PRIMEVIEW

PAEDIATRIC AND ADULT-ONSET MALE HYPOGONADISM

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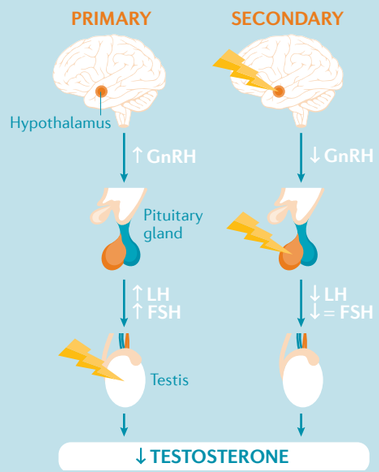
For the Primer, visit doi:10.1038/s41572-019-0087-y

Male hypogonadism is a disorder associated with symptoms of low testosterone levels and impaired spermatogenesis. The condition can arise from inherent defects in the testes or abnormalities in the regulation of testosterone secretion at the hypothalamic or pituitary level.

MECHANISMS

Primary hypogonadism, otherwise known as hypergonadotropic hypogonadism, is defined as low total testosterone with high gonadotropins. This form of hypogonadism results from malfunction at the level of the testes due to a genetic cause, injury, inflammation or infection. By contrast, central hypogonadism, or hypogonadotropic hypogonadism, involves defects of the hypothalamus or the pituitary gland. This secondary hypogonadism (defined by low testosterone with low or normal gonadotropins) is most often caused by genetic defects, intracranial masses (such as craniopharyngioma) or infiltrative disorders (for instance, Langerhans cell histiocytosis).



! In ~60% of cases, delayed puberty represents an extreme of the normal spectrum of pubertal timing rather than a sign of hypogonadism

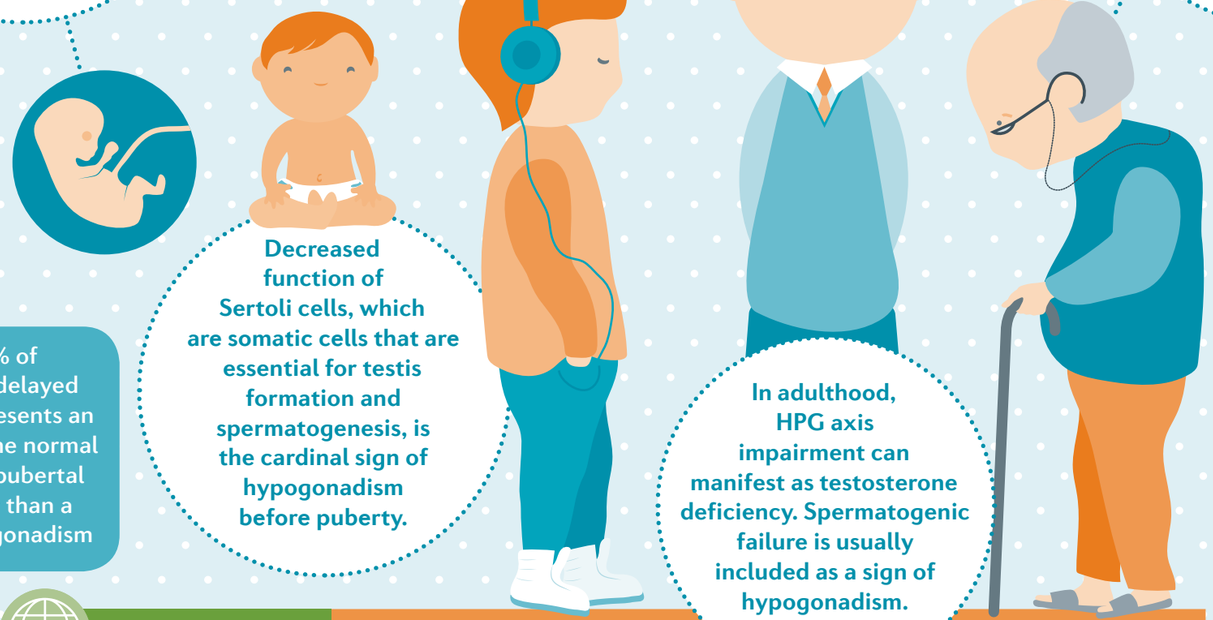
DIAGNOSIS

Hormonal deficiency during the first trimester of fetal life can result in a disorder of sex development, with a variable degree of hypovirilization and abnormalities of the external genitalia.

In normal childhood, testosterone is low and spermatozoa are not produced. However, conditions that impair the hypothalamic–pituitary–gonadal (HPG) axis (which regulates reproductive function) early in life may result in delayed puberty.

Decreased function of Sertoli cells, which are somatic cells that are essential for testis formation and spermatogenesis, is the cardinal sign of hypogonadism before puberty.

In adulthood, HPG axis impairment can manifest as testosterone deficiency. Spermatogenic failure is usually included as a sign of hypogonadism.



EPIDEMIOLOGY

Congenital conditions associated with primary hypogonadism include trisomies, such as Klinefelter syndrome and Down syndrome, and testicular dysgenesis syndrome. Acquired causes of primary hypogonadism include mumps-related orchitis, irradiation or chemotherapy, trauma to the testes or chronic alcoholism. Congenital causes of secondary hypogonadism include Kallman syndrome, whereas acquired causes include pituitary or hypothalamic dysfunction owing to a tumour, opioid use or malnutrition.

Signs and symptoms of hypogonadism depend on the age of onset, the severity of androgen deficiency and the underlying cause of the androgen deficiency.

MANAGEMENT

When specifically associated with ageing, obesity or poor health, late-onset hypogonadism is the likely diagnosis, the signs of which include but are not limited to loss of libido, erectile dysfunction and depression.

As secondary hypogonadism is, in general, characterized by low or inappropriately normal gonadotropin levels, treatment is with the gonadotropins follicle-stimulating hormone and luteinizing hormone, if fertility is desired. If fertility is not an issue, testosterone therapy is advised. In cases of primary hypogonadism, the only therapeutic option is testosterone therapy. Testosterone therapy for congenital forms of hypogonadism must be lifelong; management of acquired causes depends on whether the condition is permanent or can be resolved. However, testosterone treatment of late-onset hypogonadism remains a matter of debate owing to, for example, potential risks in older individuals. Lifestyle modifications are usually recommended before testosterone therapy is proposed.

OUTLOOK

Many questions remain unresolved in the field of male hypogonadism. For example, the optimal time to begin androgen treatment in boys with genetic conditions that underlie their primary hypogonadism is unclear. Testosterone deficiency may contribute to increased risk of cardiovascular disease in these patients, which could be avoided — but evidence is still lacking. Another important area of research is distinguishing 'normal' delayed pubertal timing from idiopathic secondary hypogonadism, which is currently not possible.

doi:10.1038/s41572-019-0093-0; Article citation ID: (2019) 5:37

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