Reviewed By
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Video Case

Infertility

Objectives:

- → Define primary and secondary infertility.
- → List the causes of male and female infertility.
- → Describe the evaluation and initial management of an infertile couple.
- → Describe the psychosocial issues associated with infertility.
- → Describe management options for infertility.
- → Describe ethical issues confronted by patients with infertility.
- → Identify the impact of genetic screening and testing of infertility associated treatments.
- → Identify the normal value of male semen analysis.
- → List the types of assisted reproductive technologies.

- → Slides
- → Important
- → Golden notes
- → Extra
- → 439 Doctor's notes
- → 441 Doctor's notes
- → 441 Female Presentation
- → Reference

Female presentation

Video Case | Editing File

Infertility

What is infertility:

- The inability to achieve pregnancy with frequent, unprotected and regular (twice a week) sexual intercourse for 12 months (in normal people) in women <35 OR 6 months in women ≥35 y/o.
    - Both male and female factors have to be evaluated in patients with infertility.
- **Fecundability** is the likelihood of conception occurring with one cycle of appropriately timed mid-cycle intercourse. With the female partner age 20, the fecundity rate is 20%(1). By age 35, the rate drops to 10%.

Factors that may contribute to infertility:

- Medical problems
- Ethical
- Financial
- Psycho-social

Who's responsible:

- Male 20%
- Female 65%
- Unexplained 15%

Male Infertility	
Causes	**Detection for good sperms**
• **Male factor (30%):** - decreased sperm count (Oligospermia) - decreased motility (Asthenospermia) - low normal forms (Teratospermia) Check note 3 from 441dr • **Unexplained (15%)** • **Unusual problems (5%)**	• **Semen analysis:** Abnormal ⟶ Repeat ⟶ Abnormal again? ⟶ refer to be assisted by urologist or reproductive endocrinologist.

Female Infertility	
Causes	**Detection for good oocyte**
• **Ovulatory dysfunction (20%)** – anovulation due to: PCOS, Thyroid disorders, age and hyperprolactinemia. • **Tubal and pelvic (30%)** ⟶ Endometriosis, pelvic adhesions, pelvic inflammatory diseases and abdominal or pelvic surgeries • **Unusual problems (5%)** ⟶ Uterine anomalies but in case of: Abnormal bleeding, pregnancy loss, preterm delivery, previous uterine surgery. Uterine assessment must be done. • **Unexplained (15%)**.	• **History of regular menses** suggest ovulatory cycles. • **Ovulation predictor kit:** To asses ovulation based on the increase LH production which can be detected by urine. • **Basal body temperature charting:** Women can monitor her ovulation by checking her daily body temperature which is the effect of high levels of progesterone during the luteal phase of the cycle.

1. 28-30% in young patients.

Initial Non-invasive Tests

Semen Analysis:

- The **first step** in the infertility evaluation is a semen analysis, which should be obtained **after 2–3 days of abstinence** and examined **within 2 h.**

Normal values

- volume >2 ml.
- pH 7.2–7.8.
- sperm density (count) >20 million/ml. (>15 million)
- sperm motility >50%.
- sperm morphology >50% normal. (~4% normal)

If values are abnormal, repeat the semen analysis in 4–6 weeks because semen quality varies with time.

Minimally abnormal

- **If**: sperm density is mild to moderately lower than normal, then **try: intrauterine insemination** → washed sperm are directly injected into the uterine cavity.
- Idiopathic oligozoospermia is the most common male infertility factor.

Severely abnormal

- **If**: semen analysis shows severe abnormalities, then **try**: intracytoplasmic sperm injection in conjunction with in vitro fertilization and embryo transfer.

No viable sperm

With azoospermia or failed ICSI, artificial insemination by donor (AID) may be used.

Anovulation:

- Of all causes of infertility, treatment of anovulation results in the greatest success.

History

irregular, **unpredictable** menstrual bleeding, most often associated with **minimal or no uterine cramping.**

Objective data

A basal body temperature (BBT) chart will **not show** the typical mid cycle **temperature elevation.**
A serum **progesterone** level will be **low**.
An **endometrial biopsy** shows **proliferative** histology.

Correctable causes

Hypothyroidism or **hyper**prolactinemia
PCOS

Initial Management of an Infertile couple

Ovulation Induction:

2nd, 3rd and fourth days do tests and investigations (mid period prolactin) ما أسوي شي

1. **The agent of choice is <u>clomiphene citrate</u>** (Selective estrogen receptor modulator) administered orally for 5 days beginning on day 5 of the menstrual cycle.
2. **<u>HMG</u>**: administered parenterally and used to induce ovulation if clomiphene fails.

- Careful monitoring of ovarian size is important because ovarian hyperstimulation is the most common major side effect of ovulation induction.
- Both Clomiphene and HMG work by stimulating the ovaries to increase follicular development.
- Clomiphene carries 10% risk of multiple gestation and HMG 25%.
- When a patient is given clomiphene, her own pituitary is being stimulated to secrete her own gonadotropins, whereas when a patient is administered HMG, the patient is being stimulated by exogenous gonadotropins.

3. **<u>Intrauterine insemination:</u>** Ejaculated semen is washed and introduced to uterine cavity by a catheter.

Assisted reproductive technologies :

- In vitro fertilization(IVF): 30% risk of multiple gestation.

○ **Indications**:

1. Blocked or absent fallopian tubes .
2. History of tubal sterilization.
3. Severe pelvic adhesions.
4. Severe endometriosis.
5. Poor ovarian response to stimulation.
6. Severe male factor infertility.
7. Failed treatment with less aggressive therapies.

- **Preimplantation genetic diagnosis:**

○ Genetic profiling of embryo prior to implantation; if the couple know that they are carriers of any inherited disease such as: cystic fibrosis or tay-sachs disease embryo can be tested for this prior implantation.

- **Psycho-social stress:**

Both normal? Ask the male (can you do anything under stress?) ^for erectile dysfunction^.

○ Social support that patients receive can have significant effect in stress level. Compared to white & Asian women black women are less likely to report encouragement for treatment from their partners & family members.

FOLLOW-UP INVASIVE TESTS

- Assessment of fallopian tube abnormalities is the next step if the semen analysis is normal and ovulation is confirmed.

Hysterosalpingogram (HSG) Wait 20 min to be sure	• A catheter is placed inside the uterine cavity, and contrast material is injected and the contrast material should be seen on x-ray images spilling bilaterally into the peritoneal cavity. • It should be scheduled during the week after the end of menses after prophylactic antibiotics to prevent causing a recurrent acute salpingitis. • No further testing is performed if the HSG shows normal anatomy. • If abnormal findings are seen, the extent and site of the pathology are noted and laparoscopy considered.
Laparoscopy	• If potentially correctable tubal disease is suggested by the HSG, the next step in management is to visualize the oviducts and attempt reconstruction if possible (tuboplasty). • If tubal damage is so severe surgical therapy is futile, then IVF should be planned.
Chlamydia antibody	• A negative IgG Antibody test for chlamydia virtually rules out infection induced tubal adhesions.

