

Sexual dysfunction

Hypogonadism: Associations, pitfalls in interpretation, and a possible “new” clinical consequence in type 2 diabetes



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Recent studies have identified that up to one third of men with type 2 diabetes may have varying degrees of hypogonadism, a prevalence far higher than previously thought (Dhindsa et al, 2004). This complex hormonal relationship is probably mediated through the pathophysiology of the metabolic syndrome, with resultant clinical consequences including erectile dysfunction (ED).

In this issue of *Diabetes Digest*, Diaz-Arjonilla and colleagues (summarised alongside) provide a timely review of the interactions between obesity, low testosterone levels and ED. While many people with diabetes may have established hypogonadism, Stanworth et al (summarised below) remind us of the importance of careful evaluation of clinical status and interpretation of blood results when making this diagnosis. In their study, they examined the effects of statin therapy (prescribed now in the majority of men with type 2

diabetes when following NICE guidelines) on biochemical parameters used to assess androgen deficiency. They noted that although total testosterone levels are lower on statin therapy, measures of active testosterone and clinical gonadal status were not affected – more evident in individuals on atorvastatin. In consequence, biochemical assessment of active (free) testosterone would seem warranted in men on statin therapy to enhance the reliability of correctly diagnosing hypogonadism. Although ED is well recognised as a consequence of hypogonadism, Grossmann et al (summarised overleaf) have also identified that androgen deficiency is more likely to be associated with anaemia and its clinical sequelae in type 2 diabetes.

As more and more evidence emerges about the prevalence, pathophysiology and management of hypogonadism in type 2 diabetes, it behoves us to have a low threshold for screening for this condition and being confident in biochemical assessment.

Dhindsa S, Prabhakar S, Sethi M et al (2004) Frequent occurrence of hypogonadotropic hypogonadism in type 2 diabetes. *J Clin Endocrinol Metab* **89**: 5462–8

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

Testosterone, obesity, metabolic syndrome and type 2 diabetes: The link

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

- 1 Obesity has been linked to a number of diseases, including cancer, erectile dysfunction (ED), cardiovascular disease and type 2 diabetes, and is implicated as a major risk factor for all of these conditions.
- 2 The authors of this review aimed to elucidate the relationships between low serum testosterone levels and erectile dysfunction in obese individuals with the metabolic syndrome or type 2 diabetes.
- 3 Excess adipose tissue is an obvious sign of obesity. This tissue produces adipokines and cytokines, which in turn causes insulin resistance and metabolic syndrome.
- 4 BMI is inversely proportional to serum total testosterone and free testosterone concentration. Low sex hormone-binding globulin in obesity also leads to lower serum testosterone levels.
- 5 Low levels of serum testosterone are commonly seen in men with type 2 diabetes or metabolic syndrome, as well as in obese individuals.
- 6 A small proportion of men with erectile dysfunction have hypogonadism, and this proportion increases if these men are obese with symptoms of the metabolic syndrome or type 2 diabetes.
- 7 The authors concluded that very low testosterone levels contribute to the development of ED in obesity, type 2 diabetes and the metabolic syndrome.

Diaz-Arjonilla M, Schwarcz M, Swerdloff RS, Wang C (2009) Obesity, low testosterone levels and erectile dysfunction. *Int J Impot Res* **21**: 89–98

DIABETES CARE

Statin therapy associated with low total testosterone

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

- 1 The authors undertook this study to investigate whether statin therapy reduces total testosterone in men with type 2 diabetes.
- 2 To examine this relationship between statin therapy and testosterone levels, 355 men with diabetes had their total testosterone measured, and were examined for any hypogonadal symptoms.
- 3 Total testosterone, sex hormone-binding globulin (SHBG), and

estradiol were measured, along with free and bioavailable testosterone.

- 4 Statin therapy was associated with lower total testosterone ($P=0.006$) and a trend toward lower SHBG levels ($P=0.034$) compared with no treatment. Only simvastatin did not cause significant reductions in testosterone or SHBG levels.
- 5 Bioavailable testosterone, free testosterone, estradiol and hypogonadal symptoms were not affected by statin therapy.
- 6 The authors recommend that levels of bioavailable testosterone or free testosterone are used for the assessment of hypogonadism in men with type 2 diabetes undergoing statin therapy, as total testosterone levels may not give an accurate picture.

Stanworth RD, Kapoor D, Channer KS, Jones TH (2009) Statin therapy is associated with lower total but not bioavailable or free testosterone in men with type 2 diabetes. *Diabetes Care* **32**: 541–6

CLINICAL ENDOCRINOLOGY

Testosterone deficiency linked with anaemia in men with type 2 diabetes

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓✓

1 Low testosterone levels are common in men with type 2 diabetes. Anaemia is also common in this population, and is associated with increased mortality and morbidity.

