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Andrology

An-drol'-uh-jee

The study of the
functions and diseases
peculiar to males,
especially of the
reproductive organs

>> FROM THE DIRECTOR

Oestrogen deficiency and the value of hormone replacement therapy (HRT) for women has long been established and has undergone extensive review by the medical community. Unfortunately there is not the same level of understanding of the male counterparts.

Testosterone or androgen deficiency can occur at any age and is thought to be significantly under-diagnosed in the community, particularly in men under the age of 60. However, beyond the age of 60 years, the frequency of androgen deficiency increases due to declining production in some men. This field of hormone replacement therapy in men is complex as there are difficulties in diagnosis and few studies of the benefits and risks of long term treatment. Confusion has arisen because some doctors have been incorrectly using testosterone for a wide variety of disorders associated with ageing.

Clouding the assessment of the value of androgen supplements is the growing abuse of these medications for performance enhancement and body building purposes. The extension of androgen abuse or illicit anabolic steroids use from its origin in sports doping into non-sporting uses for cosmetic, recreational and occupational reasons is a growing public health concern.

In this edition of "The Healthy Male", with the expert assistance of Professor David Handelsman, we explore the many facets of androgens and the role of testosterone therapy. Andrology Australia is undertaking a number of initiatives to increase understanding and improve male reproductive health care in this area.



Male Ageing — what could we or should we do?

PROFESSOR DAVID HANDELSMAN
DIRECTOR, ANZAC RESEARCH INSTITUTE

Advancing age impacts on all aspects of male reproductive health - sexuality, fertility and androgenisation - with differing extents and tempo.

The effects on androgen secretion has special significance since it could, in theory, be treatable. It remains unclear, however, whether the modest and gradual decline in blood testosterone concentrations after mid-life, of up to 1% per annum [1], warrants replenishment based on demonstrated beneficial effects on ageing tissues.

In the best available, well controlled study of androgen replacement [2,3], testosterone produced an increase in lean mass (muscle) and decrease in body fat compared with placebo. But this treatment had minimal effects on sense of well-being and failed to improve muscle strength or bone density. Further analyses showed that any benefits of testosterone were restricted to men with the lowest testosterone concentrations before starting the study. Hence, it is likely that only men with definite androgen deficiency would obtain real benefit from such treatment.

The long term safety of androgen therapy in older men is also not clear.

Recent studies indicate some benefits on cardiovascular disease in terms of vasodilatation (ability of blood vessels to dilate) [4] however this needs to be reconciled with the likelihood that androgens may foster early stages of atherogenesis (or "hardening of the arteries") [5,6].

Similarly, the effect of androgen supplementation on prostate disease is not known. Because of the strong androgen-dependence of the prostate, it remains prudent to defer androgen therapy in any men with prostate disease requiring further medical treatment.

Declining male sexual function should not be a key motivation for older men seeking androgen therapy.

The primary effect of androgens on male sexuality is in maintaining libido. Yet, the threshold for androgen effects on libido is quite low. This means that only severe androgen deficiency causes problems with sexual function. Erectile dysfunction in older men is more likely to be due to underlying vascular disease, drugs (especially antihypertensives, psychotropics and smoking), chronic medical disease (notably diabetes mellitus and severe heart, liver or kidney failure), depression and/or psychosocial factors.

From a public health perspective, androgen supplementation for ageing men cannot be recommended universally. Further research is required to define better targets including more specific therapeutic objectives and subgroups of older men who may be more responsive. In parallel, a clearer understanding of the role of androgens in the natural history of cardiovascular and prostate disease is essential.

[see page 4 for article references]



» EDUCATION UPDATE

Assisting Clinical Laboratories to Accurately Diagnose Androgen Deficiency

Underdiagnosis of classical androgen deficiency in the community has many causes including the lack of awareness and the non-specific nature of the symptoms. A significant problem is also the lack of appropriate reference ranges for male reproductive hormones for older men. As treatment of androgen deficiency is very cost-effective, establishing these ranges and educating clinicians on the complexities of this process has been given priority by Andrology Australia.

A preliminary survey conducted as part of the Royal College of Pathologists Quality Assurance Program indicated wide variation between laboratories in the reference ranges and methods used for diagnosing androgen deficiency. A well-calibrated reference range for healthy fertile men is currently not available.

The Endocrine Society of Australia has

published guidelines that are used by the Australian Government (Pharmaceutical Benefits Scheme) for subsidizing the cost of prescribing testosterone replacement. Doctors use these guidelines when deciding about the need for testosterone treatment. For these guidelines to be meaningful for the medical practitioners, the pathology testing must be accurate, consistent and as conclusive as possible.

