PRIMINARY EVALUATION OF THE INFERTILE COUPLE

Dr sara saedi
Gynecologist
Fellowship of infertility

The four basic goals of management of infertility

- To identify causes of infertility
- With proper evaluation and treatment, the majority of women will achieve pregnancy.
- To provide accurate information and to dispel the misinformation commonly gained from friends, mass media, and the Internet.
- To provide emotional support during a trying time.

- The overall long-term decline in the US birth and fertility
- 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

- Coital frequency often declines as age increases, reflecting decreasing desire or lack of a partner.
- The incidence of subclinical abortion is unknown.
- Other diseases or conditions that can adversely affect fertility (e.g., pelvic infections, leiomyomata, endometriosis) is greater in older women.

- Variations infertility rates among natural populations could reflect differences
- Genetic factors
- Socioeconomic conditions at different times and in different places.

- Success rates achieved with ART using non donor eggs also decline as age increases.
- The numbers of oocytes retrieved and embryos available and implantation, pregnancy, and live birth rates are lower in older than in younger women.

Age is the single most important factor affecting the probability of success with ART

AGE

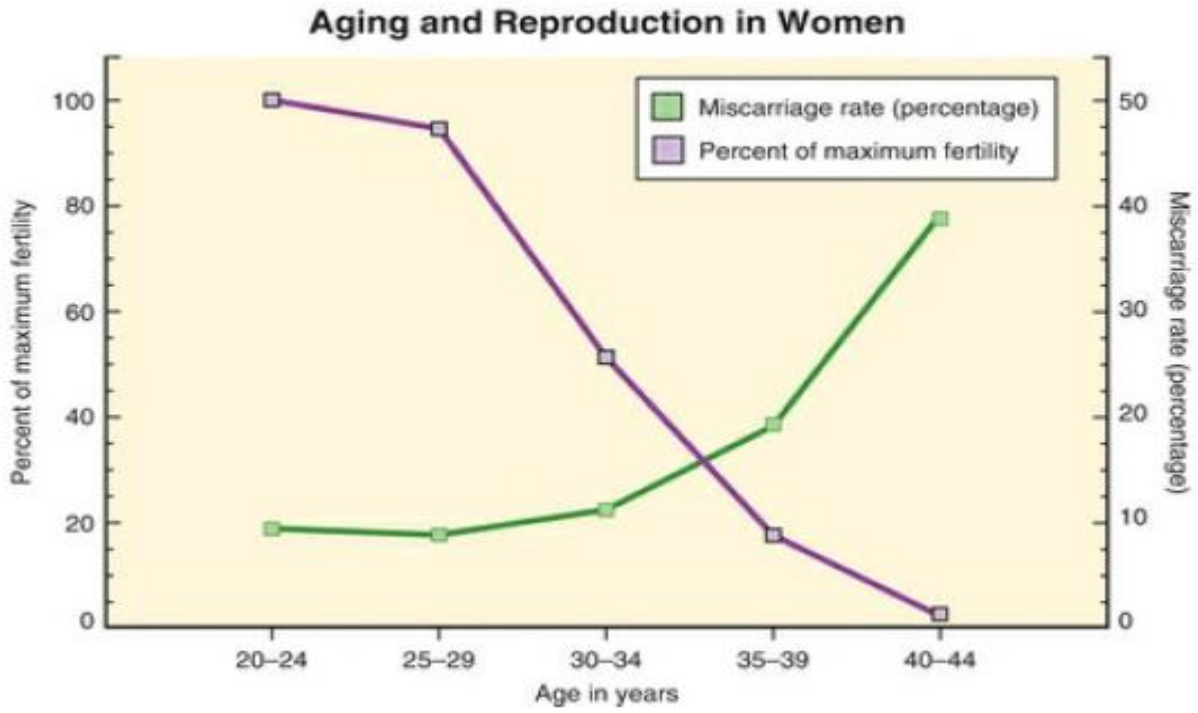
- Decline in ART live birth rates
- Increasing pregnancy waste
- Fertility decreases with increasing age
- Miscarriage rises as age advances.

- The live birth rate per embryo transfer
- 46.5% under age 35
- 38.4% for ages 35–37
- 27.4% for ages 38–40
- 15.5% for ages 41–42
- 6.6% for women aged 43–44

Miscarriage

- Low before age 30 (7–15%)
- Ages 30–34 (8–21%)
- Ages 35–39 (17–28%)
- Ages 40 and older (34–52%)

- In the 2015 US national summary of IVF outcomes, miscarriage rates
- 15% for women under age 35
- 29% at age 40
- 65% for women aged 44 and older


Aging and Reproduction in Women
Miscarriage rate (percentage)
Percent of maximum fertility
Percent of maximum fertility
Miscarriage rate (percentage)
100
80
60
40
20
0
50
40
30
20
10
0
20–24
25–29
30–34
35–39
40–44
Age in years

Physiology of Reproductive Aging

- Age-related changes
- Follicular dynamics
- Oocyte quality
- Menstrual cycle characteristics over the past 30 years.

