APPROACH TO INFERTILE COUPLES

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- Approximately 85-90% of healthy young couples conceive within 1 year, most within 6 months.

- Infertility therefore affects approximate 10-15% of couples and is an important part of the practice of many clinicians.

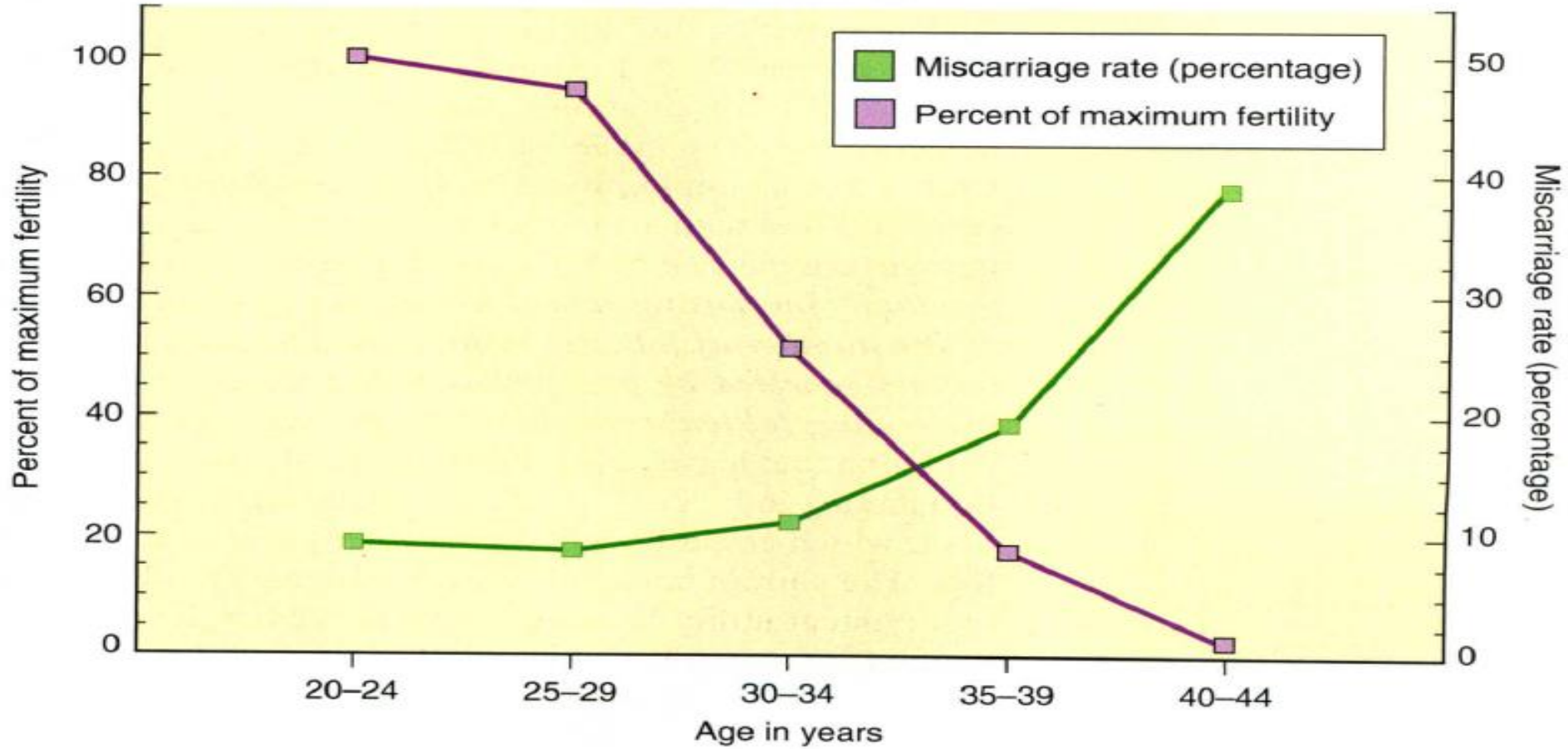
- *Fecundability* is the probability that a cycle will result in pregnancy

