

OBSTETRICS AND GYNECOLOGY

(20) Infertility

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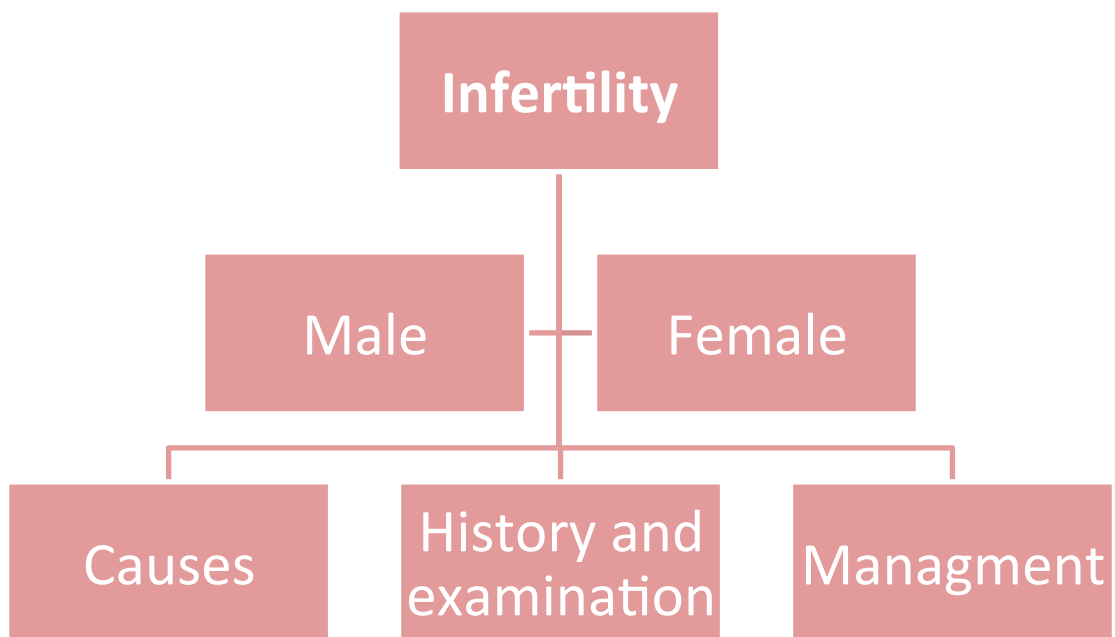
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Objectives:

Not given.



Fertility, Subfertility and Sterility

Sterility:

Absolute and **irreversible** inability to conceive. **No eggs or no sperm.**

Infertility:

Diminished capacity to conceive and bear children. **Can get pregnant but delayed.**

Clinically inability to conceive despite regular unprotected sexual intercourse over 12 months.

Pregnancy rate:

- 57% 3 months
 - 72% 6 months
 - 85% 12 months
 - 93% 24 months
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- ✓ 7% conceive in the second year justifies starting investigation for infertility after one year.
 - ✓ Female fertility decline after the age of 35 and decline more rapidly after age of 40.
 - ✓ If women 35 years of age, the **investigation should be not be delayed.** By 6 months you should go for IVF even if patient is fertile, because success rate of IVF decreases with older age.
 - ✓ Age substantially decreases the rate of conception because of lower embryo quality, reduced ovulation, and possibly decreased coital frequency. - Hacker & Moore
 - ✓ **Time and age are very important.**
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- **Primary – No previous pregnancy**
 - **Secondary – Previous pregnancy whatever the outcome**
Even if IVF, abortion, ectopic, molar or IUFD.. etc.

Prevalence: 10 – 15%

- 1/3 in the female
- 1/3 in the male
- 1/3 in the couple combined

DISORDERS:

1. Involving each of the major physical events that are necessary to

produce a pregnancy.

