Gynecology

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Female Infertility

Fecundability: probability of achieving a pregnancy within 1 menstrual cycle (25%)

Fecundity: ability to achieve a live birth within 1 menstrual cycle (6%)



Causes

- Hypothalamus
- Pituitary
- Ovary
- Uterus
- Vagina
- Fallopian tube
- Cervix



Hypothalamic-Pituitary-Gonadal Axis:



Pituitary:

- Sheehan syndrome
- Tumors: Pituitary adenoma, metastatic
- Empty sella syndrome
- Inappropriate gonadal steroid feedback:
 - estrogen excess: obesity/ tumors
 - $\circ~$ estrogen deficiency: aromatase deficiency/ ER gene mutation
 - androgen excess: adrenal or ovarian
- Hyperprolactinaemia
- Thyroid dysfunction

Hypothalamus:

- Stress
- Exercise
- Eating disorders
- Psychogenic

- Starvation/stress or severe illness
- Tumors (craniopharyngioma, metastatic tumor)
- Head injury
- Inflammation (sarcoidosis)
- Infection (tuberculosis)
- XRT
- Drugs

Ovary:

- Gonadal dysgenesis Turner's Syndrome 45XO
- XRT / Chemo for childhood malignancies
 - Premature ovarian failure
 - PCOS

Uterine abnormalities:

- Mullerian Agenesis: Mayer-Rokitansky-Kuster-Hauser syndrome
- Asherman's syndrome
- Leiomyoma
- Luteal phase deficiency
- Vaginal septum
- Tubal Disease
 - Infections/ STD/PID
 - Ruptured appendix
 - \circ Septic abortion
- Endometriosis
- Cervical



Investigations

- ž Blood work:
 - TSH
 - PRL
 - D3 FSH
 - D3 LH
 - Luteal phase Progesterone
- ž Imaging:
 - Pelvic Ultrasound
 - HSG
- ž Diagnostic
 - Laparoscopy (later)
 - Cervical(post coital test)

Marker of ovarian reserve

In the ovary, anti-Müllerian hormone (AMH) is produced by the granulosa cells. AMH levels can be measured in blood and are shown to be proportional to the number of small antral follicles. In women, serum AMH levels decrease with age and are undetectable in the post-menopausal period. AMH levels represent the quantity of the ovarian follicle pool and are a useful marker of ovarian reserve. AMH measurement can also be useful in the prediction of the extremes of ovarian response to gonadotrophin stimulation for in vitro fertilization, namely poor and hyper-response.

Ovulation testing

Various methods of predicting fertility exist, to either aid or avoid pregnancy.

Stretch test

Cervical mucus becomes clear and stretchy during the fertile window, to allow sperm to survive in and travel through it.

Ovulation Prediction Kit

Ovulation prediction kits are usually antibody tests for luteinising hormone, which peaks in urine around the time of ovulation.

Cervical position

The cervix becomes soft, high, open and wet during the fertile window.



Basal body temperature

Basal body temperature changes during the menstural cycle. Progesterone released during the menstrual cycle causes an abrupt increase in basal body temperature by 0.5°C at the time of ovulation. This enables identification of the fertile window through the use of commercial thermometers.

Progesterone level

Measurement of progesterone in the second half of the cycle to help confirm ovulation

Treatment

- \check{z} Treat the underlying cause
- ž Medical
- ž Surgical

Medical treatments

Drugs

- Clomiphene
- Human menopausal gonadotropin, hMG
- FSH
- Human chorionic gonadotropin, hCG
- Gonadotropin releasing hormone (Gn-RH) analogs
- Aromatase inhibitors
- Metformin
- Bromocriptine

Gonadotropin-releasing hormone

- \check{z} Either Gonadotropin-releasing hormone (GnRH) or
- ž any Gonadotropin-releasing hormone agonist (i.e. Lupron) may be used.
- \check{z} GnRH stimulates the release of gonadotropins (LH and FSH) from the anterior pituitary in the body.

