Does this man have testosterone deficiency?

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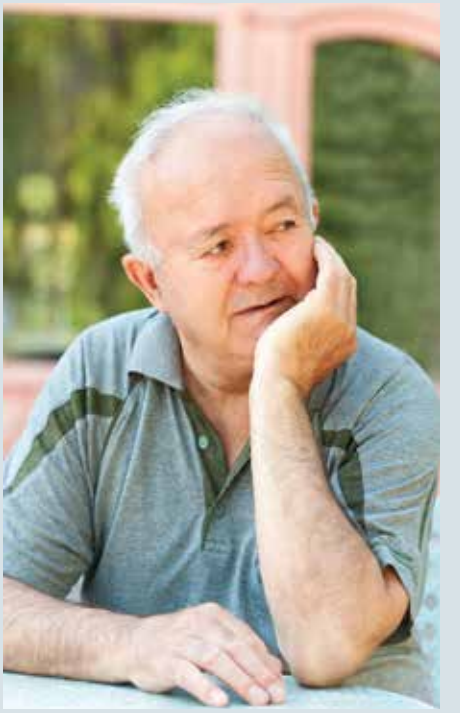

This section is about the immediate management and investigation of an acute presentation in general practice. It is inspired by, but not based on, a real patient situation.

John, aged 57 years, is a longstanding patient of your general practice. He consults you today about his 'flagging sex drive' and wonders if his testosterone level is low. He has seen and heard the advertisements in the media on testosterone and wants his testosterone levels tested. John is CEO of a large company and works long hours. He has no children, by choice, and is currently in a new relationship. He is a lifelong nonsmoker, social drinker and takes no medications. He is of a normal weight and is fit, as he exercises regularly. He has had no significant illnesses.

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What are the questions you should ask John at this point?

Answer: You should let John know that you will need to ask him some very personal questions. It is quite possible that other medical or psychological factors are responsible for his issue and these need investigation. What does John mean by 'flagging sex drive'? Does he mean reduced performance or reduced inclination? Does he have sustained erections firm enough for intercourse? If not, how long has this been happening? Can he sustain erections with masturbation or spontaneously in the morning? Has he noticed any changes in his facial hair growth, breast development or weight? Does he think that this problem is related to his new relationship, longer hours at work, anxiety, depression or anything else he can think of? Is he coping ok at work and has he noted any changes in his performance, concentration or mood? Are his energy levels normal? You should revise John's cardiovascular risk factors (e.g. diet, exercise, family history, smoking status, alcohol intake) and review his past blood test results (e.g. lipid and blood glucose levels, liver function tests).

John says he no longer has the same inclination to initiate sex and the problem has been more obvious over the past two years or so. He can sustain erections and complete intercourse but it takes more effort to achieve firm erections and his current girlfriend is concerned. He noted the same problem with his last relationship. He has noticed no change in his weight or hair growth. His work is demanding as usual, with long hours, but he says he is coping fine with this. He wonders if he has 'male menopause' and would like to try testosterone replacement therapy. You examine John.

What are the features of testosterone deficiency?

Answer: Features of testosterone deficiency include testicles that are softer and smaller than normal (measure with an orchidometer if possible), sparse pubic, body and facial hair, gynaecomastia, reduced muscle development, weight gain, loss of height (osteoporosis increases the fracture risk), small and soft prostate, and possibly reduced ejaculate (although this may be normal for the patient's age) and infertility. If both reduced ejaculate and infertility are present, there is more likely to be reduced spermatogenic function as well as reduced testosterone levels, but these may not occur together, especially in older men. In addition, the patient may complain of dysthymia, poor concentration, hot flushes and sweating. However, in some men there are few symptoms.

John's physical examination is quite normal. He has normal blood pressure (128/75 mmHg) and muscle mass. He also has normal hair distribution for his age, normal testes (both in volume and consistency) and a normal prostate on rectal examination.

What are the issues you need to discuss with John about testing for serum testosterone?
Answer: It is wise to confirm with John that he does not have erectile dysfunction, which is caused by neurological, psychological and vascular conditions. Testosterone deficiency may be associated with reduced sex drive or performance, and not necessarily with complete impotence. However, it is more likely that John's problem is related to his age or a physical or psychological change (especially as he works long hours and has a new partner). If so, testosterone replacement will have no impact on his sexual performance (erection strength or duration), but may improve libido.

You should discuss testosterone deficiency with John in detail. The interpretation of testosterone deficiency in John's age group is not always clear cut. The range of normal is standardised to young men, not men in their late 50s. It is very common for the result of testing to show mildly reduced testosterone levels in someone such as John and this is not an indication for testosterone replacement. Testosterone levels often decline very slowly in men over the years from age mid-30s onwards, although may sometimes be normal in older men in good health.

How are low testosterone levels defined and what are the PBS requirements for testosterone therapy?
Answer: Blood samples for testosterone level measurement should be taken in the morning (when testosterone levels are at their highest) and the test should be repeated if the result is abnormal. Testosterone levels fluctuate during the day and the normal (morning) eugonadal range is usually 8 to 27 nmol/L (standardised to young men, but it may vary with the laboratory).

