

INFERTILITY

Dr. Fayez zedan

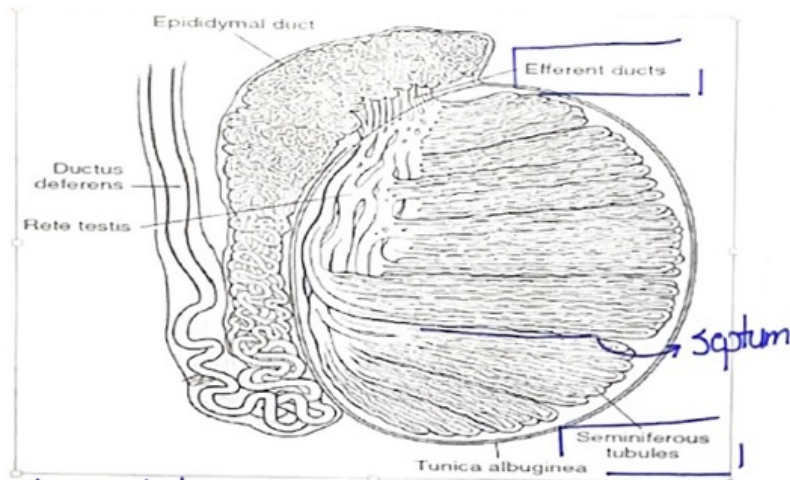
Male Reproductive Function

- 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 , spermatocytes , spermatides , spermatozoa). the combined length of tubules in the testis is approximately 250 meters.

1st
2nd
→
round, late, Mature

Septum بين Seminiferous Tubules
 Rete Testis بطلع في Seminiferous Tubules

Anatomy



(Head, body, Tail, Vas de.) epididymis ducts Rete Testis

- The human spermatozoon is approximately $60 \mu\text{m}$ 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.

بالجوار
 Oval

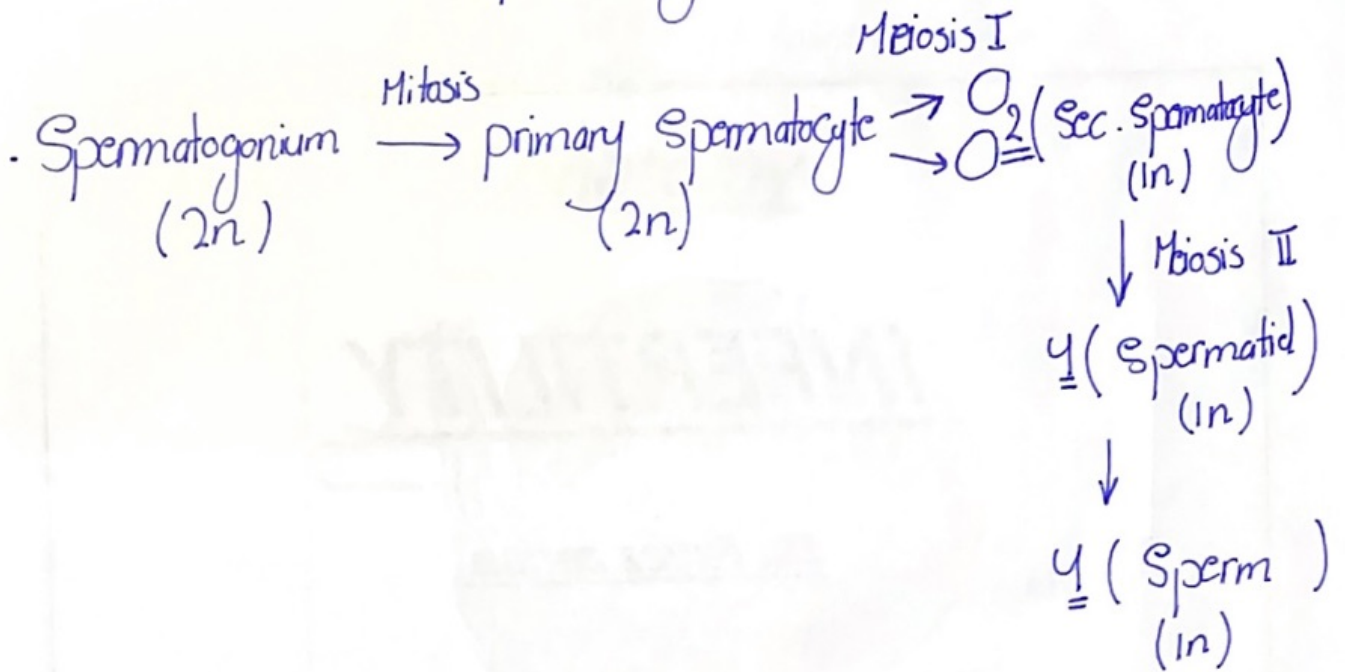
• Spermatogenesis:

