

Obstetrics & Gynecology TEAM



Infertility

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◆ very important ◆ mentioned by doctor ◆ team notes ◆ not important

Fertility - Subfertility – Sterility

Sterility: Absolute and irreversible inability to conceive.

Infertility: Diminished capacity to conceive and bear child.

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

- 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.**
- Primary – No previous pregnancy
- Secondary – Previous pregnancy whatever the outcome

Prevalence: 10 – 15%

- $\frac{1}{3}$ in the female
- $\frac{1}{3}$ in the male
- $\frac{1}{3}$ in the couple combined

Disorders: important

- Involving each of the major physical events that are necessary to produce a pregnancy.
- Production of healthy eggs.
- Production of a healthy sperm.
- Transportation of the sperm to the site of fertilization.
- Transportation of the egg and zygote to the uterus for implantation.
- Successful implantation in a receptive endometrium
- 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.

Commonest causes in the female:

- Ovulatory factor
- Tubal factor
- Endometriosis
- Failure of implantation
- Uterine factor

No oocyte production and oocyte abnormalities:

- Failure to ovulate
- The disorders are grouped into three general categories:
 - Hypothalamus
 - Pituitary
 - Ovarian Dysfunction

Anovulatory Infertility:

- Hypergonadotrophic hypogonadism – failure of the ovary to respond to gonadotrophic stimulation (very high FSH) by the pituitary gland result from **premature ovarian failure and exhaustion of the ovarian follicle pool**.
- Resistant ovary syndrome – elevated gonadotropin in the presence of good reserve follicle due to abnormalities of **FSH receptors**.
- Hypogonadotrophic hypogonadism
 - Pituitary dysfunction: failure of pituitary gland to produce gonadotropin will lead to lack of ovarian stimulation due to destruction by:
 - Pituitary tumor (adenoma)
 - Pituitary inflammation (TB - Ischemia as in Sheehan's Syndrome)
 - Pituitary damaged by radiation or surgery
 - Hypothalamic dysfunction: if pulsatile secretion of GnRH is slowed or stops (easy to treat: only give GnRH) secondary to:
 - Excessive exercise.
 - Psychological distress.
 - Anorexia nervosa.

To differentiate use biopsy:

- Hypergonadotrophic hypogonadism: no follicles
- Resistant Ovary Syndrome: follicles are present.

However this is not necessary since the management is the same.

Ovarian Dysfunction: Polycystic ovary syndrome (PCO)

Endocrine disorder: hyperprolactinemia

Hypothyroidism

Tubal infertility: (anything that causes adhesions or blockage of tubes)

- BID – Chlamydia trachomatis
- Pelvic infection or abscess from appendicitis
- Septic abortion
- Pelvic surgery. **Ectopic pregnancy.**
- T.B.
- Crohn's disease
- IUCD

Endometriosis: Severe form can lead to tubal damage due to adhesion formation caused by endometrial deposit

Uterine Factors:

- Sub mucous fibroid – occlude tubes
- Congenital uterine abnormalities
- 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.

Definition of unexplained infertility:

No pregnancy with:

- Normal semen analysis
- Confirmed ovulation
- Patent oviducts

Management:

- Wait for 3 years, 60% of couples achieve pregnancy.
- Ovulation induction and IUI and see if that works.
- If however it doesn't, we try IVF.

IVF indications:

- Severe oligozoospermia
- Irreparable tubes
- Unexplained pregnancy

Source: Kaplan

Anovulation:

- **History:** Irregular Menses
- Basal body temperature is flat (no mid cycle rise), Progesterone levels are low and Biopsy of endometrium shows proliferative changes (no evidence of progesterone)
- **Correctable causes:** hypothyroidism and hyperprolactinemia.

Tubal Disease:

- HSG, if normal no further testing
- If abnormal consider Laparoscopy to diagnose and treat tubal disease: tuboplasty OR Salpingectomy and IVF

Source: Kaplan.

History and Examination:

Personal & Social History (this was explained as a history directed to the male, though it is not in the proper place in this lecture.)

- 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:

- Age of menarche and regularity of periods
- Irregular menstrual cycle, oligomenorrhia and amenorrhoea are all suggestive of anovulation
- Amenorrhoea – menopausal symptoms
- Weight loss or gain. (PCOS patients have anovulation when there is weight gain).
- Symptoms of hyperprolactinemia and hypothyroidism.

Obstetric History:

- Enquire about previous pregnancies, outcome.
- Breast-feeding and any sustained galactorrhoea. (Hyperprolactinemia causes anovulation)
- Difficulties or treatment required prior to achieving a previous pregnancy. If the patient has had difficulties in a previous pregnancy and was successful using IVF. The next pregnancy → go directly to IVF without trying anything else.

