
Debate article

Ageing male syndrome, **andropause**, androgen decline or mid-life crisis?

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Reports of a “male menopause” have been appearing in the literature since the 1930s ^{[1] [2]}. The Heller and Myers paper of 1944 was seen by some as a ‘landmark paper where symptoms of age-related low testosterone were shown to be reversed by testosterone replacement, but not by placebo ^[3]. The “male menopause” has been referred to as the **andropause**, viropause and the male climacteric ^{[1] [4] [5] [6]}. The topic is one referred to little in mainstream medical journals. The recent *British Medical Journal* themed issue, “Men’s Health” ^[7] made no mention of the subject. It might also be asked if the symptoms are more consistent with a possible mid-life crisis, an “I Don’t Know syndrome”? ^[4] or the “irritable male syndrome” ^[8]. The word, climacteric, (from the Greek Klimacter, meaning the rung of a ladder), is a more useful term than menopause, as it suggests a gradual rather than a precipitous fall in hormone levels as occurs in a female.

The term androclise (‘clise’ in Greek means slowly diminishing) is perhaps clinically more correct than **andropause**, but still not biologically appropriate for all men. It conveys the physical and emotional changes which are often related to ageing in general, but are usually associated with significant hormone changes. Yet another and perhaps a more appropriate designation is what has been termed as the syndrome, Androgen Decline in the Ageing Male (ADAM) ^{[9] [10]}. Following the WHO meeting in Paris 2003 and the recommendations of the World Congress on the Aging Male in Prague 2004 experts have however now agreed on two definitive terms that can be used, either the Ageing Male Syndrome (AMS) or late onset hypogonadism. In contrast to the female menopause, the process in men is characterised by insidious onset and slow progression ^[11]. The clinical picture can easily be attributed to the natural and unavoidable consequences of the ageing process in males. The clinical syndrome cannot be linked directly to a decrease in the hormone testosterone as other hormones may also be involved and these

remain to be fully established. However, the response of the syndrome to Testosterone Replacement Therapy (TRT) suggests that it may be a syndrome that is amenable to therapeutic intervention ^[10]. Indeed, the onset of AMS is unpredictable and its manifestations are subtle and variable, which has led to relatively little interest in both its diagnosis and possible treatment since the concept of “male menopause” was first considered seventy 70 years ago.

Articles appear regularly in newspapers on the term “male menopause” for what is perceived as a new concept based on an analogy with the well described menopause in females which is clearly defined by the cessation of menstruation. These articles do not make clear exactly what the “male menopause” is and regularly debate whether it even exists. Nevertheless, not only does it now have two official names but at least two societies exist, the **Andropause Society** (www.andropause.org.uk) and the International Aging Male Society (www.issam.ch/), which promote research into the subject.

Before considering the concept of the Ageing Male Syndrome, it is important to be clear what a midlife crisis could be and how the two may be distinguished ^[12]. A midlife crisis is a term used frequently of men in their forties, but is sometimes also applied to women. The media has the archetype vision of seeking a younger partner, the purchase of a motorbike or sports car, ditching the family unit and the office job and the escape from domesticity fuelled by a vision of utopia. These findings may be coincidental with possible symptoms of AMS based on middle-aged men experiencing a reduced libido, energy levels and mood swings including depression ^[13] thought to be due to a fall in the male hormone, testosterone. The reasons for difficulties in distinguishing between a possible midlife crisis and AMS is that the fall in testosterone levels is slight and slow and there is no sudden cessation of fertility in the male, ^[5] unlike in female menopause.

There is a progressive reduction in testicular function in men between the ages of 25 and 75 years, with peaks in incidence between 45 and 50 years. During this time the concentration of bioavailable testosterone can fall by almost 50%, although there is a great deal of variation between individual men ^{[4] [14]}. In women oestrogen production by the ovaries drops suddenly at the menopause.

Symptoms of a possible “male menopause” reported in the literature are varied ^{[1] [15]} and although many are common to the female menopause their appearance is much more random. These symptoms can be divided into the categories of endocrine, physical, sexual and psychological.