UNEXPLAINED INFERTILITY

- A diagnosis of unexplained fertility is reserved for couples in which the semen analysis is normal, ovulation is confirmed, and patent oviducts are noted.
- Approximately 60% of patients with unexplained infertility will achieve a spontaneous pregnancy within the next three years.

Management:

- Controlled ovarian hyperstimulation (COH) with clomiphene, and appropriately timed preovulatory intrauterine insemination (IUI).
- The fecundity rates for six months are comparable with IVF with a significantly lower cost and risk.
- With IVF, eggs are aspirated from the ovarian follicles using a transvaginal approach with the aid of an ultrasound.
- They are fertilized with sperm in the laboratory, resulting in the formation of embryos. Single embryo transfer is recommended for most patients to avoid iatrogenic high-order multiple pregnancy.

FOLLOW-UP INVASIVE TESTS

Ovarian reserve testing (ORT):

- Mostly reserved for infertile women age ≥35.
- Refers to assessment of the capacity of the ovary to provide eggs that are capable of fertilization.
- It is a function of:
  - The number of follicles available for recruitment.
  - The health and quality of the eggs in the ovaries.
- Help predict whether a woman will respond to ovarian stimulation or whether it would be best to proceed directly to in vitro fertilization (IVF).
- The most significant factor affecting ORT is a woman's chronological age, with a major decrease around age 35.

Day 3 FSH level (most commonly used)	• Is expected to be low due to the feedback of estrogen from the stimulated follicles (normal!). • An increased FSH occurs if there is follicle depletion.
Anti-Müllerian hormone (AMH)	• This glycoprotein is produced exclusively by small antral ovarian follicles and is therefore a direct measure of the follicular pool. • As the number of ovarian follicles declines with age, AMH concentrations will decline.
Antral follicle count (AFC)	• Is the total number of follicles measuring 2–10 mm in diameter that is observed during an early follicular phase transvaginal sonogram. • The number of AF correlates with the size of the remaining follicle pool retrieved by ovarian stimulation. • AFC typically declines with age.

Teaching Case

A 37-year-old woman and her 37-year-old male partner present with the complaint of a possible fertility problem. The couple has been married for 2 years. The patient has a 4-year-old daughter from a previous relationship. The patient used birth control pills until one-and-a- half years ago. The couple has been trying to conceive since then and report a high degree of stress related to their lack of success. The patient reports good health and no problems in conceiving her previous pregnancy or in the vaginal delivery of her daughter who has cystic fibrosis. She reports that her periods were regular on the birth control pill, but have been irregular since she discontinued taking them. She reports having periods every 5-7 weeks. She works as a cashier, runs 12-24 miles each week for the last 2 years, and has no history of STIs, abnormal Paps, smoking, alcohol or other drugs. She has had no surgery. She has been taking a multivitamin with folic acid since trying to conceive. The patient's partner also reports good health and reports no problems with erection, ejaculation or pain with intercourse. He has had no prior urogenital infections or exposure to sexually transmitted infections. He has had unprotected sex prior to his current relationship, but has not knowingly conceived. He has no medical problems or past surgery. The couple has vaginal intercourse 3-5 times per week when he is at home. The female patient is 5'9" and weighs 130 pounds. Head and neck examination is unremarkable. Specifically there is no evidence of thyromegaly. Breast exam reveals no tenderness or masses, but she has bilateral galactorrhea on compression of the areola. Pelvic exam reveals normal genitalia, well-estrogenized vaginal mucosa and cervical mucus consistent with the proliferative phase. The uterus is anteflexed and normal in size without masses or tenderness. Several tests were ordered.

Question 1:What is the definition of infertility?

→ **Inability to become pregnant despite 12 months of trying to conceive without using contraception in women <35-years-old.**

→ **Six months of unprotected intercourse defines infertility in women 35 years and older** (due to sharp decline in fertility).

→ **About 15% of couples experience this problem.**

Question 2:What are the etiologies of infertility?

- It could be due to female factor, male factor or Mixed. However, Male factor is the commonest

Ovulatory dysfunction(20%) anovulation. PCOS	Male factor (30%) – decreased sperm count, decreased motility or low normal forms(morphology).	Tubal and pelvic (30%) tubal damage due to pelvic infection, or pelvic factors such as endometriosis or pelvic adhesions (scaring,blockage)	Unexplained (15%). Unusual problems (5%).

Question 3:What is the initial work-up for infertile couples and what tests would you add for this particular couple?

→ You have to be systematic, do the female factor respectively and male factor
→ **Ovarian reserve testing:**
→ (number one) Day 3 **FSH** 8.3 mIU/ml, **estradiol** <20 pg/ml, anti-müllerian hormone (**AMH**) 1.1 ng/ml which are considered normal , All hormonal profile **LH** also
→ Normal **TSH.**
→ **Prolactin** 60 ng/ml (normal range < 20 ng/ml).
→ **Evaluation for ovulation:** Progesterone (day 21) was 1.2 ng/ml (≥ 3 ng/ml will indicate ovulation).
→ **Hysterosalpingogram** demonstrated a normal uterine cavity with spill of radiopaque dye from both
→ fallopian tubes. The primary purpose is to assess the tubal patency which is the most important
→ function , secondary purpose is to assess the integrity of the uterine cavity.
→ **Saline infusion sonohysterography (SIS):** same as HSG but with the advantage of using ultrasound, can be done at the clinic and Avoiding the use of dye.
→ **Semen analysis** with 2 ml of semen (normal >1.5), 4 million sperm/ml (normal >15),20% motility (normal >40%), 2% normal morphology (normal >4%).
→ Discussion regarding frequency and timing of intercourse.
→ Could also review basal body temperature charting or have patient use ovulation Predictor kits.

Question 4:Offer genetic counseling and testing for cystic fibrosis mutations. Given the results of the tests, what is the differential diagnosis for the etiology(ies) of this couple's infertility?

→ Anovulation secondary to hyperprolactinemia from a potential prolactinoma
→ Oligospermia – repeat semen analysis once and consider referral to a urologist.

Question 5:What is the appropriate management for etiology of this couple's infertility?

→ Macoadenoma → refer to neurosurgery
→ Microdenoma → treat with dopamine

1. For anovulation secondary to a possible prolactinoma, the patient should have a head MRI to rule out a pituitary lesion.
   a. Treat with **Bromocriptine** to lower prolactin levels, which will usually result in regular ovulation.
   b. Or **Cabergoline** , it's the one used currently due to its specificity and less side effects
2. If she remains anovulatory after management of her prolactinoma with bromocriptine to normalize her prolactin level, ovulation induction may be offered with clomiphene citrate .
3. For oligospermia (remember to repeat the semen analysis) refer to a urologist for evaluation for correctable causes. (If severe better to refer to andrologist, unfortunately it's rare here in KSA) However, if oligospermia remains after evaluation and treatment then options include in vitro fertilization with intracytoplasmic sperm injection, intrauterine insemination with partner's sperm, intrauterine insemination with donor sperm, adoption.