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]

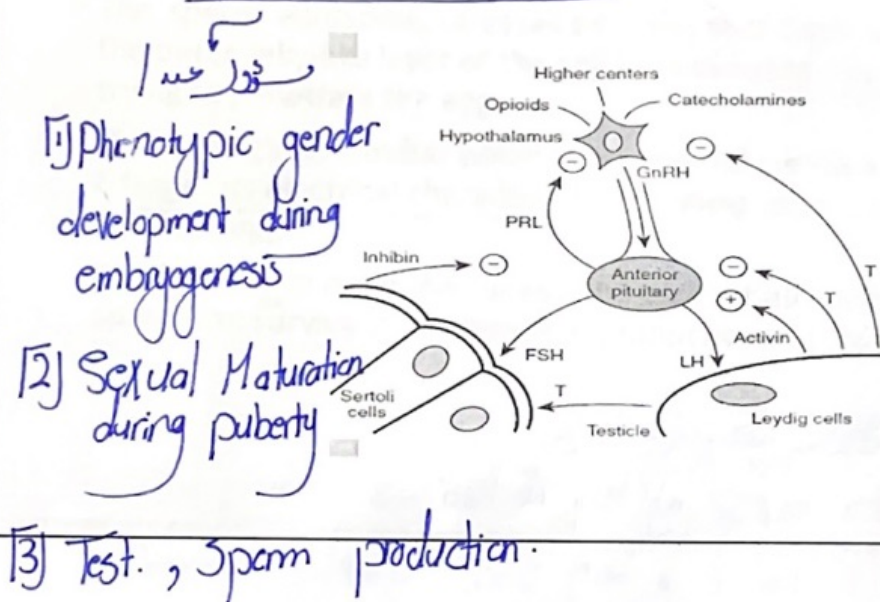
الحيوانات للتربية جناسه وال Spermatogenesis في Normal sperm
 فيه مشكلة بـ بنطاب Acrosome لحيوة Acrosome موجود داو.
 Acrosome Test Fertilization Female Male
 Test Normal Normal

Spermatogenesis



فائدة الـ Acrosome test يحدد الحيوانات المنوية في Acrosome enzyme أولاً
 عدم وجوده يعني المريس يحتاج إلى intracytoplasmic Sperm injection (زراعة)

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



رحلة الحيوانات المنوية Sperm journey

- Following ejaculation, the semen forms a gel which provides protection for the sperm from the acidic environment of the vagina. مدة تظل الجلام
- 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. بدفعه للأعلى
- The lucky few sperms who reached the egg in the Fallopian tube surround it and begin competing for entrance.

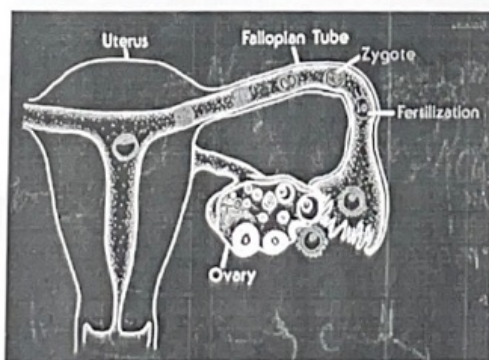
- The sperm acrosome, releases enzymes that begin to break down the outer, jelly-like layer of the egg's membrane(zona pellucida), trying to penetrate the egg.
- Once a single sperm has penetrated, the cell membrane of the egg changes its electrical characteristics ,pushing other sperms away from the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

. الحيوانات المنوية الأقوى تبقى فترة أقل .

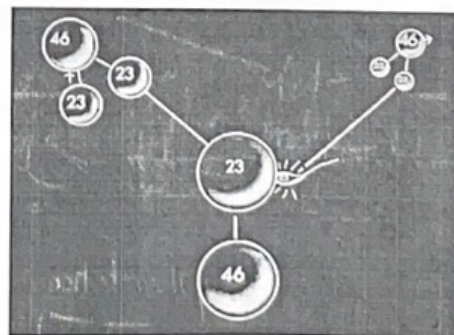
. تزيد Sexual intercourse مع حمض البورصة ← Male

Female ← حمض البورصة ← عدم n n n n

Implantation



Fertilization: sperm meets egg



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

الزوجية ما خلفوا قبل هيك

Secondary infertility:-

*infertility that occurs after previous pregnancy regardless of outcome

قديمًا الحديث عن female infertility فقط

40% Male 40% Female في السولية عن infertility

20% both

Hypothalamus + Pit. Glands.

