferent ducts: connects btw Rete testis & epididymus.

احياناً يكون هناك obstruction من الـ efferent ducts

& most commonly the obstruction is at level of epididymal tail or vas deferens

Anatomy



- ^{mature sperm} The human spermatozoon is approximately 60 μm in length, consists of head, middle piece and tail. The oval head, consists principally of a nucleus, which contains the hereditary material - DNA, and an acrosome, that contains the enzymes required for penetration of the outer membrane of the egg.

• Spermatogenesis:

cycles: within the human testis, 74 days; sperm maturation: 10-15 days.

Upon release from the testis, spermatozoa are immotile. They acquire the ability to swim during their transit through the epididymis

هذا مكان ريف
جاي بيشتري من
infertility
لانه عنده

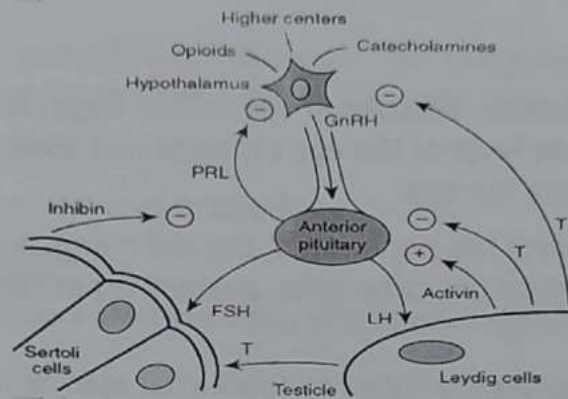
normo spermia
يعني العدد نورمال

↓
هذا بملب

acrosome
test

→ if negative → this mean the ^{الزوجان} couple needs ^{زراعة} intracytoplasmic sperm injection (ICSI)

Spermatogenesis is driven by precisely regulated and pulsatile secretions of GnRH, LH, and FSH from the hypothalamic-pituitary-gonadal (HPG) axis.



Sperm journey

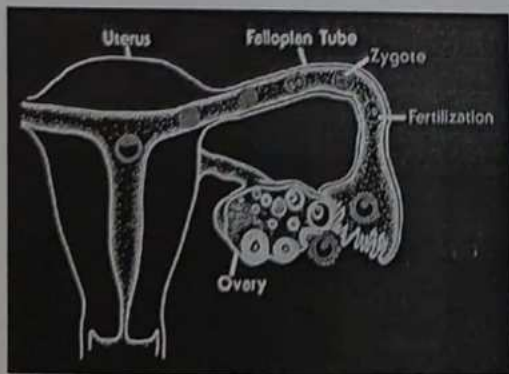
- Following ejaculation, the semen forms a gel which provides protection for the sperm from the acidic environment of the vagina.
- The gel is liquefied within 20-30 minutes by enzymes from the prostate gland. Sperms with the greatest motility travel through the cervical mucus.
- Once the sperm have entered the uterus, contractions propel the sperm upward into the fallopian tubes. Only 1 in 14 million of the ejaculated sperm will reach the Fallopian tube.
- The lucky few sperms who reached the egg in the Fallopian tube surround it and begin competing for entrance.

- The sperm acrosome, releases enzymes that begin to break down the outer, jelly-like layer of the egg's membrane (zona pellucida), trying to penetrate the egg.
- Once a single sperm has penetrated, the cell membrane of the egg changes its electrical characteristics, pushing other sperms away from the egg.
- The first sperm enter the tubes minutes after ejaculation. Motile sperm can survive in the female reproductive tract for up to 5 days.