Question 6:The husband elects to undergo testing for common cystic fibrosis mutations and is determined to be a carrier. What options are available to them to achieve a pregnancy that is less likely to lead to a child affected by cystic fibrosis? Discuss the ethical issues associated with these choices.

→ The couple could elect to use donor sperm or donor eggs. In both cases one of the parents would not be genetic parents.
→ The couple could elect to use IVF with preimplantation genetic diagnosis.
→ The couple could elect to achieve a pregnancy with none of the above techniques and accept a 1:4 risk of having a child affected with CF. They could elect to undergo antepartum testing (chorionic villi sampling, amniocentesis, etc.) to determine if the pregnancy is affected with CF.

437 notes:

Treatment steps :
1. Treat the underlying cause anovulation due to high prolactin give bromocriptine , if she has PCO give her oral contraceptives

2. If the patient wants to get pregnant from the first visit I will prescribe her folic acid.
3. Step two if she didn't get pregnant we give her clomiphene citrate
4. If she is not pregnant do IVF

Step 2 the doctor said it during the mentorship.

439 Dr. notes

- **(MCQ) Oocyte Count:**
  - In utero → ~2-7 Million
  - At birth → One million
  - At pube → 300-400 Thousand

- **Female infertility causes:**
  - Hypothyroidism → bc high TSH is similar to FSH&LH so it leads to -ve feedback
  - age → decreased oocytes count
  - hyperprolactinemia → -ve feedback (drugs,stress, breastfeeding, pregnancy, intercourse, tumor)
  - PID → contrast spillage & blockage of the tubes & adhesions & losing of the cilia function, could be caused by infections (e.g.Chlamydia) and STDs
    - Diagnosis by Hysterosalpingogram

- **Ovarian reserve and Ovulation testing**
  - Ovulation starts seven days prior to menstruation!
    - At Day 2-3 → measure FSH , LH and Estrogen levels
    - At 10-14 → use an Ovulation kit (analysing the LH surge) , also Basal Body temperature
    - At Day 21 → Progesterone (not done anymore)
    - ANYTIME → measure AMH
  - **Other fertility tests:** Prolactin, TSH , Hysterosalpingogram (HSG)

- **Ovulation Induction**
  - **1st** → Clomiphene Citrate (act by: stimulating the HBO axis allowing it to produce its own gonadotropins - indirectly stimulating the Ovarian follicles)
  - **2nd** → HMG (Purified FSH & LH from post-menopausal women's urine)
  - Intrauterine Insemination → with filtered sperms + HCG injections (to mimic the regular cycle)
  - **(MCQ)** The Fertilization occurs in the ampulla of the fallopian tube

441 Dr. notes

1. If patient comes with known case (eg. blockage tube) we start investigation immediately.
2. Couples are considered primary even if they have children from previous marriage (it's their first kid together).
3. No sperms (Azoospermia), decreased motility (asthenospermia)
4. Modalities of sperm movement:
   A. Normal
   B. Fast
   C. Local motion (يلف على نفسه)
   D. No movement
5. (A+B are the important ones >30%)
6. Do prolactin test, (if high) then do TSH, (if high) try to decrease it then the prolactin will decrease too.
7. Routine tests in clinic (FSH, LH, Prolactin, TSH)
8. We can stimulate the Oocyte with any hormone (FSH and LH) but LH is not used because FSH is better.
9. HSG is the only test for the tube nowadays.
10. (Day 3 FSH level) is more accurate than (Anti-müllerian hormon AMH) and (AFC)
11. Laparoscopy is the last choice due to invasivity and large duration of OR availability even for unexplained infertility start with everything fast (eg. IVF, Exy)

Reference

CHAPTER 34

Infertility and Assisted Reproductive Technologies

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CLINICAL KEYS FOR THIS CHAPTER

- Eighty to eighty-five percent of fertile couples will conceive after 1 year of frequent attempts. *Infertility* is defined as an undesired absence of fertility for 1 year despite frequent intercourse. About 10-15% of couples in the United States are infertile. Most infertility is subfertility, and relatively few couples are sterile.
- A steady decrease in fertility begins at about age 24 years (female partner), when the fecundity (live-birth) rate is about 22% per monthly cycle, and declines to about 5% per cycle by 40 years of age. Evaluation for infertility should begin before 1 year when the female partner's age reaches 35 years or there is an obvious problem such as oligomenorrhea (fewer than nine menstrual cycles per year).
- The known causes of infertility include male coital problems, anatomic problems involving the uterus and/or the fallopian tubes, peritoneal problems such as endometriosis and/or pelvic adhesions, and problems with the quantity or quality of cervical mucus. About 10-15% of couples are found to have unexplained infertility. Evaluation of infertility in women younger than 35 years of age should begin at 1 year.
- Evaluation of sperm quantity and quality, ovulatory function, normal reproductive anatomy, and cervical mucus should occur after history-taking and physical examination are completed. Because about 40% of infertile couples have more than one factor present, the evaluation should be complete so that a second or third factor is not overlooked and thus left untreated. Conventional treatment includes ovarian stimulation with or without intrauterine insemination, destruction of endometriosis when found, and possible surgical intervention for uterine or tubal disease. About 50-60% of couples will conceive with adequate conventional treatments.
- Assisted reproductive technologies include in vitro fertilization, intracytoplasmic sperm injection, embryo transfer without or with embryo freezing, and oocyte donation for women with abnormal or absent ovarian function. Up to 85% of couples will conceive with the addition of adequate advanced treatment.

About 10-15% of couples in the United States are involuntarily infertile. **Couples are considered infertile after unsuccessfully attempting to achieve pregnancy for 1 year.** Most of these couples are more accurately described as have varying degrees of subfertility, with some of them conceiving spontaneously during and after episodes of fertility treatment. New assisted reproductive technologies (ARTs), such as controlled ovarian stimulation with or without intrauterine insemination (IUI), in vitro fertilization (IVF) and embryo transfer, and intracytoplasmic sperm injection (ICSI), are increasing the success of treatment for infertility and subfertility.

Infertility and the Physiology of Conception

Infertility is termed *primary* when it occurs without any prior pregnancy and *secondary* when it follows a previous conception. Some conditions, such as azoospermia (absence of sperm), endometriosis, and tubal occlusion are more common in couples with primary infertility, but virtually all conditions occur in both primary and secondary infertility.

