

**Diagnostic evaluation
of
the infertile female**

M.ESLAMI MOAYED

OB&GYN

Fellowship of infertility

- diagnostic evaluation for infertility is indicated for women who fail to achieve a successful pregnancy after **12 months** or more of regular unprotected intercourse
- Since approximately 85% of couples may be expected to achieve pregnancy within that interval without medical assistance, evaluation may be indicated for as many as 15% of couples.

The overall long-term decline in the US birth and fertility rates has been attributed to several factors: Greater interest in advanced education and careers among women Later marriage and more frequent divorce Improvements in contraception and access to family planning services Delayed childbearing Decreased family size •

Time Required For Conception

Time of Exposure	% pregnant
3 months	57%
6 months	72%
1 year	85%
2 years	93%

Fertility:

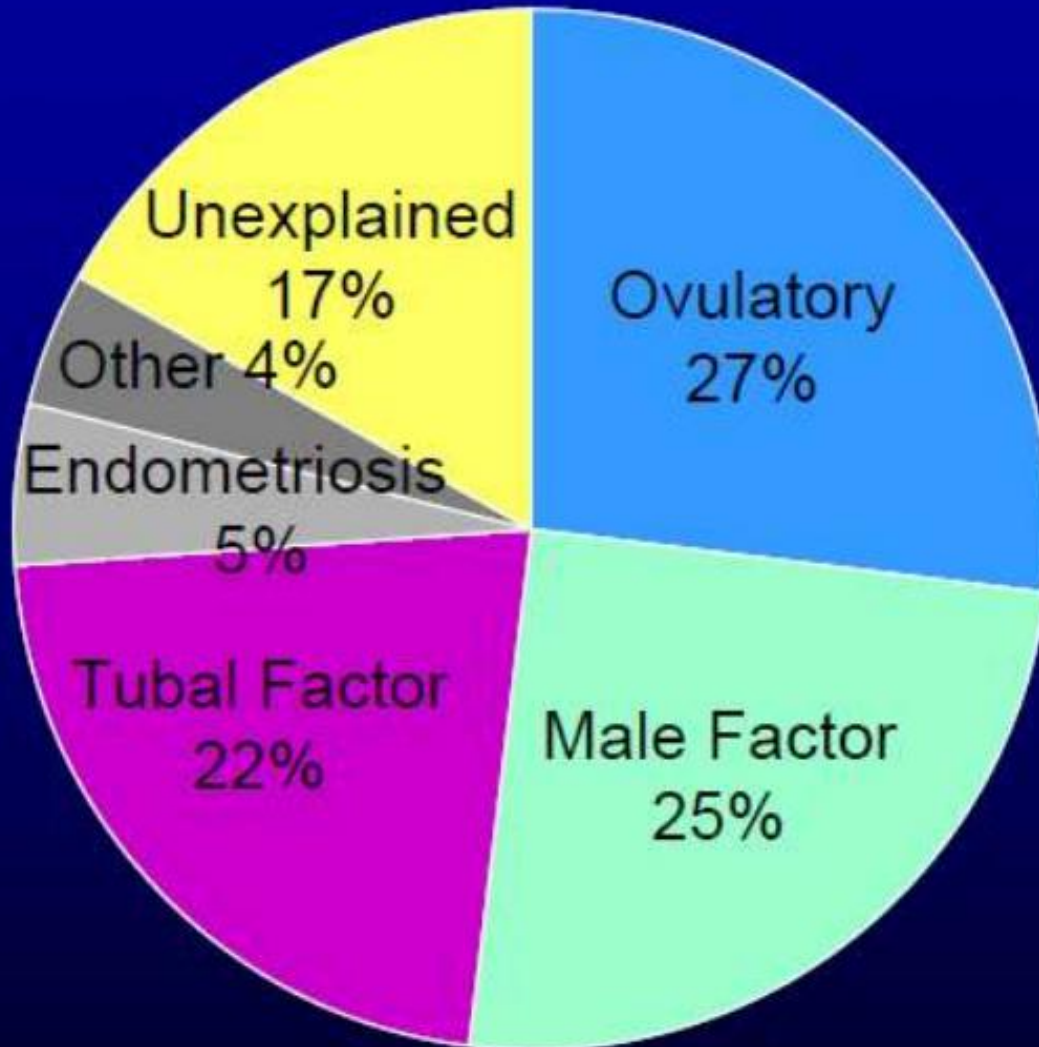
One year of unprotected coitus without conception
Affects 10-15% of couples in reproductive age group

