Klinefelter's syndrome; this diagnosis needs to be confirmed with a chromosomal karyotype. Testes that are more than 3.5 cm in longest diameter and that are either of normal consistency or are soft indicate postpubertal acquired primary hypogonadism.

If the major abnormality is a deficient sperm count with or without an elevation of FSH, differentiation between a ductal problem and acquired primary hypogonadism must be made. If spermatozoa are present, at least the ducts emanating from one testicle are patent; this condition indicates an acquired testicular defect. If the patient has no sperm in the ejaculate, a primary testicular or ductal problem may be responsible. The seminal vesicles secrete fructose into the seminal fluid. Therefore, the presence of fructose in the ejaculate should be followed by a testicular biopsy to determine whether the defect results from spermatogenic failure or from an obstruction of the ducts leading from the testes to the seminal vesicles. Absence of seminal fluid fructose indicates a congenital absence of the seminal vesicles and vas deferens.

Male Infertility

Infertility affects about 15% of couples, and male factors appear to be responsible in about 40% of cases. Female factors account for another 40%, and a couple factor is present in about 20% of cases. In addition to the defects in spermatogenesis that occur in patients with hypothalamic, pituitary, testicular, or androgen action disorders, hyperthyroidism, hypothyroidism, adrenal abnormalities, and systemic illnesses can result in defective spermatogenesis, as can microdeletions of genetic material on the Y chromosome. Disorders of the vas deferens, seminal vesicles, and prostate may also lead to infertility, as may diseases affecting the bladder sphincter that result in *retrograde ejaculation*, in which the sperm passes into the bladder rather than through the penis. Anatomic defects of the penis (as observed in patients with hypospadias), poor coital technique, and the presence of antisperm antibodies in the male or female genital tract also are associated with infertility.

Therapy for Hypogonadism and Infertility

Treatment of androgen deficiency in patients who have hypothalamic-pituitary or primary testicular abnormalities is best accomplished with exogenous testosterone administration—either intramuscular injection of intermediate-acting testosterone esters or transdermal testosterone patches or gel. Testosterone therapy increases libido, potency, muscle mass, strength, athletic endurance, and hair growth on the face and body. Side effects include acne, fluid retention, erythrocytosis, benign prostate hyperplasia, and, rarely, sleep apnea. This therapy is contraindicated in patients with cancer of the prostate.

If fertility is desired, patients with hypothalamic abnormalities may develop virilization and spermatogenesis with the use of GnRH delivered in a pulsatile fashion subcutaneously by an external pump. Direct stimulation of the testes in patients with hypothalamic or pituitary abnormalities may be accomplished with the use of exogenous gonadotropins, which increase testosterone and sperm production. If primary testicular failure is present and the patient has oligospermia, an attempt can be made to concentrate the sperm for intrauterine insemination or in vitro fertilization. If the azoospermia is caused by ductal obstruction, repair of the obstruction may be undertaken or aspiration of sperm from the epididymis may be accomplished for in vitro fertilization.

GYNECOMASTIA

Gynecomastia refers to a benign enlargement of the male breast that results from proliferation of the glandular component. This common condition is found in as many as 70% of pubertal boys and in about one third of adults 50 to 80 years old. Estrogens stimulate and androgens inhibit breast glandular development; gynecomastia results from an imbalance between estrogen and androgen actions at the breast tissue level. This condition may result from an absolute increase in free estrogens, a decrease in endogenous free androgens, androgen insensitivity of the tissues, or enhanced sensitivity of the breast tissue to estrogens. Table 65-2 lists the common conditions associated with gynecomastia.

Gynecomastia must be differentiated from fatty enlargement of the breasts without glandular proliferation and from other disorders of the breasts, especially breast carcinoma. *Male breast cancer* usually manifests as a unilateral, eccentric, hard or firm mass that is fixed to the underlying tissues. It may be associated with skin dimpling or retraction or with crusting of the nipple or nipple discharge. In contrast, gynecomastia occurs concentrically around the nipple and is not fixed to the underlying structures. Although physical examination is usually sufficient to differentiate gynecomastia from breast carcinoma, mammography may be required.

Painful and tender gynecomastia in a pubertal adolescent should be monitored with periodic examinations because, in most patients, pubertal gynecomastia disappears within 1 year. Incidentally discovered, asymptomatic gynecomastia in an adult requires a careful assessment for alcohol, drug, or medication

TABLE 65-2 CONDITIONS ASSOCIATED WITH GYNECOMASTIA

PHYSIOLOGIC CONDITIONS
Neonatal
Pubertal
Involutional
PATHOLOGIC CONDITIONS
Neoplasms
Testicular
Adrenal
Ectopic production of human chorionic gonadotropin
Primary gonadal failure
Secondary hypogonadism
Enzyme defects in testosterone production
Androgen insensitivity syndromes
Liver disease
Malnutrition with refeeding
Dialysis
Hyperthyroidism
Excessive extraglandular aromatase activity
Drugs
Estrogens and estrogen agonists
Gonadotropins
Antiandrogens or inhibitors of androgen synthesis
Cytotoxic agents
Efavirenz
Alcohol
Human immunodeficiency virus infection
Idiopathic