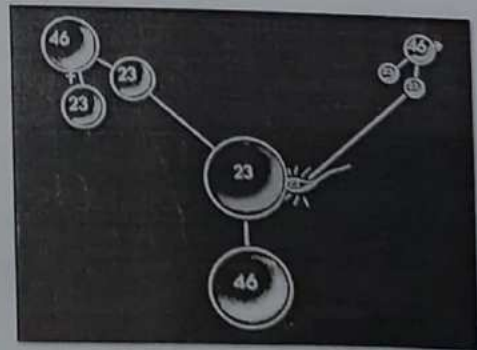
٧) *The stronger the sperm, the shorter the half life.*

اذا يوم intercourse كانت البويضة جاهزة في احتمال انجاب ذكر اكبر
 في نفس حال يوم intercourse كانت البويضة لاسم جاهزة في احتمال انجاب انثى اكبر

Implantation



Fertilization: sperm meets egg



* Couple infertility الزوجين قابلية خلوا

↳ السبب ؟
الأسباب

- ① 40% male infertility
- ② 40% Female infertility
- ③ 20% Both (male & Female) infertility.

Infertility

• Definition:

- The inability of a sexually active couple, not using any contraception, to conceive during 1 year (age < 35) or 6 months (age > 35).

Primary infertility:-

* a couple that has never conceived

Secondary infertility:-

* infertility that occurs after previous pregnancy regardless of outcome

AzooSpermia: no sperm in the ejaculate

Functional cause
obstructive cause

Etiology

Pretesticular causes:

Hypothalamic disease

- Gonadotropin deficiency (Kallmann syndrome)
- Isolated LH deficiency ("fertile eunuch")
- Isolated FSH deficiency
- Congenital hypogonadotropic syndromes

Pituitary disease

- Pituitary insufficiency (tumors, operation)
- Hyperprolactinemia → causes hypospermatogenesis.
- Exogenous hormones (androgen excess, hyper- and hypothyroidism).

46XX male \$

- normal size testis
- azospermia

له هنا من اقل
حتى لو عملنا له
testicular biopsy

من راح يلاق sperm
خالص

- *Klinefelter \$
- azospermia
 - wide pelvic
 - hair distribution "Female type"
 - very small testis
 - Gynecomastia

testicular
macroscopic biopsy

ICSI

نראה

Testicular causes :

47 XXY

- Chromosomal (Klinefelter syndrome, 46,XX male syndrome)
- Noonan syndrome (male Turner syndrome)
- Vanishing testis syndrome (bilateral anorchia)
- Sertoli-cell-only syndrome (germ cell aplasia)
- Gonadotoxins (radiation, drugs)
- Systemic disease (renal failure, liver failure)
- Testis injury (orchitis, torsion, tumour, trauma)
- Cryptorchidism ^{نموا} mumps orchitis
- Varicocele $\rightarrow 40\%$ of them have problem in spermatogenesis
- Idiopathic

of testis such in case of testis tumor

$\Rightarrow$ Post chemotherapy, or post Radiotherapy $\Rightarrow$ azospermia could develop

cryo ejaculation ^{تجميد السائل المنوي} قبلها (تجميد السائل المنوي قبلها)

Posttesticular causes:

Reproductive tract obstruction

- Congenital absence of the vas deferens (CAVD)
- Young syndrome
- Idiopathic epididymal obstruction
- Ejaculatory duct obstruction ^{infection, folly catheter, prostatic cyst, pelvic surgery}
- Acquired blockages Vasectomy
- Groin surgery
- Infection
- Functional Sympathetic n. injury, Pharmacologic

التي تأثر بها ejaculatory duct
retrograde ejaculation

* طب إذا الشخص به يعمل انقطاع او كيموي للخصية لكنه لم يبلغ بعد (قبل سن البلوغ)
هنا ممكن نعمل تجميد لل stem cells

* In case of cryptorchidism, ~~the~~ orchiopexy must be done before 2 years of old, in case of late orchiopexy $\Rightarrow$ more ~~less~~ Liable for fertility problems. 7/9/2022

Disorders of sperm function or motility

■ Immotile cilia syndromes $\Rightarrow$ necrospemia

■ Immunologic infertility

Disorders of coitus

■ Impotence

■ Hypospadias $\rightarrow$ types (glandular, coronal, sub-coronal, mid shaft, proximal penile, perioscrotal, scrotal, penineal)

■ Timing and frequency of intercourse

- normal number
- normal shape
- zero motility

trauma, mumps orchitis to confirm, do antisperm antibodies.