The PBS requirement for prescribing testosterone therapy in men with androgen deficiency has changed recently. The listing now applies to men aged 40 years or over with androgen deficiency, which is defined as:

- total testosterone level of less than 6 nmol/L; or
- total testosterone level between 6 and 15 nmol/L with high luteinising hormone (greater than 1.5 times the upper limit of the eugonodal reference range for young men, or greater than 14 IU/L, whichever is higher).

Androgen deficiency must be confirmed by measurement in at least two morning blood samples taken on different mornings. The condition must not be due to age, obesity, cardiovascular diseases, infertility or drugs. To qualify for this PBS subsidy the patient must not have an established pituitary or testicular disorder and GPs have to consult with a specialist endocrinologist, urologist or registered member of the Australasian Chapter of Sexual Health Medicine before they can prescribe testosterone for a patient.

What conditions predispose to testosterone deficiency?
Answer: Conditions that predispose to testosterone deficiency can be classed as congenital or acquired (see the Box). There is also an association between androgen deficiency and the metabolic syndrome, diabetes and obstructive sleep apnoea.

What are the contraindications of testosterone therapy in men?
Answer: Hormonally sensitive cancers (such as breast and prostate cancers) need to be excluded prior to testosterone therapy. This therapy may worsen severe congestive cardiac failure. Untreated sleep apnoea may worsen in cases of untreated testosterone deficiency. Testosterone therapy may also cause erythrocytosis; it should not be used if the haematocrit level is over 55%. In men considering having children, testosterone therapy may decrease fertility and so is contraindicated.

John wants to discuss 'male menopause'. Does it exist? What do you tell him?
Answer: Male menopause is not a definite specific stage in life, unlike female menopause. Testosterone levels normally decline very slowly over years from the mid 30s onwards, not suddenly. 'Male menopause' is not a medical concept, but rather a psychosocial one. If it exists at all, it is said to occur in midlife and coincides with certain stages in a man's career, relationships, children leaving home and attitude to his awareness of ageing and illness. It is not connected to androgen deficiency, although this may bring the concept of male menopause to medical attention.

Conditions that predispose to testosterone deficiency

Congenital
- Genetic abnormalities (e.g. Klinefelter's syndrome)
- Kallmann's syndrome
- Genitourinary developmental abnormalities

Acquired (including those of primary, secondary and androgen receptor blockade causation)
- Testicular trauma
- Undescended testicles
- Bilateral torsion
- Infections (especially mumps, gonorrhoea)
- Uncontrolled haemochromatosis
- Very advanced age (especially with obesity)
- Pituitary disease
- Radiotherapy to the groin
- Medications (e.g. spironolactone, high dose opiates, ketoconazole, oestrogens, chemotherapy, goserelin)

What initial pathology tests should you perform for John if he has not had any tests carried out in recent years?
Answer: Because of the history of change in sexual performance, it is reasonable to test John's early morning (8 to 10 am) serum total testosterone level. He should also have his liver function, full blood count, fasting lipid and blood glucose levels, prostate-specific antigen level and iron studies measured if these have not been performed recently. Iron studies are recommended to ensure John does not have haemochromatosis. This should be discussed with him.

If John's testosterone level were to be significantly low (under 6 nmol/L), what other investigations would you suggest?
Answer: He should have his morning serum testosterone level repeated and also sex hormone binding globulin tested. Luteinising hormone and follicle-stimulating hormone

Practice points

- Total testosterone levels decline in many men slowly over years, from age mid-30s onwards.
- Total testosterone levels should be measured with an early morning blood sample. If low, they should be repeated along with measurement of serum prolactin, sex hormone binding globulin, luteinising hormone and follicle-stimulating hormone levels.
- Evidence suggests that testosterone replacement in the absence of testosterone deficiency does not improve sexual function (erection strength or duration) but may improve libido. Other benefits and long-term risks of using testosterone in this setting are however unknown.
- Bone density, full blood count, fasting lipid and blood glucose levels, prostate-specific antigen level, blood pressure and other modifiable cardiovascular risk factors should be measured periodically in patients with documented testosterone deficiency.
- Hormonally sensitive cancers, such as breast and prostate cancers, need to be excluded prior to use of testosterone therapy.

levels should be measured to determine if there is a secondary (or pituitary cause) for his androgen deficiency. A serum prolactin level should also be measured. John should also have a bone density test if testosterone deficiency is confirmed.

As John has normal testicular volume, he does not need to be tested for Klinefelter's syndrome. All men with testicular volume of 4 mL or under, primary infertility or primary gonadal failure should be tested for Klinefelter's syndrome as there are other related morbidities (such as an increased risk of venous thromobo-embolism and autoimmune disease).

You receive John's results the following week. His early morning testosterone level is 12 nmol/L. You ask him back for a follow-up consultation.

What do the results show and should you prescribe testosterone therapy for John?
Answer: John's early morning testosterone level of 12 nmol/L is within the normal range of 8 to 27 nmol/L, and therefore testosterone therapy is not advised for this patient. Although testosterone therapy may increase libido, the benefits and long-term risks of using testosterone therapy in a patient such as John are unknown.

Outcome
John is happy not to have testosterone therapy and now feels that his job and the pressure of his relationship are more likely to be responsible for his reduced libido. He is reassured that his test results are all normal and, with your professional support, he plans to manage his stress levels better. ET