The Andropause: Moving Forward from Denial to Discovery

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The time has come to put to rest the barbs and criticisms of the naysayers who either question or outright deny that the andropause exists. It is also time to put to rest the hesitation and discomfort some may have with the terminology, andropause. Andropause exists and andropause is its name, and many of yesterday’s naysayers are among today’s converts.

The Four “Pauses”

Perhaps the easiest way to envisage andropause is to view it as one of the four major “—pauses” in the endocrinology of aging.1 There are many theories as to why we age and many studies trying to understand the molecular basis of aging. Yet whatever the underlying mechanisms finally turn out to be, there are at least four significant alterations of endocrine function, each of which has been designated the suffix “pause”. Whether or not this is an appropriate designation or the most descriptive of each of these endocrine changes is a moot point. The names transmit concepts that we can recognize and study, and that we can influence, if needed, with therapeutic strategies.

The four ‘pauses’ are characterized by a more gradual, albeit distinct, decline in secretory output.

Perhaps the least notorious of the “pauses” is adrenopause. As humans age, the adrenal glands diminish their production of dehydroepiandrosterone (DHEA) and its sulfate, DHEA-S.2 The third and also less familiar “pause” is somatopause, which describes the loss of growth hormone with advancing age.3 What is still unknown for both adrenopause and somatopause is whether these changes have clinical relevance or if treatment with DHEA or growth hormone will be effective.

Andropause: The Facts

Although we are still in the early chapters of the andropause story, we have gleaned considerable information about its nature and consequences, particularly since the early 1990’s when research into the effects of a decline in testosterone in the aging male was significantly increased. Since then, there been a sharp increase in andropause research, and increasing awareness of the pathophysiological events involved and the possible amelioration of some of these events by testosterone treatment.

Both total testosterone and bioavailable testosterone decline with age3,4 as a consequence of three changes that come with age (see article, page 34):

1. Decreased hypothalamic-pituitary sex hormone output.
2. Primary testicular insufficiency as manifested by decreased Leydig cell numbers and function.
3. Increased sex hormone binding globulin (SHBG) production resulting in a decrease of total testosterone.

Other factors also may intervene to reduce the concentration or effectiveness of testosterone with aging. For instance, obesity brings with it increased aromatase activity resulting in enhanced conversion of testosterone to estradiol.5

None of the above age-related changes are a matter of debate. They are a matter of reproducible scientific documentation. The fact that men become increasingly symptomatic as they age also is not a matter of debate. There is a significant increase in symptoms including lethargy, irritability, insomnia, weakness, erectile dysfunction, loss of libido, dysthymia or depression and osteopenia or osteoporosis. There have now been enough studies and accumulated anecdotal experience to know that many symptomatic men with a low level of testosterone will find relief or total amelioration of their symptomatology when given testosterone.6 This is the andropause—the low-testosterone causing symptoms relievable in part or completely by testosterone administration.7 8 All these things we know and need not be the subject of debate. The andropause exists.

Andropause: The Questions

What we don’t know with absolute certainty is the effect of prolonged testosterone treatment on the prostate gland and perhaps other organs. The single most important consideration in initiating testosterone replacement therapy is the potential prostate responsiveness to testosterone administration. There is virtually no evidence to support the idea that testosterone will induce the formation of a new prostate cancer,9 nor is there evidence to suggest a relationship between blood levels of testosterone and prostate cancer.10

There is, however, evidence to suggest that testosterone treatment may exacerbate or enhance the growth of an existing prostate cancer. Until further long-term research is available, extreme vigilance is necessary for the assessment and monitoring of andropausal men who require testosterone replacement. The argument has been put forward that making a hidden, subclinical prostate cancer clinically apparent—by either digital rectal exam or by detecting an increase in PSA levels—has actually been a positive initiative because early prostate gland cancer may be curable by aggressive treatment. Only time and careful study will clarify this point. Stressing close prostate surveillance does not diminish the viability of the entity, andropause. Andropause is not a name looking for a disease,
but is a part of the aging process, likely experienced by every aging man to one degree or another. What is needed is further understanding of its various aspects and a better appreciation of the long-term implications of testosterone replacement therapy.

**Role of the Canadian Andropause Society**

The Canadian Andropause Society (CAS) was established in 1998 to encourage more understanding, awareness, investigation and treatment of appropriately screened and diagnosed andropausal men. The CAS is a young society dealing with a newly recognized passage of life that may be physiological in a certain sense but that brings adverse clinical sequelae with it.

The CAS has several mandates (Table 1). The CAS is one of the primary Canadian organizations providing leadership in the area of men’s health, particularly in the area of hormonal regulation of that health. Because of the endocrine connection, it may be that the future will see the CAS broadening its mandate to include adrenopause and somatopause. In fact, the CAS already is providing partial funding for a multicentre Canadian research study on the adrenopause, to assess the therapeutic implications of DHEA.

One of the most confusing issues for physicians is which of the several ways of looking at testosterone and its major subfractions is most appropriate to diagnose a hypoandrogenic state. The CAS has launched a new initiative to acquire views from experts across the country on what testosterone testing recommendations should be made to physicians, laboratories and government for funding.

Testosterone has multiple positive effects in several bodily systems, including bone metabolism, muscle protein synthesis, lipids, cognition, mood and the heart. To ignore the many functions of testosterone and the possible beneficial effects of treatment in appropriately selected cases does not seem like prudent medicine. Vigilance, yes—but neglect and denial?

Canada is one of the leading countries in the world to actively pursue a clearer understanding of the andropause, its investigation and its management. The CAS feels that first and foremost is the patient, whose quality and quantity of life may be severely impacted by the endocrine sequelae of the andropause. Although we must move forward with caution, the CAS believes we must move forward.

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**Table 1**

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**References**