1) Glans
ventral
surface of
penis

* Drugs Cause retrograde ejaculation $\Rightarrow$ α blocker as (tamsulosin)
* MCC of retrograde ejaculation $\Rightarrow$ DM

Distribution of Etiology of Male Infertility

CATEGORY	NUMBER	PERCENT (%)
Varicocele	603	42.2
Idiopathic	324	22.7
Obstruction	205	14.3
Normal/female factor	119	7.9
Cryptorchidism	49	3.4
Immunologic	37	2.6
Ejaculatory dysfunction	18	1.3
Testicular failure	18	1.3
Drug/radiation	16	1.1
Endocrinopathy	16	1.1
Others (all <1%)	31	2.1

* 75% of hypospadias are distal type.

* in case of proximal hypospadias $\Rightarrow$ may cause fertilization problems

History in evaluation of infertile men:

• Fertility history:-

• Previous pregnancies (Primary or secondary infertility)

• Duration of infertility

• Previous infertility treatments

• Female evaluation

• Sexual history

• Erections

• Timing and frequency

• Lubricants

• Past history:-

• Cryptorchidism , testicular torsion, trauma

• mumps

• onset of puberty

• Midline defects (Kartagener syndrome)

• Hypospadias.

• Medical history:

• Systemic illnesses _ Diabetes mellitus, cancer

• Neurologic disease _ spinal cord injury , multiple sclerosis

• Genetic diseases _ cystic fibrosis, Klinefelter syndrome

• Infection _ prostatitis, epididymitis,

• Tuberculosis → causes obstruction in vas deferens.

• Surgical history:

- Orchidopexy
- Retroperitoneal/pelvic surgery
- vasectomy
- bladder neck/prostatic surgery

• Medication history:

- Chemotherapy/radiotherapy
- Cimetidine, ketoconazole, spironolactone, Sulfasalazine, alpha blockers,
- Antidepressants, antipsychotics. *قد يقلل ان ejaculation*

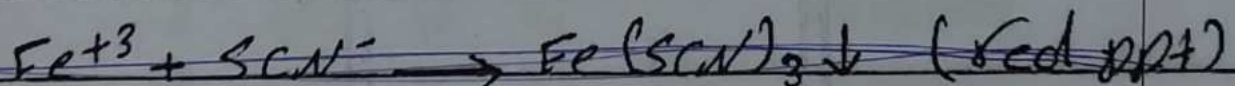
• Environmental exposures :

- Pesticides
- Heavy metals
- Social history
- Ethanol
- Smoking/tobacco , cocaine
- Anabolic steroids → *hypospermateogenesis*

آخر الزمان يقول انه التدخين < 3 سبار في اليوم يجعل كل في انتاج الحيوانات المنوية.

PHYSICAL EXAMINATION

- Virilization : decreased body hair , gynecomastia may suggest androgen deficiency
- Genital examination : curvature , chordee or hypospadias
- Scrotal contents : testis size and consistency , *site of testis , if there is scar for previous surgery*
- Vas deferens (CAVD, nodularity) , epididymis
- *varicocele* ~~Varicocele~~ *Solution: -*
- Rectal examination : prostate, seminal vesicles



azospermia with $\begin{cases} \text{normal-sized testis} \Rightarrow \text{obstructive} \\ \text{small sized testis} \Rightarrow \text{Functional} \end{cases}$

In semen ~~analysis~~ analysis 2

- ① count ≥ 15 million
- ② total motility $> 40\%$
- ③ normal form (shape) 4-30%.

Laboratory evaluation of male infertility

before semen analysis, stop intercourse 3-5 days

• Semen analysis:

Semen analysis is the primary source of information on sperm production and reproductive tract patency. However, it is not a measure of fertility.