- The process of evaluation infertile couples need to express their concerns, fears, and support groups can help to meet that need.
- Group meetings can help couples to realize that their problem is not unique and to learn how others cope with similar problems.
- Whereas severe anxieties can have adverse effects on ovulatory function and coital frequency

- To guide couples failing to conceive with other forms of treatment to alternatives
- Including IVF
- Use of donor gametes (oocytes or sperm)
- Adoption

- Counseling must ongoing process during evaluation and treatment.
- Regular visits to recommendations for further evaluation and treatment help to ensure that all of the couple’s medical, emotional, and financial needs and concerns

PREMINARY EVALUATION OF THE INFERTILE COUPLE

History

- Obstetric history including gravidity, parity, pregnancy outcomes, and associated complications.
- Menstrual history including cycle length and characteristics and onset and severity of dysmenorrhea.
- Coital frequency and sexual dysfunction.
- Duration of infertility and results of any previous evaluation and treatment.
- Medical and surgical history, including episodes of pelvic inflammatory disease or exposure to sexually transmitted infections.
- Previous abnormal cervical cancer screening results and subsequent treatment.
- Current medications and allergies.
- Occupation and use of tobacco, alcohol, and other drugs.

- Family history of birth defects, mental retardation, early menopause, or reproductive failure.
- Symptoms of thyroid disease, pelvic or abdominal pain, galactorrhea, hirsutism, or dyspareunia.

Physical Examination

- Weight and BMI.
- Thyroid enlargement, nodule, or tenderness.
- Breast secretions and their characteristics.
- Signs of androgen excess.
- Pelvic or abdominal tenderness, organ enlargement, or mass.
- Uterine size, contour, position, and mobility.
- Vaginal or cervical abnormality, secretions, or discharge.
- Mass, tenderness, or nodularity in the adnexa or cul-de-sac.

Indications for Evaluation

- The probability for achieving a live birth without treatment decreases
- Increasing age
- Duration of infertility.

- Pregnancy without treatment declines
- 5% for each additional year of female partner age
- 15–25% for each added year of infertility.
- Spontaneous pregnancies occur within 3 years ,the prognosis for success without treatment is relatively poor.

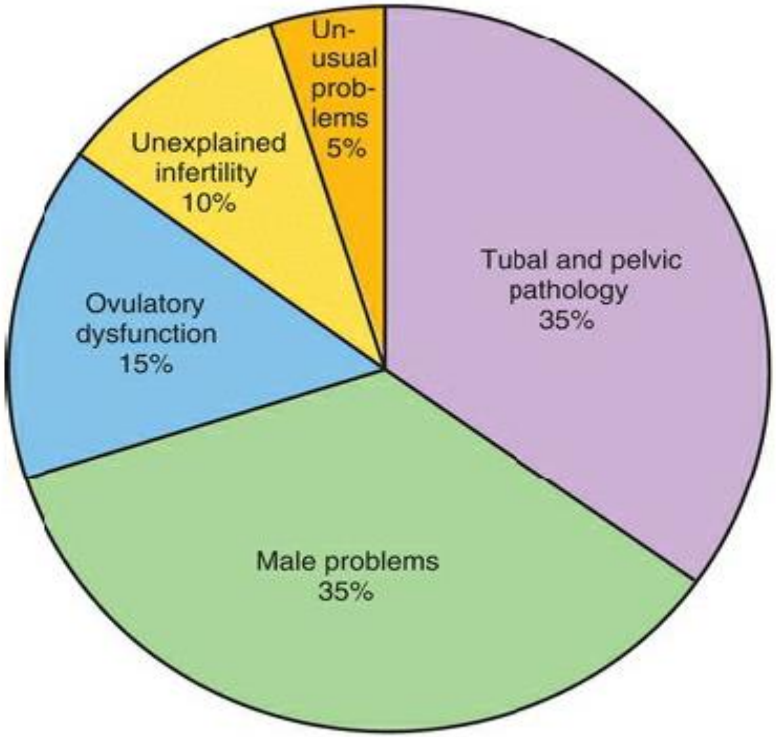
- Evaluation should be offered to all couples after a year or more of regular unprotected intercourse.
- Earlier evaluation for ,such as irregular or infrequent menses, history of pelvic infection, surgery or endometriosis, or having a male partner with known or suspected poor semen quality, after 6 months of unsuccessful effort for women over the age of 35 years.

- The cause of infertility also affects the prognosis for success
- The diagnoses of anovulation and unexplained infertility have the best prognosis.
- Prognosis is reasonably good for mild oligospermia, tubal adhesions, and mild endometriosis
- Poor for severe male factors, tubal obstruction, and severe endometriosis.

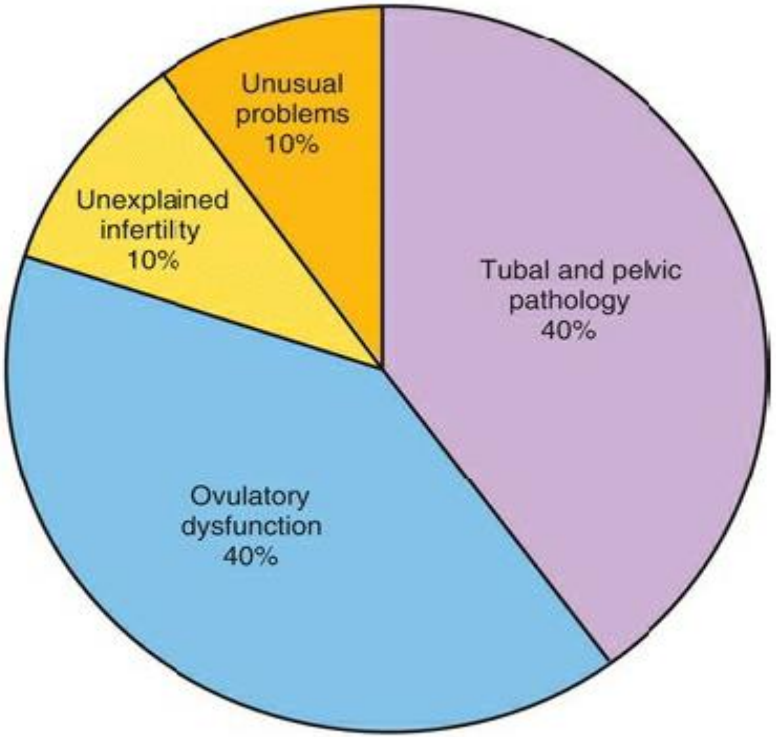
Causes of Infertility

- Ovulatory dysfunction (20–40%)
- Tubal and peritoneal pathology (30–40%)
- Male factors (30–40%)
- unexplained (10%)
- Uterine pathology is relatively uncommon