Etiology

Pretesticular causes:

Hypothalamic disease

- 1] Gonadotropin deficiency (Kallmann syndrome)
- 2] Isolated LH deficiency ("fertile eunuch")
- 3] Isolated FSH deficiency
- 4] Congenital hypogonadotropic syndromes

Pituitary disease

- 1] Pituitary insufficiency (tumors, operation)
- 2] Hyperprolactinemia → Hypogonadogenesis
- 3] Exogenous hormones (androgen excess, hyper- and hypothyroidism).

بواسطة الـ Karyotype
Hormonal study

Testicular causes :

MC

- 1) Chromosomal (Klinefelter syndrome, 46,XX male syndrome)
- 2) Noonan syndrome (male Turner syndrome)
- 3) Vanishing testis syndrome (bilateral anorchia)
- 4) Sertoli-cell-only syndrome (germ cell aplasia)
- 5) Gonadotoxins (radiation, drugs) Post Radiotherapy / chemotherapy
- 6) Systemic disease (renal failure, liver failure)
- 7) Testis injury (orchitis, torsion, tumour, trauma)
- 8) Cryptorchidism
- 9) Varicocele
- 10) Idiopathic

Normal Testis
سوي
Spermatogenesis

Mumps
orchitis.

- Cryptorchidism = undescended Testis $\Rightarrow$ Fertilization $\Rightarrow$ عجز في الحمل وخصوبة
خصوصاً لو نُزلت الـ Testis بعد 2 Years
- orchiopexy $\Rightarrow$ Before 2 Years.
- Varicocele $\Rightarrow$ 40-50% $\Rightarrow$ Spermatozoa $\Rightarrow$ تأثير الـ Spermatozoa

Posttesticular causes:

Reproductive tract obstruction

Level of obstruction.

- 1) Congenital absence of the vas deferens (CAVD)
- 2) Young syndrome Male infertility damaged airways in Lung + Sinusitis
- 3) Idiopathic epididymal obstruction
- 4) Ejaculatory duct obstruction (infection, Foley catheter)
- 5) Acquired blockages Vasectomy.
- 6) Groin surgery (Varicocelectomy, herniotomy, Pelvis عانة في)
- 7) Infection
- 8) Functional Sympathetic n. injury, Pharmacologic

α . Blocker
 $\downarrow$
Tamsulosin

$\Leftarrow$ Retrograde ejaculation / Absent of ejaculation
 $\downarrow$
MCC / DM

Klinefelter $\Rightarrow$ $XXY + 47$

لا يمكن علاج Sperm
وتعالم ICSI

و Genetic Test
لا يمكن ولادة
المريض

Azoospermia, wide pelvic, Gynecomastia
Very small Testis.

46 XX Male $\Rightarrow$ Absolute Male, Normal size of Testis

Azoospermia

Hopeless Testicular Biopsy

لا يجب فحصه عند أولاد

Bilat. Anorchia $\Rightarrow$ لا وجود للخصيتين

تقليدًا على النقطة الخاصة / أي متخضع لأي نوع من العلاج Radio/chemo لازم

العملية بتجديد مبيات (cryo-ejaculation) في مريضه عند Testicular وبيد
Tumor

تعالج orchidectomy وطلع العينه (Seminoma) ^{preservation}
Radio ^{تحتاج}
Malignant _{يعني}

Radio. قبله Azoospermia

الخطوة لما للمريض ياخذ ال Radio/chemo قبل بلوغه $\leftarrow$ يمكن ياخذ الطبيب

Testicular Tissue ^{وتجدهم ويعلم}
implantation inside
Testis.

Stem Cells
يعني

Disorders of sperm function or motility

① ■ Immotile cilia syndromes $\Rightarrow$ Necrozoospermia عندهم

② ■ Immunologic infertility $\downarrow$

Disorders of coitus

- ① Mumps orchitis
② Trauma

normal No.
normal Pome
motility Zero.

الرجل صغينه

① ■ Impotence

② ■ Hypospadias

③ ■ Timing and frequency

(بعلام
Anti-Sperm Ab.)

