Fact Sheet: Testosterone

Testing indications

- Diagnosis of hypogonadism in men – presentation may include symptoms such as reduced libido, erectile dysfunction, gynecomastia, osteoporosis, or infertility
- Diagnosis of hyperandrogenism in women – presentation may include hirsutism, acne, virilization, oligoamenorrhea, or infertility
- Investigation of infants with ambiguous genitalia or virilization
- Investigation of boys with delayed or precocious puberty
- Monitoring testosterone replacement therapy
- Monitoring antiandrogen therapy (e.g., used in prostate cancer)
- Monitoring treatment of congenital adrenal hyperplasia (CAH)
- Diagnosis of androgen-secreting tumours

Clinical information

The Leydig cells of the testis in men and the ovaries in premenopausal women are the primary sites of testosterone synthesis, with a small contribution from peripheral conversion of the adrenal androgens DHEA and androstenedione. Testicular and ovarian production is stimulated by pituitary luteinising hormone (LH) and regulated via negative feedback.

The majority of testosterone circulating is bound to proteins (predominantly SHBG and albumin), with only a small biologically active free fraction of approximately 2-3%. Measurement of total testosterone is therefore largely a measure of protein bound testosterone, and in conditions with significant alterations to these binding proteins, may not provide the best measure of biologically active testosterone. This should be considered in conditions in which SHBG is reduced, such as obesity and insulin resistance, where total testosterone may provide an underestimate of biologically active testosterone. Conversely total testosterone may be increased in conditions with increased SHBG, including hyperthyroidism and liver disease, without an increase in the biologically active fraction.

Testosterone concentrations in boys increase shortly after birth, reaching a peak at 2 to 3 months, and then fall to prepubertal levels by 6 to 12 months. Testosterone remains low until the onset of puberty, where there is a gradual rise to adult levels. Testosterone remains relatively stable in adult males until age 30-40, after which there is a gradual decline.

In girls testosterone levels are elevated at birth and fall to prepubertal levels by 6-12 months, and remain low until the onset of puberty. There is a gradual increase as puberty progresses until adult levels are reached. Testosterone then remains stable throughout adult life until menopause when concentrations fall.
## Reference intervals

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Reference interval</th>
<th>Units</th>
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<td>0.8</td>
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<tr>
<td>Premature infants</td>
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<td>6.9</td>
<td>nmol/L</td>
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*Source: ARUP laboratories’ reference interval verified locally on adult subset*
Interpretation of results

Men

In adult males low testosterone indicates hypogonadism. This can be either due to primary testicular failure where LH and FSH are increased (hypergonadotrophic hypogonadism), or central causes due to pituitary/hypothalamic disorders in which case LH and FSH are low or inappropriately normal (hypogonadotrophic hypogonadism).

A low testosterone should be confirmed with repeat testing on a separate occasion as there is a large within subject variation, meaning that an individual with a low testosterone on one occasion may be within the reference interval on repeat measurement. Testosterone for the assessment of androgen deficiency should be measured in the early morning, or soon after waking for shift workers, as this is when testosterone is at its peak.

In monitoring patients on testosterone replacement therapy, measurement of a trough level is recommended for patients using injectable of transdermal preparations. Random measurements are not recommended. The target trough testosterone concentration should be the lower half on the healthy adult male reference interval.

Increased testosterone can be seen in patients with raised SHBG, which is not associated with signs of androgen excess. Use of exogenous androgens, or tumours of the testis or adrenal glands are other causes for increased testosterone in men.

Women

Increased testosterone in women may be due to excess ovarian of adrenal production. The most common cause of increased testosterone is polycystic ovarian syndrome (PCOS). Other causes which should be considered prior to making this diagnosis include adrenal and ovarian neoplasms and non-classic congenital adrenal hyperplasia (NCAH). Very high concentrations of testosterone (> 6-7 nmol/L) are highly suggestive of a tumour, although tumours are not excluded at lower concentrations.

Measurement of early morning 17-hydroxyprogesterone in the early follicular phase is recommended to exclude NCAH. Measurement of other androgens (such as DHEAS and androstenedione) may be useful to determine the source of androgens.

Serum total testosterone should be interpreted together with SHBG. In conditions which lower SHBG, such as obesity and insulin resistance, bioavailable free testosterone may be increased despite total testosterone being within the reference interval.
Children

In boys with a clinical presentation of precocious puberty testosterone is increased above the prepubertal reference interval. Testosterone should be measured in the early morning as testosterone production occurs at night during early puberty. An increased testosterone combined with increased FSH/LH is consistent with central or gonadotrophin dependent precocious puberty. Increased testosterone with low gonadotrophins is consistent with gonadotrophin independent precocious puberty. This may be due to exogenous intake, or adrenal (e.g., adenoma/carcinoma or congenital adrenal hyperplasia (CAH)) or testicular production. Measurement of adrenal androgens (DHEA/DHEAS) may help in distinguishing between adrenal or testicular production. A testicular source can be due to an androgen producing testicular tumour, or due to stimulation by tumour hCG production, and so measurement of hCG is recommended.

Testosterone, in combination with LH and FSH, assists in the assessment of delayed puberty. In boys with delayed puberty, testosterone is in the pre-pubertal or early Tanner stage ranges. Further investigations are required to determine the cause, in particular differentiating constitutional delay of growth and puberty (CDGP), the most common cause of delayed puberty, and hypogonadotrophic hypogonadism, both of which have gonadotrophins low or normal for early Tanner stages.

Specimen:

Sample type:
Serum gel tube – Preferred
Serum non-gel tube – Accepted

Minimum volume: 0.4mL serum

Collection requirements:
For assessment of androgen deficiency in men the sample should be collected in the early morning, or shortly after waking in shift workers.

For monitoring of testosterone replacement therapy, in general, the sample should be collected predose (trough level).

Method: LC-MS/MS

Testing frequency: Twice weekly (Monday and Thursday)
Fact Sheet: Testosterone

References:

Enquiries:

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