Causes of Infertility



Couples



Women

Lifestyle and Environmental Factors

- Obesity is defined (BMI) greater than 30 kg/m2
- Overweight is defined BMI 25 kg/m2 and 30 kg/m2.
- In women, obesity is associated with menstrual dysfunction, decreased fertility, and increased risks of miscarriage and obstetric and neonatal complications.
- In men, obesity is associated with abnormal semen parameters and can adversely affect fertility.

- Smoking has well-known adverse impact on pregnancy outcome, and evidence strongly suggests that fertility is lower in both men and women who smoke.
- The mechanisms involved may include accelerated follicular depletion, menstrual cycle abnormalities, gamete or embryo mutagenesis induced by toxins in cigarette smoke.

- Marijuana inhibits the secretion of GnRH and can suppress reproductive function in both women and men. In women, marijuana use can interfere with ovulatory function
- Cocaine use can impair spermatogenesis in men and increased risk of tubal disease in women.

Heavy alcohol

- Decrease fertility in men, it has been associated with decreased semen quality and impotence.
- Conflicting evidence suggests that moderate alcohol intake can reduce fecundability.
- In both women and men, alcohol lower pregnancy rates in IVF cycles.

Caffeine

- Although moderate caffeine ingestion (200 mg daily appears not to have any adverse effects on fertility,
- Higher levels may delay conception or increase the risk of pregnancy loss.

Environmental exposures

- Exposures to perchlor ethylene in the dry-cleaning industry, toluene in the printing business, ethylene oxide, have been associated with decreased fecundity.
- Semen abnormalities have been described in men exposed to radiant heat or heavy metals.
- Environmental exposure to herbicides or fungicides has been associated with decreased fertility in women and exposure to pesticides and other chlorinated hydrocarbons with an increased risk of miscarriage.

Recommendations

- Smoking stop
- Achieve a BMI between 20 and 25 kg/m2.
- Recommendations to limit alcohol consumption to four or fewer
- Drinks per week and to limit caffeine intake to less than 200 mg/day also are for improve fertility.

Normal Reproductive Efficiency

- In normally fertile couples, cycle fecundity averages 20%
- Exceed approximately 35% even when coitus is carefully timed.

- A normal sperm can survive in the female reproductive tract and retain the ability to fertilize an egg for at least 3 and up to 5 days
- Oocyte can be fertilized successfully for only approximately 12–24 hours after ovulation.

- Infertility is defined as 1 year of regular unprotected intercourse without conception
- Infertility approximately 10–15% of couple

Fecundability

Cycle is the probability that a cycle will result in pregnancy

Fecundity

Probability that a cycle will result in a live birth

CAUSES OF MALE INFERTILITY

- Hypothalamic-pituitary disorders (1–2%), congenital, acquired, or result from systemic illness
- Primary gonadal disorders (30–40%), both congenital and acquired
- Disorders of sperm transport (10–20%)
- Idiopathic (40–50%)

	• Single gene mutations (e.g., involving the GnRH receptor, FSHβ, LHβ, or transcription factors involved in pituitary development) • Hypothalamic and pituitary tumors (e.g., craniopharyngioma, macroadenoma) • Infiltrative diseases (sarcoidosis, histiocytosis, transfusion siderosis, hemochromatosis) • Hyperprolactinemia • Drugs (GnRH analogs, androgens, estrogens, glucocorticoids, opiates) • Critical illness or injury • Chronic systemic illness or malnutrition • Infections (e.g., meningitis) • Obesity
Primary gonadal disorders	• Klinefelter syndrome • Y chromosome deletions • Single-gene mutations and polymorphisms (e.g., involving the androgen, estrogen, or FSH receptor) • Cryptorchidism • Varicoceles • Infections (e.g., viral orchitis, leprosy, tuberculosis) • Drugs (e.g., alkylating agents, alcohol, antiandrogens, cimetidine) • Radiation • Environmental gonadotoxins (e.g., heat, smoking, metals, organic solvents, pesticides) • Chronic illness (renal insufficiency, cirrhosis, cancer, sickle cell disease, amyloidosis, vasculitis, celiac disease)
Disorders of sperm transport	• Epididymal obstruction or dysfunction • Congenital bilateral absence of the vas deferens (relating to *CFTR* mutations) • Infections causing obstruction of the vas deferens (e.g., gonorrhea, *Chlamydia*, tuberculosis) • Vasectomy • Kartagener syndrome (primary ciliary dyskinesia) • Young syndrome • Ejaculatory dysfunction (e.g., spinal cord disease, autonomic dysfunction)

- A complete medical history helps in identifying or ruling out obvious risk factors, and tests to confirm ovulation and semen analysis are easy, inexpensive, and minimally invasive and quickly can identify some of the most common reproductive problems.
- In women at risk for DOR, an ovarian reserve test is also reasonable, because results may help to determine when and how further evaluation and treatment should be recommended.