- Earlier evaluation is warranted after six months of unsuccessful efforts to conceive in women **over age 35 years** and also including, but not limited to, the following:
 - **History of oligo - or amenorrhea**
 - **Known or suspected uterine/tubal/peritoneal disease or stage III–IV endometriosis**
 - **Known or suspected male subfertility**
- Where applicable, evaluation of both partners should begin at the same time.

Infertility

- Primary infertility
 - a couple that has never conceived
- Secondary infertility
 - infertility that occurs after previous pregnancy regardless of outcome

Diagnosis in Infertile Couples



Evaluation

- Successful reproduction requires proper structure and function of the entire reproductive axis, including hypothalamus, pituitary gland, ovaries, fallopian tube, uterus, cervix, and vagina.

- To assess this axis, the infertility evaluation comprises eight major elements:
 - (a) history and physical examination;
 - (b) semen analysis;
 - (c) sperm-cervical mucus interaction (postcoital testing);
 - (d) assessment of ovarian reserve;
 - (e) tests for occurrence of ovulation;
 - (f) evaluation of tubal patency;
 - (g) detection of uterine abnormalities; and

Relevant history includes the following:

- Duration of infertility and results of any previous evaluation and treatment
- Menstrual history (age at menarche , cycle length and characteristics, presence of molimina , and onset/severity of dysmenorrhea)
- Pregnancy history (gravidity, parity , pregnancy outcome, and associated complications)
- Previous methods of contraception
- Coital frequency and sexual dysfunction

- Past surgery (procedures, indications and outcomes), previous hospitalizations , serious illnesses or injuries , pelvic inflammatory disease , or exposure to sexually transmitted infections
- Thyroid disease, galactorrhea , hirsutism , pelvic or abdominal pain, and dyspareunia
- Previous abnormal pap smears and any subsequent treatment

- Current medications and allergies
- Family history of birth defects, mental retardation, early menopause, or reproductive failure or compromise
- Occupation and exposure to known environmental hazards
- Use of tobacco, alcohol, and recreational or illicit drugs

Physical examination should document the following:

- Weight, body mass index (BMI), blood pressure, and pulse
- Thyroid enlargement and presence of any nodules or tenderness
- Breast secretions and their character
- Signs of androgen excess
- Vaginal or cervical abnormality, secretions, or discharge
- Pelvic or abdominal tenderness, organ enlargement, or masses
- Uterine size, shape, position, and mobility
- Adnexal masses or tenderness
- Cul-de-sac masses, tenderness, or nodularity

Exclusion of Male Factor

Exclusion of Cervical Factor Infertility

- Abnormalities of cervical mucus production or sperm/mucus interaction rarely are the sole or principal cause of infertility.
- Examination of cervical mucus may reveal gross evidence of chronic cervicitis that warrants treatment.
- The postcoital test (PCT) allows direct analysis of sperm and cervical mucus interaction and provides a rough estimate of sperm quality.
- The test is done between days 12 and 14 of a 28- to 30-day menstrual cycle (after 48 hours of abstinence) when maximum estrogen secretion is present.
- The mucus is examined within 2 to 8 hours. (at least 5 motile sperm per high power field is considered normal).