The development of a serum panel on a reference population of healthy fertile young men is proposed to enable pathology laboratories to re-evaluate reference ranges for the different assays currently available. Guidelines for androgen measurements will then be developed.

This will be the first national approach to standardize biochemical diagnosis of androgen deficiency.

» RESEARCH ROUNDUP

monitoring the use, misuse and abuse of ANDROGENS

Appropriate clinical use of androgens is a major issue in male reproductive health and a priority area of concern for Andrology Australia. There is currently little awareness of the extent and significance of androgen use, misuse or abuse in the Australian community.

Andrology Australia has provided support for the appointment of a project officer at the ANZAC Research Institute (NSW) to review androgen abuse in high schools to look for trends and further predictors of abuse. Monitoring of androgen prescription patterns in individual States and changes in prescription patterns over the last decade will also be undertaken.

Preliminary evidence suggests that androgens are sometimes prescribed without a well established medical reason. Some common examples of

misuse of testosterone therapy when androgen deficiency has not been diagnosed include:

Male infertility

Prescription of androgens to treat male infertility can in fact be detrimental. If testosterone or other androgens are prescribed, the body's detection system recognizes that the levels of testosterone are too high and stops the production of LH and FSH. These hormonal changes in turn stop sperm production.

Erectile dysfunction or impotence

Androgen deficiency is an uncommon (< 5%) cause of erectile dysfunction. In such men, there is often an underlying disease causing the androgen deficiency, which may need treatment.

Male menopause

Ageing men who have symptoms that have been associated with androgen deficiency are sometimes described in the media as having "male menopause" or "andropause". The risks and benefits of testosterone replacement for older men with levels of testosterone that are around the lower limit of the reference range for their younger male counterparts are being researched.

Treatment of non-specific symptoms

Prescription of androgen therapy should not simply be based on symptoms. It must be corroborated by clinical blood tests that establish androgen deficiency.

It is anticipated that the final report from the study at the ANZAC Research Institute will assist in the development of future public health policy.

Focus on TESTOSTERONE THERAPY

What is testosterone?

Testosterone is the most important androgen in men. Androgens are the sex steroids or hormones that produce changes in body shape (muscle gain, fat distribution) and secondary sexual characteristics (hair and beard growth, penile growth) typical of men. It is mainly produced by a gland in the testes and it circulates in the bloodstream to act on organs or tissues at other sites. It is responsible for stimulating the production of sperm.

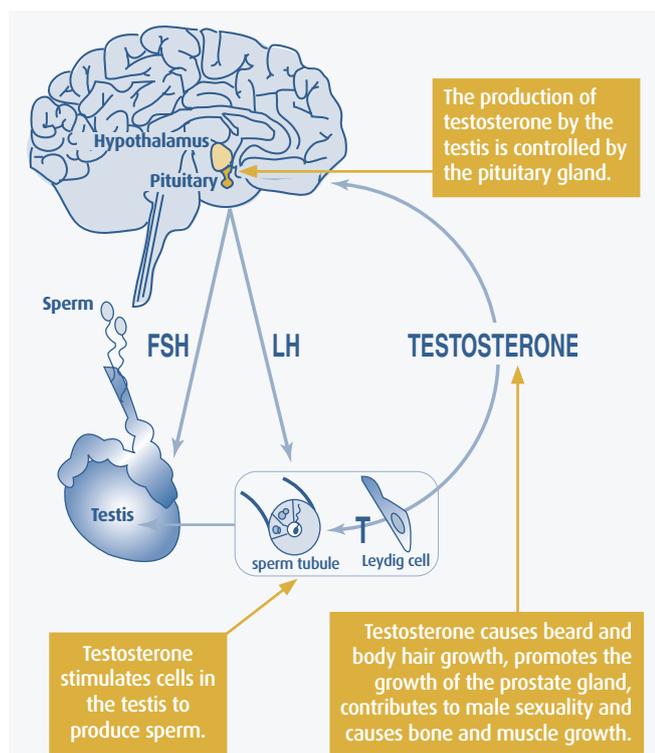
What is testosterone therapy?

Replacement testosterone is a supplement administered orally or by injection, patch or implant. This treatment is provided for men who are androgen deficient, that is, their body is unable to produce sufficient testosterone. This means that their tissues do not have enough exposure to androgens to function normally.

Do all men become androgen deficient as they age?