For successful conception to occur, the male and female gametes must join at the optimal stage of maturation, followed by transportation of the newly

TABLE 34-1

ETIOLOGIC FACTORS, DIAGNOSTIC TESTS, AND TREATMENT OPTIONS FOR INFERTILITY

Known Causes of Infertility	Diagnostic Tests and Procedures	Treatment Options	Comments
Male Factors (20-40%)	Semen analysis; testing for antisperm antibodies when suspected	IUI with washed sperm; IVF-ET with ICSI; donor insemination	Frequency of coitus without the use of toxic lubricants should be determined; paternal age could be a factor in miscarriage
Female Factors (50-65%)*			
Ovulation problems	Mid-luteal serum progesterone; LH predictor kits; serial ultrasounds	Clomiphene citrate or letrozole with or without hCG trigger for ovulation; lower-dose gonadotropins; IVF-ET; donor egg IVF-ET	Tests for ovulation are indirect and may be falsely positive; the only absolute proof of ovulation is pregnancy
Anatomic (uterine-tubal) problems	Hysterosalpingogram; saline infusion sonography; hysteroscopy; laparoscopy with chromotubation†	Tubal anastomosis to reverse sterilization procedures; tuboplasty for tubal damage; IVF-ET	When laparoscopy is performed, the tubes should be tested for patency; recent higher IVF-ET success rates make IVF-ET preferable to tubal surgery
Peritoneal problems (pelvic adhesions and endometriosis)	Laparoscopy with chromotubation† as part of infertility workup	Ablative procedures (electrocautery, laser) for endometriosis and lysis of adhesions; medical treatment for endometriosis (see Chapter 25); IVF-ET	Surgical removal of endometriomas may compromise ovarian reserve
Cervical mucus problems	Spinnbarkeit; postcoital test (Sims-Huhner); cultures for suspected infections	IUI with washed sperm; treatment for any detected infection	Postcoital test not performed by many practitioners, because of low predictive value
Unexplained Infertility (10-15%)	Laparoscopy to confirm diagnosis with negative findings	Ovarian stimulation; IVF-ET; donor insemination; donor IVF-ET; adoption	

hCG, Human chorionic gonadotropin; *ICSI,* intracytoplasmic sperm injection; *IUI,* intrauterine insemination; *IVF-ET,* in vitro fertilization and embryo transfer; *LH,* luteinizing hormone.
*Prevalence can vary in some populations due to differences in causes (e.g., infection or endometriosis).
†The use of a colored fluid such as indigo carmine to test for tubal patency.

BOX 34-1

IMPORTANT TERMS AND DEFINITIONS

- *Infertility:* Lack of fertility after 1 year of frequent attempts
- *Subfertility:* A decrease, but not an absence, of fertility potential
- *Sterility:* Complete inability to achieve fertility
- *Fecundity:* Probability of achieving a live birth in one menstrual cycle

use of an oil-based dye approximately doubled the success rate following HSG. Operative evaluation by laparoscopy is reserved for the small proportion of couples who have not conceived after 18 to 24 months or who have specific abnormalities or indications of a probable pelvic factor.

To keep the status of the evaluation in mind, it is helpful to arrange the workup under a series of five categories that can be mentally reviewed at each visit. Table 34-1 shows the approximate incidence and the tests involved in the evaluation of each factor. **In 10-15% of couples, no explanation can be found; their infertility is classified as unexplained.**

Etiologic Factors

MALE COITAL FACTORS

History

The evaluation of the male occurs early so that questions about coital frequency can be addressed and azoospermia or severe oligospermia or asthenospermia (low motility) can be identified. The history-taking from the male partner should cover any pregnancies previously sired; any history of genital tract infections, such as prostatitis or mumps orchitis; surgery or trauma to the male genitalia or inguinal region (e.g., hernia repair); and any exposure to lead, cadmium, radiation, or chemotherapeutic agents. Excessive consumption of alcohol or cigarettes or unusual exposure to environmental heat should be elicited. **Some medications, such as furantoins and calcium channel blockers, reduce sperm quality and/or function.**

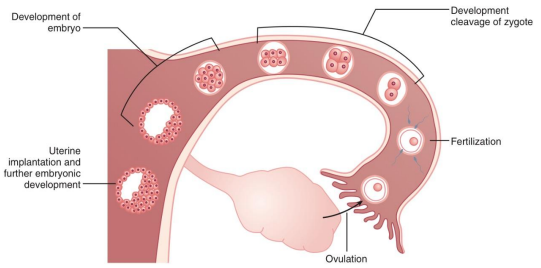

FIGURE 34-1 Sequence of events necessary for fertility: ovulation, fertilization, cleavage of zygote, continued embryo development, and implantation in the uterine cavity.

fertilized conceptus to the uterine cavity at a time when the endometrium is supportive of its continued development and implantation (Figure 34-1; see also Chapter 4). For these events to occur, the male and female reproductive systems must both be anatomically and physiologically intact, and coitus must occur with sufficient frequency for the semen to be deposited in close temporal relationship to the release of the oocyte from the follicle. **Even when fertilization occurs, it is estimated that more than 70% of resulting embryos are abnormal and fail to develop or become nonviable shortly after implantation.** According to the American Society for Reproductive Medicine (ASRM), early documented pregnancy loss (miscarriage) is considered a form of infertility when it is recurrent.

Considering the complexity of the reproductive process, it is remarkable that about **80-85% of couples achieve conception within 1 year.** More precisely, 25% conceive within the first month, 60% within 6 months, 75% by 9 months, and 90% by 18 months. The steadily decreasing rate of monthly conception demonstrated by these figures most likely reflects a spectrum of fertility extending from highly fertile couples to those with relative infertility (subfertility). After 18 months of unprotected sexual intercourse, the remaining couples have a low monthly conception rate without treatment, and many may have absolute defects that are preventing fertility (sterility). Table 34-1 lists the known causes of infertility as well as treatments for it, and Box 34-1 lists some important terms and definitions.

Evaluation of the Infertile Couple

Conception requires adequate function of multiple physiologic systems in both partners. **Infertility may result from either one major deficiency (e.g., tubal occlusion) or multiple minor deficiencies.** Failure to realize this important dictum may lead the inexperienced practitioner to overlook additional factors that might be more amenable to treatment than the one that has been identified. **Infertility in about 40% of infertile couples has multiple causes.** Therefore, for treatment to be most effective, a complete infertility evaluation should be performed for each couple. The psychological stress that is known to occur when conception is desired and is not occurring should not be overlooked or minimized. Participation in support groups such as **RESOLVE (www.resolve.org)** may help couples to cope with this stress and adjust to their situation. Couples should also be offered preconception counseling (see Chapter 7) and genetic screening for carrier status as part of their infertility care.

