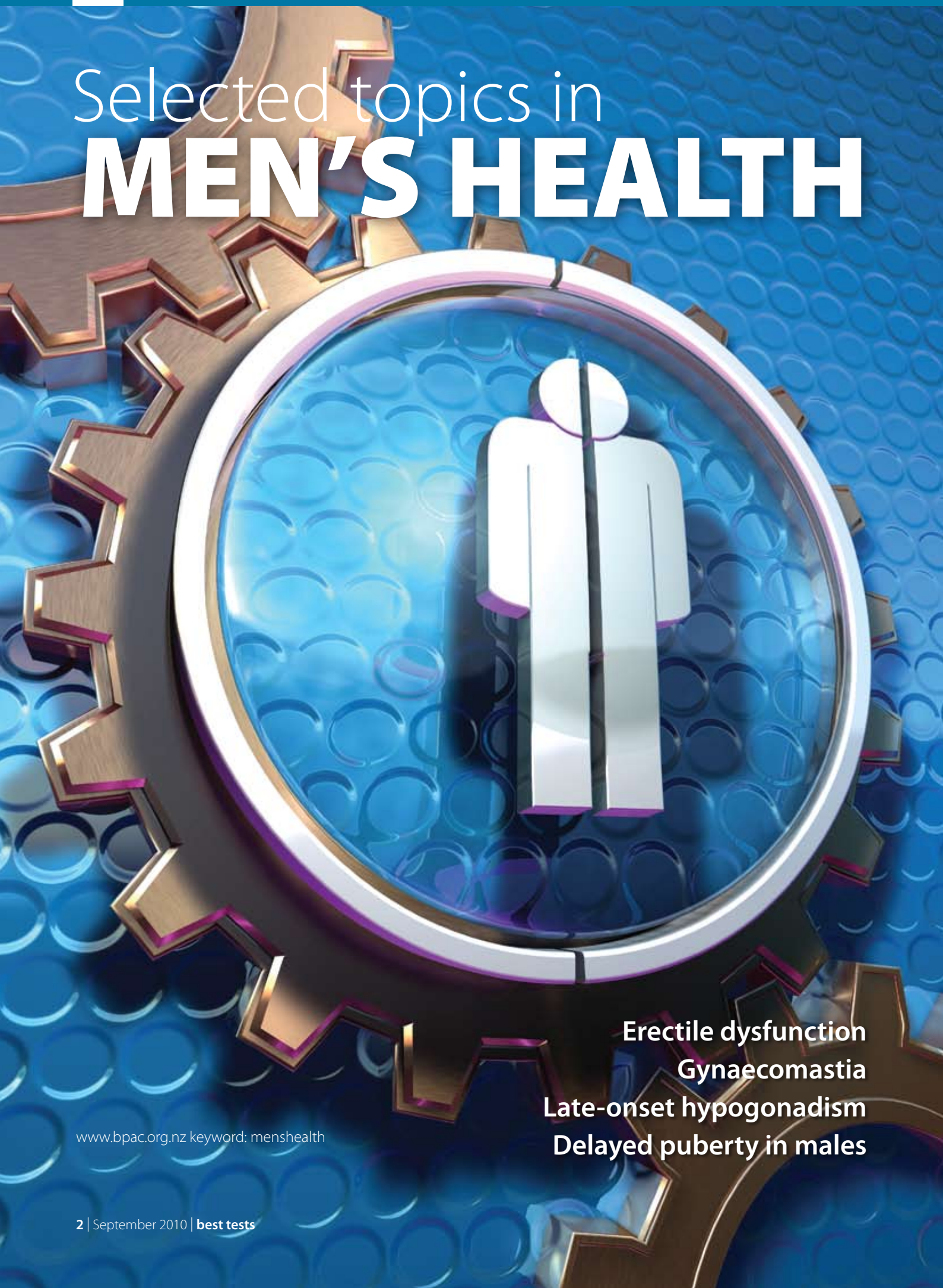
Selected topics in MEN'S HEALTH



Erectile dysfunction
Gynaecomastia
Late-onset hypogonadism
Delayed puberty in males

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Erectile dysfunction

Erectile dysfunction (ED) can be defined as the persistent inability to achieve or maintain penile erection sufficient for satisfactory sexual performance. Evaluation and consideration of treatment are indicated when ED persists for at least three months.

