

INFERTILITY

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- **Definition:**

- Infertility means inability to conceive despite a continuous regular intercourse for **at least one year** without use of any form of contraception. OR 6 months if female age 35 year or older .

- **Types:**

- **Primary**: pregnancy never occurred before.

- **Secondary**: pregnancy occurred before even once whatever its type or mode of termination.

- Requirements for occurrence of pregnancy:

- **A-Female factors:**

1- **Normal ovary:** for ovulation and production of hormones.

2- **Normal patent tube:** for normal transmission of the ova & fertilization.

3- **Normal uterine factor:** for implantation and preservation of embryo until delivery.

4- **Normal cervical and vaginal factors:** for ascent of sperms and sperm permeation.

5- **Normal hormonal and immunological status.**

- **B-Male factor:** Normal semen formation "in the testis", transport "via ductal system" and deposition of sperms in the post fornix.

Causes of infertility :

1-Female factor : 30%:

- Anovulation/oligoovulation
- Uterine factors
- Tubal disease
- Cervical factors
- Peritoneal factors

2- Male factor : 30%

3- Combined : 30%

4- Unexplained 10%

MALE CAUSES OF INFERTILITY

-These may be defective formation, transport, OR deposition of the sperms in the posterior fornix. The causes may affect quality or quantity of the sperm

1- **Congenital**: e.g. absent vas deferens..etc

2-**Traumatic**

3-**Inflammatory**: eg. prostatitis, STDs...etc.

4-**Neoplastic**: any neoplasm destructing testicular tissues.

5-**Dysfunctions**: e.g. premature and retrograde ejaculations, Abnormal seminal fluid or sperm motility / Immunological factors , varicocele .

6-**General causes**: genetics, smoking, alcoholism, liver cell failure, even idiopathic ...etc"

MALE CAUSES OF INFERTILITY

Diagnosis:

History of fertility is important

1-Clinical: by history taking and examination of the husband:

- Age and Occupation(radiation or heat exposure)
- Previous marriage and if have child
- Smoking / alcohol
- History of some diseases, trauma, surgery (hernia repair or vasectomy) ,
pelvis infections (e.g)mumps , hx chemo/radiotherapy , sexual dysfunction
...etc.

- **2-Investigations:**

C.B.C., liver function, renal function and **Semen analysis**: "the most important".

The normal **Semen analysis (after abstinence for 72 hrs)** is characterized by:

- Volume: 3-6 ml "at least more than 2 ml".
- Count: > 20 million sperms / ml.
- Normal Motility > 50 %.
- Normal Morphology: > 40 %.

- Other investigations and treatment : should requested and managed by urologist if needed .

FEMALE CAUSES OF INFERTILITY

- History and examination of female :

Menstrual cycle (regular, irregular), Previous infections & PID, Hirsutism, Dysmenorrhea, Prolactinoma & Galactorrhea, Contraception history, Family Hx of the same problem., previous marriage and children, previous infertility investigations and management .

- Sexual history (Q for both couple)

FEMALE CAUSES OF INFERTILITY

A- Anovulation/oligoovulation (ovarian).

Causes:

1-Physiological: Post OCPs , Lactation .

2-Pathological:

A- General causes: as amenorrhea and in addition:

- Age, Weight (fertility with age and overweight/obesity)
- Psychological
- Cigarettes smoking and addiction.
- Environmental toxins

B-Hypothalamic and pituitary causes (= all causes of amenorrhea).

C-Ovarian causes:

- ✓ Premature ovarian failure
- ✓ PCO
- ✓ Luteal phase defect

FEMALE CAUSES OF INFERTILITY

A . Anovulation/oligoovulation (ovarian)

Diagnosis i.e. diagnosis of an-ovulation:

1.Clinical

A-Symptoms: *absence of normal symptoms of ovulation which are (any one or more):*

- Regular cyclic menstruation.
- Ovulation pain = mid-cyclic pain "= Miettleshmirz pain".
- Ovulation spotting .
- Premenstrual mastalgia.

B-Signs: :

- Signs Document ovulation

1- increase basal body temperature early in morning.