$\downarrow$ of Sexual intercourse
= erectile dysfunction

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

- Hypospadias / opening of the urethra not located at the tip of penis

Types / Ant. or distal (75%) → لا تواجه فertilization في
- mid-penile hypospadias
- Post. or proximal

↓
فertilization لا تواجه

Distal / Glandular, Sub - Coronal

Proximal / Penoscrotal, Scrotal, Perineal

History in evaluation of infertile men:

• Fertility history:-

- Previous pregnancies →
- Duration of infertility →
- Previous infertility treatments
- Female evaluation
- Sexual history → Time, freq., erection.
- Erections
- Timing and frequency
- Lubricants

في كل سنة
هل متزوجين من ١٠ سنة

• Past history:-

- Cryptorchidism , testicular torsion, trauma
- mumps orchitis .
- onset of puberty → Cong. anomic.
- 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

↓
obstruction on Vas deferens.

→ Retrograde ejaculation.
Anejaculation تؤدي الى

شخص متزوج به استور وعنده (OA) oligasthenospermia .

↓
شخص TTT

شخص TTT و شخص TTT بکجه 'انده و حلقه

فیدر 'حلقه 'انده .

Surgical history:

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

Posttesticular
infertility

⇒ عصبان ال ⇒ Ejaculatory duct
obstruction

Medication history:

- Chemotherapy/radiotherapy
- Cimetidine, ketoconazole, spironolactone, Sulfasalazine, alpha blockers,
- Antidepressants, antipsychotics.

Retgrade ejaculation .

Environmental exposures:

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

↓
Spermatogen: المؤثرة على

hypospermogenesis .

more than 3

cig.

on day →

قد في إنتاج
الحيوانات المنوية .

PHYSICAL EXAMINATION

- Virilization : decreased body hair, gynecomastia may suggest androgen deficiency →

قد على إنتاج هورمون \$ androgen

- Genital examination : curvature, chordee or hypospadias →

intraourse .

- Scrotal contents : testis size and consistency

- Vas deferens (CAVD, nodularity), epididymis

- Varicocele

- Rectal examination : prostate, seminal vesicles

Palpated داو لا .

Functional obstructed CAVD

Functional Azoospermia ← Small Testis

• Vasectomy / elective surgical procedure for Male sterilization
 ← or permanent Contraception. ← منع الحمل بشكل دائم.

العملية جراحية بسيطة

→ يتم من خلالها

→ قطع أو إغلاق

• يمنع انتقال الحيوانات المنوية

• يمنع الحمل

• لا يؤثر على

• لا يؤثر على الخصوبة

• لا يؤثر على الرغبة الجنسية

Laboratory evaluation of male infertility

✓ 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 ⇒

النقص فيه يدل على destruction

✓ Postejaculate urine analysis ⇒

الرؤية إذا فيه sperm دالة

للناس إلى عندهم Azospermic

① Count $> 15 \text{ million.}$

② Motility $> 40\%$

③ Normal form $4-30\%$

④ No intercourse from $3-5 \text{ days,}$

⑤ No viscosity / infection.

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

Small Testis

←

Normal

الناس الى عندهم Retrograde
ejaculation عادة يكون عندهم
Orgasmic
Anorgasmia

Non-organic.
Anorgasmia ← أسباب متعلقة بالأعصاب وليس النفسية.

Adjunctive tests

- Semen leukocyte analysis → infection لروية
- Sperm-mucus interaction/ postcoital test → Mucus from cervix and Vagina ⇒ لروية حيوانات المنوية خارجة ولا في حال IUI (intrauterine insemination)
- Acrosome Reaction
- Antisperm antibody test → Autoimmune in fertility.
- Hypoosmotic swelling test
- Sperm penetrating assay
- Sperm chromatin structure
- Reactive Oxygen species
- Sperm DNA Damage → fragmentation
- Chromosomal studies and genetic analysis

Other testing

- Scrotal ultrasound → Testis Size, intra-Testicular Tumor or cyst, Testicular Microlithiasis
- Transrectal ultrasound → Dilation or Seminal vesicles. obstruction ← ejaculatory duct obstruction.
- CT scan or MRI of the pelvis
- Testis biopsy
- Vasography
- Fine-needle aspiration 'mapping' of the testes

لعرفه إذا (obstructive) Azoospermia or Not.

في حال أخذنا biopsy ولقينا Mature Sperm ← obstruction ← Vasography (معرفة إذا Distal/Proximal Contrast Parts ejac. duct obstruction urethra على Contrast).
 دألف على أي Level عند طريقه Vasography.

