



Editorial

Testosterone Deficiency Syndrome (TDS) Needs to be Named Appropriately – The Importance of Accurate Terminology

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The decline in androgen production in association with increasing age has been recognized and documented for decades [1]. The prevalence and incidence of the condition has been estimated [2] and its treatment is becoming established [3]. Controversy however still exists on the clinical relevance of diminishing plasma testosterone (T) levels [4]. The burgeoning interest in understanding the consequences of T deficit, however, has not matched our ability to name it appropriately. At a time of substantial confusion and controversy in the field, we believe that correct terminology will bring conceptual clarity and rational basis for its management. Although this may appear to be a minor issue, the penalty has been skepticism on its medical relevance and additional confusion with regards to diagnosis and treatment. Thus, we believe that a suitable designation of the condition is important. Coming after the ISA, ISSAM and EAU recommendations on late onset hypogonadism (LOH) [5], the Endocrine Society Clinical Practice Guideline for T therapy in adult men, published recently [6] is a well thought out, timely and useful document not only for endocrinologists but also for urologists and other physicians involved in the care of men with low T. However, the important and clinically relevant issue of optimal terminology was not addressed in any of these guidelines.

For over 60 years [1,7] a deficiency in T production has been designated with an assortment of names that reflect a variety of opinions. Names have been put forward with little consideration of pathophysiological principles, in some cases because of poor understanding of the endocrine mechanisms, in others because of the erroneous opinion that the condition is a simple extrapolation of gonadal senescence in women and, in a few, by the common belief that the process is exclusively associated with advanced aging (which it is) but ignoring the fact that it can be detected as early as the 3rd decade and is not uncommonly absent in the elderly. We submit that those terms are misleading malapropisms and poorly reflect the type of deficiency state under scrutiny and the nature of the hormone involved. We therefore propose that Testosterone Deficiency Syndrome (TDS) is the best option due to its simplicity, clarity, and respect for physiological and etymological principles. There is no claim of originality on our part since TDS is already used sporadically [8] and interchangeably with those listed on Table 1. In fact, the Endocrine Society's recommendations referred to deficiency syndromes, but mentioned androgens when they should have referred to T explicitly.

The reasons for this proposal are manifold. We will discuss the grounds for the inappropriateness and limitations of the predominant current termi-

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Table 1 – Terminology for the clinical picture associated with low levels of T in the adult male

Andropause
Androgen decline in the aging male (ADAM)
Partial androgen decline in the aging male (PADAM)
<i>Androgen deficiency syndromes</i>
Combined primary and secondary hypogonadism
Late onset hypogonadism (LOH)
Male climacteric
Male menopause

nology and put forward the advantages of the alternative, namely TDS.

Male climacteric and male menopause. Among the misnomers for T deficiency, these two terms are, undoubtedly, the most erroneous. They ignore the etymology of the descriptive nouns: climacteric and menopause. Climacteric comes from the Greek root klimakterikos (rung of a ladder) as an age or period of life characterized by marked physiological change and commonly associated with the menopause. Menopause (Greek *mēn* month + *pauein* to cause to cease) implies that there is a cessation of a monthly event, which is not the case with the progressive decline in T production in men. Neither term brings to mind the fact that T is involved.

Andropause offers numerous advantages over the preceding terminology primarily because, in a single word, it conveys the idea of a process similar to the menopause: a hormonal alteration occurring as a result of the cessation of gonadal function. It also, in a subtle manner, carries the connotation that it occurs later in life. In addition, andropause has been and continues to be widely used both in the lay and medical literature with a fairly good understanding of what it implies. However, on the negative side, the process in men is rarely, if ever, sudden (the exception being iatrogenic castration or gonadal injury). The testosterone decline, normally, is unpredictable in its onset and follows a protracted course, usually over several decades; it is not universal and its manifestations are nonspecific: the telltale suspension of menses, of course, is not present in men.

ADAM and PADAM. The two terms (Partial Androgen Deficiency/Decline of Aging Male) represent a significant improvement. The androgen decline observed as a result of the aging process is incontrovertible and the only objectionable portion resides on the “aging” male. What does it mean? After all we are all aging. The United Nations definition of elderly starts at 65 years [9]. Should this be the starting point for ADAM/PADAM? Probably not. By the age of 65, if it is bound to occur, the process would already be well underway; studies reported a prevalence of T decline, at this point in life, ranging from 30% to 70% [2,4,10]. It is

known that the highest levels of T, after puberty, are reached by the 3rd decade. The waning of T (and other hormones) has inexorably started by then but one would be hard pressed to describe a 30 year old person as an “elderly” man. Therefore, it appears more fitting not to incorporate “aging male” in the description for T decline. PADAM has a nicer ring but nothing else going for it. It is redundant since “decline” implies that it is also partial; complete cessation of T production simply as a result of advancing age would be a rarity. Neither ADAM/PADAM or andropause specifically indicate that the deficit is on T production. Androgens include many other gonadal and non-gonadal steroids that, although declining with aging as well, do not result in the well-defined alterations in physiological functions observed with T deficiency.

LOH and SLOH. Late onset hypogonadism and symptomatic late onset hypogonadism gained favor recently because it circumvents the derogatory connotation of aging (a major plus) [12] and emphasizes that symptoms need to be present to consider T supplementation. It carries, however, a couple of significant drawbacks: the vagaries of “late” and the inaccuracy of “hypogonadism”. What is to be considered “late”: 40? 50? 60 years? The term hypogonadism has been used synonymously with a pathological T deficiency state arising from specific diseases or dysfunctions of the hypothalamic–pituitary–testicular axis which generally require specialized investigations. This is quite different from the age-related decline in T under consideration in terms of both aetiology and severity.

1. Androgen deficiency in adult men

This was the choice of the Endocrine Society published guidelines [5]. These guidelines referred to deficiency syndromes but mentioned androgens in general when they should have referred to T specifically, since there is insufficient evidence to include other androgens such as DHEA and androstenedione while DHT is generated locally in target tissues. We are also of the opinion that highlighting the deficiency by the marker under investigation (testosterone) is a more precise reflection of the clinical syndrome than the term hypogonadism.

2. The case for Testosterone Deficiency Syndrome (TDS)

“Testosterone” is clearly understood by the medical community and the public as representative of the

main male hormone. In addition TDS does not carry the negative and often erroneous perception that it is an obligatory restricted to elderly men.

The clinical picture of TDS, composed of symptoms and signs of variable severity, is well known and widely recognized [11]. It is also recognized that the diagnosis, normally, requires the combination of clinical manifestations and biochemical support. We, therefore, have the classical requirements for describing a syndrome (Greek *syn-* together + *dra-mein* to run). The fact that TDS shares some of its manifestations with other conditions (i.e. growth hormone deficiency, depression) and that controversy rages over the accuracy of various assays and calculations for the normal ranges of blood T does not demerit the need for a more accurate taxonomy of the condition. It is generally agreed that an accurate diagnosis should include the underlying aetiology when it can be established. Such a goal can be easily accomplished by linking the generic terminology of TDS to various specific conditions, e.g. TDS in aging/elderly men, TDS in diabetes, etc.

This proposal originated from a multidisciplinary perception that the emerging picture from many years of study of T alterations related to the aging process needs a better and more specific name. Hopefully it will be considered by the medical community as a forward step [12].

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