

## Hypogonadism, Male

### Clinical Background

Hypogonadism is one of the most common endocrine disorders in men, and is characterized by low serum testosterone levels with clinical signs and symptoms of the disease and/or low sperm counts.

#### Epidemiology

- Prevalence
  - Estimated 4-5 million men in U.S. have hypogonadism
  - 20% of men  $\geq 60$  or older have hypogonadism
  - Frequency increases with obesity, type II diabetes mellitus and aging

#### Etiologies

- Primary (pathology in testes)
  - Autoimmune orchitis
  - Chemotherapy
  - Cryptorchidism
  - Dysgenetic testes
  - Klinefelter syndrome
  - Mumps orchitis
  - Myotonic dystrophy
  - Orchiectomy
  - Radiation
- Secondary (pathology in pituitary)
  - Alcohol abuse
  - Cushing syndrome
  - Drugs (corticosteroids, opiates)
  - Hyperprolactinemia
  - Iron overload
  - Pituitary lesions
  - Severe chronic illness (cancer, chronic liver disease, chronic renal disease, rheumatoid arthritis, diabetes mellitus and obesity)
  - Other genetic mutations
- Tertiary (pathology in hypothalamus)
  - Kallman syndrome
  - Prader-Willi syndrome
- Age-related hypogonadism (pathology in testes and hypothalamus)

#### Pathophysiology

- Gonadotropin-releasing hormone (GnRH) is secreted from the hypothalamus
- GnRH stimulates the release of leuteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the pituitary
- LH promotes secretion of testosterone from Leydig cells
- FSH stimulates spermatogenesis and inhibin B production from Sertoli cells inhibits FSH
- 2% of circulating testosterone is free; 98% is bound
  - 60% bound to albumin
  - 40% bound to sex hormone binding globulin

- Bioavailable testosterone = free testosterone plus albumin bound testosterone
- Substantial alterations in sex hormone binding globulin affect total testosterone level
  - Free testosterone and bioavailable testosterone levels more accurately reflect bioactive testosterone under these circumstances

#### Clinical Presentation

- Manifestations depend on the following:
  - Age of onset of hypogonadism
  - Duration of deficiency
  - Profoundness of deficiency
- Pre-pubertal/pubertal hypogonadism
  - Eunuchoidal body habitus
  - Gynecomastia
  - Small testes
  - Lack of secondary sexual characteristics
- Postpubertal hypogonadism
- Weakness
  - Decreased libido
  - Depressed mood
  - Impotence
  - Normal penile size
  - Low bone mineral density
  - Gynecomastia
  - Muscle loss
  - Abdominal adiposity

#### Treatment

- Androgen replacement

## Diagnosis

- Indications for testing – signs and symptoms of hypogonadism
- Laboratory testing
  - Screen with serum testosterone concentration (preferably between 8-10 am)
    - For children, use mass spectrometry assay
    - For adult males, use radioimmunoassay (mass spectrometry not necessary) – <300 ng/dL suggests hypogonadism
  - If total testosterone is abnormal, may consider testing for free testosterone concentrations – helpful in determining bioavailable testosterone
  - FSH/LH to differentiate between primary and secondary etiologies
    - Primary – FSH and LH are elevated
    - Secondary – LH decreased or normal
- Imaging studies
  - Testosterone <150 ng/dL – consider MRI for pituitary imaging and if LH is normal to low prolactin may be increased
    - Expect to see low LH and normal prolactin in these patients

Differential Diagnosis

- Pituitary lesions
- Dementia
- Hypothyroidism adrenal tumor
- Depression
- Diabetes mellitus
- Hemochromatosis
- Cystic fibrosis

**Lab Tests**

**Indications for Laboratory Testing**

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at [www.aruplab.com](http://www.aruplab.com).

Test Name and Number	Recommended Use	Limitations	Follow Up
Testosterone, Adult Male <b>0070130</b> Method: Electrochemiluminescent Immunoassay	Diagnose and monitor hypogonadism	This test is not recommended for females or children	
Luteinizing Hormone and Follicle Stimulating Hormone <b>0070193</b> Method: Electrochemiluminescent Immunoassay	Diagnose and monitor hypogonadism		
Testosterone, Bioavailable & Sex Hormone Binding Globulin (Includes Total Testosterone), Adult Male <b>0070102</b> Method: Electrochemiluminescent Immunoassay The concentrations of free and bioavailable testosterone are derived from mathematical expressions based on constants for the binding of testosterone to albumin and/or sex hormone binding globulin.	Diagnose and monitor hypogonadism Use for patients with suspected plasma protein abnormalities	This test is not recommended for females or children	

<p>Testosterone Free, Adult Male <b>0070111</b></p> <p>Method: Electrochemiluminescent Immunoassay The concentration of free testosterone is derived from a mathematical expression based on the constant for the binding of testosterone to sex hormone binding globulin.</p>	<p>Diagnose and monitor hypogonadism</p>	<p>Not recommended for testing females or children</p>	
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**Additional Tests Available**

Test Name and Number	Comments
<p>Testosterone, Free &amp; Total (Includes Sex Hormone Binding Globulin), Adult Male <b>0070109</b></p> <p>Method: Electrochemiluminescent Immunoassay The concentration of free testosterone is derived from a mathematical expression based on the constant for the binding of testosterone to sex hormone binding globulin.</p>	<p>Not recommended for testing females or children</p>
<p>Testosterone, Bioavailable &amp; Sex Hormone Binding Globulin (Includes Total Testosterone), Females or Children <b>0081057</b></p> <p>Method: High Performance Liquid Chromatography/Tandem Mass Spectrometry/Electrochemiluminescent Immunoassay The concentrations of free and bioavailable testosterone are derived from mathematical expressions based on constants for the binding of testosterone to albumin and/or sex hormone binding globulin.</p>	<p>This test is suggested for children due to an improved sensitivity of testosterone by LC-MS/MS</p>
<p>Testosterone Free, Females or Children <b>0081059</b></p> <p>Method: High Performance Liquid Chromatography/Tandem Mass Spectrometry/Electrochemiluminescent Immunoassay The concentration of free testosterone is derived from a mathematical expression based on the constant for the binding of testosterone to sex hormone binding globulin.</p>	
<p>Sex Hormone Binding Globulin <b>0099375</b></p> <p>Method: Electrochemiluminescent Immunoassay</p>	

Testosterone, Urine <b>0070716</b> Method: Chemiluminescent Immunoassay	
Androstenedione <b>2001638</b> Method: High Performance Liquid Chromatography/Tandem Mass Spectrometry	
Dihydrotestosterone in Serum by Tandem Mass Spectrometry <b>2002349</b> Method: High Performance Liquid Chromatography/Tandem Mass Spectrometry	

**Guidelines**

American Association of Clinical Endocrinologists Medical Guidelines for clinical practice for the evaluation and treatment of hypogonadism in adult male patients--2002 update. *Endocr Pract.* 2002; 8 (6) 440-456.

**General References**

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**References from the ARUP Institute for Clinical and Experimental Pathology®**

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**Diagnostic Algorithm(s)**

PDF algorithm(s) available at [www.arupconsult.com](http://www.arupconsult.com).

Hypogonadism Testing Algorithm

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