2. Production of healthy eggs.
3. Production of a healthy sperm.
4. Transportation of the sperm to the site of fertilization.
5. Transportation of the egg and zygote to the uterus for implantation.
6. Successful implantation in a receptive endometrium
7. Presence of other factors.

CAUSES OF INFERTILITY

- ✓ For pregnancy to occur there must be fertile sperm and egg, a means of bringing them together and a receptive endometrium to allow the resulting embryo to implant. A defect at any of these stages can lead to subfertility. *As well as a healthy functional patent tube, healthy mucus and no filling defect in the uterine cavity.*

Commonest causes in the female:

- Ovulatory factor. *Common.*
- Tubal factor. *Blocked tubes.*
- Endometriosis. *Causes adhesion and one of the main causes of infertility in KKUH clinics.*
- Failure of implantation. *Filling defect.*
- Uterine factor.

No OOCYTES production and OOCYTES abnormalities:

Failure to ovulate

The disorders are grouped into three general categories:



Any defect in the axis leads to dysfunction and infertility.

Anovulatory Infertility:

- ✓ **Hypergonadotrophic hypogonadism** – failure of the ovary to respond to gonadotrophic stimulation by the pituitary gland result from **premature ovarian failure** and exhaustion of the ovarian follicle pool. *Patients are below 40, and present with*

amenorrhea and inactive ovaries that have **no follicles** and appear small in size on US. They'll have **High FSH and low Estrogen**.

- ✓ **Resistant ovary syndrome** – elevated gonadotrophin in the **presence of good reserve follicle** due to abnormalities of FSH receptors. Same as Hypergonadotrophic hypogonadism except there are follicles and no FSH receptors. Clinically you can't differentiate between the two but it's not really necessary because the treatment is the same.
Since they have follicles they might get pregnant suddenly so never tell the patients that they will never get pregnant.
- ✓ **Hypogonadotrophic hypogonadism.**

Pituitary dysfunction: failure of pituitary gland to produce gonadotrophin will lead to lack of ovarian stimulation due to destruction by:

- Pituitary tumour – adenoma
- Pituitary inflammation - TB
- Ischemia as in Sheehan's Syndrome

Pituitary damaged by radiation or surgery

Treatment: Give FSH.

Hypothalamic dysfunction: if pulsatile secretion of GnRH is slowed or stops secondary to:

- Excessive exercise
- Psychological distress
- Anorexia nervosa

Treatment: Give Pulsatile GnRH.

Ovarian Dysfunction:

Polycystic ovary syndrome (PCO) **Excellent prognosis, and primary treatment is weight loss.**

Endocrine disorder:

- Hyperprolactinaemia
- Hypothyroidism

Tubal infertility:

- BID – **Chlamydia trachomatis. Most common organism to cause infertility.**
- Pelvic infection or **abscess from appendicitis. Have to ask of previous history of appendicitis and its complications.**

- Septic abortion
- Pelvic surgery **Causes adhesions.**
- T.B. **Causes scarring.**
- Crohn's disease
- IUCD

Tubal occlusion may occur at three locations: the fimbrial end, the mid-segment, or the isthmus-cornu. Fimbrial occlusion is by far the most common. - Hacker & Moore

Endometriosis:

Severe form can lead to tubal damage due to adhesion formation caused by endometrial deposit. **Causes scarring due to prostaglandin.**

Uterine Factors:

- Submucous fibroid – occlude tubes.
- Congenital uterine abnormalities. **Like septum (common).**
- Intrauterine adhesion due to excessive curettage. (Asherman's syndrome).

Unexplained infertility:

Complete of routine investigation fail to reveal cause in 15 - 30% of cases does not indicate absence of a cause but rather inability to identify it. The result of IVF shown there may be undiagnosed problems of oocytes or embryo quality or of implantation failure neither of which can easily be tested unless IVF is undertaken.

History and examination

History is very important to direct my investigation.

You must talk to both wife and husband.

