

## GUEST EDITORIAL

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### The Politics of Testosterone

It is dangerous to be right when the government is wrong.

—Voltaire

For reasons that are not readily apparent, there appears to be a conservative political movement that opposes the use of testosterone in older men. This was perhaps best demonstrated by the report of the Institute of Medicine, which felt that testosterone was not yet ready for prime time and that there was still a need for a number of relatively small studies to prove its efficacy [1,2]. Similarly, the guidelines of the Endocrine Society on testosterone use in older men seem, to many, to be ultra-cautious [3]. In contrast, other more-liberal guidelines and recommendations have been published [4,5]. Despite this, most regulatory agencies and third-party payers tend to display a negative view toward testosterone. In this issue of the *Journal*, the guidelines for testosterone treatment in older men, which were developed by the Canadian Society for the Study of the Aging Male, are being published. This editorial explores the reasons for the negative attitudes to testosterone-replacement therapy.

#### **There Is Insufficient Evidence That Testosterone Is Efficacious in Older Men**

Since the original studies demonstrating a salutary effect of testosterone in older men [6–8], numerous placebo-controlled studies have demonstrated that testosterone has positive effects in older men. These have been summarized in a number of recent meta-analyses [9–11]. Testosterone clearly improves sexual function (both libido and erectile function) in older men. In addition, it improves the quality of erections when hypogonadal men are treated with testosterone before receiving a phosphodiesterase-5 inhibitor [12,13] and, in some cases, can reverse total failures to respond to phosphodiesterase-5 inhibitors [14]. In addition, testosterone in low doses in borderline hypogonadal men increases muscle mass and decreases fat mass [15,16] and in higher doses, in men with a testosterone less than 12 nmol/L, improves strength [10,11]. In a recent large study (N = 322 men over 50 years of age) testosterone unde-

conote improved sexual function, increased lean body mass, decreased body fat mass, and increased bone mineral density at both the hip and the lumbar spine [17]. There are also data suggestive that testosterone will improve cognition and mood and perhaps even be useful in treating some persons with Alzheimer's disease [18–22]. Finally, there are epidemiologic data demonstrating that testosterone deficiency is associated with bothersome symptoms in older men [23–25].

In contrast to these facts, let us compare testosterone deficiency in older men to two conditions which few physicians would argue should be treated in older men, viz., hypercholesterolemia and hypertension.

Numerous epidemiologic studies have shown that low, not high, cholesterol is an excellent predictor of death in older persons [26–29]. In addition, cholesterol levels in patients, even following a myocardial infarction, fail to predict subsequent death for up to 6 years [30]. The PROSPER study, which examined the effects of pravastatin in 5,804 patients aged 70–82 years followed for 3.2 years, failed to find any hint of a change in total mortality [31]. While mortality from coronary artery disease did decrease, it was counterbalanced by an increase in new cancers, leading one to ask whether you would prefer to die from cancer or a myocardial infarct? In addition, there was no effect on cognitive function or disability.

Similarly, in the case of hypertension in persons over 85 years of age, the best mean survival is seen in persons with highest blood pressure [32]. A meta-analysis of 1,670 persons over 80 years of age who had their hypertension treated in randomized controlled double-blind trials, showed an increased total mortality and a tendency to increase cardiovascular deaths [33]. The HYVET pilot trial of 1,283 persons over 80 years of age with a 13-month follow-up showed increased total and cardiovascular mortality [34].

Based on these data it appears that physicians and regulatory agencies are much more comfortable treating older men with drugs which will kill them earlier, without improving any symptoms,

than using testosterone, a drug that improves symptoms that are important to many older men and may even reverse sarcopenia and frailty [35–41]. This is one of the best examples of “eminence” based medicine trumping evidence-based medicine in the history of medicine.

### Testosterone Increases Prostate Cancer

The prostate mafia lead by “Dr. Grossfinger” and other urologists has, with minimal evidence, convinced the medical establishment that testosterone will cause prostate cancer. In fact, prostate cancer occurs in older men at a time when testosterone levels have declined to low levels [42]. The meta-analysis by Eaton et al. [43] could show no prospective evidence that either testosterone or non-sex hormone-binding globulin-bound testosterone was correlated with the development of prostate cancer. Retrospective studies have failed to demonstrate an increase in prostate cancer in men treated with testosterone [44].

### Unrealistic Expectations

Testosterone has been claimed by some to be the ultimate anti-aging cure [45]. While the effects of testosterone are generally positive, a bit like antidepressants, they provide an important, but relatively small incremental improvement in symptoms over placebo [46]. The failure of testosterone to perform at the level of the claims of the “anti-aging” charlatans is then held against testosterone, and its legitimate use in symptomatic hypogonadal men is rejected.

### Andropause Was Invented by the Pharmaceutical Industry

In fact, the ancient Chinese Text of Internal Medicine spoke about “male menopause (which) begins gradually around the age of 50 or 60” [47].

Unfortunately, testosterone replacement in older men has had a checkered history since the original claims by Brown-Sequard that testosterone injections rejuvenated him and the exploits of the “monkey-gland” doctors led by Serge Voronoff. This history reached its low when the American Medical Association attacked the exploits of the goat-gland doctor, Dr. Brinkley [48].

### Bad Karma: It’s All about Sex

Testosterone therapy is tainted by the fact that it improves sexual enjoyment. Even in the times of

Viagra, our attitudes to sex remain similar to the concept of the English of the Victorian era, “Imagine if you give an old man testosterone, he may want to have sex”!! In the United States, the use of testosterone in women is facing a similar barrier [49,50].

### Testosterone Will Be Abused by Young People

Abuse of anabolic steroids, as demonstrated by our baseball heroes, will occur whether or not testosterone is available for old men.

### Ageism

Rabbi Abraham Herschel said:

The test of a people is how it behaves toward the old.  
It is easy to love children.  
Even tyrants and dictators make a point of being fond of children.  
But affectation and care for the old,  
The incurable, the helpless  
Are the true gold mines of a culture.

Regrettably, the lack of enthusiasm to support the use of testosterone replacement in older men is most probably simply a form of ageism. Simply put: “We have no enthusiasm to waste our money paying for you old guys to be happy.”

### Conclusion

In the end, a particular political viewpoint is in the eye of the beholder. Nevertheless, it would appear that the political failure to demonstrate enthusiasm for replacing testosterone in older men is based on ageism and the inability to accept that enhancing sexuality in older men is an appropriate pursuit.

JOHN E. MORLEY, MB, BCh  
*Division of Geriatric Medicine, Saint Louis  
University Medical Center and VA Medical Center  
(GRECC), St Louis, MO, USA*

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