- Seminal fructose ↓ seminal fructose means obstruction
- Postejaculate urine analysis

* People with retrograde ejaculation $\Rightarrow$ orgasmic anejaculation

* People with non-orgasmic anejaculation $\Rightarrow$ neurological problem or trauma

Hormonal assessment

Condition	T	FSH	LH	PRL
Normal	NL	NL	NL	NL
Primary testis failure	Low	High	NL/High	NL
Hypogonadotropic hypogonadism	Low	Low	Low	NL
Hyperprolactinemia	Low	Low/NL	Low	High
Androgen resistance	High	High	High	NL

* In case of normospermia in man complaining of infertility:-

- Do
- ① ~~Acrosome~~ Acrosome reaction
 - ② Sperm penetrating assay
 - ③ Sperm DNA damage

Adjunctive tests

- Semen leukocyte analysis → looking for infection
 - Sperm-mucus interaction/ poscoital test → after intercourse, cervix mucus is biopsied to look for viable sperm.
 - Acrosome Reaction
 - Antisperm antibody test → for autoimmune infertility
 - Hypoosmotic swelling test (HOS test) → for motility disorders (necrospemia) no viable → the patient needs to do IUI
 - Sperm penetrating assay
 - Sperm chromatin structure
 - Reactive Oxygen species
 - Sperm DNA Damage (sperm DNA fragmentation) → بين مقدرة الحيوان الحيوي على الاختراق
 - Chromosomal studies and genetic analysis
- I motile, viable sperm → do ICSI
→ I motile, non-viable sperm → لا بينج ال ICSI

* sperm penetrating assay: the ejaculate is taken from the man & eggs from the wife & from other donor female in order to compare

هنا نبيحطوا البويضات مع الحيوانات المنوية

Other testing

- Scrotal ultrasound (size of testis, intratesticular tumor or cyst, testicular microlithiasis)
- Transrectal ultrasound → dilatation of seminal vesicle
- CT scan or MRI of the pelvis → looking at pelvic part of the vas ejaculatory duct
- Testis biopsy to decide if the cause of azospermia is obstructive or not.
- Vasography → to know the level of obstruction
- Fine-needle aspiration 'mapping' of the testes

يحقن contrast
ويستخرج
من urethra → no obstruction

Testis biopsy → the sperm is mature → this means there is obstruction → Do vasography to know the level of obstruction

Characteristics of Normal Semen (World Health Organization, 1999)

Color	White, opalescent
Specific gravity	1.028
pH	7.35-7.50
Volume	2-6 mL
× Count	2×10^6 spermatozoa/mL or more
× Motility	≥50% motile (grades A + B) or 25% with progressive motility (grade A)
Morphology	>30% sperm with normal morphology
Viability	≥50% viable sperm
Pus cells	$<1 \times 10^6$ /mL of semen

Sperm parameters

- Normospermia _ Normal ejaculate
- Oligozoospermia _ Sperm concentration < 15 million/ml
- Asthenozoospermia _ $< 40\%$ spermatozoa with forward progression
- Teratozoospermia _ $< 30\%$ spermatozoa with normal morphology
- Oligoasthenoteratospermia _ OAT syndrome *count < 15 , motility $< 40\%$, normal $< 42\%$*
- Aspermia _ No ejaculate
- Azoospermia _ No spermatozoa in the ejaculate

abnormal
shape of
sperm

7/9/2022
 * Bladder neck surgeries that can cause retrograde ejaculation 7/9/2022
 ① TUIP
 ② TURP
 ③ open prostatectomy "simple" 80%.

Causes of non-obstructive Azoospermia According to testicular biopsy:

- Maturation arrest at which level of spermatogenesis.
- Germinal aplasia (Sertoli-cell-only syndrome)
- Seminiferous tubular sclerosis

* In you did testicular biopsy → and found low count of sperm → do cryopreservation of sperm.