Personal & Social History

- Age – female partners
- Occupation especially the male – **exposure to high temperature**
- Chemical and radiation can affect sperm production
- Works away from home – affect frequency of sexual intercourse around the time of ovulation
- Smoking - Alcohol

Menstrual History very important

- Age of menarche and regularity of periods **Very important because gives you a hint if the patient is ovulating or not**
- Irregular menstrual cycle, oligomenorrhia and amenorrhoea

are all suggestive of anovulation

- Amenorrhoea – menopausal symptoms
- Weight loss or gain
- Symptoms of hyper prolactinemia and hypothyroidism

Obstetric History

- Enquire about previous pregnancies, outcome
- Breastfeeding and any sustained galactorrhoea
- Difficulties or treatment required prior to achieving a previous pregnancy

Contraception

- Use of contraception pills and long acting progesterone followed by amenorrhea
- Use of long acting progesterone contraception followed by delay in the resumption of ovulation
- IUCD - ↑ risk of infection – young nulliparous leading to tubal disease

Injection contraception takes a long time for it's effects to wear off so we make the patient wait.

Sexual History

- Frequency of sexual intercourse **technique is very important to know.**
- Ejaculatory dysfunction

Other important points

- Folic acid
- Rubella vaccine
- Family history – Diabetes, endometriosis, PCO

Examination

Assessment of Body mass index, obesity and under weight cause anovulation **General examination is important to do.**

PCO or not, patients have to decrease their weight until they match a specific criteria.

Investigation

The aim to assess

- Ovulation
- Tubal patency
- Uterine factors

Assessment of Ovulation

Physiology of ovulation is very important to know.

- History of regular period

- ↑level of progesterone in serum approximately 8 days after LH surge (Mid luteal phase)
- BBT
- Endometrial histology
- Cervical mucus
- LH detection kits
- Body temperature
- Biopsy
- US

Endometrial biopsy, considered for many years to accurately reflect luteal function, has been recently shown to be a very imprecise test, causing most practitioners to abandon it as a tool to assess ovulation. - Hacker & Moore

Tubal patency tests

- HSG Benefit: can see the uterine cavity.
- Laparoscopy and dye test
- Falloscopy – assessment of tubal patency and mucosa
- Ultrasound scan and hydrotubation

Assessment of the uterus

- HSG
- Hystroscopy
- TVU with injection of N/S (Hsytrosongraphy)
- Postcoital test: provides information concerning the ability of the sperm to penetrate and survive in the cervical mucus.

Management

In general, the first 6 to 8 months of evaluation involve relatively simple and noninvasive tests and the performance of a radiologic evaluation of tubal patency (hysterosalpingography, or HSG), which can sometimes have a therapeutic effect. - Hacker & Moore

Management of anovulatory infertility:

- ✓ Patients with ovarian failure and resistant ovary syndrome will not respond to ovulation induction and are offered oocyte donation.
- ✓ Normalization of body weight in underweight and obese

patients can help to regain ovulation without the need for medical intervention.

- ✓ Medical treatment of prolactinoma.
- ✓ Ovulation induction in patients with hypogonadotropic hypogonadism with pulsatile GnRH or by Gonadotrophin.
- ✓ Ovulation induction in PCOS patients achieved by **weight normalization in obese patients** then we can start:
 - Clomiphene therapy binds to estrogen receptors in the hypothalamus, pituitary gland, ovary, endometrium, vagina, and cervix and causes production of hormones (gonadotropins) by the pituitary, which stimulates ovulation.
 - Medicinenet
 - Causes a rise of FSH and stimulation of follicular maturation.
 - Hacker & Moore
 - Gonadotrophin
 - Risk of multiple pregnancy & OHSS** Read about OHSS.

The hyperstimulation syndrome (OHSS) is a critical illness associated with marked ovarian enlargement and exudation of fluid and protein into the peritoneal cavity. The use of serum estradiol measurements, transvaginal ultrasonic scanning, and low-dose gonadotropin has greatly reduced the incidence of hyperstimulation syndrome.