Exclusion of Ovulatory Factor

- Ovulatory dysfunction will be identified in approximately 15% of all infertile couples and accounts for up to 40% of infertility in women
- It commonly results in obvious menstrual disturbances (oligo/amenorrhea), but can be more subtle.
- The underlying cause should be sought because specific treatment may be indicated and some conditions may have other health implications and consequences

- The most common causes of ovulatory dysfunction include
- **polycystic ovary syndrome, obesity, weight gain or loss, strenuous exercise , thyroid dysfunction, and hyperprolactinemia .**
- However, the specific cause of ovulatory dysfunction often remains obscure.
- Methods for evaluating ovulatory function may include any of the following:

1- Confirmation of Ovulation

- **A- Menstrual history** may be all that is required.
- In most ovulatory women, menstrual cycles are regular and predictable, occurring at intervals of 25–35 days, exhibiting consistent flow characteristics, and accompanied by a consistent pattern of menses (breast tenderness, dysmenorrhea, bloating).
- Patients with abnormal uterine bleeding, oligomenorrhea, or amenorrhea generally do not require specific diagnostic tests to establish a diagnosis of anovulation.

B- Serial basal body temperature (BBT)

- The basal body temperature (BBT) chart is a simple means of determining whether ovulation has occurred.
- The woman's temperature is taken daily with a thermometer on awakening, before any activity, and is recorded on a graph.
- After ovulation, rising progesterone levels increase the basal temperature by approximately 0.4°F (0.22°C) through a hypothalamic thermogenic effect.

C- Serum progesterone

- Midluteal phase progesterone level is another test to assess ovulation.
- A concentration greater than 3.0 ng/mL in a blood sample drawn between days 19 and 23 is consistent with ovulation, whereas a concentration greater than 10 ng/mL implies adequate luteal support.

D- Urinary luteinizing hormone (LH)

- Determinations using various commercial “ovulation predictor kits” can identify the midcycle LH surge that precedes ovulation by one to two days.
- Urinary LH detection provides indirect evidence of ovulation and helps to define the interval of greatest fertility: **(the day of the LH surge and the following two days)**

E- Transvaginal ultrasonography

- Transvaginal ultrasonography can reveal the size and number of developing follicles and also provide presumptive evidence of ovulation and luteinization by demonstrating progressive follicular growth, sudden collapse of the preovulatory follicle, a loss of clearly defined follicular margins, the appearance of internal echoes, and an increase in cul-de-sac fluid volume

- Other evaluations aimed at defining the best choice of treatment may be indicated for anovulatory infertile women.
- **Serum thyroid-stimulating hormone** (TSH) and **prolactin** determinations can identify thyroid disorders and/or hyperprolactinemia, which may require specific treatment.

- In women with amenorrhea, **serum follicle-stimulating hormone (FSH)** and **estradiol** measurements can distinguish women with
 - **Ovarian failure (high FSH,low estradiol)**
,whom may be candidates for oocyte donation,
from those with
 - **Hypothalamic amenorrhea (low or normal FSH,low estradiol)**, who will require exogenous gonadotropin stimulation for ovulation induction.

2- Assessment of Ovarian Reserve

- The concept of “ovarian reserve” views reproductive potential as a function of the number and quality of remaining oocytes.
- Decreased or diminished ovarian reserve (DOR) describes women of reproductive age having regular menses whose response to ovarian stimulation is reduced compared to those women of comparable age.

- These tests may provide prognostic information in women at increased risk of diminished ovarian reserve, such as women who:
 - 1) are over age 35 years;
 - 2) have a family history of early menopause;
 - 3) have a single ovary or history of previous ovarian surgery, chemotherapy, or pelvic radiation therapy;
 - 4) have unexplained infertility
 - 5) have demonstrated poor response to gonadotropin stimulation; or
 - 6) are planning treatment with assisted reproductive technology(ART)

- Tests utilized to assess “ ovarian reserve ”

Include :

- **cycle day 3 FSH and estradiol measurements,**
- **a clomiphene citrate challenge test**
- **an early follicular phase antral follicle count (via transvaginal ultrasonography), or**
- **a serum antimuellerian hormone (AMH) level**

Cycle Day 3 FSH and Estradiol

- FSH obtained on cycle day 2–5 is commonly used as a measure of ovarian reserve.
- High values (10–20 IU/L) have been associated with both poor ovarian stimulation and the failure to conceive.

