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## Introduction: the politics of testosterone

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### ■ There's more to testosterone than just sex

I suspect that if testosterone wasn't associated with sexual function then there would be no need to write this chapter. In addition the smouldering media debate and medical discourse which have flared up from time to time concerning the use of testosterone therapy (TTh) would probably have died out.

Testosterone is a word used loosely in everyday life by people who may not know much about it. One hears comments like 'male aggression fuelled by testosterone'. A quick Internet search produced comments by the Urban Dictionary: "During the war grandpa was a testosterone-fuelled madman killing lots of enemies".<sup>1</sup> Often, the only things that the general public know about testosterone are the negative aspects. When Abraham Morgentaler was interviewed by Abdulmageed Traish, about testosterone and negativity he stated: That perspective is made even worse by ads that we see on TV or in the media that promote supplements that are, I suppose, allegedly intended to boost testosterone, to make men more 'manly'.<sup>2</sup>

When checking the definition of manly, it is not meaning male aggression implying that testosterone treatment will turn men into rampaging bull elephants, or start committing sexual abuse or violence. Manliness is a term of approval, when a man feels good about himself, feels strong both physically and mentally, earns respect from his partner and demonstrates traits approved by society. When I see the partners of patients with low testosterone levels they often say "He has lost his oomph", or "I want him to be strong and support me again". One of my patients with both clinical symptoms and several laboratory tests demonstrating low testosterone described himself as a "Weak, feeble creature".

One of the factors that has fuelled the fire of T criticism is its misuse among young men, especially those involved with bodybuilding and sport. These athletes and so-called "sportsmen" cheat by using anabolic androgenic steroids (AAS) in order to gain an advantage over their competitors by adding muscle bulk to make them physically stronger. Medically qualified clinicians increase

the sleaze, undercover and improper use of testosterone by issuing prescriptions to these so called "Olympians". The use of (AAS) has been an international political football with nations being accused of cheating, excluded from competing, or medals retracted. The Countries alleged of doping their athletes bounce back with denials and claims of improper testing or false results. Of worrying concern is the continuing increase in AAS for body image and cosmetic reasons in the UK.<sup>3</sup> Sometimes the medical profession are complicit in prescribing T illegally to such patients and to men that have normal physiological T levels and without signs or symptoms of TD.

As I write this chapter, another Political/Sporting/Media/Testosterone storm is brewing, as the first transgender athlete is set to compete at an Olympics. Three key imperatives, in order to compete in sport, are inclusion, fairness and safety. The International Olympic Committee requires a trans woman to achieve testosterone levels below 10nmol/L for a year to be eligible for women's competition. Critics say that factors such as muscle mass, muscle strength and bone density should also be taken into consideration. Inclusion therefore comes at the expense of fairness to both trans and biological females. Trying to keep all parties happy seems to me to be an insolvable problem at present.

A quick "straw poll" of ten random adults "in the street" as to: "What is the first word that comes into your mind when I mention the word testosterone?" produced the following result. Six said "sex" and four answered "aggression". The public are generally unaware that there is a medical condition called Testosterone Deficiency (TD) which can affect not only the general health but also the quality of life of the affected person.<sup>4</sup>

Many Health Care Professionals (HCPs) seem reticent to proactively search for TD in at risk groups such as men with Type 2 Diabetes (T2D), where the incidence of TD is 40%.<sup>5</sup> However when asked, most will check for thyroid function as part of the annual check-up, even though the pick-up rate of finding thyroid disease is much lower.

## ■ **The media and testosterone**

The media continue to have a love hate relationship with testosterone, extolling its value one week and denigrating it the next. Figures 1.1 and 1.2 are typical and illustrate headlines at either end of the press demographic spectrum. They love to use the expression 'male menopause' as it reads well in print. The term 'male menopause' is inappropriate as men do not have 'menses' (periods) and only very rarely (following surgery or trauma for example) does TD occur suddenly 'pause'.

It may not be helpful if men read headlines such as: "My energy is back: how testosterone replacement therapy is changing men's lives", in national newspapers.<sup>6</sup> Because of the link to sex and their embarrassment there could be a tendency for men to be tempted into Quackery seeking help from 'fringe' private clinics or online

**Figure 1.1.** Peta Bee, The Times  
15<sup>th</sup> June 2021.



sources of testosterone. These men often fall through the net of not being properly investigated and monitored.