Causes of obstructive Azoospermia:

1. Epididymal obstruction

Congenital forms	Idiopathic epididymal obstruction
Acquired forms	Postinfective (epididymitis)
	Postsurgical (epididymal cysts)

2. Vas deferens obstruction

Congenital forms	Congenital absence of the vas deferens
Acquired forms	Postvasectomy
	Postsurgical (hernia, scrotal surgery)

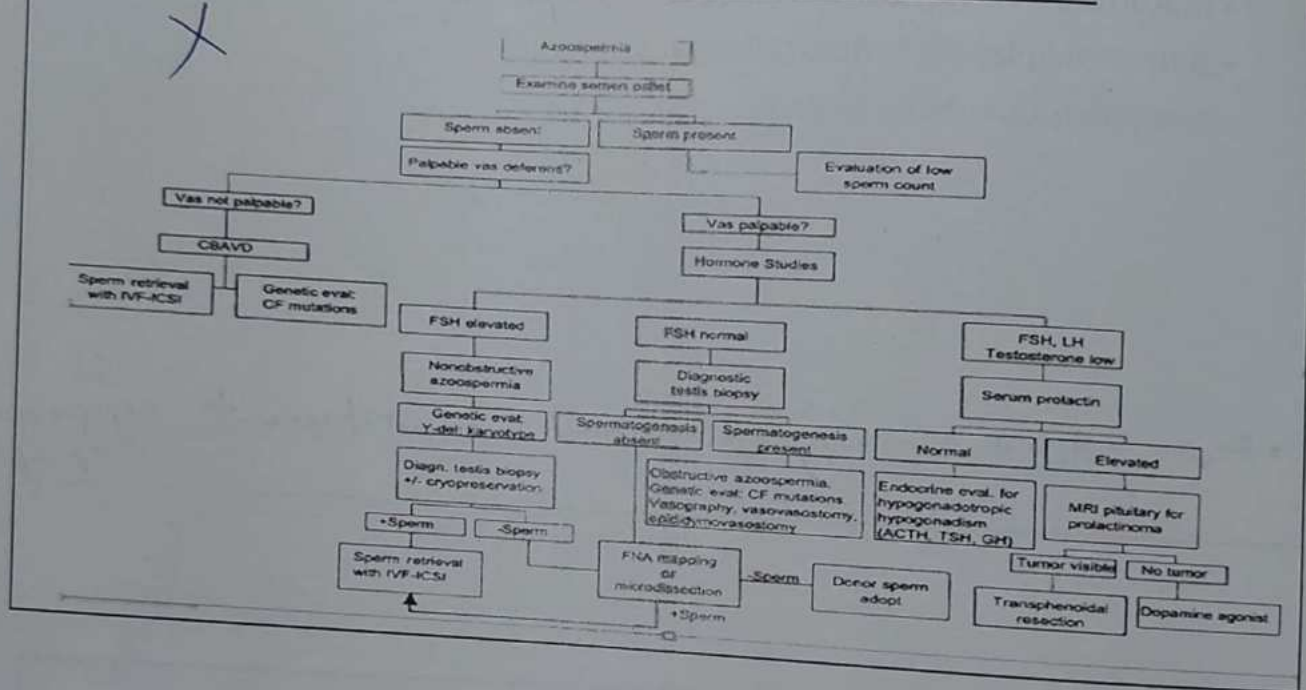
3. Ejaculatory duct obstruction

Congenital forms	Prostatic cysts (Müllerian cysts)
Acquired forms	Postsurgical (bladder neck surgery)
	Postinfective

لو كانت عند المريض (هي من الغالب asymptomatic) epididymal cyst
 المريض لا يحس ، يفضل انما ما تنسأل لانه لو كان مقلد لـ post surgical obstruction

* In radical prostatectomy $\frac{\text{نسيج}}{\text{ال}}$ para obturator & parailiac LNs.

Clinical approach for azoospermia



Treatment of Infertile

- Infertility places a great emotional burden on the infertile couple.
- The quest for having a child becomes the driving force of the couples relationship.
- It is important to address the emotional needs of these patients.
- The treatment of male infertility depends upon the underlying cause.

