



# Infertility

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# Definition

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- Infertility is defined as the inability to become pregnant after 12 months of regular, unprotected intercourse.
- In a survey from 2006 to 2010, more than 1.5 million U.S. women, or 6% of the married population 15 to 44 years of age, reported infertility
- 6.7 million women reported impaired ability to get pregnant or carry a baby to term.
- Among couples 15 to 44 years of age, nearly 7 million have used infertility services at some point.



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- 85% of couples conceive spontaneously within 12 months if having intercourse regularly
  - Generally, evaluation should be offered to couples who have not conceived **after one year** of unprotected vaginal intercourse.
  - Counseling about options should be offered to couples who are not physically able to conceive (i.e., same-sex couples or persons lacking reproductive organs)
  - Women **older than 35 years** or couples with **known risk factors** for infertility may warrant evaluation **at six months**



# ETIOLOGY

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**Table 1. Etiology of Infertility**

<i>Factors</i>	<i>Percentage</i>
Combined factors	40
Male factors	26 to 30
Ovulatory dysfunction	21 to 25
Tubal factors	14 to 20
Other (e.g., cervical factors, peritoneal factors, uterine abnormalities)	10 to 13
Unexplained	25 to 28

*Information from references 5 through 8.*

# Evaluation of Men

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## **Causes:**

infection

injury

toxin exposures

anatomic variances

chromosomal abnormalities

systemic diseases

sperm antibodies

Other(smoking, alcohol use, obesity, and older age)

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**Male**

Genetic etiology:  
Y deletions  
XXY (Klinefelter syndrome)

Y deletions: small testes  
Klinefelter phenotype: small testes, tall,  
gynecomastia, learning disabilities

Both syndromes result in normal semen  
volume but low sperm count  
Y deletions may present as normal hormone  
levels or have an elevated FSH level  
Klinefelter syndrome typically results in low  
testosterone level and an elevated FSH level

Y deletions can be passed to offspring if intracytoplasmic  
sperm injection is used with in vitro fertilization; genetic  
counseling is indicated

Other genetics:  
*CFTR* gene (cystic fibrosis)  
5T allele (cystic fibrosis)

Absence of the vas deferens

Low volume semen analysis

Because of the inheritance pattern, genetic testing of the partner  
is warranted, and counseling is indicated if she is a carrier

Obstruction of the vas  
deferens or epididymis  
Ejaculatory dysfunction

History of infection, trauma, or vasectomy; normal  
testicular examination

Low volume semen analysis; transrectal  
ultrasonography can identify obstruction

Rare cause of infertility; evaluation reserved for fertility  
specialist

Systemic disease  
(not all-inclusive):  
Hemochromatosis  
Kallmann syndrome  
Pituitary tumor  
Sarcoidosis

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Low FSH level; low testosterone level; check  
prolactin level and, if elevated, perform  
imaging for pituitary tumor

Infiltrative processes that cause a small number of infertility  
cases; however, effective treatment is available

Unclear etiology

Normal testicular examination

Normal FSH level; normal semen volume; low  
sperm count

Subspecialist may consider testicular biopsy to determine  
obstructive vs. nonobstructive azoospermia

# Evaluation of Men

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## **1-Hx and Ph/E:**

previous fertility, pelvic or inguinal surgeries, systemic diseases, and exposures

## **2-Laboratory Evaluation:**

semen analysis

\*If the semen analysis result is abnormal, further evaluation is indicated

## **3-Others:**

testicular biopsy, genetic testing, and imaging

\* **Postcoital testing** and **antisperm antibody** testing are no longer considered useful

# Evaluation of Men

**Table 2. World Health Organization  
2010 Semen Analysis Reference Guidelines**

<i>Characteristic</i>	<i>Normal reference</i>
Morphologically normal	4%
Motility (progressive)	32%
Motility (total)	40%
Sperm count	39 million per ejaculate; 15 million per mL
Vitality	58%
Volume	At least 1.5 mL

NOTE: **oligospermia** = sperm count < 15 million per mL; **asthenozoospermia** = < 40% of the sperm are motile; **teratozoospermia** = normal morphology < 4%. If an individual has all three low sperm conditions, it is known as **OAT syndrome**, which is typically associated with an increased likelihood of genetic etiology of the infertility. Total motility differs from progressive motility only in the notation of forward movement.

Information from reference 18.

- If oligospermia or azoospermia present:

R/O hypogonadism

Check morning levels of **total testosterone** (NL= 240 to 950 ng per dL) and **FSH**(NL= 1.5 to 12.4 mIU per mL) to differentiate between **primary and secondary disorders**

