The male menopause: does it exist?

AGAINST: Problems of senescence in men are not analogous to female menopause [see opposing view p. 76](#)

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The normal menopause—that is, the final cessation of menstruation—is caused by primary ovarian failure. The estrogen deficiency that results often causes vasomotor instability (flushing and sweating attacks), genital atrophy (vaginal dryness and discomfort), and bladder irritability, together with difficulties in cognition and loss of a general feeling of well-being. This climacteric syndrome, readily reversible by estrogen treatment,¹ is obviously gender-specific. We have to ask whether it really provides a helpful analogy for the features Jaques described as the penultimate age of man²:

... The sixth age shifts
Into the lean and slipper'd pantaloons,
With spectacles on nose and pouch on side,
His youthful hose well sav'd, a world too wide
For his shrunk shank; and his big manly voice,
Turning again toward childish treble, pipes
And whistles in his sound.

In thinking about this, we do well to consider how many of the changes in men as they pass from middle to old age should be attributed to the passage of years and how many to a decline in hormone concentrations. An endocrine explanation is attractive because it raises the possibility of hormonal therapy for symptoms that occur at this time of life. The findings of a careful review of the literature are at best suggestive. But we still have a way to go.

First, what hormonal changes occur in aging men? Certainly gonadal function wanes: by age 80 years, serum total testosterone concentrations have fallen to about 75% and free testosterone concentrations to about 50% of what they were at age 20.³ The fall of free testosterone (that is, of the fraction that is biologically available to the tissues) is amplified by a difficult-to-explain but regularly observed increase in concentrations of the sex hormone-binding globulin.⁴ The fall in testosterone production is caused partly by testicular failure and partly by changes in pitu-

itary gonadotropin secretion.⁴ The key difference from the menopause, however, is the gradual nature of the change in men compared with the precipitate fall of estrogen concentration in women.⁵

Second, what are the biologic changes that can be related to these endocrine alterations? The association of a symptom with a particular hormone concentration does not indicate causation. Therefore, before attributing to testosterone deficiency the reduction in sexual activity, the decline in muscle bulk to which Jaques referred, and the decline in skeletal mineralization that may all occur in elderly men, we are obliged to prove that hormone replacement therapy in physiologic doses reverses these processes. We must, in other words, shift the argument from epidemiologic to interventional studies. The history of this treatment is that it began with a number of persuasive trials of full-dose testosterone treatment of both young and older men with hypogonadism.⁶⁻⁹ When, however, physiologically appropriate doses of testosterone were administered to elderly men, the results were less impressive. For example, for 3 years, Snyder and colleagues treated a group of almost 100 healthy men older than 65 years with testosterone patches in doses sufficient to raise their serum testosterone concentrations into the range appropriate for men in their 20s.¹⁰ The overall effects on bone mineral density were no different from those obtained with placebo. Although lean body mass increased significantly (1.9 [SD 0.3] kg), principally in the trunk, and fat mass decreased (-2.9 [->0.5] kg), principally in the arms and legs, Snyder and colleagues were unable to detect a significant increase in muscle strength, as measured in extension and flexion of the knee with a dynamometer.¹¹

So far as sexual activity is concerned, the role of testosterone in elderly men is still not well defined.^{12,13} Circulating concentrations of testosterone in older men are usually well above those needed for a normal sexual response, although the proportion of men complaining of erectile dysfunction rises dramatically with age, such that 50% of men between the ages of 50 and 70 years complain of impotence.¹⁴ As many as 80% of cases of erectile dysfunction are now thought to have a medical cause, such as diabetes mellitus, cardiovascular disease (especially angina and after myocardial infarction), neurologic disorders (multiple sclerosis and spinal injury), pelvic surgery (prostatectomy), and trauma. Indeed, some have suggested that the development of erectile dysfunction should be regarded as sentinel of disease and an indication for careful medical assessment.

Recent work, reviewed elsewhere,¹⁵ has shown that what ultimately determines potency is the ability of muscles in the walls of the artery supplying the penis to relax and so permit engorgement to occur. Nitric oxide released from parasympathetic nerve endings in response to sexual stimulation causes guanylate cyclase to produce

cyclic guanosine monophosphate (cyclic GMP), which relaxes arterial smooth muscle. Cyclic GMP is metabolized by a specific phosphodiesterase. Sildenafil citrate (Viagra) inhibits this enzyme, prolongs arterial relaxation, and so enhances erection. As for impotence in an older man, unless hypogonadism can be clearly shown, treatment with sildenafil (with appropriate warnings about cardiovascular risks and drug interactions with nitrites) is likely to be safer and more efficacious than injections of testosterone esters.

The analogy of the female menopause is not helpful in understanding or trying to manage the problems of senescence in men. Moreover, the endocrinology of aging is much broader than that term suggests. As Lamberts and associates have pointed out, although the fragility of elderly people might be related to a gonadopause, an adrenopause (the age-related fall of dehydroepiandrosterone sulfate concentrations), or a somatopause (the decline in secretion of growth hormone and insulinlike growth factor), actually in old people, the commonest endocrine disorders are diabetes mellitus and hypothyroidism.¹⁶ These conditions are definitely treatable.

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