The prevalence of ED increases with age.[1] The Massachusetts Male Aging Study was the first major epidemiological investigation of ED and one of the largest population-based studies in this field to date. It was estimated that 52% of non-institutionalised men aged between 40 and 70 years, had some degree of ED – 17% minimal, 25% moderate and 10% complete.[2]

Causes: organic or psychogenic

ED may result from organic or psychogenic causes (or components of both). Even in men with an obvious organic cause, there are psychological factors that may play a role in either exacerbating or sustaining the condition.

There is much variation among men with ED in the way they present, in terms of severity of the disorder and associated co-morbidities.[1]

Men with an organic cause for their ED usually present with a gradual onset and the difficulty becomes progressively worse over time.[2]

Conversely, when the cause of ED is psychogenic, it can occur suddenly with a complete and immediate loss of sexual function which may vary with the partner or situation. It may also be difficult to differentiate between ED from organic or psychogenic causes. A useful clinical indicator is that men with psychogenic ED usually continue to experience early morning erections.[1, 2]

Most causes of ED were once considered to be psychogenic, but evidence suggests that up to 80% of cases have an organic cause.[1] Organic causes include vasculogenic, neurogenic and hormonal aetiologies (Table 1). Vasculogenic aetiologies represent the largest group, with arterial or inflow disorders being the most common. Abnormalities of venous outflow (corporeal veno-occlusive mechanism) are much less common.

Hormonal dysfunction, contrary to popular opinion, is a rare cause of ED. Hormonal treatment produces little improvement in ED other than in men with severe androgen deficiency. Regardless of the primary aetiology, a psychological component frequently coexists.[3]

Diagnostic evaluation of erectile dysfunction

When a patient first presents with ED, it is essential to obtain a full history (both medical and sexual) and perform a targeted clinical examination.

A detailed medical history is important as many disorders are associated with ED including hypertension, diabetes mellitus, ischaemic heart disease, dyslipidaemia, chronic kidney disease, hypogonadism, neurological and psychiatric disorders and many chronic illnesses. Genitourinary and rectal surgery, and medicines such

Table 1: Common causes of erectile dysfunction[2]

Organic	Psychogenic
■ Vascular disease ■ Diabetes mellitus ■ Medicines e.g. antidepressants, psychotropics, antihypertensives ■ Cigarette smoking ■ Alcohol ■ Neurological disorders ■ Severe hypogonadism	■ Performance anxiety ■ Generalised anxiety ■ Major depression

as antihypertensive and psychotropic drugs, may also cause ED. Chronic misuse of alcohol, marijuana, codeine, pethidine, methadone or heroin is also associated with a high prevalence of ED.[4]

Examination should include measurement of blood pressure and evaluation for peripheral vascular disease and diabetes and an assessment for possible hypogonadism (gynaecomastia, reduced androgenic body hair and decreased testicular volume).

Laboratory tests

There is a lack of consensus regarding the best choice of laboratory tests for the evaluation of patients with ED. Given the association of ED with vascular disease and diabetes, it is recommended that a cardiovascular risk assessment is performed and screening for diabetes is undertaken.

Some guidelines propose measurement of testosterone as part of the initial work up for all cases of ED,[5] whereas others suggest testosterone measurement is only necessary if the history or clinical examination indicates possible hypogonadism.[6] More recently, due to insufficient evidence to determine net benefits and harms, the American College of Physicians announced that it was unable to recommend either for or against routine use of hormonal blood tests or hormonal treatment in the management of patients with ED[7] (see sidebar). It was recommended that clinicians consider the presence or absence of symptoms of androgen deficiency (decreased libido, fatigue) and of physical findings (reduced androgenic hair, gynaecomastia, testicular atrophy) before measuring hormone levels in individual patients.

Testosterone replacement

Testosterone therapy is not usually indicated for ED in men with normal testosterone levels.[8]

Testosterone replacement is appropriate when a man with ED is diagnosed with hypogonadism. Adverse effects associated with exogenous testosterone therapy include gynaecomastia, increased haematocrit, alterations in lipid profile, hypertension and infertility.