2-Changes in characters of cervical mucous (become slippery)

FEMALE CAUSES OF INFERTILITY

- **A- Ovarian factor = Anovulation.**

2. Investigations:

A- Lab:

- ✓ Day 3 FSH & LH
- ✓ Day 21 Progesterone level in blood
- ✓ L.H level in plasma and urine.
- ✓ E2
- ✓ Prolactin
- ✓ Testosterone, and its derivatives in hyperandrogenism.
- ✓ TFT
- ✓ Anti-müllerian hormone (AMH) levels can also be helpful in predicting ovarian reserve

FEMALE CAUSES OF INFERTILITY

- **A- Ovarian factor = Anovulation.**

B- Radiological:

- U.S For serial measurements of follicular growth and maturation, "the mature Graffian follicle is about 18-25 mm".

C- Histopathological:

- Premenstrual endometrial biopsy show NO secretory changes OR luteal phase defect.

FEMALE CAUSES OF INFERTILITY

Treatment of ovarian factor:

1-Correction of general condition:

- Treatment of general causes e.g. D.M, T.B.....etc.
- Treatment of hypothyroidism
- Treatment of hypothalamic and pituitary causes.
- Treatment of hyper-prolactinemia (Bromocriptine and Cabergolin as anti-prolactin).
- Progesterone for luteal phase defect in second half of cycle .

FEMALE CAUSES OF INFERTILITY

Treatment of ovarian factor:

2-Induction of ovulation:

by using any of the followings ---→

- ✓ 1. **Clomiphen citrate (Clomid) = antiestrogen** :oral ~~50-100~~ mg/day from the 3rd day for 5-7 days (first line medication~)

Mechanism -By blocking the receptors of estrogen so blocking the negative feed back mechanism on hypothalamus and pituitary with subsequent increase in F.S.H & L.H and thus ++follicular growth and ovulation

-It increases the sensitivity of the ovary to gonadotrophins

- ✓ 1. **Gonadotrophins.** (FSH OR HMG) *human menopausal gonadotropin*
- ✓ 2. **H.C.G = human chorionic gonadotrophins.** (injection to trigger ovulation)
- ✓ 3. **Tamoxifen** as selective direct estrogen receptor inhibition.
- ✓ 4. **Metformin** as ant-insulin in PCOS.

Ovarian hyper-stimulation

- It is a common complication of induction of ovulation as the ovaries may enlarge up to 12 cm OR more with risk of peritoneal irritation and OR ovarian rupture.
- It may be mild moderate or severe.
- In mild form; there is abdominal distension, pain, sickness and diarrhea.
- In moderate form; there may be excess fluid in the abdomen leading to more pain and discomfort.
- In severe form; the case may be life threatening as there may be free fluid in the abdomen (low albumin), heamoconcentration and hypercoagulability.

Ascites

B- Tubal factor of infertility

Causes:

1. **Congenital:** tubal aplasia, hypoplasia, diverticulum.
2. **Traumatic:** trauma during operation followed by adhesions.
3. **Inflammatory:** following P.I.D ---: adhesions "the commonest cause in the tube".
4. **Neoplastic:** e.g. small cornual fibroid closing the tubal ostia.
5. **Endometriosis:** causing pelvic adhesions.
6. **Disturbed physiology:** e.g. Poor ciliary movement.

Diagnosis:

Investigations:

A-Hystrosalpingograhv = H.S.G: the main line used for diagnosis by "tubal patency tests".

The idea:

- Inject radio opaque dye in the uterus to pass through the tubes to the peritoneal cavity.
- Then the lower abdomen and pelvis are photographed.