For those men that had gone to a bona fide National Health service (NHS) clinician they were then made to feel guilty by another headline; “Increasing demand for testosterone on

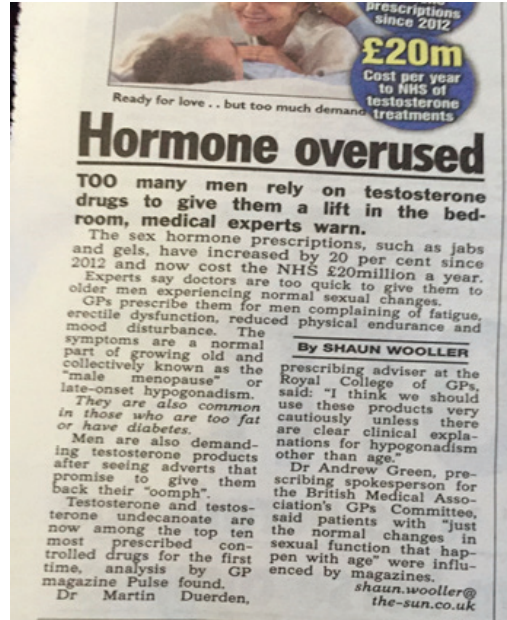
NHS costing tax payers £20 million”.<sup>7</sup> The article implied that “obesity, stress or diabetes, which can cause low testosterone, taking effect in an aging body” could be reversed “By tackling these conditions appropriately” and therefore shouldn’t have been given testosterone. From my clinical experience although patients with TD, obesity and Type 2 Diabetes (T2D) are aware of these issues, and are on the correct management and medication, they find it practically impossible achieve targets for weight or HbA1c. However, if they are prescribed TTh they can gradually reach these targets. Haider *et al.*<sup>8</sup> achieved remission in over a third of their hypogonadal T2D participants treated with TTh. This contrasted with no remissions of T2D or reductions in HbA1c or glucose in the control group. Furthermore there were fewer deaths, myocardial infarctions, strokes and diabetic complications in the TTh group vs the controls.

Why didn’t that appear as a front page headline? I suspect because of the image that testosterone has built up over the years.

## ■ Testosterone deficiency: a new pseudo-condition?

Pharma companies are sometimes accused of “disease mongering” in having created a new “pseudo-condition” of Testosterone Deficiency (TD) in order to promote their medication to an unsuspecting public and trying to ‘hoodwink’ the medical

**Figure 1.2.** Shaun Wooller, The Sun  
24<sup>th</sup> September 2016.



profession into prescribing it. These Pharma sceptics consider the interest in testosterone to be a recent affair based on the drug industry's rush to find treatments for "lifestyle problems". I would suggest that nothing could be further from the truth as writings have been discovered going back many centuries, linking the testes with sexual function. Likewise, aphrodisiacs such as pills, pastes and potions for the penis, have formed many a tale or recipe across many cultures and centuries.

### Sushrata of India 140 B.C. wrote:

"By eating the testes of a he-goat with (an adequate quantity of) salt and powdered long-pepper (Pippali), fried in clarified butter prepared from churning milk (and not from curd), a man is enabled to visit a hundred women."

Sushruta Samhita, volume 4: Cikitsasthana by Kaviraj Kunja Lal Bhishagratna | 1911

Leonardo da Vinci,<sup>9</sup> in the sixteenth century, wrote this on the side of one of his anatomical diagrams "Are not the testicles the cause of ardour?"

In 1767 John Hunter undertook the first documented testicular transplantation by grafting the testicles from a cock into the abdomen of a hen. Arnold Berthold, in 1849, concluded that a substance produced in the testes affected behavioural and sexual characteristics via the blood stream. An enthusiastic 'transplanter', in the 1920s, was Serge Voronoff, who used slices of primate testis and grafted them to the testicular capsule in humans. Apparently, he operated on 300 men and claimed that hormonal secretion lasted 1-2 years reducing over time due to graft fibrosis.

The pace was speeding up to find the active substance. In 1927, Lemuel Clyde McGee demonstrated a biologically active substance from bull testicles. The first 15g of androgen was isolated from 15,000 -25,000litres of policeman's urine. A Dutch group including Karoly David, Elizabeth Dingemanse, Janos Freud and Ernst Laqueur used several tons of bull testicles to isolate the chief secretion product from the testes and the main androgen in the blood which they called testosterone in 1935. The word testosterone comes from 'testo' (testes), 'ster' (sterol), and 'one' (ketone). Meanwhile the race to publish the chemical synthesis of testosterone was achieved by three groups led by Adolf Butenandt, Ernst Lacueur and Leopold Ruzicka in the same year.

Both the discovery of the biochemical substance and its chemical synthesis meant that modern endocrinology blossomed and the 'therapeutic door' was opened for sexual hormones with perhaps overenthusiastic prescribing of such treatments and patients encouraged by the word and 'promise' of 'rejuvenation'. The Journal of the American Medical Association (JAMA) hinted at this possibility in 1939 when their editorial commented:

"Recently many reports have appeared in medical journals claiming that a climacteric occurs in middle aged men. Brochures circulated by pharmaceutical

manufacturers depict the woeful course of aging man. None too subtly these brochures recommend that male hormone substance, like a veritable elixir of youth, may prevent or compensate for the otherwise inevitable decline".<sup>10</sup>

There is a misconception whereby T is just labelled as a sex hormone. Whilst it does have an impact on sexual drive and function, like many hormones it has an effect on many parts of the body. These numerous attributes will be expanded on in the following chapters.