Surgical treatment

- Varicocele_ varicocelectomy
- Vasectomy_ vasectomy reversal or epididymovasostomy or vasa vasosa anastomosis.
- Ejaculatory duct obstruction: TURED transurethral resection of ejaculatory duct
- Spinal cord injury; injured the pelvic sympathetic nerves:
Electroejaculation RIVI
- Cryptorchidism: Orchidopexy
- Sperm retrieval techniques: MESA, TESE, PESA, TESA

27 إذا لم ينجح orchidopexy و ما انتقل الربي abdomen و ما انتقل الربي abdomen
هنا لازم تشال لأنه ممكن احتمال tumor transformation

Medical therapy

- Hypogonadotropic Hypogonadism:
- Human chorionic gonadotropin (hCG) at a dose of 1500 to 2000 IU two to three times per week for 4 to 6 months , then human menopausal gonadotropin(hMG) is administered at a dose of 75 IU two to three times per week, and recombinant FSH usually uses doses of 37.5 to 75 IU three times per week

- Hyperprolactinemia _ bromocriptine or cabergoline.
- Hypothyroidism—Both elevated and depressed levels of thyroid hormone Alter spermatogenesis. Replacement or removal of low or excessive thyroid hormone is effective treatment for infertility.
- Immunologic infertility corticosteroid suppression, ART....

- Empiric medical therapy when no identified cause can be detected 40% of patient

- 1) Antiestrogens :clomephene citrate,tamoxifen
- 2) Antioxidants :vit E , L-carnitine
- 3) Zinc , folic acid

- 4) Food supplementation , stop smoking

- If neither surgery nor medical therapy is appropriate for male infertility treatment, assisted reproductive techniques (ART) can be used to achieve a pregnancy.

Life style & environmental modification

السبب في علة "بغير من الليل" spermatogenesis

Assisted Reproduction

ART: Assisted reproductive disease.

- Indications for ART:
- Tubal disease
- Male-factor infertility
- Endometriosis
- Premature ovarian failure
- Polycystic ovarian syndrome
- Immunologic infertility
- Unexplained infertility

Treatment Options

Advice	Assessment
OI	Ovulation Induction
IUI	Intrauterine Insemination
IVF	In Vitro Fertilisation
ICSI	Intra Cytoplasmic Sperm Injection
SSC	Surgical Sperm Collection tesa,
Donor	Sperm, Eggs or Embryos

مننا تعتبر حرام شرعاً
لأنها تتدخل في
الأنساب

Intrauterine Insemination (IUI):

شرعاً number of sperm > 9 million

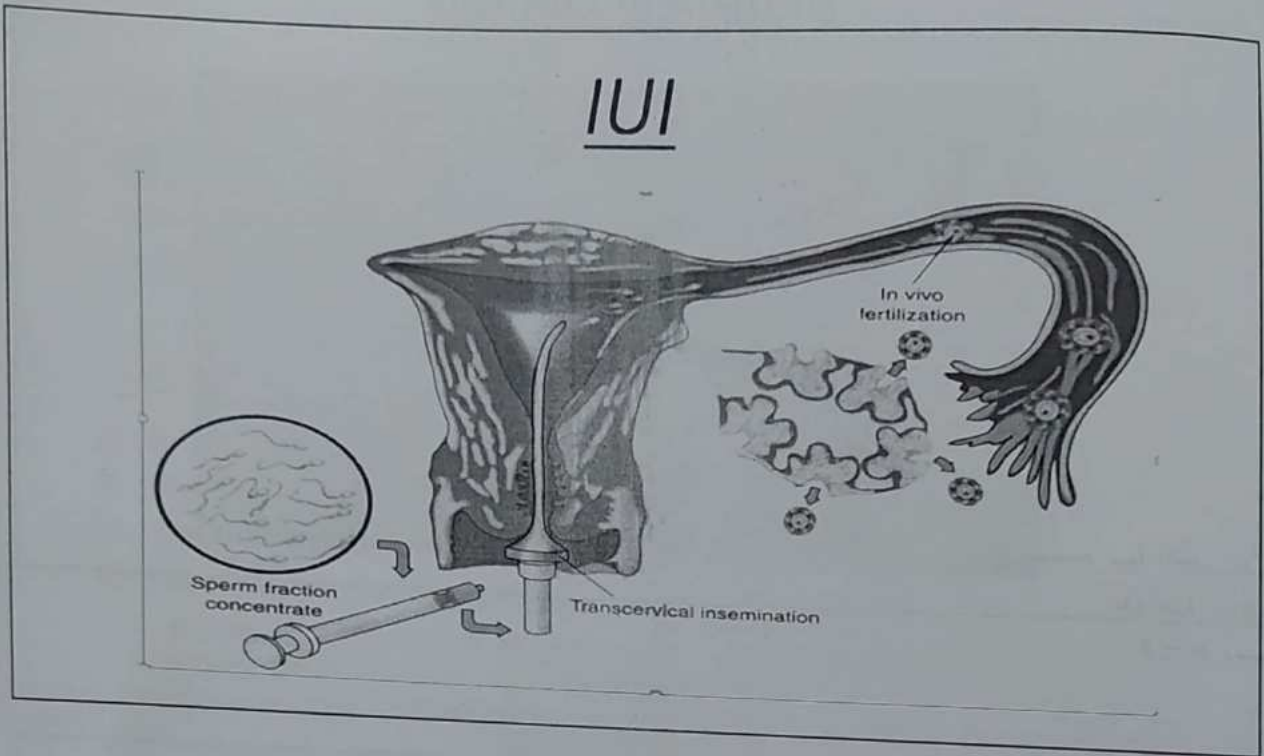
- Involves the placement of a washed pellet of ejaculated sperm within the female uterus, beyond the cervical barrier.
- Success rate 8 - 16% per cycle.
- Less expensive , less invasive for mild male factor and cervical factor