Age substantially decreases the rate of conception because of reduced embryo quality and likely reduced coital frequency. On the basis of a large study of donor insemination (ensuring proper timing of exposure), the strictly age-related reduction appears to be about one-third for women ages 35 to 45 years. It is reasonable to begin the basic evaluation at 6 months in older patients and to consider starting treatment for unexplained infertility earlier in women older than 35 years of age.

Evaluation and therapy may be started earlier (<1 year) when obvious defects are identified, or they may be delayed (e.g., when a correctable factor such as infrequent intercourse is identified).

In general, the first 6 to 8 months of evaluation involve relatively simple and noninvasive tests as well as the performance of a radiologic evaluation of tubal patency (hysterosalpingography [HSG]), which can sometimes have a therapeutic effect. **In some studies,**

Physical Examination

A physical examination is done upon referral to a urologist when semen analysis is abnormal. The normal location of the urethral meatus should be noted. An abnormal anatomic location could result in the deposition of semen in a less favorable location during intercourse. Testicular size should be estimated by comparison with a set of standard ovoids. The presence of a varicocele should be elicited by asking the patient to perform a Valsalva maneuver in the standing position.

Investigations

A semen analysis should be performed following a 2- to 4-day period of abstinence. The entire ejaculate should be collected in a clean, nontoxic container. Until relatively recently, the full range of normal variation was not appreciated. The characteristics of a normal semen analysis by percentile are shown in Table 34-2.

An excessive number of leukocytes (>10 per high-power field) may indicate infection, but special stains are required to differentiate polymorphonuclear leukocytes from immature germ cells. Semen quality varies greatly with repeated samples. **An accurate appraisal of abnormal semen requires at least three analyses.** Periodic reassessment is necessary.

Endocrinologic evaluation of the male with subnormal semen quality may uncover a specific cause. Hypothyroidism can cause infertility, but there is no place for the empirical use of thyroxine. **Low levels of gonadotropins and testosterone may indicate hypothalamic-pituitary failure. An elevated prolactin concentration may indicate the presence of a prolactin-producing pituitary tumor. An elevated level of follicle-stimulating hormone (FSH) generally indicates substantial parenchymal damage to the testes,** as inhibin, produced by the Sertoli cells of the seminiferous tubules, provides the principal feedback control of FSH secretion. A response to any treatment is unlikely in the presence of an elevated level of FSH. However, the level of FSH is not helpful in predicting whether sperm will be recovered with testicular sperm extraction.

TABLE 34-2

WORLD HEALTH ORGANIZATION REFERENCE VALUES FOR SEMEN CHARACTERISTICS

	Percentiles				
Characteristics	5th*	25th	50th	75th	95th
Semen volume (mL)	1.5	2.7	3.7	4.8	6.8
Sperm concentration (million/mL)	15	41	73	116	213
Total sperm (million/mL)	39	142	255	422	802
Total motility (%)†	40	53	61	69	78
Normal forms (%)	4	9	15	24.5	44

Data were generated from semen parameters of fertile men whose partners achieved a pregnancy within 12 months.
*Values in the 5th percentile are considered abnormal.
†Percentage of progressive plus nonprogressive.

Treatment

The couple should be advised to have intercourse approximately every 1 to 2 days during the periovulatory period (e.g., days 12 through 16 of a 28-day cycle). **Because infrequent coitus is a common contributing factor, firm advice in this regard can be beneficial.** This "scheduled intercourse" can be disruptive and stressful, however, and insemination using the husband's or partner's sperm may relieve considerable pressure on a couple.

The woman should be advised to lie on her back for at least 15 minutes after coitus to prevent rapid loss of semen from the vagina. Lubricants may be toxic to sperm. **A nontoxic lubricant, Pre-Seed, has been developed for infertile couples.**

For optimal fertility, smoking and the use of alcohol or marijuana should be reduced or, preferably, stopped. The use of saunas, hot tubs, or tight underwear should be discouraged, as should exposure to other environments that raise scrotal temperature, because these factors may affect spermatogenesis.

Low semen volume may provide insufficient contact with the cervical mucus for adequate sperm migration to occur. When a high semen volume coexists with a low count, infertility may result because a lower density of sperm contacts the cervical mucus. **At present, these abnormalities of volume (as well as other factors mentioned below) are most commonly treated with sperm washing and IUI. Figure 34-2 illustrates the method of IUI.**

If low sperm density (oligospermia) or low motility (asthenospermia) is caused by hypothalamic-pituitary failure, injections of human menopausal gonadotropins (hMGs) may be effective. The suppressive effects of **hyperprolactinemia** on hypothalamic function **can be reversed by the administration of a dopamine agonist such as bromocriptine or cabergoline. When low semen quality coexists with a varicocele** (dilation and incompetence of the spermatic veins), **improved semen quality, particularly motility, may occur with ligation of this venous plexus.** Various medications (clomiphene, human chorionic gonadotropin [hCG], testosterone, letrozole, and hMG) have been tried when no cause is apparent (idiopathic oligoasthenospermia), but none has proved consistently effective. Because approximately 3 months is required for spermatogenesis and sperm transportation to occur, frequent semen checks during treatment are unnecessary and serve only to discourage the patient.

Reference

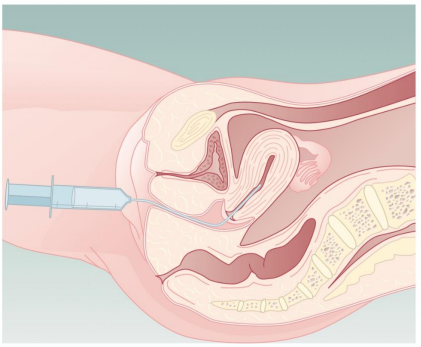

FIGURE 34-2 Illustration of the method of intrauterine insemination (IUI). Washed sperm are gently injected into the uterine cavity at the estimated time of ovulation. Untreated semen should not be used for IUI.

If semen quality cannot be improved, IUI with close timing of the insemination to the precise point of ovulation may be effective. By washing and concentrating the sperm into a small volume by centrifugation, large numbers of sperm can be placed into the uterus. When unwashed sperm is used it should be placed only on the cervix and not inside the uterus. Accurate timing may be accomplished either by measurement of daily luteinizing hormone (LH) concentrations or by controlled stimulation of the cycle with clomiphene or hMG, followed by administration of hCG when follicular diameter, as visualized by ultrasonography, indicates maturity. Insemination may then be carried out within a few hours of ovulation, which occurs 36 to 44 hours following the LH surge or hCG injection. When urinary LH testing is used, there is a delay of several hours between the onset of the surge and the positive urine test. It is advisable to test in the afternoon or evening, with insemination the following morning.

IVF is an effective treatment for the male factor because, with ICSI (intracytoplasmic sperm injection), only one motile sperm (with the tail removed) for each egg is required. Finally, insemination with donor sperm is effective when the male factor is refractory to treatment.