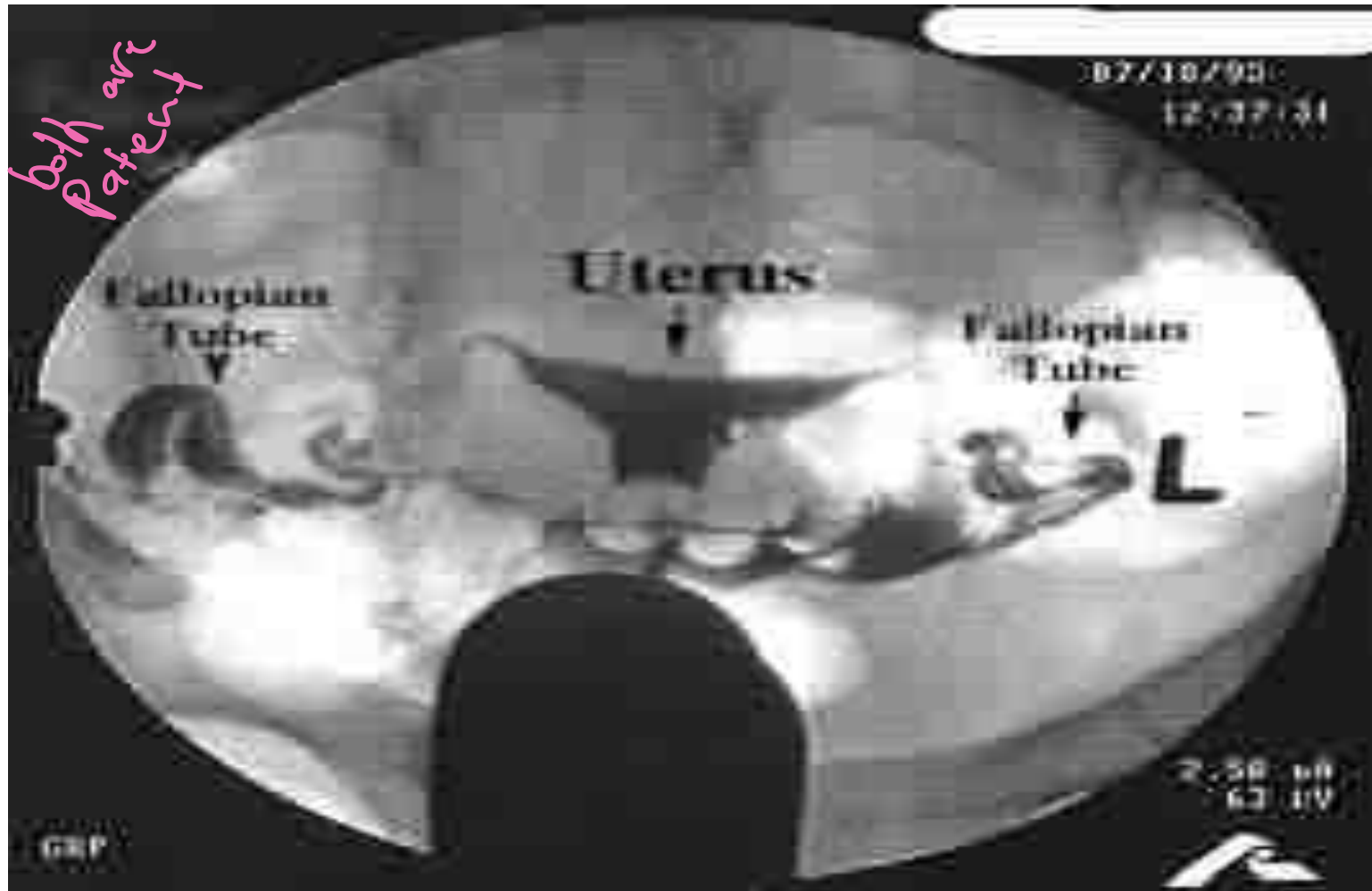
Timing of the test: it should be done postmenstrual to minimize chances of interrupting a pregnancy

