

COMMENTARY

The diagnosis of late life hypogonadism

This first article in the 'Expert Opinion' section in this journal [1] is a bold voyage into the stormy waters surrounding the nomenclature, diagnosis and indications for treatment of androgen deficiency in the adult male. It offers a seemingly logical, positive and constructive way forwards for the clinician faced with the difficult choices which arise in daily clinical practice in this field. It also goes further than usual in giving the patient the benefit of the doubt which inevitably arise in the doctor's mind when faced with the question to treat or not to treat the characteristic pattern of symptoms of what might preferably be called the 'testosterone deficiency syndrome' (TDS) [2].

On the vexed question of terminology, late life hypogonadism sounds more specific than it actually is. Can a man in his forties, perhaps halfway through his lifespan, be said to suffer from such a condition? Also, calling the condition hypogonadism seems to presuppose that it is the 'gonadal status' that is mainly at fault, almost entirely due to insufficient testosterone production. It is like focusing exclusively on insulin levels and pancreatic function in maturity onset diabetes. However, as pointed out, it may often be increased resistance to androgen action resulting from excess sex hormone binding globulin activity, any of the androgen receptor polymorphisms, or a vast range of other metabolic factors at the cellular level, which can be the usually multifactorial source of the problem [3].

Again, in an analogy with insulin in maturity onset diabetes, the symptom complex characteristic of TDS could be considered as being due to 'an absolute or relative deficiency of testosterone or its metabolites according to the needs of that individual at that time in his life' [4].

The great complexity of the mechanisms of action of testosterone on different organs, cells and metabolic pathways is likely to frustrate the quest for the holy grail of the ideal questionnaire to diagnose TDS. Of the many available, the best designed and validated appears to be the Aging Male Symptoms (AMS) questionnaire [5]. This has the added advantage of being available in over 20 different languages, and scaleable, so that it can be used for monitoring responses to treatment as well as diagnostic purposes [6]. Despite its name, it is less

age-related in the scores it gives than the Androgen Deficiency in Aging Males (ADAM) questionnaire. However, neither of these commonly used questionnaires can predict low testosterone levels with any degree of specificity, and in a recent study of both, no relationship was found between symptomatology and any of a battery of eight endocrine assays, including total and free testosterone, other than possibly age-related declines in DHEA and IGF-1 [2].

Neither are total and free, nor bioavailable testosterone the definitive measures of androgen deficiency that endocrinologists would like them to be. Conditions of sampling, physiological and health-related factors, analytical variation, and above all interpretation of results according to arbitrary and of inappropriate norms, can combine to invalidate decisions made on androgen assays being given priority over symptoms [7]. As reiterated in this opinion, it is an inconvenient truth that one man may have total and free testosterone levels that lie anywhere within the normal reference range, and still have symptoms which respond to treatment, and another have low levels without symptoms.

Although this opinion offers what is described as a 'radical proposal', it is an approach to this clinical dilemma which an increasing number of clinicians are adopting. It coincides with the emerging view that "the lack of correlation between the clinical picture and the most commonly used biochemical confirmatory tests, again, clearly points to the paramount importance of the clinical evaluation. An emphasis and reliance on serum T alone hinders the clinician's ability to manage testosterone deficiency syndromes (TDS)" [2].

This opinion is welcome in that it shifts the tipping point in the decision to treat more towards the clinical assessment and symptomatology rather than widely varying and often invalid laboratory measures. It is suggested that the level of total testosterone is just the tip of the iceberg of androgen deficiency and clinicians should steer their patients towards a therapeutic trial of treatment accordingly. If this basically safe form of treatment produces symptom relief and an improved quality of life for years on end, it is likely to indicate that it is not just a placebo effect, but a fully justified form of 'mainstream medical

treatment' [8] for a very common, important, under-diagnosed and, above all, under-treated condition.

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References

1. Morley JE. The diagnosis of late life hypogonadism. *Aging Male* 2007;10:217–220.
2. Morales A, Spevack M, Emerson L, Kuzmarov I, Casey R, Black A, Tremblay R. Adding to the controversy: pitfalls in the diagnosis of testosterone deficiency syndromes with questionnaires and biochemistry. *Aging Male* 2007;10:57–65.
3. Carruthers M. The paradox dividing testosterone deficiency symptoms and androgen assays. *J Sex Med* 2007; In Press.
4. Carruthers M. ADAM: Androgen Deficiency in the Adult Male – causes, diagnosis and treatment. London and New York: Taylor & Francis. 2004.
5. Heinemann LAJ, Zimmerman T, Vermeulen A, Thiel C, Hummel W. A new 'aging males' symptoms' (AMS) rating scale. *Aging Male* 1999;2:105–114.
6. Heinemann LA, Moore C, Dinger JC, Stoehr D. Sensitivity as outcome measure of androgen replacement: the AMS scale. *Health Qual Life Outcomes* 2006;4:23.
7. Carruthers M, Trinick TR, Wheeler MJ. The validity of androgen assays. *Aging Male* 2007;10:165–172.
8. Morgentaler A. Cultural biases and scientific squabbles: the challenges to acceptance of testosterone therapy as a mainstream medical treatment. *Aging Male* 2007;10:1–2.

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