OVULATORY FACTORS

History

Most women with regular cycles (every 22 to 35 days) are ovulating, particularly if they have premenstrual molimina (e.g., breast changes, bloating, and mood change). Recent studies indicate reduced fecundity associated with very irregular cycles. A discussion of oligomenorrhea and its underlying causes is presented in Chapter 33.

Investigations

The simplest screening tests for confirming reasonably normal ovulation are serial measurement of urinary LH, which assesses the duration of luteal function, and the mid-luteal level of serum progesterone, which assesses the level of luteal function. The interval from the urinary LH surge to the onset of menses should be at least 12 days. An older test of ovulation, the basal body temperature, is now seldom used. A progesterone level of greater than 5 ng/mL indicates ovulatory activity, but mid-luteal concentrations usually exceed 10 ng/mL in cycles in which conception has occurred. Because of the marked pulsatile secretion of progesterone, a level between 5 and 40 ng/mL can be found in the normal luteal phase.

In spite of ovulation, an inadequate luteal phase may be responsible for infertility. **Endometrial biopsy, considered for many years to accurately reflect luteal function, has recently been shown to be a very imprecise test, causing most practitioners to abandon it as a tool for assessing ovulation.**

Treatment

Use of fertility drugs such as clomiphene citrate or gonadotropins will correct any luteal insufficiency in women with unexplained infertility.

In women whose menses are less frequent than every 35 days (oligomenorrhea), it is helpful to induce more frequent ovulation, thus increasing the opportunity for pregnancy and improving the ability to time coitus. Ovulation induction should always be preceded by a thorough workup for thyroid disease, hyperprolactinemia, and polycystic ovarian syndrome (PCOS) (see Chapter 33) because conditions causing anovulation (e.g., hypothyroidism) may be worsened by pregnancy or may complicate it. In addition, ovarian failure seldom responds to attempts to induce ovulation.

The choice of the most appropriate technique for ovulation induction is determined by the patient's specific diagnosis. With this approach, regular ovulation can be restored in more than 90% of anovulatory women. Provided that these patients persevere with treatment for an adequate period of time and no other infertility factors are present, their fertility should approximate that of normal women.

Pituitary insufficiency requires the injection of hMG (FSH and LH). Hypothalamic amenorrhea is caused by infrequent or absent pulsatile release of gonadotropin-releasing hormone (GnRH). GnRH is highly effective when administered in small pulses subcutaneously or intravenously in these patients every 90 to 120 minutes by using a small, portable infusion pump. Because this treatment is not currently available in the United States, hMG is used instead, but with a much higher risk of multiple pregnancy. **Hyperprolactinemia and its suppressive effect on the hypothalamus are specifically treated by use of dopamine agonists such as bromocriptine (Parlodel) or cabergoline (Dostinex).**

Most of the remaining patients with anovulation have some form of PCOS and generally respond to clomiphene, an orally active antiestrogen. Anovulation occurs in patients with polycystic ovaries because of chronic, mild suppression of FSH release. These women often have increased ovarian and adrenal androgen production. Clomiphene, by inhibiting the negative feedback effect of endogenous estrogen, causes a rise of FSH and stimulation of follicular maturation. One of the principal causes of excessive ovarian androgen production is higher circulating insulin concentrations because of insulin resistance. Metformin can also be used alone and may result in ovulation and pregnancy in some women. Recently, the aromatase inhibitor letrozole has been reported to be superior to clomiphene for ovulation induction, particularly in women with PCOS. Letrozole is currently not approved for this use by the U.S. Food and Drug Administration (FDA).

Other less frequently used treatments to induce ovulation in PCOS are laparoscopic "ovarian drilling," whereby multiple small craters are created by using a laser or cautery, and dexamethasone, which increases the ovarian response to clomiphene. Surgery is not often recommended, due to the possibility of causing scarring around the ovaries and tubes.

If ovulation does not occur with clomiphene or letrozole, follicular development may be occurring, but the normal LH surge may fail to occur. This results in lack of follicular rupture. **Assessment by serial pelvic ultrasonography and carefully timed hCG administration may lead to normal ovulation. If follicular maturation is not occurring, ovulation induction will require low-dose FSH or hMG.**

The main complications of ovulation induction are related to excessive stimulation of the ovaries. Substantial enlargement of the ovary with clomiphene citrate can generally be avoided by examining the ovaries before each treatment course and by using the lowest effective dose. Cystic ovarian enlargement is not an uncommon complication of hMG treatment, but it almost always regresses spontaneously. **The hyperstimulation syndrome is a serious illness associated with marked ovarian enlargement and exudation of fluid and protein into the peritoneal cavity.** The use of serum estradiol (E2) measurements, transvaginal ultrasonic scanning, and low-dose gonadotropin have greatly reduced the incidence of hyperstimulation syndrome. By starting at 50 to 75 U and increasing the dose by 25 to 50 U every 7 days if follicular maturation is not detected, a marked reduction in the incidence of multifollicular development, hyperstimulation, and multiple pregnancy can be achieved. **Multiple pregnancy occurs in 8-10% of clomiphene conceptions, with less than 1% of cases exceeding twins.** Multiple gestation occurs in 20-30% of hMG conceptions, and 5% of these conceptions are multiple births of more than two. Ultrasonic monitoring reduces this risk if the hCG is withheld in the presence of an excessive number of mature follicles. **Current use of a lower-dose regimen of hMG or pure FSH reduces the overall risk of multiple pregnancy to about 5%.**

CERVICAL FACTORS

During the few days before ovulation, the cervix produces profuse watery mucus (called ***spinnbarkeit***) that exudes out of the cervix to contact the seminal ejaculate. To assess its quality, the patient must be seen during the immediate preovulatory phase (days 12 to

FIGURE 34-3 The cervix produces profuse watery mucus during the few days before ovulation. The *spinnbarkeit* refers to the ability of the mucus to "stretch" at least 6.5 cm.

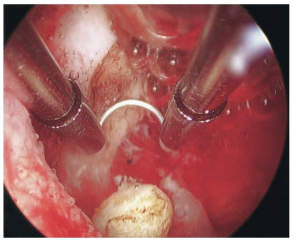

FIGURE 34-4 A significant submucosal polyp seen at the time of hysteroscopy.

14 of a 28-day cycle). Spuriously abnormal results can be reduced by timing the test to the morning after the urinary LH surge.

Investigations

The amount and clarity of the mucus is recorded. **The spinnbarkeit may be tested by touching the mucus with a piece of pH paper and lifting vertically. The mucus should extend in a thread to at least 6 cm (Figure 34-3).** The pH should be 6.5 or greater. **A postcoital (Sims-Huhner) test may be performed 2 to 12 hours after intercourse to assess the number and motility of spermatozoa that have entered the cervical canal.** The number of sperm, however, does not correlate well with semen quality, recovery of sperm from the cul-de-sac, or subsequent fertility. Consequently, the predictive value of this test for fertility is low, and many practitioners have abandoned this postcoital test. Empirical treatment with IUI for the cervical factor on a presumptive basis or when clomiphene is used (antiestrogenic effect) may avoid the morbidity and expense of injectable fertility drugs (gonadotropins).