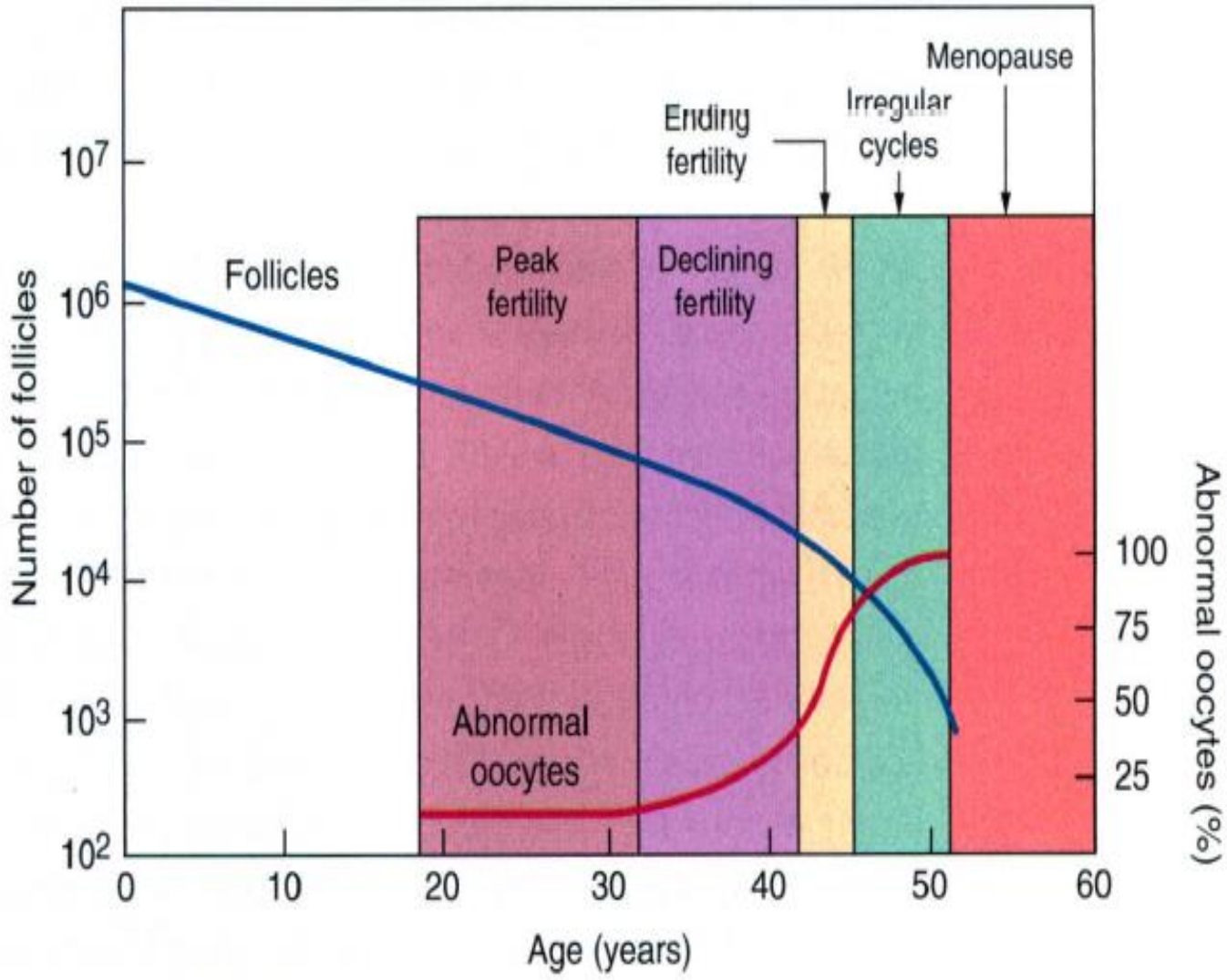
- *Fecundity* is the probability that a cycle will result in a live birth.

Aging and Fertility

- fertility in women peaks between the ages of 20 and 24, decreases relatively little until approximately age 30 to 32, and then declines progressively.

Aging and Reproduction in Women





Adapted from[17, 156]

miscarriage rates were:

- below 15% for women under age 35
- almost 30% at age 40
- and over 50% for women age 44 and older.