Contraception:

- Use of contraception pills and long acting progesterone followed by amenorrhoea
- Use of long acting progesterone contraception followed by delay in the resumption of ovulation
- IUCD ↑ risk of infection – young nulliparous leading to tubal disease (not given to young patients)

Sexual History:

- Frequency of sexual intercourse.
- Ejaculatory dysfunction.

Other important points

- Folic acid to prevent neural tube defects
- Rubella vaccine to prevent congenital rubella syndrome
- Family history – Diabetes, endometriosis, PCO

Examination:

Assessment of body mass index, **obesity and under weight cause anovulation**

Investigation: The aim to assess:

- Ovulation
- Tubal patency
- Uterine factors

Assessment of Ovulation: important

- History of regular period.
- ↑ Level of progesterone in serum approximately 8 days after LH surge (Mid luteal phase) indication of ovulation.
- BBT **basal body temperature rises at ovulation.**
- Endometrial histology (secretory phase is an indication of ovulation).
- Cervical mucus (mucus becomes ‘Spinnbarkeit’ at ovulation).
- LH detection kits (to advise when is the best time to have intercourse).

Under the influence of estrogens, cervical mucus becomes abundant, clear, and stretchable, somewhat like egg white. The stretchability of the mucus is described by its spinnbarkeit, from the German word for the ability to be spun. Only such mucus appears to be able to be penetrated by sperm. After ovulation, the character of cervical mucus changes, and under the influence of Progesterone it becomes thick, scant, and tacky. Sperm typically cannot penetrate it. Wikipedia.

Tubal Patency Tests:

- HSG.
- Laparoscopy and dye test.
- Falloposcopy – assessment of tubal patency and mucosa.
- Ultrasound scan and hydrotubation.

Assessment Of The Uterus:

- HSG.
- Hysteroscopy.
- TVU with injection of N/S (Hysterosonography).
- Postcoital test: provides information concerning the ability of the sperm to penetrate and survive in the cervical mucus. Maybe the problem is only in the thick mucus.

Management of Anovulatory Infertility:

- Patients with ovarian failure and resistant ovary syndrome will not respond to ovulation induction and they 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

Ovulation induction medication: (under hospital observation)

- Clomiphene therapy (ant estrogen that feeds back to pituitary to produce more FSH)
- Gonadotropin therapy
- Risk of multiple pregnancy & OHSS (ovarian hyperstimulation syndrome is the most serious consequence of induction of ovulation)

Surgical methods are either **ovarian drilling or wedge resection** the theory was that the thick tunica albugenia prevented the release of the ovum. **Not used anymore.**

Disadvantages: tubal damage and adhesion from destruction of the ovarian stroma and reduction of ovarian reserve

Advantages: No risk of multiple pregnancy and 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 IVF-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

- Steroidogenesis Leydig cells between seminiferous tubule. Testosterone – (LH)
- Spermatogenesis. Sertoli cells (inhibin) – (FSH)
- Both lead to production of healthy spermatozoa.

Cryptorchidism: Infection – orchitis – mumps

Other Factors That May Cause Male Infertility:

Occupation – excess heat – radiation – toxic - Lifestyle – smoking - alcohol - Drugs (salfasalyasin) - Ejaculation – disorders – Retrograde ejaculation (semen goes into urine) - 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.
- Chromosome Karyotype.
- Semen Analysis: **have to know it by heart.**

Volume	2–6ml
Liquefa	within 30 min
Density	20-250 million/ml
Motility	> 50% progressive movement
Morphology	>30% of sperms are of normal morphology

Semen Analysis: If abnormal repeat after 4-6 weeks because sperm count varies through time.

Obtain 2-3 days abstinence and examine within 2 hours.

Overweight men generally have a low sperm count. (Kaplan)

Azoospermia:

Obstructive - Non obstructive.

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 – Intra Uterine Insemination

ZIFT Zygote Intrafallopian Transfer

GIFT Gamete Intrafallopian Transfer

IVF In Vitro Fertilization

ICSI Intra-Cytoplasmic Sperm Injection

Kaplan Summary:

Question	Answer	Management
Criteria of Infertility	12 months of unprotected intercourse	
1. Anovulation	BBT is flat, Progesterone levels are low and biopsy shows proliferative tissue.	Clomiphene or HSG
2. Male Factor	Semen analysis. Repeat if abnormal.	IUI, ICSI or AID
3. Tubal disease	HSG	Laparoscopy repair or IVF
Unexplained	1, 2 & 3: no problem If that doesn't work	Clomiphene + IUI IVF