Physical Examination

- Examination of the penis
- Palpation of the testis and measurement of their size
- The presence both the vasa and epididymides
- Presence of any varicocele
- Secondary sex characteristics, including body habitus, hair distribution, and breast development

MALE FACTOR

- Semen analysis is therefore always an appropriate and important initial step in the evaluation of the infertile couple
- When semen quality is normal, attention naturally turns to the female partner.

Semen Analysis

- The initial evaluation for male factor infertility should include at least one semen analysis.
- If abnormal, another semen analysis should be obtained after at least 4 weeks.
- Semen collection should be provided, to include a defined abstinence period of 2–3 days.

THE FEMALE INFERTILITY EVALUATION

Follicular Depletion

- Oocytes peaks around the 20th week 6–7 million oocytes arrested at the first meiotic prophase
- Oocytes declines to 1–2 million at birth
- 300,000–400,000 by puberty
- By age 40, the number of follicles shrinks to approximately 25,000
- Menopause, there remains less than 1,000 follicles.

Endocrinology of Reproductive Aging

- The end of the reproductive period
- (FSH) levels begin to rise,(LH) concentrations remain unchanged.
- Inhibin B levels (derived primarily from smaller antral follicles) decrease as or even before FSH concentrations begin to increase.
- Inhibin A levels also decline, but only in the later stages of reproductive aging, after the onset of menstrual irregularity.

- Preovulatory follicular fluid inhibin concentrations are similar in young and older cycling women suggests that the number of remaining follicles is more important.

- Age and FSH levels increase
- Follicular phase becomes shorter
- LH levels and luteal phase duration remain unchanged.
- Estradiol levels rise earlier, suggesting that higher FSH levels stimulate more rapid follicular development.

- The earlier increase in follicular phase FSH level also frequently results in more than one dominant follicle explaining the higher prevalence of dizygotic twinning in older cycling women.

- However, women generally take notice only when cycles become irregular, marking the beginning of the menopausal transition.
- The menopausal transition begins at an average age of 46 years, but can arrive as early as age 34 and as late as age 54 years.

Genetics of Reproductive Aging

- There is good correlation between menopausal age in mothers and daughters and between sisters, suggesting that genetic factors play an important role in determining menopausal age.
- Approximately 10% of women become menopausal by the age of 45

- Genes affecting reproductive hormones
- (FSH, FSHR, LH, LHR, CYP17, CYP19)
- The initial growth of follicles (GDF9, BMP15, GPR3) impact follicular
- Polymorphisms in the gene the receptor for (AMHR2) were associated with menopausal age

The Aging Follicle and Oocyte

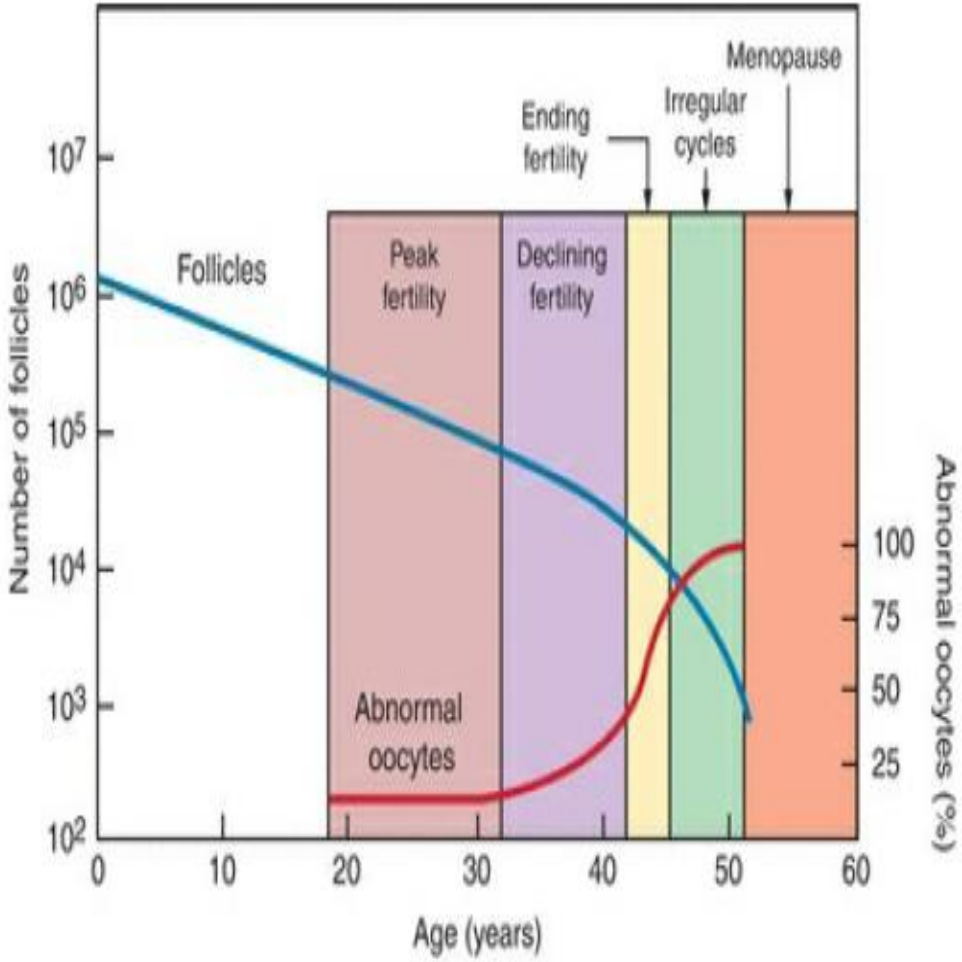
- Number of remaining ovarian follicles steadily declines with increasing age
- In stimulated cycles suggest that aging follicles also become progressively less sensitive to gonadotropin stimulation.
- As age increases, the total dose and duration of treatment required to stimulate multiple follicular development increase.