The initiation of testosterone replacement is not a simple issue and requires careful consideration and supervision by a specialist.[9] It is important conditions such as polycythaemia and prostate malignancy are excluded.

Gynaecomastia

Gynaecomastia (GM), a benign enlargement of male breast tissue, is a common condition which indicates an imbalance between free oestrogen and androgen action in the breast tissue. True GM can be distinguished from an accumulation of adipose tissue (lipomastia or pseudogynaecomastia) in which glandular tissue is not palpable. Breast enlargement can also be rarely caused by a primary or secondary breast malignancy. If there is doubt about the cause of GM, further evaluation is required.[10]

There are several situations in which GM occurs physiologically. Transient neonatal GM lasting one to two months is a common phenomenon which occurs in 65–90% of neonates.[10] It is caused by the transplacental passage of maternal oestrogen. GM is also common during mid to late puberty, when relatively higher levels of oestrogen are produced by the testes and peripheral tissues, before testosterone reaches adult levels. In 95% of cases this resolves within one to two years.[10] As men age, the frequency of GM again increases and is assumed to be related to a fall in free testosterone levels.[10]

In the early stages of the development of GM, the breast tissue is in a "proliferative" stage, but as the ductal system increases, eventually fibrosis develops. GM is generally reversible if managed early, however once GM has evolved to the stage of extensive fibrosis, the process may be irreversible and is unlikely to regress, either spontaneously or with medical therapy.[11]

There are numerous conditions associated with GM (see sidebar). These include disorders which either impair

androgen production (hypogonadism) or increase oestrogen levels (rare tumours, cirrhosis, thyrotoxicosis). Some medicines can cause gynaecomastia, therefore review of a patients medicine list is important.

A physical examination is useful for differentiating true GM from pseudo-gynaecomastia. In patients with true GM a concentric, rubbery or firm mound of tissue around the nipple-areolar complex can be felt, whereas in patients with pseudo-gynecomastia, this is not found. A hard or firm mass palpable outside the areolar area may suggest the presence of a tumour and further follow-up is recommended.[12]

Diagnosis of gynaecomastia

Although laboratory evaluation may be appropriate, abnormalities are not detected in the majority of patients with GM. Endocrine evaluation in adolescent patients, and in adult patients with longstanding fibrotic GM, is contentious.

If an adult male presents with unilateral or bilateral GM that is of acute onset, particularly if tender, and if the patient's history and physical examination do not reveal the cause, then serum testosterone, LH, oestradiol and hCG are usually sufficient. Other tests depend on clinical findings or suspicion.[13]

In older men, GM may be the result of late onset hypogonadism (see below) and measurement of morning testosterone and LH is reasonable. A low testosterone and elevated LH suggests primary testicular failure, whereas a low testosterone with normal or low LH suggests secondary hypogonadism.

Estimated prevalence of underlying disease processes in gynaecomastia

In males seeking medical attention for GM, it is estimated that the prevalence of underyling aetiologies is as follows:[10]

- Persistent pubertal gynaecomastia – 25%
- Medicines – 10–25%
- No detectable abnormality – 25%
- Cirrhosis or malnutrition – 8%
- Primary hypogonadism – 8%
- Testicular tumors – 3%
- Secondary hypogonadism – 2%
- Hyperthyroidism – 1.5%
- Chronic renal insufficiency – 1%

Referral

Referral to an endocrinologist should be considered, after initial screening investigations, for any patient with pathological GM which is not related to use of a medicine or another recognised cause (cirrhosis, renal failure, thyrotoxicosis).

Treatment with tamoxifen 20 mg daily for up to three months may be initiated if the GM is of recent onset. This results in regression of GM in up to 80% of patients.[10]

Late-onset hypogonadism

As healthy men age, the serum concentration of testosterone, particularly free testosterone but also total testosterone, declines by 0.4 – 2.6% per year after the age of 40 years. This results in a total testosterone level that is below the normal laboratory range in approximately 25% of men aged over 70 years and 50% aged over 80 years.

As testosterone levels fall, a variety of physical changes occur, including loss of muscle mass and strength, an accumulation of adipose tissue, reduced bone density and sexual dysfunction. These features are also commonly seen in patients with true androgen deficiency.

