

# Etiologies of female infertility

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# Etiologies of female infertility

- \_female factor infertility :37 percent
- \_male factor infertility : 8 percent
- \_male and female factor infertility:35percent
- \_The remaining couples had unexplained Infertility.

# Most common identifiable female factors

- \_Ovulatory disorders (25 percent)
- \_Endometriosis (15 percent)
- \_Pelvic adhesions (12 percent)
- \_Tubal blockage (11 percent)
- \_Other tubal abnormalities (11percent) Hyperprolactinemia (7 percent)

# Ovulatory disorders

**oligoovulation** or anovulation results in infertility.

WHO has classified anovulation into three main groups, and recognizes hyperprolactinemia as additional etiology.

# Oocyte aging

**Age** is an important factor affecting a woman's fertility.

\_ovary reaches its apex of **6 to 7 million follicles** in the **mid-gestation** female fetus.

\_followed by a steady attrition from **1 to 2 million** follicles **at birth** to **300,000 follicles** at the onset of **puberty**.

# The rate of follicle loss accelerates

The rate of follicle loss accelerates after the woman reaches her **mid-thirties** .

Other insults to the ovary such as cigarette **smoking, radiation, chemotherapy**, and **autoimmune disease** also accelerate follicular loss.

**.Women with a depleted ovarian follicle pool may continue to ovulate regularly, but have infertility due to the poor quality of oocytes remaining in the terminal follicular pool**

# FALLOPIAN TUBE

## ABNORMALITIES/PELVIC ADHESIONS

Tubal disease and pelvic adhesions prevent **normal transport** of the oocyte and sperm through the fallopian tube.

The primary cause of tubal factor infertility is: **pelvic inflammatory disease**

**severe endometriosis**

**adhesions from previous surgery**

**non tubal****nontubal infection** (appendicitis, inflammatory bowel disease)

pelvic tuberculosis

salpingitis isthmica nodosa

Women with **distal tubal obstruction** may develop **hydrosalpinges**, which decrease the success rate of in vitro fertilization (IVF). obstruction to **sperm migration**

reduce fertility by **retrograde flow** of tubal contents into the endometrial cavity, which creates a hostile environment to

**implantation** of an embryo. Removal of the hydrosalpinges increases the success of IVF.



# UTERUS

Uterine fibroids are **common**  
**benign** smooth muscle  
monoclonal **tumors**.

that fibroids with a **submucosal** or  
**intracavitary** component can lower  
**pregnancy** and **implantation** rates.

# Uterine anomalies

- ▶ Uterine abnormalities are thought to cause infertility by interfering with normal **implantation**. Müllerian anomalies are a significant cause of **recurrent pregnancy loss (RPL)**, with the *septate uterus associated with the poorest reproductive* outcome .

Other structural abnormalities associated with infertility include endometrial polyps, and synechiae from prior pregnancy-related curettage.

# ENDOMETRIOSIS

Mechanisms which decrease fertility in women with endometriosis include :

anatomic distortion from pelvic adhesions damage to ovarian tissue by endometrioma formation and surgical resection

production of substances such as cytokines and growth factors which impair the normal processes of ovulation, fertilization, and implantation.

# CERVICAL FACTORS

Normal mid cycle midcycle cervical mucus facilitates the transport of sperm.

Congenital malformations and trauma to the cervix (including surgery) may result in stenosis and inability of the cervix to produce normal mucus, thereby impairing fertility.

# INHERITED THROMBOPHILIA

Inherited thrombophilias do not appear to be related to unexplained infertility .

A large retrospective study reported **no** significant association with common thrombophilias, including factor V Leiden and lupus anticoagulant, and diminished in vitro fertilization success .

# IMMUNE FACTORS

Women with some autoimmune diseases are at **increased risk of infertility** unrelated to direct effects of these antibodies on fertilization and implantation. premature ovarian failure has also been described in women with **systemic lupus erythematosus** and **myasthenia gravis**.

Women with untreated **celiac disease** may have an increased frequency of reproductive abnormalities, including **infertility, miscarriage, and intrauterine growth restriction**.