- Hypoosmotic swelling Test / للمرضى الذين عندهم مشكلة في حركته
Motility مثل Necrozoospermia

100%
immotile.

الزراعة
في IVF / ICSI بدك تعرف ههنا الحيوانات المنوية عالية

وما بتحرك ولا ميتة
ما بتنفذ في ICSI
↓
بتنفذ في ICSI

- Sperm penetrating assay / الفكرة من هذا ال Test انو تعرف
ههنا المسألة عند الرجل ولا زوجته من
خلال بويضات بتأخذ من امرأة ثانية في مركز الزراعة وتنشأ Fertilization

- Sperm DNA frag. Test / Deletion of DNA في الحيوانات المنوية
يوضح قلة الحيوانات المنوية
على الإخصاب DNA

- Male with Normospermia ⇒ ① Acrosome Test
② DNA
③ penetrating assay

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	$\geq 50\%$ motile (grades A + B) or 25% with progressive motility (grade A)
Morphology	$> 30\%$ sperm with normal morphology
Viability	$\geq 50\%$ viable sperm
Pus cells	$< 1 \times 10^6$ /mL of semen

سليم
الفرغوني
دكتور المختار

Sperm parameters

- Normospermia _ Normal ejaculate
- Oligozoospermia _ Sperm concentration < 20 million/ml
- Asthenozoospermia _ $< 50\%$ spermatozoa with forward progression
- Teratozoospermia _ $< 30\%$ spermatozoa with normal morphology (4-30)
- Oligoasthenoteratospermia _ OAT syndrome Count < 15
- Aspermia _ No ejaculate
- Azoospermia _ No spermatozoa in the ejaculate

Normal form $\Rightarrow$ No fertilization

- OAT \$/Count < 15
- Mobility < 40
- Normal Forme < 4

→ Functional

Causes of non-obstructive Azoospermia

According to testicular biopsy:

- Maturation arrest ⇒ Level على مستوى Late spermatid / spermatocyte
- Germinal aplasia (Sertoli-cell-only syndrome)
 - ↓ No spermatogenesis
- Seminiferous tubular sclerosis
 - ↓ No cells.

Mature sperm or
but very low
count
↓
Testicular
Tissue.

Causes of obstructive Azoospermia:

① Epididymal obstruction

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

ما يعطى لو المريض
بـو مختلف .

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

↪ Retrograde ejaculation .

في ٣ عمليات على Bladder Neck

تعمل Retrograde ejaculation

① Transurethral resection of prostate (TURP)

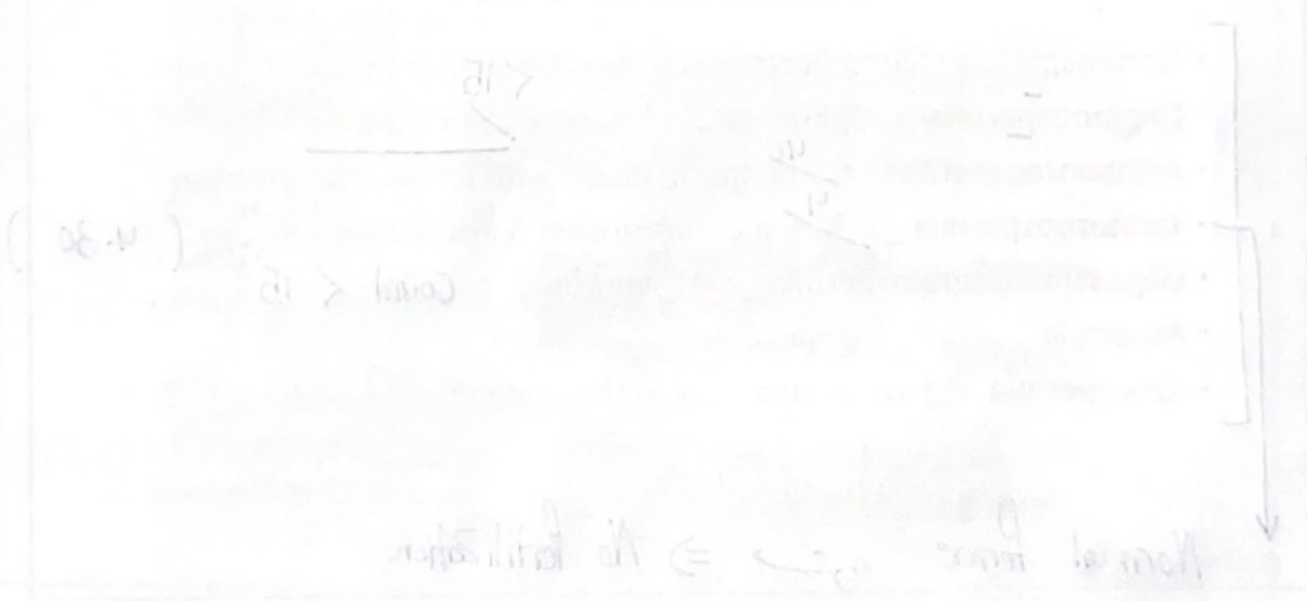
② Transurethral incision " " (TUIP)