- Ovarian follicular development and preovulatory follicular fluid hormones in older and younger cycling women do not suggest any age-related decline in follicular function, once growth and development begin.
- Preovulatory follicles in older and younger women are similar in size and inhibin content, and follicular fluid progesterone levels and estrogen/androgen ratios are even higher in older than in younger women.

- The age-related decline in female fertility
- Increase in risk of miscarriage
- Increase in the proportion of abnormal oocytes in an aging and shrinking follicular pool.

- Number of follicles decreases
- Oocyte quality also declines, because of an increase in meiotic nondisjunction
- Resulting in an increasing rate of oocyte and embryo aneuploidy in aging women.
- Therefore, in the zygote, there were more aneuploidies resulting from errors in meiosis II than meiosis I.

- Miscarriage risk and the prevalence of aneuploid oocytes are relatively low and change little until approximately age 35
- Increase progressively, 70% at age 40
- 100% after age 45.
- Trisomies are by far the most common abnormality observed, followed by polyploidies and monosomy X (45,X).



Adapted from[17, 156]

Aging and the Uterus

- Aging does not appear to have any significant adverse effect on the uterus.
- Even though benign uterine pathology (leiomyomata, endometrial polyps, adenomyosis) is more common in older women, there is limited evidence to suggest that uterine age itself has a major impact on fertility.

- Live birth rates in donor egg IVF cycles relate to the age of the donor, not the age of the recipient.
- In one large series, miscarriage rates increased from 14% in women matched with egg donors aged 20–24 to 44% for women whose donors were over age 35.

Aging and Male Fertility

- The relationship between age and fertility in men is discussed
- Several studies have shown that semen volume, sperm motility, progressive motility, and morphologically normal sperm significantly decrease with male

- Overall, the available evidence suggests a negative correlation between male age and pregnancy rates.
- The time to conception increases with male age.
- However, because there is little or no overall measurable decline in male fertility before age 45–50

Ovarian Reserve Assessment

- Ovarian reserve tests are aimed at identifying individuals at risk for a disease, in this case “diminished ovarian reserve” (DOR).
- It is important to emphasize that such tests cannot and do not establish a diagnosis of DOR; they only identify women more likely to exhibit a poor response to gonadotropin stimulation and potentially have a lower likelihood of achieving pregnancy with treatment.

- The purpose of ovarian reserve testing is to correctly identify women with DOR, it will be most useful in women at high risk for DOR.
- When applied in a low prevalence population, many women with a normal ovarian reserve will have a false-positive result and be categorized as having DOR.

Ovarian reserve tests

- Biochemical tests such as FSH, estradiol, inhibin B, (AMH), such as the clomiphene citrate challenge test
- Ultra sonographic measures of ovarian reserve include the antral follicle count (AFC) and ovarian volume.

Basal FSH and Estradiol Concentrations

- Serum FSH concentration was one of the earliest and commonly used tests of ovarian reserve, diminished ovarian reserve (DOR).
- FSH concentration is best obtained during the early follicular phase (cycle days 2–4).

- FSH levels greater than 10 IU/L (10–20 IU/L) have high specificity (80–100%) for predicting poor response to stimulation
- Single elevated FSH concentration (>10 IU/L) does not have high specificity for predicting poor response to stimulation or failure to achieve pregnancy.
- Serial testing in efforts to select the ideal cycle for treatment does not improve outcomes in women with fluctuating FSH concentrations.

- The basal serum estradiol concentration, by itself, has little value as an ovarian reserve test, but can provide additional information that helps in the interpretation of the basal FSH level.

- When the basal FSH is normal and the estradiol concentration is elevated (>60–80 pg/mL), the likelihood of poor response to stimulation is increased and the chance for pregnancy decreased.
- When both FSH and estradiol are elevated, ovarian response to stimulation is likely to be very poor.

Clomiphene Citrate Challenge Test

- Before (cycle day 3 FSH and estradiol) and after (cycle day 10 FSH) treatment with
- clomiphene citrate (100 mg/day, cycle days 5–9).

Inhibin B

- Inhibin B is secreted primarily during the follicular phase by the granulosa cells of smaller antral follicles.
- inhibin B is generally not regarded as a reliable measure of ovarian reserve.

AMH

- Antimüllerian hormone is produced by the granulosa cells of preantral and small antral follicles, **Because** AMH derives from preantral and small antral follicles, levels were thought to be gonadotropin-independent

AMH

- In the general IVF population, low AMH threshold values (0.2–0.7ng/mL) have predicting poor response to stimulation (≤3 follicles or ≤2–4 oocytes), but have proven neither sensitive nor specific for predicting pregnancy.

- AMH is a very promising screening test for DOR but is likely to be more useful in a general IVF population or in women at high risk for DOR than in women at low risk for DOR.
- Low threshold values have good specificity for poor response to ovarian stimulation, but not for predicting pregnancy.