# GENETIC CAUSES

Infertile couples have been shown to have a higher prevalence of karyotype abnormalities (trisomies, mosaics, translocations) than the general population .

The **most common aneuploidies** associated with infertility are:

**45, X** (Turner syndrome) in women

**47, XXY** (Klinefelter syndrome) in men.



# infertility evaluation

An infertility evaluation is usually initiated after **one year** of regular unprotected intercourse in women under age **35 years** and after **six months** of unprotected intercourse in women age **35 years and older**

However, the evaluation may be initiated **sooner** in women with:  
irregular menstrual cycles

Known risk factors for infertility:

such as endometriosis

a history of pelvic inflammatory disease

reproductive tract malformations.

# INITIAL APPROACH

**Both partners** of an infertile couple should be evaluated.

The infertility specialist then uses this information to counsel the couple about the **possible etiologies** of their infertility and to offer a **treatment plan** targeted to their specific needs.

# History and physical examination

Findings on history and physical examination may suggest the cause of infertility and thus help focus the diagnostic evaluation.

The most important points in the history are:  
Duration of infertility and results of previous evaluation and therapy

### Menstrual history:

regular monthly cycles with menses (breast tenderness, ovulatory pain, bloating) suggest that the patient is ovulatory, severe dysmenorrhea suggest endometriosis. cycle length may also be a general indicator of ovarian reserve

Medical, surgical, and gynecologic history (including sexually transmitted infections, pelvic inflammatory disease) to

look for conditions, procedures, or medications potentially associated with infertility.

symptoms of thyroid disease, galactorrhea, hirsutism, pelvic or abdominal pain, dysmenorrhea, or dyspareunia.

- Obstetric history
  - Sexual history, including sexual dysfunction and frequency of coitus.
- Family history
  - Personal and lifestyle history including age, occupation, exercise, stress, dieting/changes in weight, smoking, and alcohol use.

# Physical examination

- body mass index (BMI)
- In the setting of primary amenorrhea, incomplete development of secondary sexual characteristics is a sign of hypogonadotropic hypogonadism.
- short and stocky, with a squarely shaped chest, suggests Turner syndrome in patients with absent periods
- Tenderness

- Palpable tender nodules in the posterior cul-de-sac, uterosacral ligaments, or rectovaginal septum are additional signs of endometriosis.
- Vaginal/cervical structural abnormalities or discharge suggest the presence of a müllerian anomaly, infection, or cervical factor.
- Uterine enlargement, irregularity, or lack of mobility are signs of a uterine anomaly, leiomyoma, endometriosis, or pelvic adhesive disease.



# Diagnostic tests

- Semen analysis to detect male factor infertility.
  - Documentation of normal ovulatory function. Women with regular menses with molimina are almost always ovulatory.
  - A test to rule out tubal occlusion and assess the uterine cavity. We usually perform a hysterosalpingogram (HSG), or hysterosalpingo-contrast sonography
- laparoscopy with chromotubation
- A test or tests of ovarian reserve such as:
  - cycle day 3 follicle-stimulating hormone (FSH) and estradiol
  - clomiphene citrate challenge test
  - anti-müllerian hormone
  - antral follicle count.

# Basal body temperature

Progesterone released from the **corpus luteum** at the time of ovulation has potent effects on the hypothalamus, one of which is to increase body temperature.

The woman takes her temperature by putting the thermometer under her tongue every morning while she is still in the basal state and records the temperature on a chart.

an **approximately 0.5°F** rise in body temperature can be detected in the luteal phase of the menstrual cycle compared with the follicular phase. In a normal cycle, the temperature rise begins **one or two days after the LH surge and persists for at 10 days.**

# Assessment of ovarian reserve

We test ovarian reserve with an **AMH** level and a **day 3 FSH** and **estradiol levels**.

Other tests such as:

**antral follicle count.**

# Anti-mullerian hormone

AMH **<0.5 ng/mL** predicts reduced ovarian reserve with less than 3 follicles in an IVF cycle.