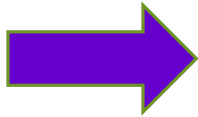


# Evaluation Of Women

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## **Etiology:**

### **Ovulation disorders**



Uterine abnormalities

Tubal obstruction

Peritoneal factors

Cervical factors

- **Group I** : Hypothalamic Pituitary failure (10%)

amenorrhea and low gonadotropin levels

low body weight or excessive exercise

- **Group II**: Dysfunction of hypothalamic-pituitary-ovarian axis (85%)

polycystic ovary syndrome and hyperprolactinemia

- **Group III**: Ovarian Failure (5%)

can conceive only with oocyte donation and in vitro fertilization

**Table 3. Etiology and Evaluation of Infertility**

<i>Condition</i>	<i>History and physical examination</i>	<i>Laboratory and radiologic testing</i>	<i>Comments</i>
<b>Female</b>			
Endometriosis or pelvic adhesions	History of abdominal or pelvic surgery; history consistent with endometriosis	Rarely helpful	Generally diagnosed on laparoscopy; consider in women with otherwise unexplained infertility
Hypothalamic amenorrhea	Amenorrhea or oligomenorrhea; low body mass index	Low to normal FSH level; low estradiol level	Encourage weight gain
Ovarian failure/insufficiency	Amenorrhea or oligomenorrhea; menopausal symptoms; family history of early menopause; single ovary; chemotherapy or radiation therapy; previous ovarian surgery; history of autoimmune disease	Elevated FSH level; low estradiol level	Consider additional tests of ovarian reserve (antral follicle count, antimüllerian hormone level, clomiphene [Clomid] challenge test)
Ovulatory disorder	Irregular menses; hirsutism; obesity (polycystic ovary syndrome); galactorrhea (hyperprolactinemia); fatigue; hair loss (hypothyroidism)	Progesterone level < 5 ng per mL (15.9 nmol per L); elevated prolactin level; low TSH level	Check TSH and prolactin levels based on clinical symptoms
Tubal blockage	History of pelvic infections or endometriosis	Abnormal hysterosalpingography result	Usually necessitates subspecialist referral for treatment
Uterine abnormalities	Dyspareunia; dysmenorrhea; history of anatomic developmental abnormalities; family history of uterine fibroids; abnormal palpation and inspection	Abnormal hysterosalpingography or ultrasonography result	May necessitate subspecialist referral for treatment

# Evaluation Of Women

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## **1-History:**

menstrual history, timing and frequency of intercourse, previous use of contraception, previous pregnancies and outcomes, pelvic infections, medication use, occupational exposures, substance abuse, alcohol intake, tobacco use, and previous surgery on reproductive organs.

**2-ROS and Ph/E** of the endocrine and gynecologic systems

## **3-Others:**

preconception screening and vaccination for preventable diseases such as rubella and varicella, sexually transmitted infections, and cervical cancer, based on appropriate guidelines and risk

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### Women with regular menstrual cycles:

Check serum progesterone **at day 21** to confirm ovulation

### Women with irregular cycles:

Check serum progesterone **seven days before presumed onset of menses**, and **repeated weekly** until menses.

A progesterone level of 5 ng per mL (15.9 nmol per L) or greater implies ovulation.

### Anovulatory women

- R/O treatable causes such as thyroid disorders or hyperprolactinemia
- FSH↑(greater than 30 to 40 mIU per mL) with a Estradiol↓ ovarian failure
- low or normal FSH level (less than 10 mIU per mL) and a estradiol↓ hypothalamic pituitary failure
- Basal body temperatures: not recommended

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FSH ↑ (10 to 20 mIU per mL) drawn on day 3 of the menstrual cycle is associated with infertility.

serum estradiol ↑ (greater than 60 to 80 pg per mL) in conjunction with a normal FSH level: lower pregnancy rates (due to ovarian insufficiency or diminished ovarian reserve).

**Other tests of ovarian reserve:**

- clomiphene (Clomid) challenge test, antral follicle count, and antimüllerian hormone level
- predict response to ovarian stimulation with exogenous gonadotropins and ART
- poor to moderate predictive value despite widespread use.

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Women with no clear risk of tubal obstruction : **Hysterosalpingography**

Women with risk factors for tubal obstruction( such as endometriosis, previous pelvic infections, or ectopic pregnancy) : **Hysteroscopy or Laparoscopy with dye**

**Endometrial biopsy** : only in women with suspected pathology (chronic endometritis or neoplasia).

**Postcoital testing of cervical mucus:** no longer recommended

# Treatment of Male Infertility

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- Abnormal semen analysis :referral to a male fertility specialist or reproductive endocrinologist
- Anatomic variance or obstruction: referral for surgical evaluation and treatment
- Endocrinopathy (such as hyperprolactinemia: treat the underlying cause
- Varicocele: corrective surgery (?)
- Antiestrogens and gonadotropin therapy
- Antioxidants such as zinc, vitamin E, or l-carnitine
- IUI
- IVF

# Treatment of Anovulatory Conditions

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## **WHO group I ovulatory disorders :**

Achieve a normal body weight.

Pulsatile administration of GnRH or gonadotropins with LH activity to induce ovulation

## **Women in WHO group II (overweight /PCO) :**

weight loss, exercise, lifestyle modifications to restore ovulatory cycles and achieve pregnancy

Clomiphene has also proven effective for ovulation induction in women with polycystic ovary syndrome.

Metformin (Glucophage)



# Treatment of Unexplained Infertility

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- Urinary luteinizing hormone kits
- Basal body temperature measurements
- Cervical mucus changes

# Lifestyle Factors

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Abstain from tobacco use

Limit alcohol consumption

Body Mass Index less than 30 kg per m<sup>2</sup>

## Infertility Evaluation