في IUI :-

- يتم فحص حجم البويضة و من المتوقع تنقل
- بناءً على الزوج عينة السرموي و يتم غسلها washing
- يتم ادخال catheter في عنق الرحم و من خلال يتم ادخال الحيوانات المنوية الى الرحم

IUI تتمه تتخلل يومين ورا بعض

IUI



دخلت لتستخدم

In Vitro Fertilization (IVF):

سperm count $\geq 500,000$

- The technique of letting fertilization of the male and female gametes occur outside the female body (in Petri dishes) 500,000 to 5 million motile sperm often used.
- Techniques usually used in IVF include:
- Transvaginal ovum retrieval (OCR) _a small needle is inserted through the vagina and guided via ultrasound into the ovarian follicles to collect the fluid that contains the eggs.
- Embryo transfer is the step in the process whereby one or several embryos are placed into the uterus .

Indications:-

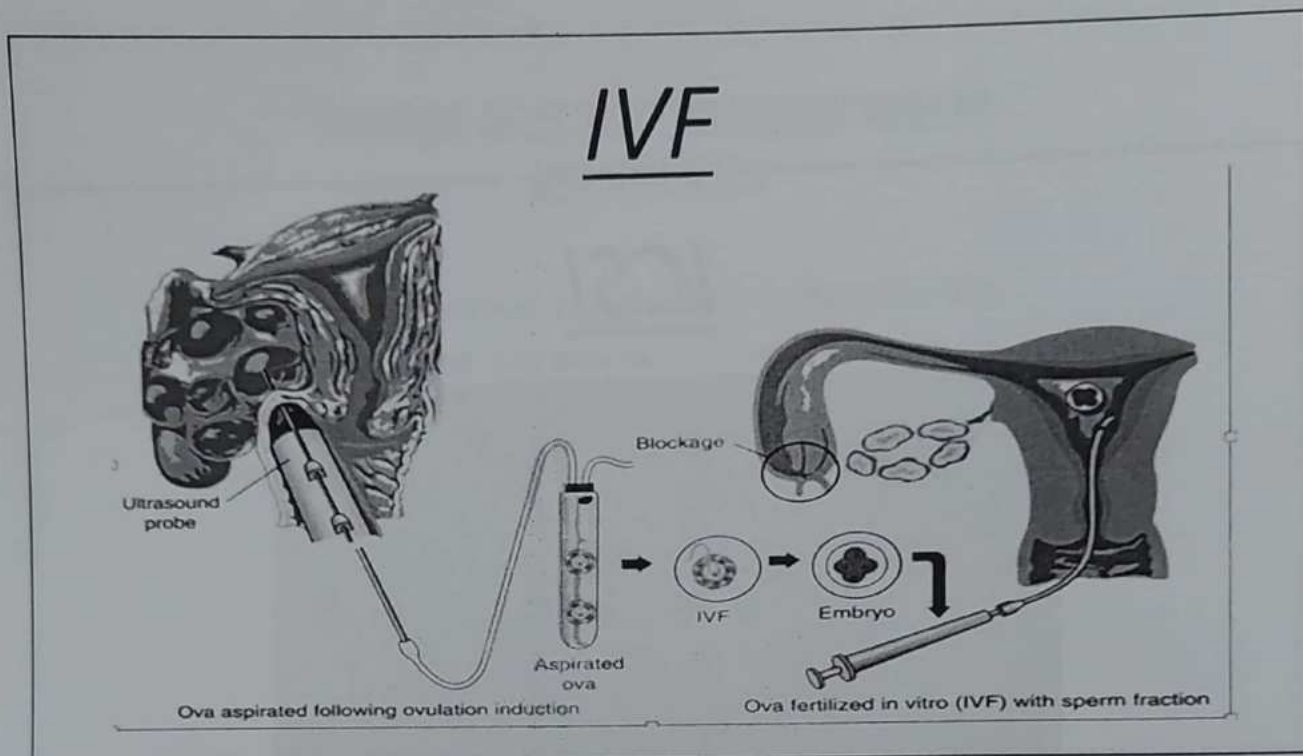
- 1) Prolonged unexplained
- 2) Tubal factor
- 3) Severe male factor