AMH **<1.0 ng/mL** predicts baseline ovarian reserve with a likelihood of limited eggs at retrieval. AMH **>1.0 ng/mL** but **<3.5 ng/mL** suggests a **good** response to stimulation. AMH **>3.5 ng/mL** predicts a vigorous response to ovarian stimulation and caution should be exercised in order to avoid ovarian **hyperstimulation** syndrome.

# Assessment of fallopian tube patency

HSG as the **first-line test** for evaluation of tubal patency because of therapeutic, as well as diagnostic benefits.

laparoscopy with chromotubation

# Hysterosalpingogram

- HSG is the standard of care to look for tubalocclusion in all patients.
- Water or lipid-soluble contrast media is used to fill the uterus and fallopian tubes. • HSG also provides information about the uterine cavity.
- HSG is not useful for detecting peritubal adhesions or endometriosis.

# Assessment of the uterine cavity

Modalities to assess the uterine cavity :

saline infusion sonohysterography  
three-dimensional sonography  
hysterosalpingography (HSG)  
hysteroscopy.

Saline infusion sonohysterography

# LAPAROSCOPY

Laparoscopy may be indicated in women in whom **endometriosis** or **pelvic adhesions/tubal disease** is suspected based on physical examination, HSG, or history.



# Karyotype

There is a general consensus to counsel and offer to karyotype the male partner if there is **severe oligospermia**, as these men are at higher risk of karyotypic abnormalities.

We suggest karyotyping women :

**with premature ovarian insufficiency  
or a family history of early ovarian insufficiency (prior to  
age 40) and both partners if there have been recurrent  
pregnancy losses.**

# Treatment

Once the cause of infertility is identified, therapy aimed at correcting **reversible etiologies** and overcoming **irreversible** factors can be implemented.

lifestyle modifications to improve fertility, such as smoking cessation, reducing excessive caffeine and alcohol consumption.

The patient should be involved in fertility treatment choices. These choices involve four major factors: **effectiveness** (live birth rate), **burden of treatment** (frequency of injections and office visits), **safety** (risk of ovarian hyperstimulation and multiple gestation), and **financial costs**.

# OVULATORY DISORDERS

WHO class 1 – Hypogonadotropic hypogonadal anovulation is the least common, occurring in 5 to 10 percent of cases. Examples of women in this category: are women with hypothalamic amenorrhea from functional etiologies such as excessive exercise or low body weight.

WHO class 2 – Normogonadotropic normoestrogenic anovulation is the most common, accounting for 70 to 85 percent of cases. Women with polycystic ovary syndrome usually fall into this category.

WHO class 3 – Hypergonadotropic hypoestrogenic anovulation occurs in 10 to 30 percent. Women with primary gonadal failure (previously called premature ovarian failure) or gonadal dysgenesis, comprise the majority of these cases.

## Options include

- Weight modulation
- Clomiphene citrate
- Aromatase inhibitors
- Gonadotropin therapy
- Metformin
- Laparoscopic ovarian diathermy
- Bromocriptine or other dopamine agonist
- Assisted reproductive technology

class 2 patients.

WHO class 1 patients respond best to therapy involving lifestyle modification organotropins. Some WHO class 3 patients respond to gonadotropin therapy and in vitro fertilization (IVF), but those who fail require oocyte donation.

# Ovulation induction agents

# TUBAL FACTOR INFERTILITY AND ADHESIONS

# In vitro fertilization



# ENDOMETRIOSIS

surgical resection of endometriosis, ovulation induction plus intrauterine insemination, and assisted reproductive technologies.

# UTERINE FACTOR INFERTILITY

endometrial submucous fibroid polyp,  
septate uterus, or uterine synechiae.

# UNEXPLAINED INFERTILITY

Therapy with **clomiphene with intrauterine** insemination (IUI) may be employed as initial treatment due to the low cost and low risk of side effects.

If the patient does not conceive after clomiphene with IUI:

**gonadotropin injections with IUI**  
**assisted reproductive technologies**