2 The authors of this Australian study set out to determine whether anaemia is linked to low testosterone levels in men with type 2 diabetes.

3 This cross-sectional cohort study comprised 464 men with type 2 diabetes attending a diabetes outpatient clinic in Melbourne, Australia. Men with a diagnosis of hypogonadism or end-stage renal disease, or those on testosterone replacement or erythropoietin therapy, were excluded.

4 Approximately 24% of the study participants had anaemia. This was associated with the presence and severity of chronic kidney disease, systemic inflammation, increased age, and reduced iron availability. Testosterone levels of participants were also associated with reduced haemoglobin levels.

5 Participants with lower total testosterone levels (<10 nmol/L; 43% of the cohort) were more likely to suffer from anaemia (adjusted odds ratio [AOR] 1.7; 95% confidence interval [CI] 1.1–2.8), and anaemia was twice as common in those with a free testosterone level <0.23 nmol/L (AOR 2.0, 95% CI 1.2–3.1).

6 The authors concluded that the increased frequency of anaemia in men with type 2 diabetes may be due to a deficiency of testosterone.

Grossmann M, Panagiotopoulos S, Sharpe K et al (2009) Low testosterone and anaemia in men with type 2 diabetes. *Clin Endocrinol (Oxf)* **70**: 547–53

JOURNAL OF SEXUAL MEDICINE

Cardiorespiratory fitness protects against ED

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓✓

1 The authors undertook this study to determine the prevalence and correlates of erectile dysfunction (ED) in the Look AHEAD study cohort.

2 Inclusion criteria were those of the Look AHEAD study, plus the

participants had to have been sexually active in the preceding 6 months or in a committed relationship.

3 Around half (49.8%) of the men reported mild or moderate degrees of ED, and 24.8% had complete ED. ED was significantly associated with age, baseline HbA_{1c}, history of hypertension, and metabolic syndrome.

4 Cardiorespiratory fitness was found to be protective of ED in a multivariable analysis ($P < 0.001$).

5 This study confirms a link between ED and cardiovascular risk factors.

Rosen RC, Wing RR, Schneider S et al (2009) Erectile dysfunction in type 2 diabetic men: relationship to exercise fitness and cardiovascular risk factors in the Look AHEAD trial. *J Sex Med* **6**: 1414–22

ANDROLOGIA

Testosterone a marker for metabolic syndrome

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓✓

1 This study aimed to investigate the relationship between testosterone levels in obese men with components of metabolic syndrome (MS).

2 The authors enrolled 34 men with a BMI >27 kg/m² who met the criteria of MS, aged <40 years; twenty men aged <40 years with a

BMI <25 kg/m² were enrolled as a comparator group.

3 It was found that with increasing BMI, levels of serum leptin, triglycerides, insulin, total cholesterol, the waist circumference, visceral fat and blood pressure were higher, whereas insulin sensitivity and serum testosterone levels were lower – more so in people with a BMI >30 kg/m².

4 The authors concluded that plasma testosterone levels correlate with several factors of MS, and suggest that serum testosterone levels could be used as a marker of the condition.

Goncharov NP, Katsya GV, Chagina NA, Gooren LJ (2009) Testosterone and obesity in men under the age of 40 years. *Andrologia* **41**: 76–83

JOURNAL OF SEXUAL MEDICINE

ED therapy in type 1 and type 2 diabetes

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓✓

1 This study aimed to determine whether specific and unique mechanisms underlie erectile dysfunction (ED) in type 1 and 2 diabetes by using animal models.

2 The authors conducted a literature search of Pubmed to find all current literature relating to the underlying mechanisms.

3 Impaired cavernosal vasodilation has been established in type 1 diabetic rodents, and appears to be mediated by a defect in non-adrenergic-non-cholinergic nerve signalling, as well as impairment in penile endothelial function. In type 2 diabetic animals, there is minimal impairment in parasympathetic-mediated dilatatory function, but there is evidence of endothelial dysfunction.

4 The authors concluded that therapy for ED should be specific to either type 1 or 2 diabetes, but more work needs to be done on the underlying mechanisms.

Chitale K (2009) Type 1 and type 2 diabetic-erectile dysfunction: same diagnosis (ICD-9), different disease? *J Sex Med* **6**(Suppl 3): 262–8

“The increased frequency of anaemia in men with type 2 diabetes may be due to a deficiency of testosterone.”