③ Simple prostatectomy → في ١.٨.٢٠٠٠
المرضى

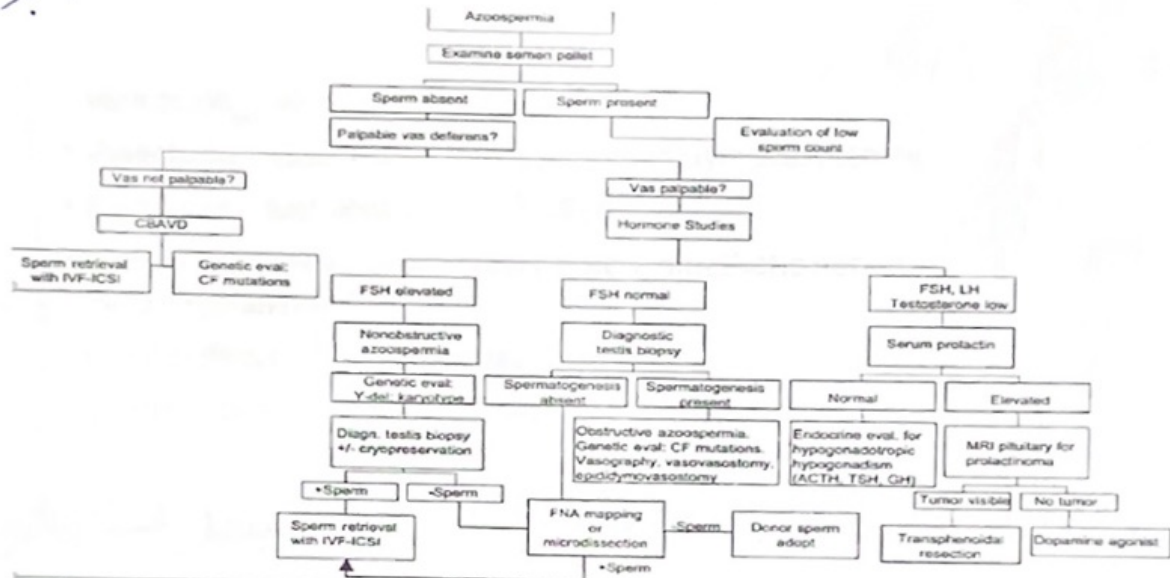
• Radical prostatectomy / Remove of prostate and seminal vesicles and LNs and post. urethra.

↓
• Para-obturator

• Para-iliac.



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.

لا ادعم نفسيًا.

Surgical treatment

- Varicocele_ varicocelectomy
- Vasectomy_ vasectomy reversal or epididymovasostomy
- Ejaculatory duct obstruction: TURED
- Spinal cord injury; injured the pelvic sympathetic nerves: Electroejaculation
- Cryptorchidism: Orchidopexy
- Sperm retrieval techniques: MESA, TESE, PESA, TESA

في حالة ال Testis كانت intra-abd. والمريض Adult يفضل استئصالها
لأنه فيها tumor Tran.

Medical therapy

ملاحظة

- 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....

hypo, hyper
معالجة

نقطة

• Empiric medical therapy when no identified cause can be detected

- 1) Antiestrogens : clomiphene citrate, tamoxifen
- 2) Antioxidants : vit E , L-carnitine
- 3) Zinc , folic acid
- 4) Food supplementation

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

مسألة في دراسة حالة
عند المريض (٠/٠) في المزرع

Empiric
TFT

→ (لوقت في صريفه Spermatogenesis) فابنم بالليل , متعاطي , Smoker.