Treatment

Any cervical infection should be treated by prescribing a 10-day course of doxycycline, 100 mg twice daily, for both partners. Persistent chronic cervicitis may be treated with cryotherapy if antibiotic treatment fails. Poor mucus quality can be treated with **washed sperm and IUI.**

UTERINE AND TUBAL FACTORS

Abnormalities of the uterine cavity are seldom the cause of infertility. Large submucosal myomas or endometrial polyps, as seen in Figure 34-4, may be associated with infertility and first-trimester spontaneous abortions (miscarriages). The role of intramural myomas is not clear, although myomectomy in some uncontrolled studies has been associated with conception in 40-50% of couples and some other studies with IVF have shown reduced conception with intramural myomas. Subserosal fibroids (see Figure 19-3) do not affect fecundity.

Tubal occlusion may occur at three locations: the fimbrial end, the mid-segment, or the isthmus-cornu. Fimbrial occlusion is by far the most common. Prior salpingitis is a common cause of tubal occlusion, although about one-half of cases are unassociated with any such history. Isthmic-cornual occlusion can be congenital or caused by mucus plugs, endometriosis, tubal adenomyosis, or prior infection. Mid-segment occlusion can be seen following surgery or infection with tuberculosis.

Investigations

Tubal abnormalities may be diagnosed by HSG (hysterosalpingography) or laparoscopy. To perform HSG, an occlusive cannula is placed in the cervix, and the instillation of a radiopaque dye is followed by image intensification under fluoroscopy. Selected radiographs are taken for permanent documentation (Figure 34-5). Anesthesia generally is not required. A water-soluble dye is used initially to confirm tubal patency because of the adverse effects of sequestration of an oil-based dye within the lumen of an occluded tube. If patency is confirmed, an oil-based dye (if available) may then be instilled because of its prominent therapeutic effect in women with unexplained infertility. If only one tube fills with dye, the HSG should be considered normal, as this finding is usually, although not

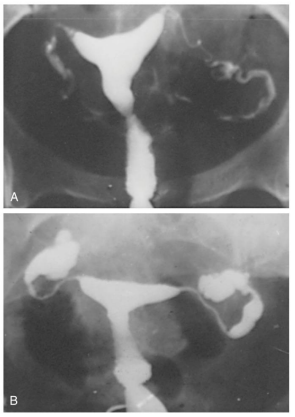

FIGURE 34-5 Normal hysterosalpingograms showing free spill of contrast material **(A)** and bilateral hydrosalpinges **(B)**.

invariably, caused by the dye following the path of least resistance.

Serious infections can result from HSG. A normal pelvic examination and prophylactic doxycycline should reduce this risk to a minimum.

Treatment

In most circumstances, microsurgical tuboplasty is more effective than conventional surgical techniques for reversal of tubal occlusion. About 60-80% of patients achieve pregnancy after reversal of sterilization using microsurgical techniques. Tubal anastomosis may be carried out laparoscopically, with good results in experienced hands.

When performed for fimbrial occlusion, neosalpingostomy is associated with a success rate of 20-30%, although it has reached 40% with long-term follow-up. Most often this is done by laparoscopy. Because a hydrosalpinx reduces the success rate of IVF by about 50%, any hydrosalpinx not repaired should be removed, or its communication with the uterus can be interrupted by using cautery or clips.

For an isthmic-cornual occlusion caused by disease, clearing the obstruction with oral danazol has been reported when the occlusion coexists with peritoneal endometriosis. Selective catheterization has restored patency in the majority of proximal occlusions and should be the first line of therapy. Microsurgical resection and reanastomosis is associated with a 50-60% pregnancy rate. **If the intramural portion of the tube is occluded, reimplantation is required, with a new opening made into the endometrial cavity.** A substantially lower rate of success is achieved in this circumstance; a laparotomy is required; and similar success can be achieved with a single cycle of IVF.

At least 10% of conceptions after repair of diseased tubes are ectopic pregnancies. Anastomosis of healthy tubes carries a risk of ectopic pregnancy of about 3-5%. This possibility must always be considered in the management of an early pregnancy following tuboplasty. As IVF and embryo transfer success rates continue to increase and costs decrease, this procedure may be preferred to tubal surgery in most cases.

PERITONEAL FACTORS

Laparoscopy identifies previously unsuspected pathologic conditions in about 30% of women with unexplained infertility. Endometriosis is the most common finding. Periadnexal adhesions may be found and may hold the fimbriae away from the ovarian surface or entrap the released oocyte.

Endometriosis may interfere with tubal motility, cause tubal obstruction, or cause adhesions that directly disturb the pickup of the oocyte by the fimbriae. Other mechanisms of endometriosis-associated infertility must exist as well, because even minimal endometriosis has some negative effect. In a randomized study of laparoscopic cautery versus no treatment for minimal endometriosis, treatment resulted in one of eight affected women conceiving. These same women, however, may conceive with other treatments used for unexplained infertility. **There is a strong trend toward omitting laparoscopy in women who have no symptoms indicating peritoneal disease and who have a normal pelvic examination, a normal HSG result, and a normal pelvic ultrasound.** A serum titer for antichlamydial antibodies may be helpful if this approach is taken, to avoid overlooking occult pelvic adhesions.

Treatment of endometriosis depends on its extent; this is discussed fully in Chapter 25. **If substantial adhesions or endometriomas are present, laparoscopic surgery is preferable because these conditions generally do not respond to medical management. With advanced operative laparoscopic techniques, most endometriosis can be removed or ablated** without laparotomy by using advanced instrumentation, lasers, or fulguration.

Reference

Danazol, GnRH analogues (agonists and antagonists), or oral medroxyprogesterone acetate are effective treatments for symptomatic disease, with continuous oral contraceptive therapy being generally inferior. If minimal disease with scattered implants is found, simple cautery at the time of laparoscopy should suffice.

Periadnexal adhesions may be lysed by operative laparoscopy. Microsurgical techniques diminish adhesions. The most effective adjunct in preventing recurrent scarring is the placement of an artificial tissue barrier, separating the raw surfaces during the early period of healing.

Because of the current high success rate with IVF, that treatment is very often given as an alternative to the above surgeries. It is particularly important to conserve ovarian function as much as possible. **IVF is preferable to removal of an endometrioma** because of the compromised ovarian function that often results from ovarian surgery.

Unexplained Infertility

No cause is found for infertility in 10-15% of patients who have documented ovulation, normal semen analyses, and a normal HSG result. The problem may be primarily one of sperm transportation because IUI with washed sperm appears to increase the rate of conception. Some studies have shown subtle abnormalities of follicular growth and ovulation, partly explaining the increased fecundity associated with fertility drugs.

