

## Hormone Replacement, Hypogonadism, and ADAM

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## DESCRIPTION

Hypogonadism and ADAM Male hypogonadism, also known as Testosterone Deficiency Syndrome (TDS), results from a failure of the testes to produce adequate androgen. This syndrome is characterized by low circulating levels of androgens, most often decreased bioavailable testosterone. The diagnosis of hypogonadism relies on the combination of laboratory measurements of serum testosterone and clinical signs and symptoms of androgen deficiency. Decreased libido is the symptom most often associated with hypogonadism, but patients may also exhibit fatigue, Erectile Dysfunction (ED), and body composition changes. A patient may have normal libido, sexual function, and energy levels despite having low testosterone levels. Such asymptomatic men can be a diagnostic challenge to the clinician. Discrepancies among hypogonadal men arise not only from different individual thresholds to the actions of testosterone, but also from the varying etiologies that underlie hypogonadism. Primary hypogonadism, or hypergonadotropic hypogonadism, is characterized by low levels of circulating androgens despite high levels of pituitary gonadotropins, and is often referred to as primary testicular failure. Klinefelter's syndrome (47,XXYor mosaic 46,XY/47,XXY) is the classic example of primary hypogonadism. Interestingly, some patients may have normal testosterone levels but have low bioavailable testosterone levels due to elevated estrogen and Sex-Hormone Binding Globulin (SHBG) levels. However, Luteinizing Hormone (LH) is usually elevated and Follicle-Stimulating Hormone (FSH) is markedly elevated in these patients. Other causes of primary testicular failure range from infection and trauma to drug use and exposure to chemotherapeutic agents or radiation. Chemotherapy is a well-known cause of azoospermia, although many cases are temporary and reproductive function is usually recovered over time. Secondary hypogonadism, or hypogonadotropic hypogonadism, generally refers to conditions

resulting from decreased release of LH and/or FSH with the defect being in the hypothalamus or the pituitary. Kallman's syndrome is a congenital hypogonadal syndrome with delayed pubertyanosmia, and midline facial defects resulting from impaired migration of Gonadotropin-Releasing Hormone (GnRH)-releasing neurons to the hypothalamus during the embryonic period. Idiopathic hypogonadotropic hypogonadism results in a similar clinical picture. Any damage to the hypothalamus or pituitary before puberty can result in low gonadotropin levels. Infection, tumors, exposure to radiation, surgery, and infarction of the hypothalamus or pituitary gland can lead to low levels of gonadotropins and resultant hypogonadism. For example, elevated prolactin secretion from pituitary prolactinomas causes a decrease in gonadotropin secretion and subsequent hypogonadism. Androgen deficiency of the aging male (ADAM) is a cause of secondary hypogonadism that often goes unrecognized. This phenomenon of hypogonadism due to aging has also been described as testosterone deficiency syndrome, late-onset hypogonadism, and andropause. Symptoms of this condition resemble those of 'normal' aging and include changing body composition (osteopenia, increased adiposity, decreased muscle mass), decline in energy and stamina, decreased cognitive function, decreased libido, and erectile dysfunction [American Society for Reproductive Medicine Practice Committee]. Testosterone levels in men begin to decline in the late third or early fourth decade and diminish at a constant rate thereafter. Longitudinal studies, such as the Massachusetts Male Aging Study, suggest that total testosterone decreases at a rate of about 1.6% annually, with a concomitant 1.3% annual increase in SHBG after age 40.The fraction of circulating testosterone that is bound to SHBG is inactive, so its increase results in even lower levels of bioavailable testosterone. An estimated 30% of men aged 7079 have low serum total testosterone and approximately 70% have low bioavailable testosterone levels

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