- Hacker & Moore

Surgical methods are either ovarian drilling or wedge resection. The theory was that the thick tunica albugenia prevented the release of the ovum.

Disadvantage: Tubal damage and adhesion form destruction of the ovarian stroma and reduction of ovarian reserve.

Advantage: No risk of multiple pregnancy & OHSS.

Management of tubal infertility:

Can be treated with tubal surgery, IVF and embryo transfer (IVF-ET) or selection salpingography. Although tubal surgery is no longer recommended for severe tubal disease since the introduction of IVF-ET, it still has a place in less severe forms of the disorder.

Management of endometriosis-related infertility:

- ✓ Depends on the severity of the condition and the presence of any other infertility factors. The medical methods are inappropriate in an infertile patient either induce anovulation or teratogenicity.
- ✓ Conservative surgical treatment of minimal or mild endometriosis may improve natural conception rates postoperatively. Diagnostic laparoscopy and diathermy to endometriosis can be delivered at the same session.
- ✓ Severe endometriosis for IVF-ET.

Management of unexplained infertility:

Conservative management, ovulation induction with or without intrauterine insemination, and IVE-ET are the main approaches to managing unexplained infertility. It provides information about fertilization and egg and embryo quality. Owing to its high cost, IVF-ET is usually seen as a last resort in unexplained infertility.

Management of uterine factor infertility:

- ✓ Myomectomy either laparoscopically or by laparotomy.
- ✓ Entry into the uterine cavity should be avoided if possible, and adhesion barriers and microsurgical technique to reduce the risk of adhesions.
- ✓ Hysteroscopy: Resection of submucous fibroids depending on the size of the fibroid and its degree of protrusion into the uterine cavity.
- ✓ Risk of haemorrhage, uterine perforation and endometrial scarring leading to intrauterine adhesions.

Male Infertility

Testes: Under GnRH

1 - Steroidogenesis

Leydig cells between seminiferous tubule

→ Testosterone – (LH)

2 - Spermatogenesis

Sertoli cells (inhibin) – (FSH)

Both lead to production of healthy spermatozoa.

Cryptorchidism:

Infection – orchitis – mumps

Occupation – excess heat, radiation, toxic environment

Lifestyle – smoking, alcohol

Drugs – sulfasalazine

Ejaculation – disorders – Retrograde

Premature Ejaculation - Impotence

- Congenital abnormalities
- Chromosomal anomalies
- Traumatic causes
- Coital Abnormalities
- Vascular
- Hormonal
- Inflammatory
- Immunological
- Environmental

EXAMINATION:

- ✓ General Health
- ✓ Presence of 20 sexual characteristics
- ✓ Genital Examination:
 - Epididymis
 - Testes

INVESTIGATION:

- ✓ **Hormonal:**
 - Testosterone
 - FSH

Endocrine evaluation of the male with subnormal semen quality may uncover a specific cause. Hypothyroidism can cause infertility, but there is no place for the empirical use of thyroxine. Low levels of gonadotropins and testosterone may indicate hypothalamic-pituitary failure. An elevated prolactin concentration may indicate the presence of a prolactin-producing pituitary tumor. An elevated level of follicle-stimulating hormone (FSH) generally indicates substantial parenchymal damage to the testes. - Hacker & Moore

✓ **Chromosome Karyotype.**

✓ **Semen Analysis:**

- Volume - 2 – 6ml
- Liquefaction time - within 30 min.
- Density - 20-250 million/ml
- Motility - > 50% progressive movement

If there's any problem with these parameters we go for IUI. Semen analysis table at page 12.

An accurate appraisal of abnormal semen requires at least three analyses. Periodic reassessment is necessary. - Hacker & Moore

AZOOSPERMIA:

- Obstructive
- Non obstructive

Treat with IVF.

PRINCIPLE OF MANAGEMENT

Deal with the couple together.

