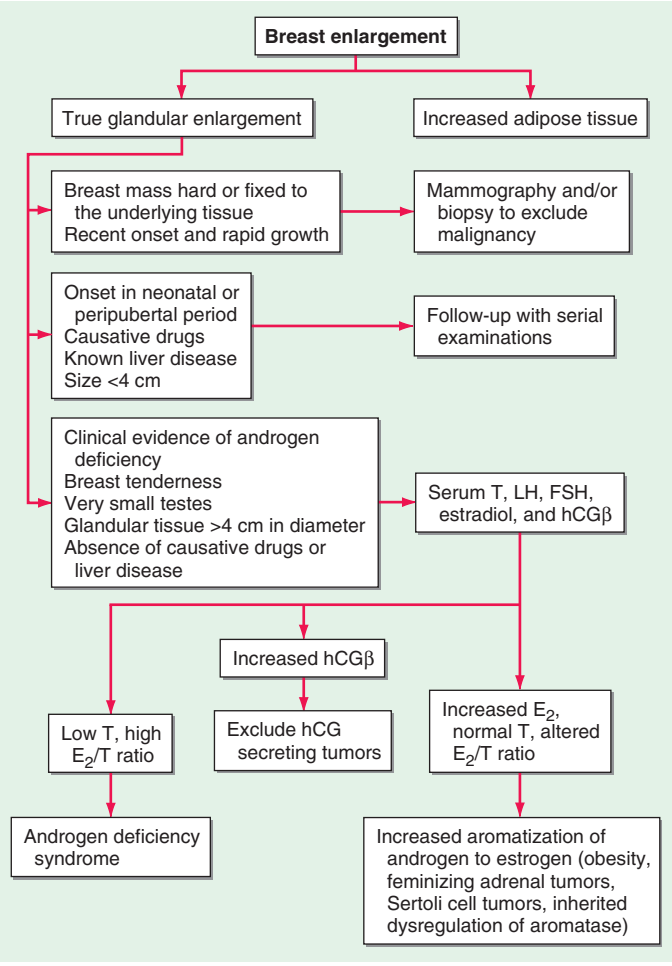

FIGURE 411-5 Evaluation of gynecomastia. E_2, 17β-estradiol; hCGβ, human chorionic gonadotropin β; T, testosterone.