Complications: Neurogenic shock, hemorrhage due to trauma,

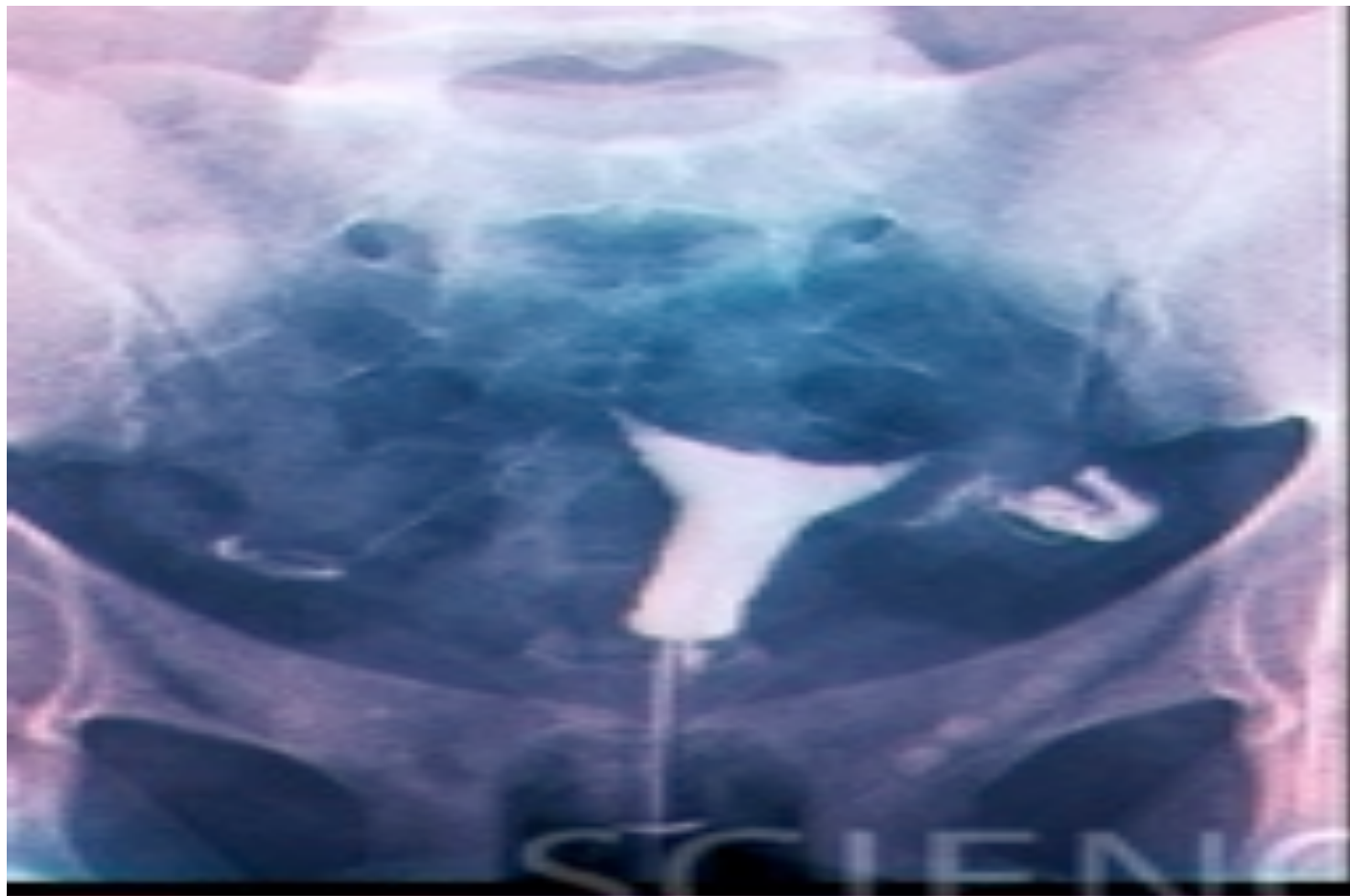
Infection , perforation of uterus , endometriosis , oil embolism , dye allergy

HSG

both are
patent



HSG



Values of HSG :

1-Diagnostic for: intrauterine and tubal disorder

2- Therapeutic for:

- Removal of mucous plug that may close the tube.
- Removal or absorption of thin adhesions.
- Straightening of kinked tube or relieve of uterotubal spasm..

B-Laparoscopy with dye injection:

by injection of methylene blue dye through the cx if passed from the fimbrial end = patent tubes.

B- Tubal factor of infertility

Treatment:

➤ IVF

C- Cervical factor of infertility

Causes

1. Congenital:
2. Traumatic
3. Inflammatory: endocervicitis, "common organisms are chlamydia and gonorrhea".
4. Neoplastic: cervical fibroid and masses blocking or distorting the cx
5. Immunological i.e. presence of anti-sperm antibodies.
6. Hormonal: especially decreased estrogen causing decreased mucous and rendering it thick.

