

Carruthers ME. An Androgen Resistance Syndrome (ARS) in the Adult Male?

Aging Male 2006; 9: 5. (18071) There are many theoretical parallels, as well as biochemical links, between the insulin resistance seen in maturity onset diabetes and metabolic syndrome, and androgen resistance. As with insulin, the resistance to androgens may vary between tissues, and decide the physical, mental and pathological expression of their actions throughout life. The mechanisms of androgen resistance in the adult male can be considered as follows:

Receptor Polymorphism: The androgen receptor gene is the most mutated in the human body, and shows marked individual and racial differences giving different responses to testosterone treatment and hormonal contraception. Longer CAG repeats make men more resistant to the action of androgens, and are linked with obesity and insulin resistance.

Longer GGN repeat lengths can also be linked to androgen resistance and may be the cause of 'Testicular Genesis Syndrome', which includes testicular maldescent, hypospadias, testicular cancer and infertility.

Age-related Receptor Changes: With age, the number of androgen receptors can decrease, and down-regulation occur.

Protein Binding: Free testosterone can vary between 1 and 3% of the total, depending on the amount and affinity of its binding proteins. Sex Hormone Binding Globulin (SHBG) increases with age, hyperthyroidism, cirrhosis, and low carbohydrate, high fibre diets. Certain drugs, notably anticonvulsants, can raise SHBG, and precipitate androgen deficiency symptoms. The binding affinity of SHBG is affected by metabolites such as free fatty acids, and environmental factors such as xenoestrogens and antiandrogens.

Endocrine Factors: Variations in 5 α -reductase activity can be due to genetic polymorphism, dietetic or pharmacological factors. Similar factors apply to aromatase activity, which may also vary with age. Other counter-regulatory factors include increased catecholamines and glucocorticoids, or growth hormone deficiency.

Summary: these factors can combine to make resistance to the action of androgens as important as insufficient production in relation to the symptomatology and pathology of androgen deficient states.