-

Clomiphene Citrate Challenge Test

- The CCCT involves measurements of serum FSH before and after treatment with clomiphene citrate (100 mg daily, cycle days 5–9), typically on cycle day 3 and cycle day 10.
- An elevated FSH concentration after clomiphene stimulation therefore suggests DOR.
- Cycle day 10 FSH levels have a higher sensitivity but lower specificity compared to cycle day 3 FSH concentrations

Antral Follicle Count

- Antral follicle count (AFC) is the sum of antral follicles in both ovaries, as observed with transvaginal ultrasonography during the early follicular phase.
- Antral follicles have been defined as measuring 2–10 mm or 3–8mm in mean diameter in the greatest 2-dimensional plane.
- A low AFC (range 3–10 total antral follicles) has been associated with poor response to ovarian stimulation and with the failure to achieve pregnancy

Serum Antimullerian Hormone (AMH) Level

- Serum concentrations of AMH, produced by granulosa cells of early follicles, are gonadotropin-independent and therefore remain relatively consistent within and between menstrual cycles in both normal young ovulating women and in women with infertility
- Therefore an AMH level can be obtained on any day of the menstrual cycle.
- Overall, lower AMH levels (<1 ng/mL) have been associated with poor responses to ovarian stimulation, poor embryo quality, and poor pregnancy outcomes in IVF

Endometrial biopsy (EBM)

- Endometrial biopsy (EBM) and histology can demonstrate secretory endometrial development, which results from the action of progesterone and thus implies ovulation.
- Dating the endometrium using traditional histologic criteria was long considered the “gold standard” among methods for evaluating the quality of luteal function and for diagnosis of luteal phase deficiency (LPD).

UTERINE ABNORMALITIES

- Abnormalities of uterine anatomy or function are relatively uncommon causes of infertility in women, but should be excluded.
- Methods for evaluation of the uterus include the following:
- **Hysterosalpingography (HSG)** defines the size and shape of the uterine cavity and can reveal developmental anomalies (unicornuate, septate, bicornuate uteri) or other acquired abnormalities (endometrial polyps, submucous myomas,) having potential reproductive consequences.

- **Ultrasonography (US)** can be used to diagnose uterine pathology, including myomas
- **Sonohysterography**, involving transvaginal ultrasonography after introduction of saline into the uterine cavity better defines the size and shape of the uterine cavity and for detection of intrauterine pathology (endometrial polyps, submucous myomas, synechiae)

- **Hysteroscopy** is the definitive method for the diagnosis and treatment of intrauterine pathology.
- As it is also the most costly and invasive method for evaluating the uterus, it generally can be reserved for further evaluation and treatment of abnormalities defined by less invasive methods such as HSG and sonohysterography

evaluation of tubal patency

- Tubal disease is an important cause of infertility and should be specifically excluded.
- The methods for evaluating tubal patency are complementary and not mutually exclusive
- Accurate diagnosis and effective treatment of tubal obstruction often requires more than one of the following techniques:

- **Hysterosalpingography (HSG)**, using either a water- or lipid-soluble contrast media, is the traditional and standard method for evaluating tubal patency and may offer some therapeutic benefit.
- HSG can document proximal and distal tubal occlusion, demonstrate salpingitis isthmica nodosa, reveal tubal architectural detail of potential prognostic value, and may suggest the presence of fimbrial phimosis or peritubular adhesions when escape of contrast is delayed or becomes loculated, respectively.