Aging and the Uterus

- Aging does not appear to have any significant adverse effect on the uterus.
- Although the prevalence of benign uterin pathology (leiomyomata, endometrial polyps, adenomyosis)increases with age,little evidence exists to indicate it has much overall impact on fertility in women.

Aging and Male Fertility

- Modest age-related decreases in semen volume, sperm motility, and morphologically normal sperm, but not sperm density, have been observed.

- *the available evidence indicates that pregnancy rates decrease and time conception increases as male age increases.*

- *However, because there is little decline in male fertility before age 45-50, male factors contribute little to the age-related decline in fertility.*

Ovarian Reserve Tests

- Like all screening tests, ovarian reserve tests are aimed at identifying individuals at risk for "diminished ovarian reserve" (DOR).

Basal FSH and Estradiol

- The basal FSH concentration is the simplest and still most widely applied measure of ovarian reserve.

- *FSH levels greater than 10 lU/L (10-20 lU/L) have high specificity (80-100%)for predicting poor response to stimulation.*

- In a 2008 study, FSH concentration above 18 lU/L had 100% specificity for failure to achieve a live birth.

Antimullerian Hormon (AMH)

- Antimullerian hormone (AMH) is produced by the granulosa cells of preantral and small antral follicles.

- *AMH is a very promising screening test for DOR.*

- *Low threshold values(0.2-0.7 ng/mL) have good specificity for poor response to ovarian stimulation.*

Antral Follicle Count (AFC)

- The antral follicle count (AFC; total number of antral follicles measuring 2-10 mm in both ovaries) thus provides an useful measure of ovarian reserve.

- A low AFC (threshold value of 3 to 4 follicles) has high specificity for predicting poor response to ovarian stimulation and treatment failure.

ovarian reserve testing can best be justified for women with any of the following characteristics:

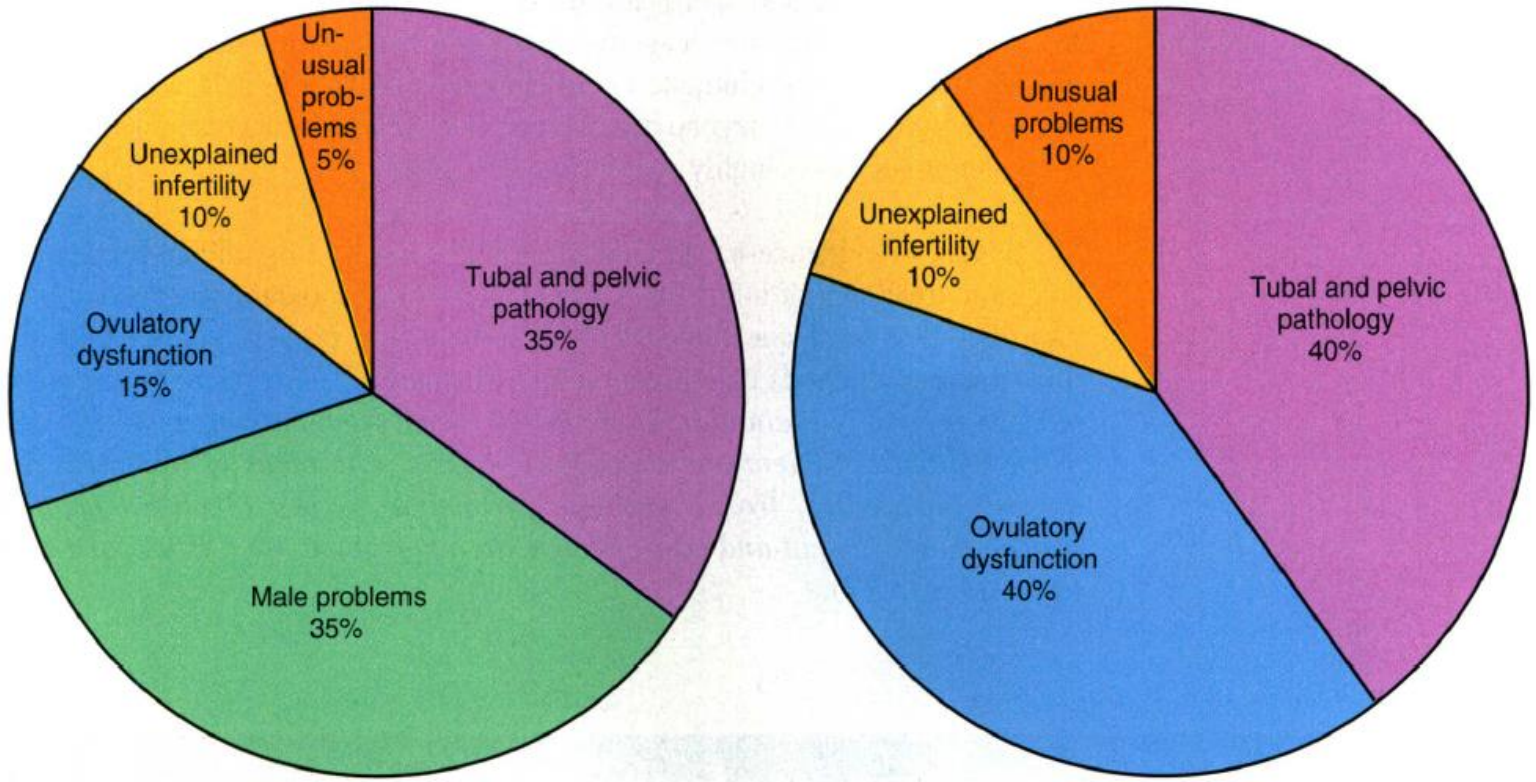
1. Age over 35.
2. Unexplained infertility.
3. Family history of early menopause.
4. Previous ovarian surgery (ovarian cystectomy or drilling, unilateral oophorectomy), chemotherapy, or radiation.
5. Smoking.
6. Demonstrated poor response to exogenous gonadotropin stimulation.