Assisted Reproduction

- 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

طعام اختيار
دائماً

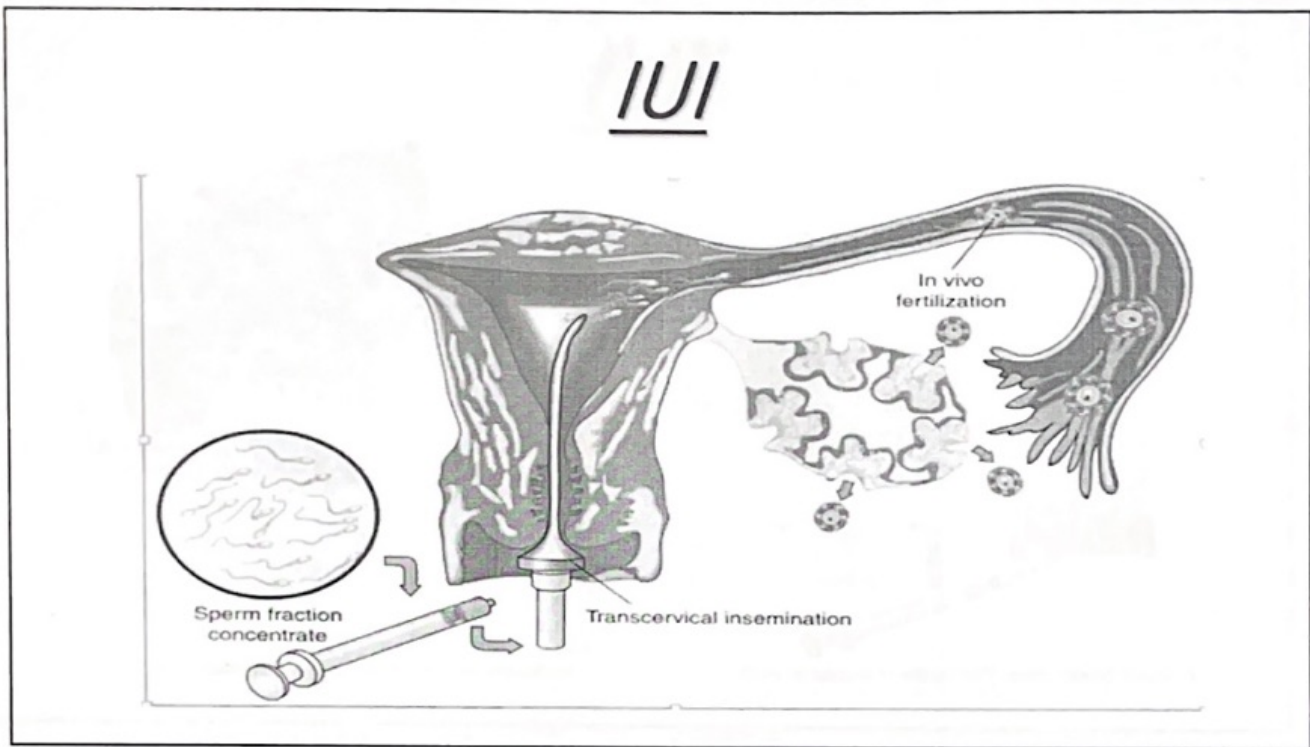
Intrauterine Insemination (IUI):