In other cases, a defect in the ability of the sperm to fertilize the egg may be present because a lower rate of fertilization is noted in couples with unexplained infertility who undergo IVF compared with couples in whom there is a tubal cause for infertility. **Another male problem that may not be detected by routine evaluation is the presence of antisperm antibodies.**

Other possible mechanisms of unexplained infertility include minimal endometriosis and mildly reduced ovarian reserve (reduced number of normal oocytes without hormonal abnormalities such as elevated FSH levels).

IUI, usually with controlled ovarian stimulation (stimulation of multiple follicles with clomiphene citrate or letrozole and/or gonadotropins and hCG timing of insemination), is employed next. The final therapeutic option is IVF.

Assisted Reproductive Technologies

The last resort for infertile couples with any of the aforementioned factors and failure of lesser treatments is the procedure of IVF and embryo transfer (Figure 34-6). In most cases of tubal occlusion in which the rate of success with tubal repair is low (<30%), IVF is preferable to surgery because of the more rapid conception rate and the lower ectopic pregnancy rate (<3% vs. >6% following tubal surgery). **Even severe male factors can be effectively treated with IVF by using ICSI (intracytoplasmic sperm injection), with fertilization rates of 60-70% of injected oocytes and pregnancy rates similar to those of nonmale factor IVF (30-35%).**

TECHNIQUE

A GnRH analogue, such as the GnRH agonist (GnRH-a), is given to prevent premature LH release. It is commonly started in the mid-luteal phase or overlapped with an oral contraceptive. After ovarian suppression (with GnRH-a), **the ovaries are stimulated with FSH or hMG, or both,** on the second or third day of the next cycle. Follicular size is assessed by transvaginal ultrasonic scanning.

An injection of hCG (usually 10,000 U) is given on the basis of follicular size and estradiol levels to induce the resumption of meiosis and completion of oocyte maturation. Thirty-five hours after the hCG injection, multiple oocytes are aspirated under transvaginal ultrasonic guidance. An antagonist (which is the FDA-approved analogue for use in IVF) may be used instead of the agonist and has the advantage of then allowing an agonist to be used to trigger ovulation rather than using hCG as the trigger. This has been shown to reduce the incidence of ovarian hyperstimulaton in some studies.

After a further period of in vitro maturation, washed sperm are added or a single sperm is injected (ICSI) into each oocyte. **Fertilization may be identified 14 to 18 hours after insemination by the visualization of two pronuclei.** The conceptus is then transferred to the uterine cavity 2 to 4 days after oocyte retrieval (early transfer) or at 5 to 6 days (blastocyst stage) by means of a tiny catheter (see Figure 34-6). In some cases, the hatching process is aided by making an artificial opening in the zona pellucida ("assisted hatching"). **Surplus embryos not transferred at the time of the IVF treatment can be frozen, stored, and transferred in a later menstrual cycle in the event of failure or for additional pregnancies.** As freezing-and-thawing methods have improved, many programs are not transferring fresh embryos in highly stimulated cycles when egg retrieval occurs. This "freeze-all" method can allow for the performance of preimplantation studies. Selected embryos are then thawed and transferred in more physiologic cycles. This technique may have other advantages in terms of pregnancy complications and does not decrease the overall success rate (see Figure 34-6, *B*).

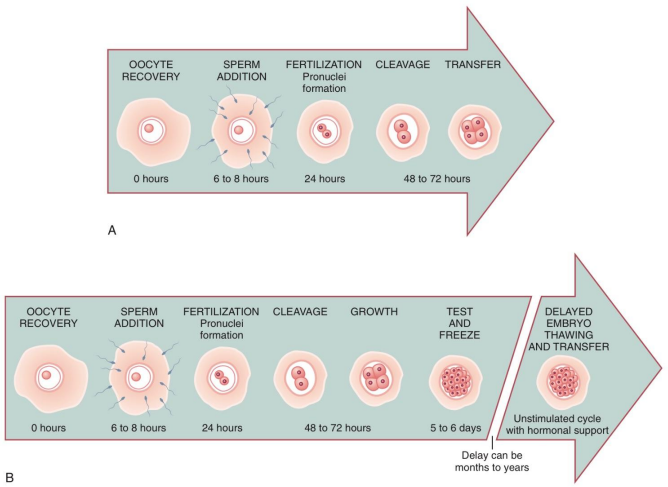

FIGURE 34-6 Approximate time-course for in vitro fertilization and embryo transfer in same cycle as stimulation **(A)** or delayed after embryo freezing and thawing **(B)**.

OUTCOMES

The pregnancy rate with IVF is highly variable from center to center because of the complexity of the techniques required, whereas the pregnancy rate with gamete intrafallopian transfer, a technique whereby oocytes and washed sperm are mixed and placed into the fallopian tube or tubes, is more consistent. **The mean live delivery rate per retrieval with IVF currently approximates 30-40%, with about 2-3% of pregnancies being ectopic. This rate of ectopic pregnancy is at least double the rate with spontaneous conceptions (about 1%). The site of the ectopic pregnancy may also be affected by ARTs.** Most studies have not shown any significant increase of fetal abnormalities when treated couples are compared with subfertile couples (not fertile ones) who conceive without fertility treatment.

EGG DONATION

It is possible to achieve pregnancy with IVF and embryo transfer using donor eggs. This has a higher success rate than regular IVF (approximately 50%). The eggs generally come from young fertile women (known or anonymous volunteers). The recipient can be programmed for optimal uterine receptivity by replacement doses of estradiol and progesterone. Estradiol and progesterone must be continued until the placenta takes over late in the first trimester. **The excellent success of egg donation mandates the conservation of the uterus whenever future fertility is desired, even if the ovaries must be removed.**

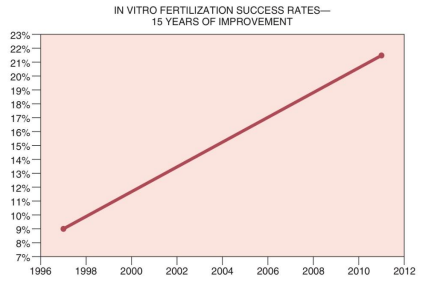

FIGURE 34-7 Average percentages of live-birth rates in women younger than 38 years of age resulting from nondonor, fresh embryo transfers from 1997 through 2011. (Data from Centers for Disease Control and Prevention (CDC), 1997-2012. Available from www.cdc.gov/art/reports/index.html.)

Overall Success of Infertility Therapy

Conventional therapies, when adequately performed, result in conception in about 50-60% of infertile couples, and the application of the advanced treatments described above should enable about 80-85% of couples who are infertile to conceive. The success rate of IVF as reported to the Centers for Disease Control and Prevention (CDC) has been improving each year, as shown in Figure 34-7.

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