Clomiphene

 ž is a selective estrogen receptor modulator (SERM). It is the most widely used fertility drug. It is used as an ovarian stimulator by inhibiting the negative feedback of estrogen at the hypothalamus. As the negative feedback of estrogen is inhibited, the hypothalamus secretes GnRh which in turn stimulates the anterior pituitary to secrete LH and FSH which help in ovulation.

Aromatase inhibitors

Although primarily a breast cancer treatment, aromatase inhibitors can also work as fertility medication, probably through a mechanism similar to clomiphene.

Gonadotropins

Gonadotropins are the hormones in the body that normally stimulate the gonads (testes and ovaries). For medication, they can be extracted from urine or by genetic modification.

For example, the so-called menotropins consist of LH and FSH extracted from human urine from menopausal women. FSH and FSH analogues are mainly used for ovarian hyperstimulation as well as reversal of anovulation.

There are also recombinant variants which are created by inserting the DNA coding for it into bacteriae. The bacterial DNA is then called Recombinant DNA. Examples of recombinant FSH are Follistim and Gonal F, while Luveris is a recombinant <u>LH.</u>

Human chorionic gonadotropin

ž Human chorionic gonadotropin (hCG) is normally produced during pregnancy. However, it can also replace LH as an ovulation inducer.

Others

- ž dopamine agonist, such as cabergoline or bromocriptine. For treatment of hyperprolactinaemia
- ž Metformine in PCOS

COMPLICATIONS

Fertility drugs have the risk of multiple pregnancies

- Injectable fertility drugs increase the chance of multiple births
- Careful monitoring: blood tests, hormone tests, ultrasound measurement of ovarian follicle size

Because of risk of ovarian hyperstimulation syndrome

Ovarian hyperstimulation syndrome (OHSS)

is a medical condition affecting the ovaries of some women who take fertility medication to stimulate egg growth. Most cases are mild, but rarely the condition is severe and can lead to serious illness or death. OHSS is divided into the categories mild, moderate, severe, and critical. In mild forms of OHSS the ovaries are enlarged (5–12 cm) and there may be additional accumulation of ascites with mild abdominal distension, abdominal pain, nausea, and diarrhea. In severe forms of OHSS there may be hemoconcentration, thrombosis and distension, oliguria (decreased urine production), pleural effusion, and respiratory distress. Early OHSS develops before pregnancy testing and late OHSS is seen in early pregnancy.



Surgical treatment

- ž Hysteroscopy A hysteroscopy is an outpatient procedure in which a narrow fiberoptic telescope inserted into uterus through the cervix, to look for and sometimes remove adhesions inside uterus.
- ž Laparoscopy -

A laparoscopy is surgical procedure in which a narrow fiberoptic telescope inserted through an incision near navel to look for and sometimes remove adhesions in pelvic cavity, remove ovarian cysts or remove or repair a fluid-filled hydrosalpinx or ovarian drilling

- ž Fallopian Tube Sterilization Reversal (reanastomosis) A tubal reversal is a surgical procedure performed to reconnect the two ends of the fallopian tubes in an effort to reverse sterilization.
- ž Hydrosalpinx removal A hydrosalpinx is an obstructed fallopian tube that leads to an accumulation of fluid. Removal of the affected tube can increase IVF success rates.

Combined infertility

- ž In some cases, both the man and woman may be infertile or sub-fertile, and the couple's infertility arises from the combination of these conditions.
- ž In other cases, the cause is suspected to be immunological or genetic; it may be that each partner is independently fertile but the couple cannot conceive together without assistance.

Unexplained infertility

 ^ž up to 20% of infertile couples have unexplained infertility. In these cases abnormalities are likely to be present but not detected by current methods. Possible problems could be that the egg is not released at the optimum time for fertilization, that it may not enter the fallopian tube, sperm may not be able to reach the egg, fertilization may fail to occur, transport of the zygote may be disturbed, or implantation fails. It is increasingly recognized that egg quality is of critical importance and women of advanced maternal age have eggs of reduced capacity for normal and successful fertilization.

Thank You,,,



Fertilization