Guiding Principles for Evaluation and Treatment of Infertility

- From the beginning, the evaluation of infertility should focus on the *couple* and not on one or the other partner, regardless of past reproductive performance.

Time Required for Conception Among Couples Who Will Attain Pregnancy[342]	
Months of Exposure	*% Pregnant*
3 months	57%
6 months	72%
1 year	85%
2 years	93%

Causes of Infertility



Couples **Women**

- *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, but an oocyte can be fertilized successfully for only approximately 12-24 hours after ovulation.*

- *Consequently, virtually all pregnancies result from intercourse occurring sometime within the 6-day interval ending on the day of ovulation.*

The prevalence of each cause of infertility varies with age.

- Ovulatory dysfunction is more common in younger than in older couple
- tubal and peritoneal factors have a similar prevalence
- male factors and unexplained infertility are observed somewhat more often in older couples.

Indications for Evaluation

- *Evaluation should be offered to all couples who have failed to conceive after a year or more of regular unprotected intercourse, but a year of infertility* is *not a prerequisite for evaluation.*

Earlier evaluation is *justified for women*

- *with irregular or infrequent menses,*
- *history of pelvic infection or endometriosis,*
- *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.*

Preliminary Evaluation of the Infertile Couple

- Any evaluation of infertility must begin with a careful history and physical examination, which often will identify symptoms or signs that suggest a specific cause and help to focus evaluation on the factor(s) most likely responsible.

History

- Gravidity, parity, pregnancy outcomes and associated complications.
- 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.
- Past surgery, its indications and outcome, and past or current medical illnesses, including episodes of pelvic inflammatory disease or exposure to sexually-transmitted infections.

- Previous abnormal pap smears 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 character.
- Signs of androgen excess.
- Pelvic or abdominal tenderness, organ enlargement, or mass.
- Vaginal or cervical abnormality, secretions, or discharge.
- Mass, tenderness, or nodularity in the adnexa or cul-de-sac.

Male Factor

- male factors explain or contribute significantly to infertility in up to 35% of couples.
- Semen analysis is therefore always an appropriate and important initial step in the evaluation of the infertile couple.

Transvaginal Ultrasonography

- The last and most complicated test of ovulation involves serial transvaginal ultrasonography (TVUS), which permits direct observation of events in the ovary just before and immediately after ovum release.

- Serial TVUS provides detailed information about the size and number of preovulatory follicle and the most accurate estimate of when ovulation occurs.

Uterine Factor

- Abnormalities of the uterus are a relatively uncommon cause of infertility, but should always be considered.