Symptoms of a possible Ageing Male Syndrome

Because the intention is to detail the extent of AMS there is an overlap between the following categories

Endocrine

Flushes, erectile dysfunction (which can also have other causes such as cardiovascular disease or diabetes), reduced erectile quality, diminished nocturnal erections, increase in abdominal and visceral adipose tissue and waist size, dry skin on face or hands, joint and muscle aches, decrease in body hair and skin alterations.

Physical (somatic)

Decreased vigour, easily fatigued, diminished muscle mass and strength, loss of lean muscle mass and decrease in bone mineral density resulting eventually in osteoporosis.

Sexual

Decreased libido, reduced sexual activity, poor erectile function, limited quality of orgasm, reduced volume of ejaculate and weakness of ejaculation.

Psychological

Changes in mood, poor concentration, loss of motivation, becoming lackadaisical, reduced memory, anxiety, depression, irritability, general decrease in intellectual activity, decline in libido and insomnia.

All these symptoms and signs need not be present to define AMS. The severity of one or more of these symptoms and signs does not necessarily match that of others. Their uneven appearance and development is not yet understood as there is considerable variation between men. The symptoms are, however, also the natural and unavoidable consequence of ageing in men.

A validated screening questionnaire called the Saint Louis University ADAM questionnaire has been developed and based on some of these symptoms. This can objectively be used to ascertain whether men can be categorised as being menopausal and so androgen deficient [\[10\]](#)

.The questions used are as follows:

1. Do you have a decrease in libido (sex drive)?
2. Do you have a lack of energy?
3. Do you have a decrease in strength and/or endurance?
4. Have you lost height?
5. Have you noticed a decreased "enjoyment of life"?
6. Are you sad and/or grumpy?
7. Are your erections less strong?
8. Have you noticed a recent deterioration in your ability to play sports?
9. Are you falling asleep after dinner?
10. Has there been a recent deterioration in your work performance?

A positive questionnaire result is defined as a “yes” answer to questions 1 or 7 or any three other questions. This can be used to identify men with a high likelihood of androgen deficiency and so an associated symptom complex to define the AMS.

Testosterone patches are now being used in America in an attempt to treat and possibly reverse such endocrine, physical, sexual and psychological symptoms. But, is this phenomenon just being used as an explanation for various non-specific symptoms associated with the ageing process ^[11] ? Studies have found that increases in serum testosterone levels can overcome androgen deficiency and so increase sexual interest and have a significant effect on erectile dysfunction despite a reduction in sensitivity of the target organ to testosterone (‘target tissue insensitivity’) ^{[15] [16] [17] [18] [19]} . Testosterone has been recorded to be effective in 6-45% of erectile dysfunction cases ^[6] .

A relative indicator of androgen deficiency in an ageing male is the measurement of serum bioavailable testosterone. In other words testosterone that is free or weakly bound to serum albumin ^[20] . This is decreased primarily from testicular Leydig cell impairment and factors that alter the hormones; luteinizing hormone (LH) and follicle-stimulating hormone (FSH). In addition, many other hormones may play a part in the symptoms of AMS. For example, human growth hormone, insulin-like growth factor and dehydroepiandrosterone ^[21] .

Prevalence of erectile dysfunction increases significantly with age ^[22] . Consultation rates are generally low in men and the opportunity for recognising such symptoms are limited and should perhaps be explored, if appropriate, whenever a patient consults. It is possible therefore that many of these symptoms, whether they be hormonal or psychological, can go unrecognised and untreated.

The use of testosterone patches may present problems such as the potential activation of testosterone sensitive sub-clinical adenocarcinoma of the prostate gland that may normally have remained inactive throughout a patient’s life ^{[4] [5]} . After one year of testosterone replacement therapy (TRT) a recent study of 75 hypogonadal men with prostatic intraepithelial neoplasia (PIN) found they did not have a greater increase in prostate-specific antigen (PSA) or a significantly increased risk of cancer than men without PIN. These results suggest that TRT is not contraindicated in men with a history of PIN ^[23] . Considerable speculation still surrounds testosterone treatment and the prostate gland.