AIM OF INVESTIGATION:

- To give an explanation of the cause
- To form basis for treatment.
- Prognosis

Assisted Conception A.R.T

- **AIH - IUI**

Artificial insemination by husband (AIH) and Intrauterine insemination (IUI): A procedure in which a fine catheter (tube) is inserted through the cervix (the natural opening of the uterus) into the uterus (the womb) to deposit a sperm sample directly into the uterus.

- **ZIFT**

Zygote intrafallopian transfer (ZIFT): A technique in which a woman's egg is fertilized outside the body, then implanted in one of her fallopian tubes.

- **GIFT**

Gamete intrafallopian transfer (GIFT): A technique in which the male and female germ cells required to begin formation of a human

embryo are injected into a woman's fallopian tubes of the female for fertilization.

- **IVF**

In vitro fertilization: A laboratory procedure in which sperm are put in a special dish with unfertilized eggs to achieve fertilization. The embryos that result can be transferred into the uterus or frozen (cryopreserved) for future use.

- **ICSI**

Intracytoplasmic sperm injection (ICSI): A test-tube fertilization procedure in which a sperm is injected directly into an egg to achieve fertilization.

– Medicinenet.

Semen analysis

Semen volume	Normal:	2–5 milliliters (mL) (0.002–0.005 L in SI units) per ejaculation
	Abnormal:	An abnormally low or high semen volume is present. This may sometimes cause fertility problems.
Liquefaction time	Normal:	20–30 minutes after collection
	Abnormal:	An abnormally long liquefaction time is present. This may be a sign of an infection.
Sperm count	Normal:	20 million spermatozoa per milliliter (mL) or more 0 sperm per milliliter if the man has had a vasectomy
	Abnormal:	A very low sperm count is present. This may mean infertility. But a low sperm count does not always mean that a man can't father a child. Men with sperm counts below 1 million have fathered children.

Sperm shape (morphology)	Normal:	More than 30% of the sperm have normal shape. Kruger criteria: More than 14% of the sperm have a normal shape.
	Abnormal:	Sperm can be abnormal in several ways. They may have two heads or two tails, a short tail, a tiny head (pinhead), or a round (rather than oval) head. Abnormal sperm may not be able to move normally or to penetrate an egg. Some sperm that aren't normal are usually found in every normal semen sample. But a high percentage of abnormal sperm may make it harder for a man to father a child.
Sperm movement (motility)	Normal:	More than 50% of the sperm show normal forward movement after 1 hour.
	Abnormal:	Sperm must be able to move forward (or "swim") through cervical mucus to reach an egg. A high percentage of sperm that can't swim well may make it harder for a man to father a child.
Semen pH	Normal:	Semen pH of 7.1–8.0
	Abnormal:	An abnormally high or low semen pH can kill sperm or affect how well they can move or can penetrate an egg.
White blood cells	Normal:	No white blood cells or bacteria are found.
	Abnormal:	Bacteria or a large number of white blood cells are present. This may be a sign of an infection.

<http://www.webmd.com/infertility-and-reproduction/guide/semen-analysis?page=3>

Summary

- ✓ Infertility is clinically described as inability to conceive despite regular unprotected sexual intercourse over 12 months.
- ✓ Investigation usually starts after 1 year but If the women is 35 years of age or older, the investigation should be not be delayed.
- ✓ Primary: No previous pregnancy, Secondary: Previous pregnancy whatever the outcome or the mean.
- ✓ For pregnancy to occur there must be fertile sperm and egg, a means of bringing them together and a receptive endometrium to allow the resulting embryo to implant. A defect at any of these stages can lead to subfertility.
- ✓ History is very important to direct my investigation.
- ✓ Ovulation induction in PCOS patients is achieved by weight normalization in obese patients then we can start pharmacological therapy like Clomiphene therapy or Gonadotrophin.
- ✓ Semen analysis is very important to know if it's the wife or the husband that is infertile.