- **Saline infusion sonography (SIS)** is a test to determine tubal patency using fluid and ultrasound.
- **Laparoscopy** and chromotubation with a dilute solution of methylene blue or indigo carmine (preferred) introduced via the cervix can demonstrate tubal patency or document proximal or distal tubal obstruction.
- The procedure also can identify and correct tubal factors such as fimbrial phimosis or peritubal adhesions, which may not be identified with less invasive methods such as HSG.

Chlamydia Antibody Test (CAT)

- The detection of antibodies to Chlamydia trachomatis has been associated with tubal pathology; however, this test has limited clinical utility.
- Compared to laparoscopy, the CAT has lower sensitivity for detection of distal tubal disease

evaluation of peritoneal factor

- Peritoneal factors such as endometriosis and pelvic or adnexal adhesions may cause or contribute to infertility.
- History and/or physical examination findings may raise suspicion but rarely are sufficient for diagnosis.
- Peritoneal factors also should be considered in women with otherwise unexplained infertility.
- Transvaginal ultrasonography can reveal otherwise unrecognized pelvic pathology that may have reproductive implications, such as an endometrioma

- **Laparoscopy** with direct visual examination of the pelvic reproductive anatomy is the only method available for specific diagnosis of peritoneal factors that may impair fertility.
- However, the impact of minimal and mild endometriosis on fertility is relatively small , and most women with significant adnexal adhesions have historical risk factors (pelvic pain, moderate or severe endometriosis, previous pelvic infection or surgery) or an abnormal HSG.

- Consequently, laparoscopy is most clearly indicated for those with symptoms or risk factors or an abnormal HSG or ultrasonography who have no other clear indications for ART (e.g., severe male factor infertility); its yield in asymptomatic women with normal imaging is low.
- Given individual circumstances, there may be a place for diagnostic laparoscopy for young women with a long period(>3 years) of infertility but no recognized abnormalities

Assisted Reproductive Technologies (ART)

- Explosion of ART has occurred in the last decade.
- These technologies help provide infertile couples with tools to bypass the normal mechanisms of gamete transportation.
- Probability of pregnancy in healthy couples is 30-40% per cycle, live birth rate 25%.
 - this varies depending on age

Intrauterine insemination (IUI)

- A type of artificial insemination — is a procedure for treating infertility.
- Sperm that have been washed and concentrated are placed directly in uterus around the time the ovary releases one or more eggs to be fertilized.
- The hoped-for outcome of intrauterine insemination is for the sperm to swim into the fallopian tube and fertilize a waiting egg, resulting in a normal pregnancy.

- The most common reasons for IUI are a low sperm count or decreased sperm mobility.
- However, IUI may be selected as a fertility treatment for any of the following conditions as well:
 - Unexplained infertility
 - A hostile cervical condition, including cervical mucus problems
 - Cervical scar tissue from past procedures which may hinder the sperms' ability to enter the uterus
 - Ejaculation dysfunction

IUI is not recommended for the following patients:

- Women who have severe disease of the fallopian tubes
- Women with a history of pelvic infections
- Women with moderate to severe endometriosis

How does IUI work?

- Before intrauterine insemination, ovulation stimulating medications may be used, in which case careful monitoring will be necessary to determine when the eggs are mature.
- The IUI procedure will then be performed around the time of ovulation, typically about 24-36 hours after the surge in LH hormone that indicates ovulation will occur soon.

- A semen sample will be washed by the lab to separate the semen from the seminal fluid.
- A catheter will then be used to insert the sperm directly into the uterus.
- This process maximizes the number of sperm cells that are placed in the uterus, thus increasing the possibility of conception.
- The IUI procedure takes only a few minutes and involves minimal discomfort.
- The next step is to watch for signs and symptoms of pregnancy.

How successful is IUI?

- The success of IUI depends on several factors.
- If a couple has the IUI procedure performed each month, **success rates may reach as high as 20% per cycle** depending on variables such as female age, the reason for infertility, and whether fertility drugs were used, among other variables.
- While IUI is a less invasive and less expensive option, pregnancy rates from IUI are lower than those from IVF.



THANKS