

DIAGNOSTIC EVALUATION FOR POSTPUBERTAL PATIENTS WITH HYPOGONADISM

Patient History

- Loss of libido
- Sexual dysfunction
- Low-volume ejaculate
- Impotence
- Use of medications, herbal preparations or OTC medications
- Possible exposure to diethylstilbestrol in utero
- Midline defects or cryptorchidism, anosmia or hyposmia (suggestive of Kallmann's syndrome)
- Genetic family history
- Rule out endocrine deficiencies

Physical Examination

- Amount and distribution of body hair (including beard, axillary and pubic)
- Male-pattern escutcheon (note ethnic origin)
- Gynecomastia
- Galactorrhea (suggestive of hyperprolactinemia and hyperestrogenism)
- Testes measured by Prader orchidometer or calipers (normal adult testes between 20-30 mL [vol] and 4.5-6.5 cm x 2.8-3.3 cm)
- Small and firm testes implies prepubertal damage; small and soft testes implies postpubertal damage
- Scrotal examination—presence of scrotal masses or varicoceles should be noted
- Penis length ranges from 10 to 17 cm; the width in the flaccid state > 3 cm
- Nonpalpable prostate suggests low testosterone

American Association of Clinical Endocrinologists Medical Guidelines for Clinical Practice for the Evaluation and Treatment of Hypogonadism in Adult Male Patients— 2002 Update

Adapted from AACE
Hypogonadism Task Force
Clinical Practice Guidelines

Evaluation and Treatment of Hypogonadism in Adult Male Patients

Current Clinical Situation:

- Men with hypogonadal disorders have symptoms that are often denied by the patient and ignored by the physician; physicians need to be aware of the disorder and to discuss these issues with their at-risk patients
- Decreased testosterone levels may increase the risk of osteoporosis, sexual dysfunction, fatigue, cardiovascular disease, and mood disturbances

Postpubertal Clinical Signs and Symptoms of Hypogonadism

- Progressive decrease in muscle mass
- Loss of libido
- Impotence
- Oligospermia or azoospermia
- Occasionally, menopausal-type hot flashes (with acute onset of hypogonadism)
- Poor ability to concentrate

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LABORATORY STUDIES: DETERMINE CAUSE/EXTENT OF HYPOGONADISM

Tests

- Testosterone (determined in morning, repeated if subnormal)
- Gonadotropins measured if low testosterone is established
- GnRH Stimulation Test
- Clomiphene Stimulation Test
- hCG Stimulation Test
- Prolactin Level
- Semen Analysis

Testing Parameters

- Hypogonadism stimulates production of high sex hormone-binding globulin (SHBG), which should be measured in addition to total hormone level. Measurement of total testosterone can be enhanced by measuring free testosterone index
- FSH has longer half-life and is more likely to provide adequate results in a single blood sample
- Injection of 100 µg GnRH causes higher than expected levels of LH (3- to 6-fold increase) and FSH (20% to 50% increase) in hypogonadism
- Clomiphene interrupts the negative feedback loop of the hypothalamic-pituitary axis and results in doubling LH and increasing FSH by 20%-50%
- hCG (5,000 IU intramuscularly); monitoring pre- and 72-hour post-testosterone levels
- Prolactin level may be evaluated for presence of prolactinoma; high prolactin levels can reduce GnRH, libido, and potency
- Semen analysis to assess fertility. A fertile sample is usually associated with a mobility of more than 50% and a sperm count that exceeds 20 million/mL. Normal volume is 1.5 to 6.0 mL. Absence of fructose suggests obstruction of ejaculatory ducts or congenital absence of both vasa deferens and both ejaculatory ducts

Additional studies: bone densitometry, pituitary imaging, genetic studies, testicular biopsy and scrotal exploration, and testicular ultrasonography. Refer to complete guidelines for recommendations.

TREATMENT RECOMMENDATIONS

Therapeutic Goals

- Restoration of sexual function, libido, well-being, and behavior
 - To reach physiological serum levels of testosterone between 280-800 ng/dL, along with physiologic ranges of dihydrotestosterone and estradiol
- Produce and maintain virilization
 - Testosterone therapy improves secondary sex characteristics such as increased muscle mass and growth of beard, pubic and axillary hair, and phallus growth
- Optimize bone density and improve osteoporosis
 - Marginal improvement of bone density is seen with testosterone replacement
- Possibly normalize growth hormone levels in elderly men
 - Testosterone treatment results in significant increase in 24-hour mean serum growth hormone value and mean growth hormone pulse amplitude
- Potentially affect risk of cardiovascular disease
- Restore fertility in cases of hypogonadotropic hypogonadism

TESTOSTERONE THERAPY

Testosterone Preparations

- FDA approval for clinical use: transdermal patches, scrotal patches, transdermal gels, orally administered agents, and IM preparations of testosterone
- Orally administered testosterone does not achieve sufficient physiologic blood levels over time and is not recommended for use in the United States
- Parenteral testosterone preparations (long-acting testosterone esters) achieve peak levels approximately 72 hours after IM injection, followed by a slow 1-2 week decline
- Scrotal patch delivery systems are convenient but costlier than IM
- Transdermal gel delivery systems show positive effects on libido and mood by about 30 days of therapy
- Gel preparations are well tolerated and associated with minimal skin irritation in comparison with testosterone patches

Contraindications

- Testosterone replacement is contraindicated in men with prostate cancer, male breast cancer, or untreated prolactinoma. Testosterone treatment can stimulate tumor growth in androgen-dependent neoplasms
- Symptomatic prostatism should be evaluated before testosterone treatment is considered
- Sleep apnea and polycythemia (which may lead to hyperviscosity) are relative contraindications
- Parental preparations of high-dose testosterone may provide the convenience of longer time intervals, but are associated with greater fluctuations in testosterone levels which may result in fluctuating symptoms in patients. Full virilization may take as long as 3-4 years
- Daily evening application generally results in normal serum testosterone levels which mimic normal diurnal changes in serum testosterone and, in contrast to scrotal patches, achieve normal dihydrotestosterone and estradiol levels
- Testosterone treatment tends to reduce sperm count and testicular size and should not be used in men currently seeking fertility