C- Cervical factor of infertility

Diagnosis

Cervical culture

Postcoital tests: for patients with history or physical exam findings suggestive of cervical factor

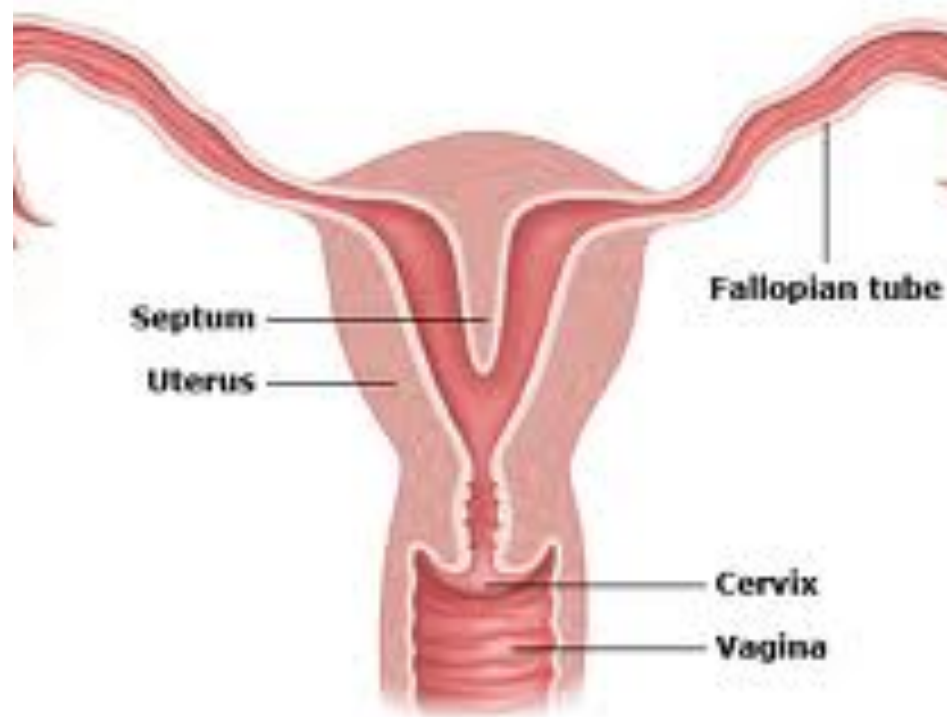
The validity of the test is controversial,

Treatment :

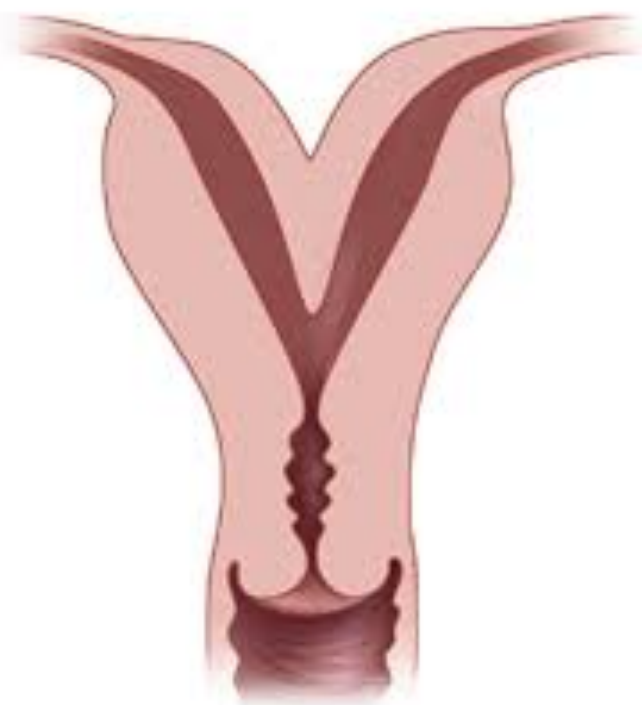
Treat underlying cause

D- Uterine factor of infertility

- Uterine factors include leiomyomata, intrauterine synechiae (Asherman syndrome), septae, and other müllerian anomalies.
fibrad - adhesions
- **Investigation :**
 - ✓ **Pelvic US**
 - **Saline infusion ultrasonography** (sonohysterography [SHG])
 - **HSG**
 - **Hysteroscopy** :Reserved for those patients with HSG or SHG results that need further evaluation
 - **Laparoscopy** :Spatet and biocornate uterus are similar in HSG and differentiate b/w them by Laparoscopy



Bicornuate Uterus



D- Uterine factor of infertility

according to cause

Treatment of the cause e.g.