- If for no other reason, they may adversely affect the outcome of pregnancies achieved by successful treatment of male, ovarian, and tubal factors.

- There are basic methods for evaluation of the uterine cavity:

1. hysterosalpingography,
2. transvaginal ultrasonography
3. saline sonohysterography
4. hysteroscopy

- Each has advantages and disadvantages and the choice among them should be tailored to the needs of the individual patient.
- HSG is the traditional method and most often still the best initial test because it also evaluates tubal patency.

Congenital Uterine Anomalies

- *Developmental uterine anomalies have long been associated with pregnancy loss and obstetric complications, but affected women generally are not infertile.*

- The prevalence of uterine anomalies in infertile women and fertile women with normal reproductive outcomes is similar, approximately 2-4%.

- The prevalence of uterine anomalies is higher among women with recurrent miscarriage (10-13%).

- septate uterus is the most common anomaly (35%), followed by bicornate (26%), arcuate (18%), didelphys (8%), and agenesis (3%).

- *In women with a septate uterus and recurrent pregnancy loss, live birth rates are approximately 10% before hysteroscopic septum resection and 75-80% after surgery, indicating that hysteroscopic metroplasty restores an almost normal prognosis for term delivery*

Uterine Myomas

- Myomas can be identified in 20-40% of all reproductive aged women and in 5-10% of infertile women.
- myomas are the only abnormal finding in 1-2% of women with infertility.

- *submucous myomas reduce IVF success rates by approximately 70%, intramural myomas by approximately 30%, and subserosal myomas have no adverse impact on outcomes.*

- *Submucous myomas increase risk for miscarriage after successful IVF at least 3-fold, and intramural myomas by more than half.*

Endometrial Polyps

- Polips are generally rare in young women and increase in incidence with age.

- The overall prevalence of polyps in infertile women ranges between 3% and 10%

- 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 on the circumstances leading to its discovery.*

Tubal Factor

- Tubal and peritoneal pathology is among the most common causes of infertility and the primary diagnosis in approximately 30-35% of both younger and older infertile women.

- *A history of pelvic inflammatory disease (PID), septic abortion, ruptured appendix, tubal surgery, or ectopic pregnancy strongly suggests the possibility of tubal damag*

- HSG and laparoscopy are the two classic methods for evaluation of tubal patency in infertile women; each provides information the other does not and each has advantages and disadvantages.

- HSG images the uterine cavity and reveals the internal architecture of the tubal lumen, neither of which can be evaluated by laparoscopy.
- Laparoscopy provides detailed information about the pelvic anatomy that HSG cannot, including adhesions, endometriosis and ovarian pathology.

Hysterosalpingography (HSG)

- HSG is best scheduled during the 2-5 day interval immediately following the end of menses, to minimize risk for infection and to prevent any possibility that the procedure might be performed after conception.

- *Treatment with antibiotics (doxycycline 100 mg twice daily for 5 days, beginning 1-2 days before HSG) is prudent when tubal disease is highly suspected.*

laparoscopy

- Laparoscopy is regarded generally as the definitive test for the evaluation of tubal factors.

- Issues concerning scheduling, the use of antibiotics, and the risks of infectious complications are the same as for HSG.

Unexplained Infertility

- Unexplained infertility is a diagnosis of exclusion, after systematic evaluation fails to identify a cause.
- The incidence of unexplained infertility ranges from 10% to as high as 30% among infertile populations, depending on diagnostic criteria

- *The diagnosis of unexplained infertility implies evidence of normal semen quality, ovulatory function, a normal uterine cavity, and bilateral tubal patency.*

- In the past, the diagnosis also required laparoscopy (excluding pelvic adhesions and endometriosis), but laparoscopy is no longer performed routinely, with unexplained infertility.

- Instead, transvaginal ultrasonography is performed to detect unsuspected ovarian pathology, such as endometriomas.

- much of infertility previously attributed to cervical factors, luteal phase deficiency, and mild endometriosis or adhesions is now "unexplained."

- Unexplained infertility likely represents the abnormalities of sperm or oocyte function, fertilization, implantation, or embryo development that cannot be detected reliably by standard methods of evaluation.

- before treatment is recommended, an ovarian reserve test also is prudent.

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