



FIGURE 414-1 Causes of infertility. FSH, follicle-stimulating hormone; LH, luteinizing hormone.

function of age in women has led to recommendations that women >34 years old who are not at increased risk of infertility seek attention after 6 months, rather than 12 months as suggested for younger women, and receive an expedited work-up and approach to treatment.

APPROACH TO THE PATIENT: Infertility

INITIAL EVALUATION

In all couples presenting with infertility, the initial evaluation includes discussion of the appropriate timing of intercourse and discussion of modifiable risk factors such as smoking, alcohol, caffeine, and obesity. The range of required investigations should be reviewed as well as a brief description of infertility treatment options, including adoption. Initial investigations are focused on determining whether the primary cause of the infertility is male, female, or both. These investigations include a semen analysis in the male, confirmation of ovulation in the female, and, in the majority of situations, documentation of tubal patency in the female. In some cases, after an extensive workup excluding all male and female factors, a specific cause cannot be identified, and infertility may ultimately be classified as unexplained.

PSYCHOLOGICAL ASPECTS OF INFERTILITY

Infertility is invariably associated with psychological stress related not only to the diagnostic and therapeutic procedures themselves but also to repeated cycles of hope and loss associated with each new procedure or cycle of treatment that does not result in the birth of a child. These feelings are often combined with a sense of isolation from friends and family. Counseling and stress-management techniques should be introduced early in the evaluation of infertility. Importantly, infertility and its treatment do not appear to be associated with long-term psychological sequelae.

FEMALE CAUSES

Abnormalities in menstrual function constitute the most common cause of female infertility. These disorders, which include ovulatory dysfunction and abnormalities of the uterus or outflow tract, may present as amenorrhea or as irregular or short menstrual cycles. A careful history and physical examination and a limited number of laboratory tests will help to determine whether the abnormality is

(1) hypothalamic or pituitary (low follicle-stimulating hormone [FSH], luteinizing hormone [LH], and estradiol with or without an increase in prolactin), (2) polycystic ovary syndrome (PCOS; irregular cycles and hyperandrogenism in the absence of other causes of androgen excess), (3) ovarian (low estradiol with increased FSH), or (4) a uterine or outflow tract abnormality. The frequency of these diagnoses depends on whether the amenorrhea is primary or occurs after normal puberty and menarche (see Fig. 69-2).

The approach to further evaluation of these disorders is described in detail in Chap. 69.

Ovulatory Dysfunction In women with a history of regular menstrual cycles, evidence of ovulation should be sought (Chap. 412). Even in the presence of ovulatory cycles, evaluation of ovarian reserve is recommended for women age >35 years if they are interested in fertility. Measurement of FSH on day 3 of the cycle (an FSH level <10 IU/mL on cycle day 3 predicts adequate ovarian oocyte reserve) is the most cost-effective test. Other tests include measurement of FSH in response to clomiphene citrate (blocks estrogen negative feedback on FSH), antral follicle count on ultrasound, and anti-müllerian hormone (AMH); <0.5 ng/mL predicts reduced ovarian reserve although there is variability between labs).

Tubal Disease Tubal dysfunction may result from pelvic inflammatory disease (PID), appendicitis, endometriosis, pelvic adhesions, tubal surgery, previous use of an intrauterine device (IUD), and a previous ectopic pregnancy. However, a cause is not identified in up to 50% of patients with documented tubal factor infertility. Because of the high prevalence of tubal disease, evaluation of tubal patency by hysterosalpingogram (HSG) or laparoscopy should occur early in the majority of couples with infertility. Subclinical infections with *Chlamydia trachomatis* may be an underdiagnosed cause of tubal infertility and requires the treatment of both partners.

Endometriosis Endometriosis is defined as the presence of endometrial glands or stroma outside the endometrial cavity and uterine musculature and accounts for 40% of infertility not due to ovulatory disorders, tubal obstruction, or male factor. Its presence is suggested by a history of dyspareunia (painful intercourse), worsening dysmenorrhea that often begins before menses, or a thickened rectovaginal septum or deviation of the cervix on pelvic examination. Mild endometriosis does not appear to impair fertility; the pathogenesis of the infertility associated with moderate and severe endometriosis may be multifactorial with impairments of folliculogenesis, fertilization, and implantation, as well as adhesions. Endometriosis is often clinically silent, however, and can only be excluded definitively by laparoscopy.

MALE CAUSES (SEE ALSO CHAP. 411)

Known causes of male infertility include primary testicular disease, genetic disorders (particularly Y chromosome microdeletions), disorders of sperm transport, and hypothalamic-pituitary disease resulting in secondary hypogonadism. However, the etiology is not ascertained in up to one-half of men with suspected male factor infertility. The key initial diagnostic test is a *semen analysis*. Testosterone levels should be measured if the sperm count is low on repeated examination or if there is clinical evidence of hypogonadism. Gonadotropin levels will help to determine a gonadal versus a central cause of hypogonadism.

TREATMENT INFERTILITY

In addition to addressing the negative impact of smoking on fertility and pregnancy outcome, counseling about nutrition and weight is a fundamental component of infertility and pregnancy management. Both low and increased body mass index (BMI) are associated with infertility in women and with increased morbidity during pregnancy. Obesity has also been associated with infertility in men. The treatment of infertility should be tailored to the problems unique to each couple. In many situations, including unexplained infertility,