- Surgery, adhesiolysis in Asherman's.
- Polypectomy OR myomectomy in fibroid.
- Removal of septum if septate uterus

F- Pelvic and peritoneal factor

Any gross pathology in the pelvis may disturb the function / movement of tubes / ovaries like endometriosis , adhesions or PID

Diagnosis

Laparoscopy.

Ultrasound can diagnose endometrioma / hydrosalpinx

Treatment of the cause.,

Endometriosis: remove endometrioma > 3 cm if present , lysis and excision of endometriosis if indicated

>> mild endometriosis >> ovulation induction +/- IUI

>> if failed or moderate / severe endometriosis >> IVF

PROTOCOL FOR MANAGEMENT OF INFERTILE COUPLE

- 1-History taking and examination of the wife.
- 2-History taking and examination of the husband.
- 3-Investigation of the husband starting by semen analysis.
- 4-Investigation of the wife:
 - Evaluation of ovulation : day 3 FSH , LH , E2 , DAY 21 PROGESTERONE , urinary LH , BIPHASIC basal body temperature chart , PROLACTIN , TFT, Testosterone
 - ✓ Uterine factor investigation : pelvic us , sonohystrogram and hysteroscopy (if needed)
 - ✓ Evaluation of tubal patency : HSG , laparoscopy (if needed)
 - ✓ Cervical factor investigation. PCT if needed
- 5-Treatment started only after complete investigation and actual diagnosis of the cause(s).

SUMMARY OF INVESTIGATION

- Semen analysis
- Day 3 FSH , LH , E2 , DAY 21 PROGESTERONE , PROLACTIN , TFT , androgen profile if hyperandrogen .
- PELVIC US / SONOHYSTEROGRAM (IF NEEDED)
- HSG
- POSTCOITAL TEST IF NEEDED
- LAPROSCOPY / HYSTEROSCOPY IF NEEDED

ASSISTED REPRODUCTIVE TECHNOLOGIES



A.R.T = ASSISTED REPRODUCTIVE TECHNOLOGY

Types: there are many types e.g.

- **Intrauterine Insemination= IUI** :cannula is used to deliver sperm into the endometrial cavity after either spontaneous or induced ovulation with ovulation trigger .
- **In vitro fertilization and embryo transfer = I.V.F-E.T** i.e. the embryo resulted after fertilization by 2-3 days is transferred in the uterine cavity.
- **Intracytoplasmic Sperm Injection =ICSI**

Indications:

- ✓ 1-Male factors of infertility: low sperm count, low sperm motility, and abnormal morphology associated with reduction in fertilizing ability
- ✓ 2-Tubal causes or peritoneal :e.g. moderate to severe endometriosis
- ✓ 3-Unexplained infertility.
- ✓ 4-Immunologic infertility or genetic disorders.
- ✓ 5-Ovulatory dysfunction not responding to ovulatory drugs.
- ✓ 6. Couples seeking preimplantation genetic diagnosis

Steps of IVF-ET cycle:

- Initial consultation and assessment.
- Controlled induction ovulation and ovulation trigger .
- Trans-vaginal oocyte retrieval.
- In vitro fertilization of the ova.
- Embryo culture till blastocyst stages and then embryo transfer in the uterine cavity.
- Excess embryos not used for transfer can be cryopreserved for an unlimited period