توضع الحيوان المنوي مع البويضة
betry dish

بعدين لحظاتها حضانه و يتم مراقبه
الانقسام ، اذا هارفت اجنية جدين

يتم الرجاء الاجنية في ال uterus

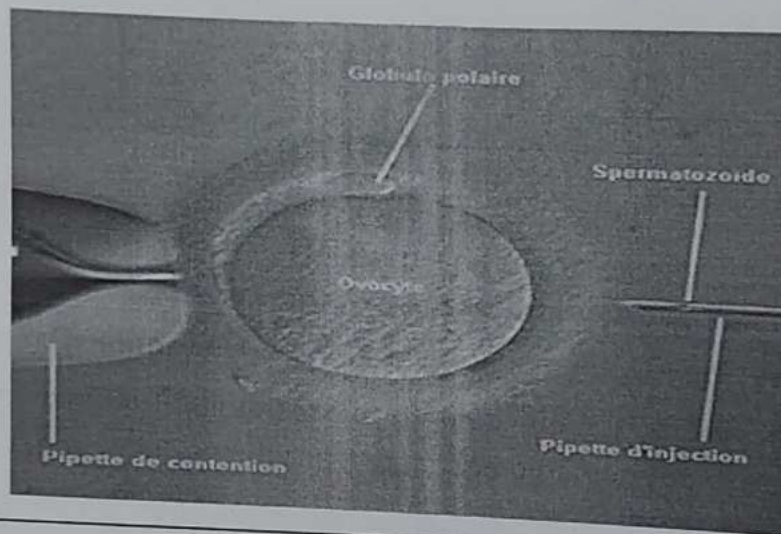
هنا تقدم يتم sex selection بي بره
عندها ولاد و بهابنت او عندها بنات و بهاولد



Intracytoplasmic sperm injection (ICSI):

- The sperm requirement for egg fertilization has dropped from hundreds of thousands for IVF to 1 viable sperm for ICSI. The procedure involves a single sperm carefully injected into the center of an egg using a microneedle.
- The most effective method for severe immunological infertility But with the highest cost tens of thousands of dollars.

ICSI



Complications

- Multiple pregnancy
- Ovarian hyperstimulation syndrome (OHSS)
- Ovaries may enlarge and cause pain and bloating
- Higher risk in PCOS women
- Bleeding or infection
- Low birth weight
- Birth defects

Human sperm cryopreservation

Indications:

- Before surgical, chemical or radiological cancer therapy
- Temporary or permanent absence of the husband.
- Before vasectomy.
- Cryopreservation of testicular tissue in boys with testicular cancer.