Testosterone levels in men begin to fall from the age of 40 years. Some estimates suggest that the prevalence of androgen deficiency may be as high as 10% by the age of 65 years with this figure rising to about 20% by the age of 70 years. However, many men aged over 80 years will have relatively normal androgen levels. The lifestyle or risk factors that may account for this inter-individual variation are still not characterized.

Unlike women, whose oestrogen levels fall rapidly when they go through menopause, men's testosterone levels fall much more gradually and over a longer period of time.



Can younger men be androgen deficient?

One in 200 men under 60 years of age suffer from androgen deficiency. These men require androgen replacement under the supervision of their doctor. Causes of androgen deficiency in younger men may include:

- » Testicular problems in which there is poor production of testosterone by the testes occurs as a result of a number of problems, such as genetic disorders (e.g. Klinefelter's Syndrome), undescended testis, infections (e.g. mumps after childhood) or chemotherapy or radiotherapy given for cancer treatment;
- » Diseases of the pituitary gland stop the production of the hormones (LH and FSH) that are needed to drive the testes. The commonest pituitary gland problem is the presence of a benign tumour called an adenoma.
- » Diseases of the hypothalamus. A rare genetic disorder known as Kallmann's syndrome stops the production of GnRH from the hypothalamus that is needed to drive the pituitary gland and the production of LH and FSH. Low levels of LH and FSH from the pituitary in turn leads to poor hormonal drive of the testes. Rare tumours or congenital abnormalities of the hypothalamus can also lead to low levels of LH and FSH from the pituitary.

Why the need for close monitoring when on testosterone therapy?

Monitoring of androgen therapy in older men is more intensive than for younger men because of the higher prevalence of age-related diseases. The growth of the prostate is controlled by androgens. Testosterone causes the prostate gland to increase in size in some older men. Any prostate cancer, if present, may therefore increase in size. Consequently, prior to commencing androgen therapy, prostate disease requiring further treatment must be excluded.

Does "Male Menopause" exist?

Ageing men who have symptoms that have been associated with androgen deficiency are sometimes described in the media as having "male menopause" or "andropause". Terms such as these are misleading and have little place in meaningful medical or scientific discussion. Menopause refers to the stopping of menstrual cycles (periods) which can only be applied to women. Unlike women whose oestrogen levels fall rapidly when they go through menopause, men's testosterone levels fall much less, more gradually and variably as well as over a much longer period of time. The risks and benefits of testosterone replacement for older men with "normal" gradual declines in testosterone levels are yet to be determined.



Professor David J Handelsman
MBBS, PhD, FRACP

Professor David Handelsman is a major figure in Andrology in Australia. He is an expert in all aspects of male reproductive health, medicine and biology and holds the honour of being Australia's first Professor of Andrology, a position to which he was appointed in 1996 by the University of Sydney. In 1999 Concord Hospital made him Director of the first Department of Andrology at an Australian hospital. He is currently the Inaugural Director of the ANZAC Health and Medical Research Foundation and of its newly constructed ANZAC Research Institute at Concord.

Professor Handelsman gained his undergraduate medical degree at the University of Melbourne. He has a PhD in medicine from the University of Sydney and in 1984 was awarded the NHMRC Neil Hamilton Fairley Fellowship to undertake postgraduate training as a specialist physician in endocrinology in USA. He continued these studies in both Germany and Australia.

Over a 20 year career he has contributed to over 440 publications including over 200 scientific papers. His experience and knowledge are great assets for Andrology Australia.

Body Image in Young Men

Late last year the British Medical Journal, in an editorial feature on men's health [7], reported on some concerns raised by Professor David Castle (Melbourne's Mental Health Research Institute) regarding the growing obsession with appearance of young men in our society.

The condition known as body dysmorphic disorder effects as many men as it does women. It involves exaggerated concerns about the appearance of the body, particularly skin, hair, nose, eyes and genitals.

A form of the disorder that occurred almost exclusively in men called muscle dysmorphia has recently been identified. Men suffering from this condition are preoccupied with their musculature, believing their bodies to be too small and "puny".

The result is commonly compulsive working out at the gym and painstaking attention to diet and dietary supplements. The fear is that muscle dysmorphia may lead to potentially dangerous anabolic steroid use or abuse of androgen therapies. Professor Castle quotes a London study indicating that 6-7% of high school boys have used these drugs to enhance their appearance.

The cause of the disorder is unknown and probably multifactorial, however recent social pressures for boys and men to be large and muscular is considered to be a major contributing factor to the development of this disorder and subsequent androgen abuse.

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