

most accurate results will be obtained with these highly sensitive assays (5). Currently, many assays for gonadotropins lack the sensitivity to detect values below the normal range, unlike the modern thyrotropin assays for thyroid disease. Additional studies, such as gonadotropin-releasing hormone (GnRH) testing, by an endocrinologist may help in the further assessment of these patients.

Both FSH and LH are secreted in short pulses. FSH has a longer half-life than does LH and is more likely to provide adequate results on a single blood sample. In addition, most patients with progressive hypogonadism will have increased FSH levels well before LH levels increase. Because LH has a shorter half-life than does FSH, errors may be introduced in measurements made on single samples. Pooled samples for LH done 20 to 30 minutes apart are more accurate than single-sample determinations (albeit less convenient). Persistent borderline values may be further evaluated with dynamic endocrine testing. These tests may include the GnRH stimulation test, the clomiphene stimulation test, and the human chorionic gonadotropin (hCG) stimulation test. These specialized, dynamic studies should be conducted and interpreted by an endocrinologist and may have limited clinical value.

Dynamic Tests

GnRH Stimulation Test.—In the GnRH stimulation test (11,12), intravenous injection of 100 µg of GnRH causes serum LH levels to increase threefold to sixfold during a period of 30 to 45 minutes and FSH levels to increase between 20 and 50%. Various degrees of primary testicular failure cause higher than expected peak values for LH and FSH. Men with hypothalamic or pituitary disease may have a reduced or normal response that is often inadequate for distinguishing between a pituitary and a hypothalamic disorder. If the pituitary gland is primed with repeated doses of GnRH, this stimulation test may provide a more sensitive and reliable result.

Clomiphene Stimulation Test.—In the clomiphene stimulation test, 100 mg of clomiphene citrate is given for 5 to 7 days as an evocative test of the hypothalamic-pituitary axis. Clomiphene acts by interrupting the negative feedback loop and thereby stimulating release of gonadotropin from the pituitary. A doubling of LH and a 20 to 50% increase in FSH are normal results indicative of an intact hypothalamic-pituitary response (13).

hCG Stimulation Test.—Various protocols are used for hCG stimulation testing. In general for postpubertal male patients, a single dose of hCG (5,000 IU intramuscularly) is administered, and pretherapy and 72-hour posttherapy testosterone measurements are done (some protocols use 1,000 to 4,000 IU of hCG or multiday dosing) (14).

Prolactin Level

In men with acquired hypogonadotropic hypogonadism, who usually have a reduced libido and impotence,

a prolactin level should be determined to evaluate for the presence of a prolactinoma or other cause of hyperprolactinemia. High prolactin levels can reduce GnRH and testosterone levels. In addition, a high prolactin level can reduce libido and potency even in men treated with therapeutic doses of testosterone. About 5% of men who complain of impotence will have an increased prolactin level (15). Further endocrinologic evaluation with magnetic resonance imaging (MRI) scanning of the pituitary gland is indicated for unexplained hyperprolactinemia.

Semen Analysis

A semen analysis (12) is the primary test to assess the fertility potential of the male patient. Semen should be collected by masturbation after 2 to 5 days of abstinence and evaluated within 2 hours. Variability between specimens is common; with low or borderline samples, follow-up consisting of evaluation of three or more samples should be done during a 3-month period. A fertile sample is usually associated with a motility of more than 50% and a sperm count that exceeds 20 million/mL (16). In general, semen volume should range from 1.5 to 6 mL. Morphologic features should be examined for abnormalities.

A fructose test should be done on a semen sample showing azoospermia. Because fructose is secreted by the seminal vesicles, absence of fructose may indicate complete obstruction of the ejaculatory ducts or congenital absence of both vasa deferens and both ejaculatory ducts.

Most often, a semen analysis is done in an otherwise asymptomatic man during the course of an infertility evaluation. For such an assessment, a semen analysis should be done early to determine appropriate further evaluation and therapeutic options.

Other Studies

Bone Densitometry

Because hypogonadism frequently results in low bone density and increased fracture risk, baseline hip and spine bone densitometry studies should be performed to assess the initial situation and allow future interventions to be based on any deterioration in bone density that may occur over time. Such baseline studies are especially important in men treated for prostate cancer and rendered hypogonadal. In addition to addressing the underlying condition, treatment options to maintain bone mass may include testosterone therapy (but not in the setting of prostate cancer) or bisphosphonates. At present, alendronate has been approved by the US Food and Drug Administration (FDA) for use in osteoporosis in male patients. In addition, therapy should include sufficient calcium, exercise, and vitamin D. Anabolic agents, such as parathyroid hormone, may become therapeutic options in the future for men with osteoporosis. Regardless of treatment, bone density studies should be repeated in 1 to 2 years to determine whether bone mass is being appropriately maintained.