Antral Follicle Count

- The antral follicle count (AFC; total number of antral follicles measuring 2–10 mm in both ovaries) thus provides an indirect but useful measure of ovarian reserve.
- A low AFC has high specificity for predicting poor response to ovarian stimulation and treatment failure, making it a useful test AFC threshold value of three to four follicles has high specificity for predicting poor response to ovarian stimulation and failure to conceive

Ovarian Volume

- Low ovarian volume (<3 mL) has high specificity (80–90%) and widely ranging sensitivity (11–80%) for predicting poor response to ovarian stimulation women at high risk.
- Overall, ovarian volume has very limited clinical utility as an ovarian reserve test.

Ovarian reserve testing

- Age over 35
- Unexplained infertility to identify unsuspected loss of ovarian reserve
- Family history of early menopause
- Previous ovarian surgery (ovarian cystectomy or drilling, unilateral oophorectomy), chemotherapy, or radiation
- Smoking
- Demonstrated poor response to exogenous gonadotropin stimulation

- An abnormal test result does not preclude the possibility of pregnancy. Except perhaps when grossly abnormal, test results should not be used to deny treatment, but only to obtain prognostic information that may help to guide the choice of treatment and best use of available resources.
- Although the probability of pregnancy may be low, many with abnormal test results

- Irregular or infrequent menses indicate ovulatory dysfunction
- A history of previous hysteroscopic or reconstructive uterine surgery or recently developing symptoms of menorrhagia suggest an abnormality of the uterine cavity

- Previous uncomplicated first- and second-trimester pregnancy terminations generally do adversely affect subsequent fertility.
- Worsening dysmenorrhea, new onset of dyspareunia, or physical findings of focal tenderness or cul-de-sac nodularity suggest endometriosis.
- A history of pelvic infection, septic abortion, ruptured appendix, ectopic pregnancy, abdominal myomectomy, or adnexal surgery should raise suspicion for tubal or peritoneal disease.

Screening Tests

- Cervical test
- A blood type, Rh factor, and antibody screening (in Rh-negative women) also is recommended
- CBC screening for thalassemias and hemoglobinopathies
- Women with a family history of fragile X–with premature ovarian insufficiency should be offered fragile X permutation carrier

- All women attempting pregnancy with undocumented previous rubella infection or vaccination should be tested for immunity and vaccinated if sero negative.
- CDC has determined that women need not avoid pregnancy for more than 1 month after vaccination.
- The CDC also recommends that all women without history of previous infection or evidence of immunity or vaccination against varicella (chicken pox) receive two doses of vaccine and avoid pregnancy for 1 month after each dose.

INFECTION TEST

- (STIs) is recommended for all women for syphilis hepatitis B ,(HIV-1),chlamydia and gonorrhea screening
- For women receiving inseminations of donor sperm considers syphilis, hepatitis B and C, HIV-1, HIV-2, chlamydia, gonorrhea, and CMV, (HTLV) types I and II

- For male partners of women receiving inseminations of donor sperm, recommends HIV-1 and HIV-2 and recommends other STI screening similar to the female partner.
- For recipients of donor oocytes or embryos and their male partners, recommends screening for syphilis, hepatitis B and C, HIV-1, HIV-2, chlamydia,gonorrhea, and CMV.

OVARIAN FACTOR

- Overall, disorders of ovulation account for approximately 15% of the problems identified in infertile couples.
- The only positive proof that assures the occurrence of ovulation is pregnancy.

Menstrual History

- Women with regular menses are almost always ovulatory.
- Women with irregular or infrequent menses may ovulate, but not consistently, and do not require specific diagnostic tests to prove what is already obvious.

Basal Body Temperature

- BBT is measured each morning, upon awakening and before arising.
- BBT is typically low and fluctuates between during the follicular phase of the cycle, modestly but distinctly higher (0.4–0.8 degrees) during the luteal phase, and falls again to baseline levels just before or after the onset of menses.

BBT

- The ideal BBT recording is distinctly biphasic and reveals a cycle between 25 and 35 days in length, with menses beginning 12 days or more after the rise in temperature.