## ■ The Internet: friend or foe?

Our patients for one reason or another are turning to the internet for information about medical conditions. Whilst social media can be a powerful tool for educating patients and HCPs, it can also be a festering source of disinformation. The term 'disinformation' refers to 'false information deliberately and often covertly spread in order to influence public opinion or obscure the truth'.<sup>11</sup> Men experiencing sexual problems may resort to the internet before seeking help from a clinician because of embarrassment.<sup>12</sup> Warren *et al.*<sup>13</sup> assessed the patient utilisation and reliability of YouTube videos (YTVs) concerning male hypogonadism and TTh. They found that most of these YTVs were unreliable but that there were some reliable ones. The YTVs featuring a physician were more reliable and less biased but received fewer viewings than unreliable ones. They also noted that many patients (over 38 million views) were using YTVs as an educational resource for male hypogonadism and TTh. Unfortunately, these findings were consistent with previous studies evaluating YTVs and sexual health information. Many nations and international groups have looked at policing social media platforms.<sup>14</sup> Having established that lawsuits cannot effectively stop Internet misinformation, Sableman looked at whether social media companies could be encouraged to curb such issues. However he concluded: "*In short, self-policing by social media companies is unlikely to keep political misinformation off of their pages*".<sup>15</sup> If that is the state of affairs for political Internet misdemeanours what hope do the medical profession have in preventing unreliable YTVs?

## ■ Past myths and future management of testosterone

Two myths surrounding testosterone have caused concern among Physicians. One going back over 80 years was practically etched in stone, concerning the link between testosterone and prostate cancer. The second in 2013-14 was the allegation that testosterone therapy caused increased cardiovascular risk including heart attack, stroke and death. Both rocked the medical profession to its very foundation, caused a media and legal frenzy, but deprived suitable patients from treatment with testosterone. These topics are discussed more fully in the book together with references. However, the weight of evidence suggests that testosterone therapy does not increase cardiovascular or prostate cancer risk.



Testosterone has pleiotropic properties in producing many effects in many parts of the body. This, until the last few years has been one of the problems in dissipating research evidence among the medical profession. Each medical speciality kept in its own 'silo' whether it is teaching students, on hospital wards, societies, journals or conferences. So communication, sharing experience, research and case studies were fragmented. Hopefully, more integrated journals, conferences and teaching communications will bring together a mélange of HCPs who will be able to have intelligent debate and deliberation so that a consensus of reliable information can be cascaded down to clinicians, the media and patients alike.

Critics of testosterone replacement argue that it is a natural aging process – so why medicalise it? However, research has shown that 75% of men, in old age, maintain normal testosterone levels.<sup>16</sup> Looking at the patient holistically demonstrates that dentists do not generally decline to treat patients when their teeth start to crumble and fall out. When their hearing, eyesight and joints begin to fail do we as clinicians refuse to help them? Concerning hormone replacement, general practitioners actively and routinely check for thyroid function in at risk groups and replace and monitor hormone replacement where necessary. We often prescribe insulin for diabetics and in women offer hormone replacement therapy when indicated.

Surely we owe it to patients, their partner and families to operate within guidelines<sup>17</sup> to actively look for, investigate, treat to within physiological levels and monitor those with testosterone deficiency? This needs to be within the framework of a state health provider (such as the NHS in the UK) or a properly registered bona fide private clinic. There is a need for education of patients, clinicians and the media in demonstrating that there is more to testosterone than just sex.

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# 2

## Diagnosis and terminology in hypogonadism

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### ■ Introduction

Hypogonadism (testosterone deficiency) is a clinical and biochemical syndrome that stems from a reduced production of testosterone and sperm cells by the testis. It can adversely affect multiple bodily systems and is associated with a marked decrease in quality of life. Hypogonadism is primarily classified according to it being a congenital or acquired disorder; the anatomical level of dysfunction: at testicular (primary hypogonadism), hypothalamic- pituitary (secondary hypogonadism) or combined levels and recognises affected men with idiopathic, metabolic or iatrogenic conditions resulting in testosterone deficiency. Treatment decisions should include lifestyle measures and a holistic review of the patient.

This chapter aims at:

1. Shedding some light on definitions and terminology in patients with testosterone deficiency (hypogonadal patients).
2. Outlining its epidemiology.
3. Exploring the underlying pathophysiology.
4. Discussing issues surrounding diagnosis.
5. Drawing a conclusion.

### ■ Definitions and terminology

For the purpose of this chapter, we will refer to the term 'hypogonadism'. However, other nomenclature used in the literature include male hypogonadism, men with testosterone deficiency (TD) and testosterone deficiency syndrome (TDS).

Regarding the decreasing plasma androgen levels in ageing men, in the past, 'andropause', 'male menopause' and 'male climacteric' have been used. However, these terms are generally regarded as inaccurate, since the precipitous changes that occur in women are lacking in men. Unlike menopause, the decrease in testicular function in men is gradual and symptoms can be more non-specific. Indeed, many older men (up to 80%) continue to have free androgen levels in the low normal