In the short term, testosterone in ageing men improves the male physique (lean body mass), cognitive function, but its possible effect on the cardiovascular system is unknown ^[24] although fluid retention may be a problem. Treatment is thought to have little or no effect on bone density or muscle strength. Such risks need, however, to be carefully balanced before the general use of testosterone patches is recommended ^[5] as long-term risks might be of gynaecomastia, polycythaemia, prostatic stimulation and an uncertain effect on cardiovascular disease. The consequence of testosterone on lipid and glucose levels and blood clotting is not known, but for ageing men going through a possible adropause, the risk of coronary artery disease is increased and fibrinolytic capacity is reduced so TRT may be beneficial, but this remains to be evaluated fully. A recent paper indicates that low testosterone levels could be associated with a greater risk of Alzheimer’s disease and future research is necessary to determine whether higher endogenous free testosterone levels through TRT offer protection against a diagnosis of Alzheimer disease in older men ^[25] .

If testosterone is to be given it would seem logical to take some baseline measurements first and see if they alter as a result of the therapy. These include: lipids, PSA, full blood count, testosterone, LH and FSH. Testosterone can be given orally, topically, by intramuscular injection or with an implant. As a result of a high first pass and conversion to inactive metabolites, oral medication needs to be taken three times a day. It can be given by injection or applied as a gel formulation or absorbed using a skin patch. When given transdermally it can most ideally mimic

the diurnal physiological variations observed in normal human testosterone secretion ^[9]. However, as with many medications applied through patches enabling absorption through the skin, local irritation and sensitivity can be a problem.

Although some reports suggest that TRT provides benefits for men with AMS, controversy remains regarding indications for its use. To address potential concerns, large-scale and long-term studies would need to be initiated where men could be monitored to exclude potential prostate and cardiovascular sequelae. A recent review paper discusses what is known (and not known) about the risks of TRT ^[26].

The existence of a “male menopause” is a contentious area and one of much debate, particularly given the low consultation rates of men and the low reporting rates of possible symptoms. Some doctors believe that the symptoms attributed to a possible “male menopause” are more likely to be the result of non-hormonal explanations. These might include lifestyle issues such as alcohol and drug misuse, other medications, marital problems, financial problems, stress and burnout and so may be more consistent with a possible mid-life crisis ^{[15] [16]}. It would seem appropriate and is generally recommended that these factors are considered, discussed and if possible dismissed before any potentially harmful male hormone treatment is cautiously contemplated ^[15].

Although, there is some evidence to support a hormonal basis for an AMD, several of the symptoms may be related to the perception with increasing age of a threat to the masculinity of men. It might even be suggested that such a threat manifests itself in the form of a mid-life crisis where middle aged men feel the urge to seek the company of younger women, and adventure ^[1]. Indeed, many of the non-specific symptoms listed earlier could be manifestations of depression and so fuel the controversy as to whether a “male menopause” really exists.

There is a belief that men are reared by society to be strong, so when they feel threatened by these perceived changes which they cannot control, some feel the need to prove their youth and masculinity to those around them ^{[27] [28]}. Associated physical symptoms could well be attributed to a “male menopause”. These should be carefully distinguished from psychological, emotional and even spiritual symptoms, which could more likely be the basis of a postulation for the occurrence of a mid-life crisis and the realisation of one’s mortality exacerbated by increasing vulnerability to illness and fatigue.

It would be unscientific to dismiss the concept of a “male menopause” and a suggestion that improvement in health in male midlife can never be achieved ^{[28] [29]}. It is an important and somewhat neglected area of research. To study the area clinically, andrology clinics are needed, just as there are menopause clinics for women. In the UK andrology remains a subspecialty of urology and there is a need for it to become an independent specialty like gynaecology. In other countries it may become part of associated specialties such as endocrinology. The concept of a “male menopause” remains an interesting, important and exciting area of future research.

Summary

- The ageing male syndrome has also been referred to as the **andropause**, viropause, male climacteric, ADAM (Androgen Decline in the Aging Male) syndrome, Ageing Male Syndrome (AMS) or late onset hypogonadism.
- Possible symptoms can be divided into the four categories of endocrine, physical, sexual and psychological.
- Testosterone Replacement Therapy (TRT) may have a role in treating symptoms. The pros and cons of TRT are discussed, together with the long-term dilemmas in relation to the prostate gland and cardiovascular disease.
- Symptoms may also be consistent with lifestyle issues and a possible mid-life crisis or depression.
- This is a contentious area, but whether middle aged men are suffering hormonal deficiencies or psychological problems, they should not go untreated.

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