Serum Progesterone Concentration

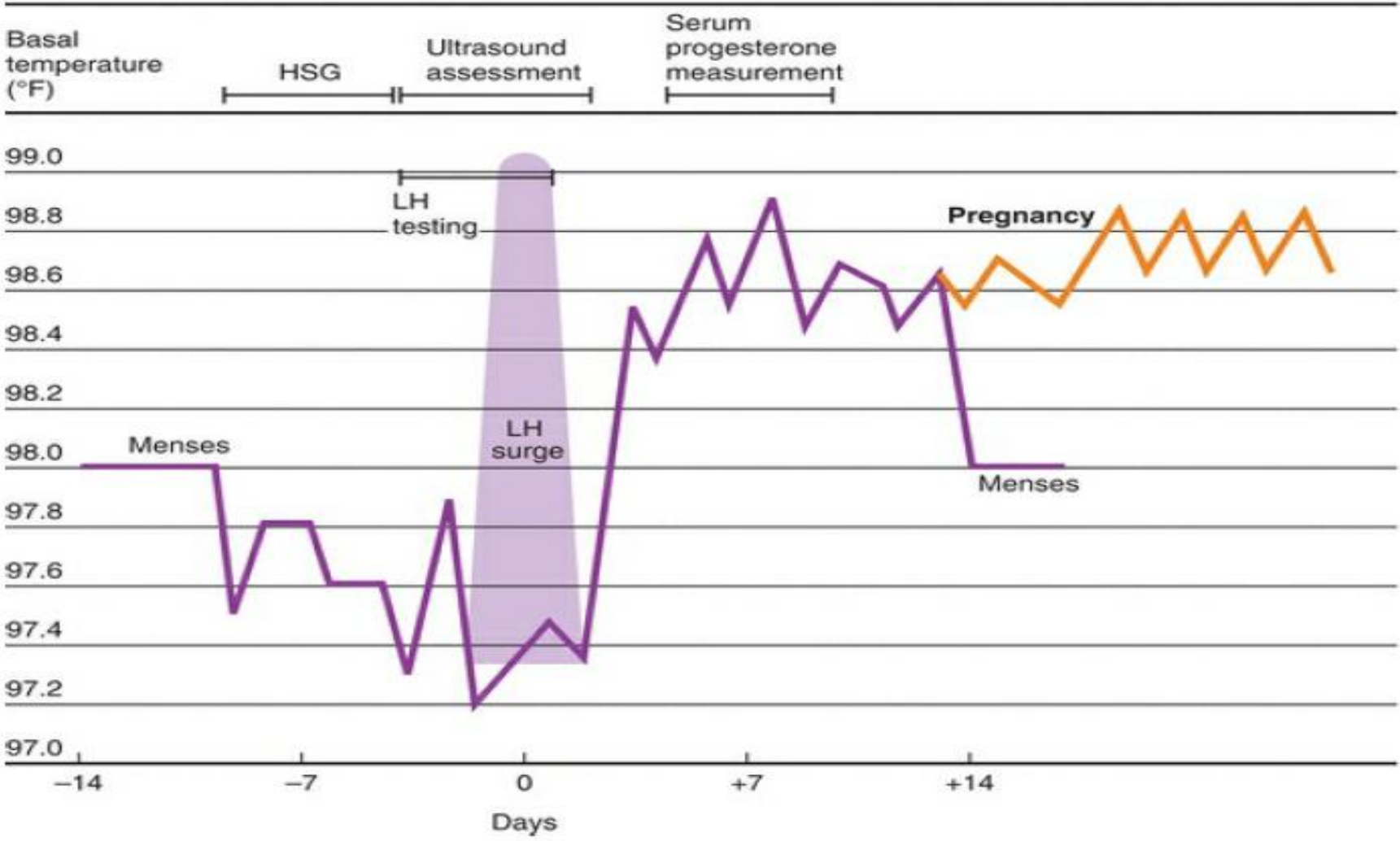
- A progesterone concentration less than 3 ng/mL implies anovulation, except when drawn immediately after ovulation or just before the onset of menses, when lower levels naturally might be expected.
- The serum progesterone level should be drawn approximately 1 week before the expected onset of menses, when the concentration is at or near its peak.
- The best time to test will vary with the overall length of the menstrual cycle, aiming for approximately 1 week before the expected menses

Urinary LH Excretion

- The midcycle LH surge is a relatively brief event, typically lasting between 48 and 50 hours from start to finish. LH has a short half-life and is rapidly cleared via the urine.
- Ovulation predictor kits turn positive when the urinary LH concentration exceeds a threshold level normally seen only during the LH surge.
- Beginning 2 or 3 days before the surge is expected, based on the overall length of the cycle.
- The first positive test provides all relevant information

LH SURGE

- Ovulation generally occurs 14–26 hours after detection of the LH surge and almost always within 48 hours.
- Consequently, the interval of greatest fertility includes the day the surge is detected and the following 2 days
- The day after the first positive test generally is the one best day for timed intercourse or insemination


Basal temperature (°F)
HSG
Ultrasound assessment
Serum progesterone measurement
99.0
98.8
98.6
98.4
98.2
98.0
97.8
97.6
97.4
97.2
97.0
LH testing
Pregnancy
Menses
LH surge
Menses
−14
−7
0
+7
+14
Days

Endometrial Biopsy and Luteal Phase Deficiency

- In the absence of treatment with exogenous progesterone or a synthetic progestin, a secretory endometrium implies recent ovulation.
- Histologic endometrial dating cannot guide the clinical management of women with reproductive failure and has no place in the diagnostic evaluation of infertility.

Transvaginal Ultrasonography

- The preovulatory follicle grows approximately 2 mm per day (range: 1–3 mm/day).
- After ovulation, the follicle collapses, margins become less distinct, the density of internal echoes increases, and the volume of cul-de-sac fluid increases.

- When confirm ovulatory function, as in those with regular monthly menses, a properly timed serum progesterone concentration is the simplest and most reliable method.
- When circumstances require accurate prediction of ovulation, as in couples having infrequent intercourse or those requiring insemination, urinary LH monitoring generally is the most cost-effective and appropriate choice.
- In the few who require insemination but consistently fail to detect a mid cycle LH surge, serial TVUS can provide the necessary information

- Estrogen during the follicular phase,mucus becomes more abundant and watery, less cellular, and more easily penetrated by sperm.
- Progesterone inhibits cervical mucus production and renders it opaque, viscid, and impenetrable.

- Abnormal post coital test results were common, usually due to improper timing
- The best time was 2 days before the LH surge when TVUS demonstrated a preovulatory follicle.
- Other explanations for poor-quality mucus were cervicitis, previous treatment for cervical intraepithelial neoplasia (cryotherapy), and treatment with clomiphene citrate.
- The post coital test for diagnosis of cervical factor is no longer recommended.

UTERINE FACTOR: ANATOMIC AND FUNCTIONAL ABNORMALITIES

- The anatomic uterine abnormalities that can adversely affect fertility include :congenital malformations, leiomyomas, and intrauterine adhesions; endometrial polyps
- The only functional uterine abnormality of specific interest in the evaluation of infertility is chronic endometritis.
- There are three basic methods for evaluation of the uterine cavity: HSG, TVUS or saline sono hysterography, and hysteroscopy.