- 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

نسبة النجاح

① No' > 9 Million

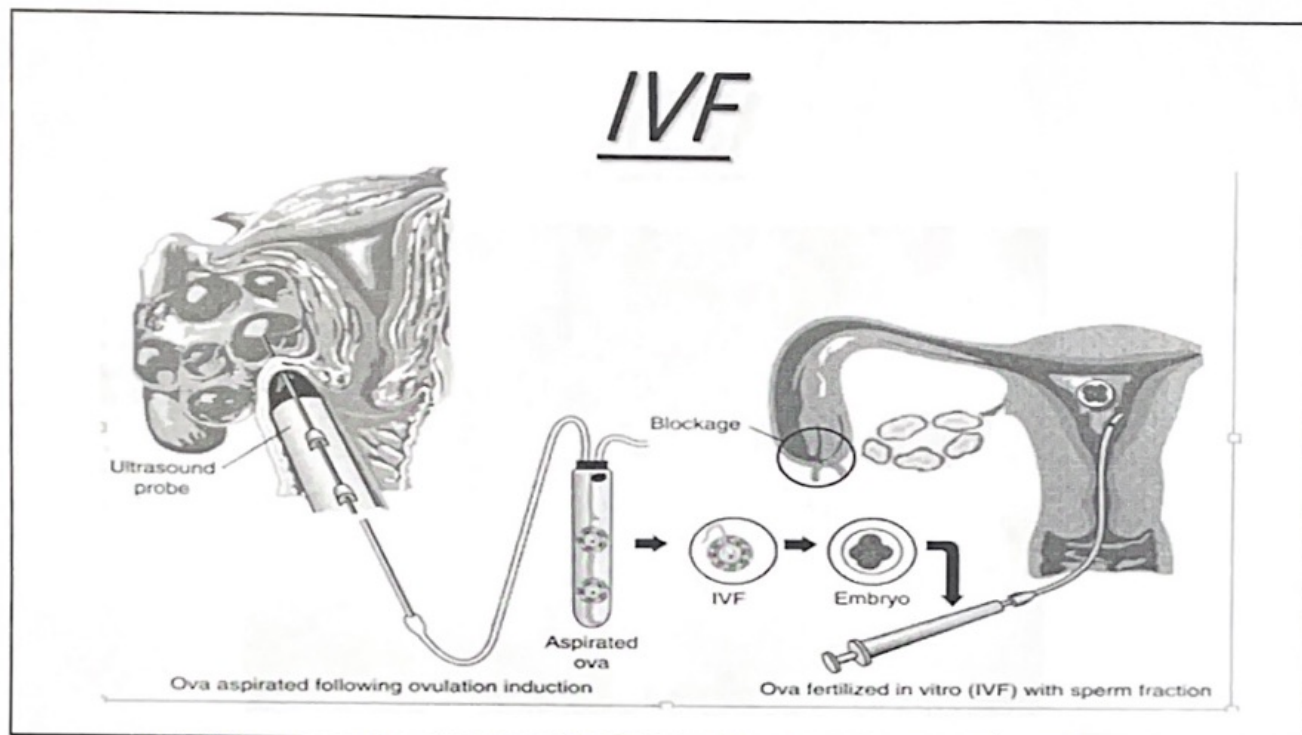
حقن ال Sperm داخل الرحم وتغلب بوسه ورا بوسه .
في الناحية التي يتموت الحيوانات المنوية في
Mucus of Vagina



بداية

In Vitro Fertilization (IVF): → **مبدأ، ICSI**

- 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



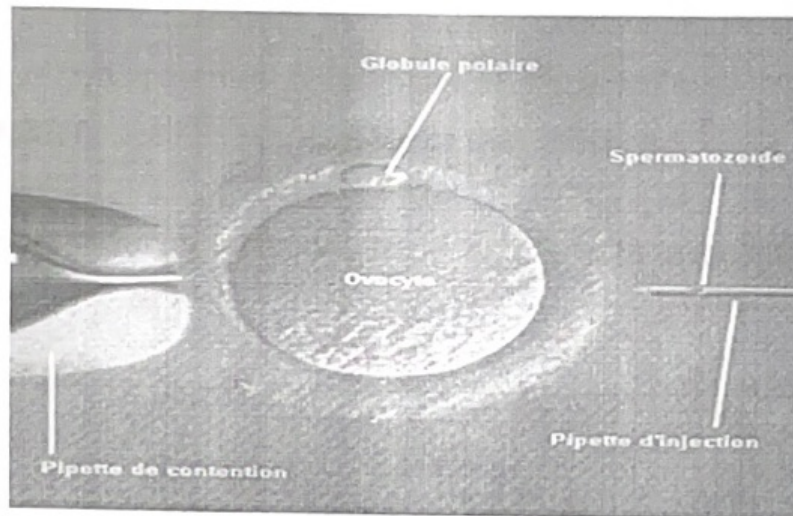
١. ابويضات لحقة بـ ١. هوانات منوية تفحص بعد ٤٨ ساعة ثم حبار
 ٢. اجنة وانقسام ترجم لا uterus. على نقل Sex selection.

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.

• Success 40-50%.

ICSI



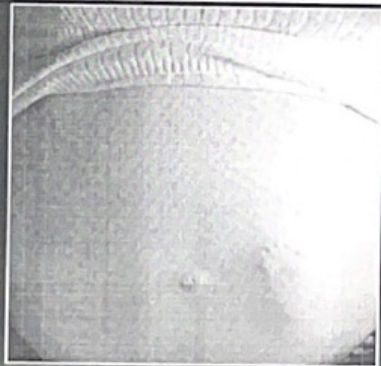
Complications

- 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.

في الجوده .



THANK YOU