

Sexual dysfunction

The rise, fall and re-emergence of testosterone treatment in men with diabetes and erectile dysfunction



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When I first commenced training at medical school, the fashion was to try most men with diabetes on testosterone if they presented with erectile dysfunction (ED). This was regardless of

baseline assessment of the testosterone axis and was administered in the belief that whatever the cause, ED could be overcome by a boost of this androgen.

Clinical trials (using fairly crude assessments of the testosterone axis) then appeared to establish that hypogonadism was perhaps no more common in diabetes than the general population and that empirical androgen replacement was not of benefit to a number of diabetic men with ED. Moreover, supraphysiological levels of testosterone even may be harmful.

However, in recent years these views have been re-challenged. More detailed and widespread assessment of men with diabetes has indicated that, in this population,

hypogonadism is more widespread than previously thought. In particular, the association between the metabolic syndrome, insulin resistance and hypogonadism is now well established and is supported by two excellent articles featured in this edition of *Diabetes Digest* (Haring et al, 2009; Yeap et al, 2009; summarised alongside and below).

“It is important to be vigilant for the possibility of hypogonadism in men with diabetes and erectile dysfunction.”

While severe hypogonadism is fairly evident clinically, mild hypogonadism (in which ED and psychological factors may predominate) in men with diabetes is more common. In consequence, it is important to be vigilant for the possibility of hypogonadism in men with diabetes and ED. While considering a therapeutic trial of androgen replacement with careful monitoring in people with borderline low circulating levels, El-Sakka et al (2009; summarised overpage) raise the intriguing possibility that improved glycaemic control may help to restore normal testosterone levels in men with type 2 diabetes. The interplay between glycaemic control, the testosterone axis and ED merits further investigation.

EUROPEAN JOURNAL OF ENDOCRINOLOGY



Low testosterone associated with insulin resistance

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

1 Studies have shown that insulin resistance (IR) is a risk factor for cardiovascular disease, being associated with metabolic syndrome and type 2 diabetes.

2 The authors of this study analysed 2470 men without diabetes (aged ≥ 70 years), to establish whether low testosterone or sex hormone-binding globulin (SHBG) levels in older men are associated with insulin resistance independently of central obesity.

3 Total testosterone, SHBG, luteinising hormone (LH) and insulin levels were measured by assaying early morning sera.

4 A progressive decline in levels of total testosterone, free testosterone and SHBG was observed across increasing quintiles of HOMA2-IR (all $P < 0.001$) and correlated inversely with log HOMA2-IR ($r = -0.27, -0.14$ and -0.24 , respectively; all $P < 0.001$).

5 Once adjustments for age, BMI, waist circumference, HDL and triglyceride levels had been made, total testosterone was independently associated with log HOMA2-IR (beta = 0.05, $P < 0.001$); SHBG was not.

6 The authors concluded that in older men, lower total testosterone is associated with insulin resistance independently of measures of central obesity. In addition, this relationship was seen with testosterone levels in the low to normal range.

Yeap BB, Chubb SA, Hyde Z et al (2009) Lower serum testosterone is independently associated with insulin resistance in non-diabetic older men: the Health In Men Study. *Eur J Endocrinol* **161**: 591–8

DIABETES

Low testosterone predicts MetS

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

1 This German study aimed to assess the relationship between serum testosterone and dehydroepiandrosterone sulphate (DHEAS) levels with metabolic syndrome (MetS) in men.

2 Using data from the Study of Health in Pomerania, a population-based prospective cohort of adults aged 20–79 years, 1004 men without baseline MetS were analysed for testosterone and DHEAS.

3 A total of 480 men developed MetS after 5 years of follow-up; testosterone levels were found to decrease with increasing numbers of metS components.

4 MetS was predicted by testosterone in the lowest quartile (relative risk [RR], 1.38; 95% confidence interval [CI], 1.13–1.69), particularly in men aged 20–39 years (RR, 2.06; 95% CI, 1.29–3.29).

5 In young men especially (aged 20–39 years), low testosterone levels were found to be a strong predictor for MetS. Baseline DHEAS did not show an independent association with MetS.

Haring R, Völzke H, Felix SB et al (2009) Prediction of metabolic syndrome by low serum testosterone levels in men: results from the study of health in Pomerania. *Diabetes* **58**: 2027–31

UROLOGY

Testosterone linked to glycaemic control in T2D

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

1 This prospective office-based study sought to assess the impact of glycaemic control on androgen pattern in men with type 2 diabetes-associated erectile dysfunction (ED).

2 A total of 159 men (mean age 53.9 ± 9.2 years) with type 2 diabetes and ED were enrolled; 84.9% were overweight or obese and 28.9% were current or former smokers.