Diagnosis of late-onset hypogonadism

The association between aging-related testosterone reduction and late-onset hypogonadism in men remains

a controversial concept due to the high prevalence of hypogonadal symptoms in the aging male population and the non-specific nature of these symptoms.

The issue is further complicated by the impact of a variety of medical conditions on the male gonadal axis, the diurnal variation in testosterone levels (more than one pre-9am sample is essential) and the limitations of available total and free testosterone assays.[13] Androgen deficiency has a broad differential diagnosis, ranging from primary testicular disorders (such as orchitis, chemotherapy, Klinefelter's syndrome) to central disorders (pituitary tumours, haemochromatosis, diabetes). Appropriate treatment for a patient with an unequivocally low testosterone level may therefore require more than just androgen replacement.

Androgen replacement could be considered in elderly men with clinically significant symptoms of androgen deficiency and low morning total testosterone on more than one occasion. However, there is a lack of consensus from international experts on the thresholds for normal testosterone levels.

Delayed puberty in males

Delayed puberty in males is defined by the absence or incomplete development of secondary sexual characteristics by age 14 years, i.e. the age at which 95% of males have initiated sexual maturation.[15] An increase in testicular size is the first sign of sexual maturation. If there has been some increase in testicular volume then the patient can be reassured that they are likely to progress through puberty normally, although perhaps later than their peers.[15]

Delayed puberty in boys may be due to:

- Functional causes e.g. constitutional delay in puberty, chronic illness, excessive exercise, malnutrition, stress
- Associated pathologies e.g. hypothalamic or pituitary tumours
- Genetic causes e.g. Klinefelter's syndrome

Constitutional delay of puberty

The most common cause of delayed puberty is constitutional delay in growth and puberty. This diagnosis, as opposed to permanent central hypogonadism, can only be made retrospectively once full sexual maturation has occurred. At the expected time of puberty, the height of males with constitutional growth delay begins to deviate further from the growth curve because of delay in the onset of the pubertal growth spurt. Catch-up growth, onset of puberty and the pubertal growth spurt occur later than average, but result in normal adult stature, sexual development and fertility.[15]

Evaluation

For a boy aged under 16 years, watchful waiting should reliably distinguish those with constitutional delay (who will eventually spontaneously progress through puberty) from those with other causes of delayed puberty. A positive family history for constitutional delay of puberty, especially in the father, can be useful for helping to confirm this. Reassessment of the patient may be considered after six months.[16]

A thorough history should identify nutritional problems, medical illness or excessive exercise. When examining the patient include measurements of height, weight, arm span (see below) and presence of secondary sexual characteristics. Sometimes these features may be present but unnoticed by the patient or family and identifying them can be reassuring. Serial measurements made over one to two years can often be helpful.[15]

An arm span exceeding the height by more than 5 cm suggests delayed epiphyseal closure secondary to hypogonadism (sex steroids are required for epiphyseal closure).

Males with constitutional delay of puberty typically have a delayed bone age, indicating residual growth potential. An x-ray of the left wrist and hand to evaluate bone age may be obtained.[15]

Classification of delayed puberty according to LH and FSH levels

Delayed puberty syndrome can be classified according to the circulating levels of the gonadotrophins LH and FSH:

- High serum LH and FSH levels are associated with various causes of gonadal disease, termed primary hypogonadism
- Low or normal LH and FSH levels indicate disorders at the hypothalamic-pituitary level, termed secondary hypogonadism. Rarely, this can be due to hypothalamic dysfunction, hypopituitarism, hypothyroidism or hyperprolactinaemia.

Constitutional delay of puberty is typically associated with low levels of LH and FSH.

Laboratory tests for delayed puberty in males

- Tests directed at possible medical or nutritional disorders, based on history and examination findings e.g. CBC, liver function, creatinine, coeliac serology
- Hormonal tests: LH and FSH, serum testosterone, serum prolactin, TSH (and FT4 if a pituitary cause is suspected)

Random growth hormone (GH) testing is of little value because of the pulsatile nature of GH secretion by the pituitary.

Depending on the results of these initial tests, further testing may be indicated, but specialist advice is recommended.

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