Intracytoplasmic Sperm Injection : SAME IVF STEP EXCEPT

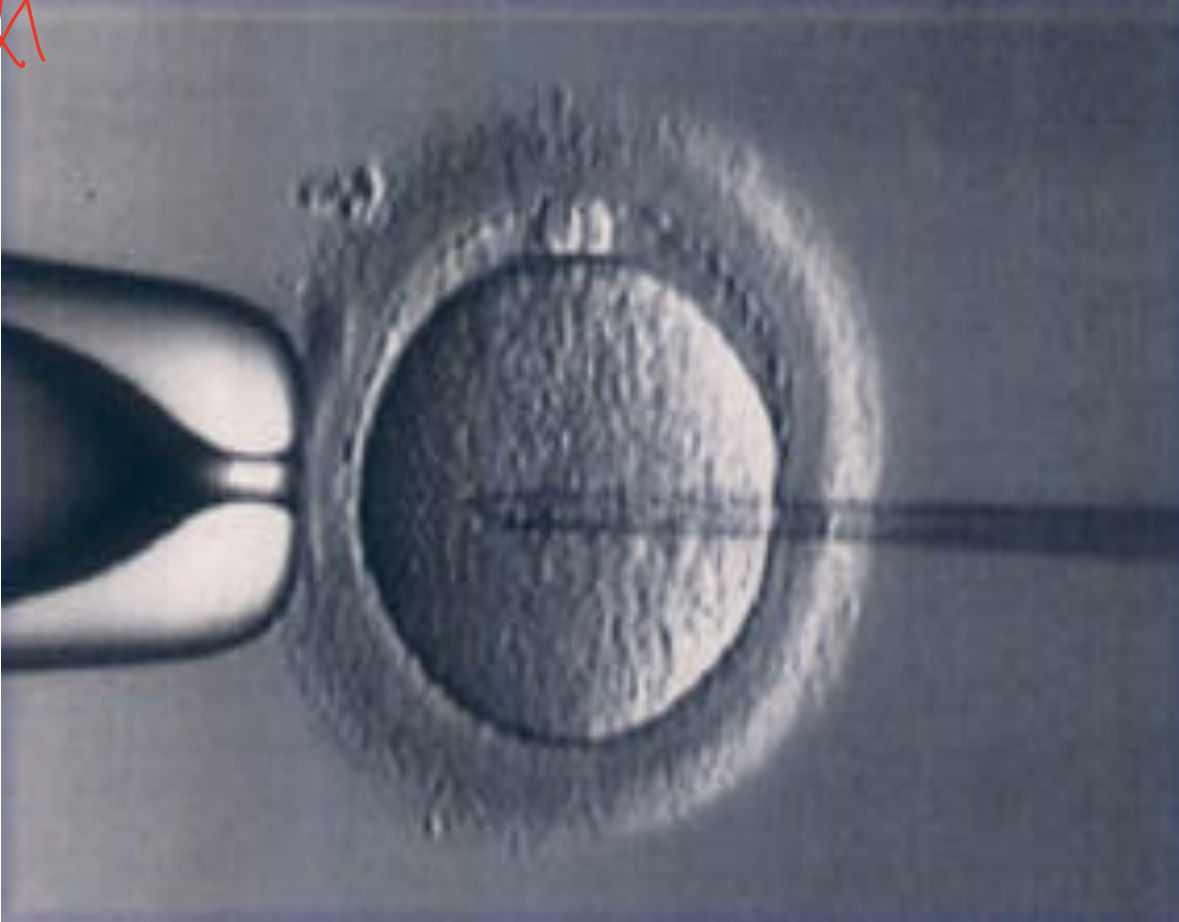
In ICSI, a single spermatozoon is injected microscopically into each oocyte, and the resulting embryos are transferred into the uterus

- indications: For infertility refractory to IUI/IVF , Severe abnormal semen analysis OR if PGD NEEDED .

IVF



ICSI



Preimplantation genetic diagnosis

- The process of PGD proceeds by biopsy and genetic analysis of either oocyte or embryo

- ***Indications Of PGD***

1. Single-Gene Disorders: As cystic fibrosis.
- 2- Aneuploidy Testing of women who are of advanced reproductive age, have a history of recurrent pregnancy losses, or have undergone multiple failed IVF cycles.
- 3- Sex Selection : medically for x-linked disorder(e.g muscular dystrophy) or nonmedical use (has limited application)

Q

45. A 28 year old woman has a 3 year history of primary infertility. She presents with increasing symptoms of steady, aching lower abdominal pain at the time of menses. The pain persists throughout menstruation and often after, and radiates into the rectum. Tender nodules in the uterosacral ligaments are noted on pelvic examination. Which one of the following would be the most contributory investigation?

Endometriosis

- a) Postcoital test
- ☒ b) Diagnostic laparoscopy
- c) Hysterosalpingogram on day 9 of her cycle
- d) Endometrial biopsy on day 26 of her cycle
- e) Basal body temperature charting

THANK YOU