3 Diabetes control comprised lifestyle modification in addition to oral antidiabetes and/or insulin therapy, and participants were followed-up every 4 weeks for assessment and adjustment of their treatment regimens.

4 Measurements of HbA_{1c}, ED severity, total testosterone (TT), dehydroepiandrosterone sulphate (DHEAS) and insulin level were taken at baseline, 3 months and 6 months.

5 At baseline, 25.8% of participants had low TT, 6.3% had low DHEAS and 30.2% had hyperinsulinaemia.

6 Significant increases were observed in TT levels at 3 and 6 months (4.2 ± 1.9 vs. 4.7 ± 2.1 and 5.3 ± 2.2 ng/mL, respectively), along with significant decreases in insulin level (23.7 ± 17.4 vs. 22.8 ± 15.3 and 17.8 ± 13.9 μ U/mL, respectively).

7 Good diabetes control or decreased fasting blood glucose were significantly associated with normal TT levels at 3 and 6 months.

8 The results suggest significant associations between diabetes control and normal TT levels at 3- and 6-month follow-up.

El-Sakka AI, Sayed HM, Tayeb KA (2009) Androgen pattern in patients with type 2 diabetes-associated erectile dysfunction: impact of metabolic control. *Urology* **74**: 552–9

SURGERY FOR OBESITY & RELATED DISEASES

Sexual dysfunction in women seeking bariatric surgery

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

1 Using the validated Female Sexual Function Index (FSFI), female sexual dysfunction (FSD) was assessed in 102 female bariatric surgery candidates.

2 An FSFI score of ≤ 26.55 was used to identify individuals with FSD;

these were compared with published norms available for female sexual arousal disorder (FSAD) and healthy controls.

3 Sixty-one women had FSD (FSFI total scores of ≤ 26.55); FSFI scores for the bariatric surgery candidates (26.4 ± 6.3) were lower than the control group (30.5 ± 5.3) and higher than the FSAD group (19.2 ± 6.6 ; all $P < 0.0001$).

4 Severely obese women seeking bariatric surgery were found have diminished sexual function, which supports the use of validated assessment of FSD in this population.

Bond DS, Vithiananthan S, Leahey TM et al (2009) Prevalence and degree of sexual dysfunction in a sample of women seeking bariatric surgery. *Surg Obes Relat Dis* **5**: 698–704

UROLOGY

T2D associated with severe ED in MetS

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

1 To determine the effect of T2D on erectile dysfunction (ED) in men with metabolic syndrome (MetS), 93 individuals (aged 30–70 years) were split into two groups and assessed (group 1, $n=37$, no T2D or abnormal fasting glucose; group 2, $n=56$, T2D).

2 Severe ED was present in 11 men in group 1 (29.7%) and 42 men in group 2 (75%) ($P < 0.001$).

3 Abnormal blood pressure (BP), serum HDL, and serum triglyceride (ST) ratios were 48.6%, 75.7%, and 86.5% in group 1 and 51.8%, 53.6% and 73.2% in group 2, respectively ($P_{BP}=0.933$; $P_{HDL}=0.053$; $P_{ST}=0.205$).

4 T2D was found to be significantly associated with severe ED, with the relative risk as high as 7.1 ($P_{T2D} < 0.001$).

5 The authors concluded that T2D was strongly associated with severe ED in men with MetS, and components of MetS should be taken into consideration when diagnosing and treating ED.

Aslan Y, Sezgin T, Tuncel A et al (2009) Is type 2 diabetes mellitus a cause of severe erectile dysfunction in patients with metabolic syndrome? *Urology* **74**: 561–4

JOURNAL OF UROLOGY

Antioxidant therapy restores erectile function in rats

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

1 The authors hypothesised that antioxidant therapy may restore erectile function in diabetic rats by inhibiting apoptosis in the rat crura.

2 Forty rats were randomised to five groups: healthy controls, rats

with diabetes (RWD), RWD plus the antioxidant tempol, RWD plus insulin, and RWD plus tempol and insulin.

3 Intracavernous pressure in RWD was significantly increased compared with untreated RWD following therapy with tempol or insulin alone.

4 Combined insulin and tempol therapy returned apoptosis to normal in RWD.

5 The authors concluded that antioxidant therapy using tempol and insulin can restore erectile function in RWD by inhibiting apoptosis.

Hirata H, Kawamoto K, Kikuno N et al (2009) Restoring erectile function by antioxidant therapy in diabetic rats. *J Urol* **182**: 2518–25

“Type 2 diabetes was strongly associated with severe erectile dysfunction in men with metabolic syndrome.”