Hysterosalpingography

- HSG accurately defines the size and shape of the uterine cavity, provides clear images of most uterine developmental anomalies (unicornuate, septate, bicornuate, and didelphys),also identifies submucous myomas and intrauterine adhesions that can have important reproductive implications.
- HSG had 75% sensitivity for detection of intrauterine adhesions and only 50% sensitivity for detection of endometrial polyps.

Transvaginal Ultrasonography and Saline Sonohysterography

- TVUS is another method for evaluation of uterine factors in infertile women.
- Saline sonohysterography, involving TVUS during or after introduction of sterile saline through a catheter designed for the purpose

- During the proliferative phase, the endometrium is relatively hypo echoic and grows in thickness to yield a prominent “triple line” or trilaminar pattern. prominent “triple line” or trilaminar pattern.
- During the secretory phase, the endometrium grows little more, and increases in echodensity

- In the diagnostic evaluation of infertile women, trans vaginal ultrasonography can identify important uterine pathology but provides no useful measure of endometrial function or receptivity.

- For identification of congenital :TVUS+HSG
- 3D ultrasonography showed 100% specificity and sensitivity for diagnosing congenital uterine anomalies in two studies, and its concordance with specificity and sensitivity of laparoscopy and hysteroscopy

Hysteroscopy

- Hysteroscopy is the gold standard method for both diagnosis and treatment of intrauterine pathology that may adversely affect fertility.

Congenital Uterine Anomalies

- Developmental uterine anomalies have long been associated with pregnancy loss and obstetric complications
- The prevalence of uterine anomalies in infertile women and fertile women with normal reproductive outcomes is similar, approximately 2–4%.

- Septate uterus was the most common anomaly among infertile women (3%), followed by arcuate (2%), bicornuate (1.1%), unicornuate (0.5%), and didelphys (0.3%).
- Septate uterus is the anomaly most highly associated with reproductive failure and obstetrical complications, including first- and second-trimester miscarriage, preterm delivery, fetal mal presentation, intrauterine growth restriction, and infertility.

- Hysteroscopic septum resection is
- Women over age 35
- Women with infertility of long duration
- Women with other indications for surgical treatment, and women who require IVF or other treatments
- Increased risk of multi fetal gestation and pregnancy loss.

Uterine Myomas

- Displacement of the cervix
- Decreasing exposure to sperm
- Enlargement or deformity of the uterine cavity
- Interfering with sperm transport Obstruction of the interstitial segment of the fallopian tubes
- Distorted adnexal anatomy, Distortion of the uterine cavity or increased or abnormal myometrial contractions, inhibiting sperm or embryo transport
- Impaired uterine blood flow, chronic endometritis, or decreased endometrial receptivity, interfering with implantation

- Submucous myomas reduce IVF success rates by approximately 70%
- Intramural myomas by approximately 20–40%
- Subserosal myomas have no adverse impact on outcomes
- Submucous myomas increase risk for miscarriage after successful IVF at least threefold and intramural myomas by more than half.
- The careful selection of patients most likely to benefit from myomectomy is far more important than the choice of surgical technique.

Intrauterine Adhesions (Asherman Syndrome)

- Intrauterine adhesions can be asymptomatic or cause menstrual disorders(hypomenorrhea, amenorrhea, dysmenorrhea), pain, recurrent miscarriage, or infertility.
- The inability to pass a uterine sound, or a negative progestin challenge in amenorrheic women suggest the diagnosis.
- When suspected, HSG and saline sonohysterography confirm the presence of intrauterine adhesions.

Endometrial Polyps

- Molecular mechanisms have been implicated in their pathogenesis
- Endometrial hyperplasia
- Overexpression of endometrial aromatase and gene
- Saline sonohysterography is the most useful method of imaging for detection of endometrial polyps

- Polypectomy may improve reproductive performance in infertile women.
- Treatment must be individualized, depending on the size of a polyp, associated symptoms, and circumstances leading to its discovery.

- Tubal factor: Tubal occlusion and adenexal adhesion (PID), septic abortion, ruptured appendix, tubal surgery, or ectopic pregnancy strongly suggests the possibility of tubal damage.
- Proximal tubal obstruction is essentially an all-or-none phenomenon
- Distal tubal occlusive disease exhibits a spectrum ranging from mild (fimbrial agglutination) to severe (complete obstruction).

- HSG and laparoscopy are the two classic methods for evaluation of tubal patency in infertile women
- Sono hysterography is recognized as having greater sensitivity than HSG for detection of intrauterine pathology.
- Chlamydia antibody tests can be as accurate as HSG or even laparoscopy for detection of tubal pathology

Tubal Surgery in the Era of ART

- The decision between surgery and IVF should be based on the following:
- The age of woman
- Ovarian reserve
- Prior fertility status
- Number of children desired
- Site and extent of tubal damage
- Presence or absence of other factors necessitating IVF
- Surgeon's experience
- Success rate of IVF program
- Patient preference, that is, religious belief, cost, and insurance coverage for each option

UNEXPLAINED INFERTILITY

- The diagnosis of unexplained infertility implies
- Normal semen analysis,
- Normal ovulatory function
- Normal uterine cavity
- Unilateral tubal patency

- In summary, IVF is clearly the most effective treatment for couples with unexplained infertility, regardless whether it is the first or the last treatment.

Thank you

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