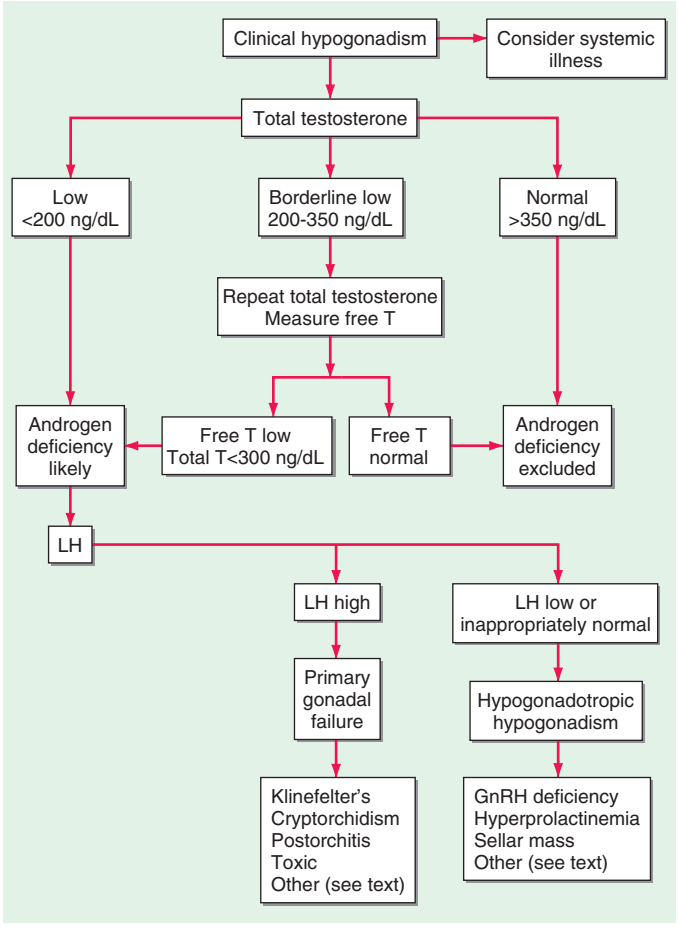

FIGURE 411-6 Evaluation of hypogonadism. GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone; T, testosterone.

whom surgery cannot be performed, treatment with antiestrogens such as tamoxifen (20 mg/d) can reduce pain and breast tissue size in over half the patients. Estrogen receptor antagonists, tamoxifen and raloxifene, have been reported in small trials to reduce breast size in men with pubertal gynecomastia, although complete regression of breast enlargement is unusual with the use of estrogen receptor antagonists. Aromatase inhibitors can be effective in the early proliferative phase of the disorder. However, in a randomized trial in men with established gynecomastia, anastrozole proved no more effective than placebo in reducing breast size. Tamoxifen is effective in the prevention and treatment of breast enlargement and breast pain in men with prostate cancer who are receiving antiandrogen therapy.

AGING-RELATED CHANGES IN MALE REPRODUCTIVE FUNCTION

A number of cross-sectional and longitudinal studies (e.g., The Baltimore Longitudinal Study of Aging, the Framingham Heart Study, the Massachusetts Male Aging Study, and the European Male Aging Study) have established that testosterone concentrations decrease with advancing age. This age-related decline starts in the third decade of life and progresses slowly; the rate of decline in testosterone concentrations is greater in obese men, men with chronic illness, and those taking medications than in healthy older men. Because SHBG concentrations are higher in older men than in younger men, free or bioavailable testosterone concentrations decline with aging to a greater extent than total testosterone concentrations. The age-related decline in testosterone is due to defects at all levels of the hypothalamic-pituitary-testicular axis: pulsatile GnRH secretion is attenuated, LH response to GnRH is reduced, and testicular response to LH is impaired. However, the gradual rise of LH with aging suggests that testis dysfunction is the main cause of declining androgen levels. The term *andropause* has been used to denote age-related decline in testosterone concentrations; this term is a misnomer because there is no discrete time when testosterone concentrations decline abruptly. The approach to evaluating hypogonadism is summarized in Fig. 411-6.

In epidemiologic surveys, low total and bioavailable testosterone concentrations have been associated with decreased appendicular skeletal muscle mass and strength, decreased self-reported physical function, higher visceral fat mass, insulin resistance, and increased risk of coronary artery disease and mortality, although the associations are weak. An analysis of signs and symptoms in older men in the European Male Aging Study revealed a syndromic association of sexual symptoms with total testosterone levels below 320 ng/dL and free testosterone levels below 64 pg/mL in community-dwelling older men. In systematic reviews of randomized controlled trials, testosterone therapy of healthy older men with low or low-normal testosterone levels was associated with greater increments in lean body mass, grip strength, and self-reported physical function compared with placebo. Testosterone therapy also induced greater improvement in vertebral but not femoral bone mineral density. Testosterone therapy of older men with sexual dysfunction and unequivocally low testosterone levels improves libido, but testosterone effects on erectile function and response to selective phosphodiesterase inhibitors have been inconsistent. Testosterone therapy has not been shown to improve depression scores, fracture risk, cognitive function, response to phosphodiesterase inhibitors, or clinical outcomes in older men. Furthermore, neither the long-term risks nor clinical benefits of testosterone therapy in older men have been demonstrated in adequately powered trials. Although there is no evidence that testosterone causes prostate cancer, there is concern that testosterone therapy might cause subclinical prostate cancers to grow. Testosterone therapy is associated with increased risk of detection of prostate events (Fig. 411-7).