# Late-onset hypogonadism (LOH): an emerging pathophysiological entity requiring the physician's attention

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Late-onset hypogonadism (LOH) is an emerging pathophysiological entity. Not everybody is familiar with LOH or even recognizes its existence. Since the 19th century women's life expectancy has become progressively greater than that of men and therefore their ailments associated with aging from the climacteric onwards attracted medical attention much earlier than male aging health problems. In addition, male aging problems start at a later age than the climacteric occurs in women. However, men's life expectancy is also continuously increasing: in Europe a newborn male now has a life expectancy of about 75 years, and a 60-year-old man has a statistical possibility of reaching 80 years of age. The increasing number of aging men forces physicians to focus on their health problems.

Hypogonadism is defined as any impairment of testicular function, endocrine or exocrine, or both, resulting in lack of androgenicity and infertility. If the cause of hypogonadism resides in the testes themselves, it is characterized as primary; if causes lie in the hypothalamus or pituitary the term secondary hypogonadism is used (for review[1]). Cross sectional[2] and longitudinal studies[3] have shown that testosterone slowly declines with advancing age. Testosterone stays above the lower limit of normal in many aging men, but declines below that threshold in a percentage of men and this percentage increases progressively with advancing age.[4] The Leydig cell reserve capacity for testosterone biosynthesis is impaired as evidenced by decreasing response to hCG stimulation, indicating a primary testicular element in causing these changes. At the same time, amplitude and order of LH pulses as well as the pituitary's capacity to respond do GnRH stimulation of LH secretion are impaired, indicating a secondary element in the aging process of the hypothalamo-pituitary-testicular system. While spermatogenesis continues fertility can be maintained lifelong albeit at a reduced level.[5] In conclusion, testicular function declining with progressing age is caused by impaired testicular as well as pituitary function. When in this process testosterone levels drop below the lower limit of normal it is justified to speak of late-onset hypogonadism (LOH) which has a combined pituitary and testicular aetiology. However, LOH is not only a biochemical diagnosis, clinical symptoms are at least equally important and prompt the patient to ask for medical advice.

Once the diagnosis of LOH has been established the therapeutic consequence would be testosterone substitution as in other forms of hypogonadism. While testosterone substitution in primary and secondary hypogonadism has belonged to the standard therapeutic repertoire for over 60 years, comparatively few studies to date have dealt with the benefits and risks of testosterone substitution in LOH. Especially, long-term studies on the effects of testosterone substitution in LOH are lacking and research is now focussed on the effects of testosterone in aging men. Nevertheless, some benefits e.g. for body composition, bones, metabolism, sexual functions and cognition are already know and further possible benefits e.g. for the cardiovascular system[6], in diabetes treatment[7] and the metabolic syndrome[8] are emerging. Also implications for the prostate and lower urinary tract symptoms (LUTS) are under investigation. So far, the dogma prevails that testosterone should not be given to a patient with prostate carcinoma which has to be excluded before any testosterone treatment.

Although testosterone has been available for clinical use for over 60 years the treatment options for substitution therapy were rather limited until quite recently. New transdermal, buccal and injectable testosterone preparations, however, now result in the desired pharmacokinetic profile mimicking a serum testosterone and profiles of healthy younger men (for review[9]) and offer the possibility of treating LOH.

Testosterone treatment of LOH, however, should by no means be administered to aging men indiscriminately. Testosterone should be given to aging men only under strict criteria and under tight surveillance. In this regard, the International Society of Andrology (ISA) and the International Society for the Study of the Aging Male (ISSAM) set up a panel of experts which was later joined by the European Association of

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Urology (EAU) to draft recommendations for the investigation, treatment and monitoring of LOH which are reprinted in this issue.[10] These recommendations translate current scientific and clinical knowledge about LOH into practice. They provide the physician with guidelines for dealing with aging men suffering from LOH.

The question remains who should deal with LOH and patients afflicted by it? Unlike for women who have a medical speciality dealing with female reproductive and health problems throughout their life cycle, men often do not know whom to consult. Isn't it about time that a medical (sub-) speciality deals specifically with male problems? There are now about 40 learned societies around the globe dealing with "andrology", but there are very few countries where andrology has reached professional status in the medical system. Germany is the first country in Europe recognising andrology as a sub-speciality for endocrinologists, urologists and dermatologists and hopefully for the benefit of men, other countries will follow soon.

Andrology concentrates on five areas: infertility, hypogonadism, erectile dysfunction, male senescence (especially LOH) and male contraception. All these areas have made significant diagnostic and therapeutic progress in recent years so that the critical mass warranting a (sub-) speciality has accumulated. Establishing andrology as a medical discipline marks an important step towards gender equality in health care.

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