

Pitteloud N, Hardin M, Dwyer AA, Valassi E, Yialamas M, Elahi D et al.

Increasing insulin resistance is associated with a decrease in Leydig cell testosterone secretion in men.

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Abstract: Insulin resistance is associated with low testosterone (T) levels in men, the mechanism of which is unclear. Thus, the aim of this study was to evaluate the hypothalamic-pituitary-gonadal axis in men with a spectrum of insulin sensitivity. Twenty-one men (aged 25-65 yr) had a glucose tolerance test and assessment of insulin sensitivity using a hyperinsulinemic-euglycemic clamp. Insulin sensitivity, expressed as the M value (milligrams per kilograms(-1) per minute(-1)), was calculated from the glucose disposal rate during the final 30 min of the clamp. Eighteen subjects had blood sampling every 10 min for 12 h to assess LH pulsatility. Hypogonadism was then induced with a GnRH antagonist, followed by sequential stimulation testing with GnRH (750 ng/kg, iv) and human chorionic gonadotropin (hCG; 1000 IU, im) to assess pituitary and testicular responsiveness, respectively. Nine subjects had normal glucose tolerance, nine had impaired glucose tolerance, and three had diabetes mellitus. There was a positive relationship between M and T levels ( $r = 0.46$ ;  $P < 0.05$ ). No relationship was seen between M and parameters of LH secretion, including mean LH levels, LH pulse amplitude, LH pulse frequency, and LH response to exogenous GnRH administration. In contrast, a strong correlation was observed between M and the T response to hCG ( $r = 0.73$ ;  $P < 0.005$ ). Baseline T levels correlated with the increase in T after hCG administration ( $r = 0.47$ ;  $P < 0.05$ ). During the clamp, T levels increased from a baseline level of  $367 \pm 30$  to  $419 \pm 38$  ng/dl during the last 30 min ( $P < 0.05$ ). From these data we conclude that insulin resistance is associated with a decrease in Leydig cell T secretion in men. Additional studies are required to determine the mechanism of this effect