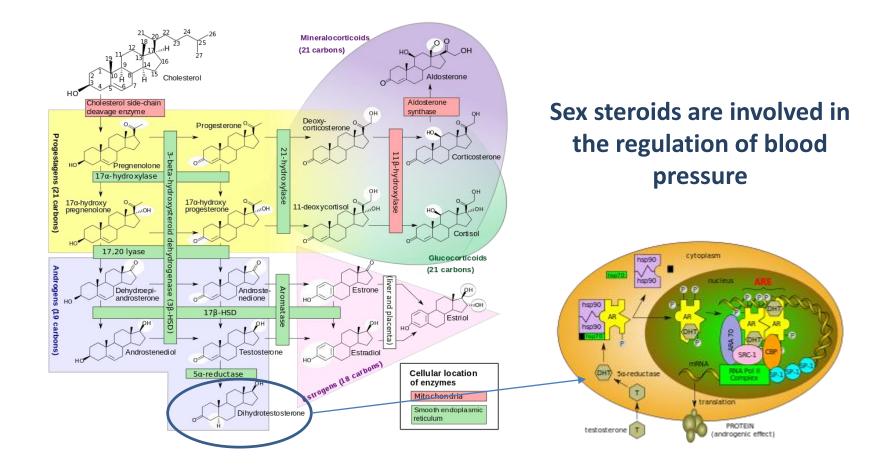


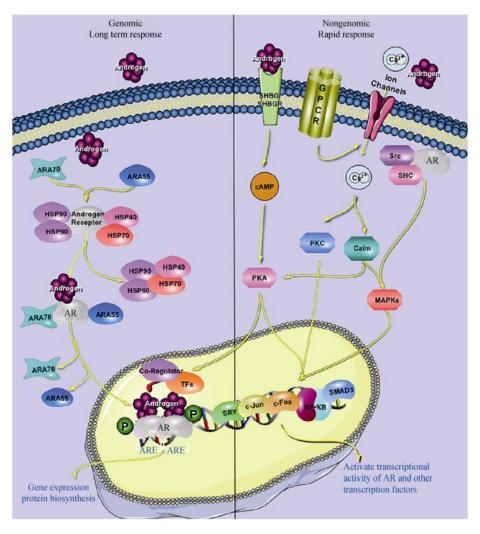
Physical Activity and Health Promotion

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Lesson 6 Hypothesis on the action of androgens in promoting hypertension





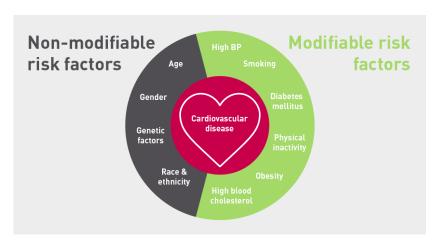
The androgen signal pathways 1.

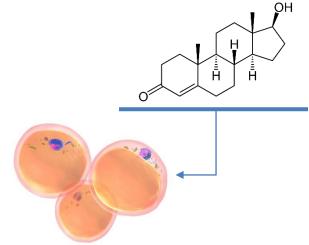
Genomic pathway by binding to the AR and translocation into the nucleus

2.

Nongenomic stimulation of second messenger cascades

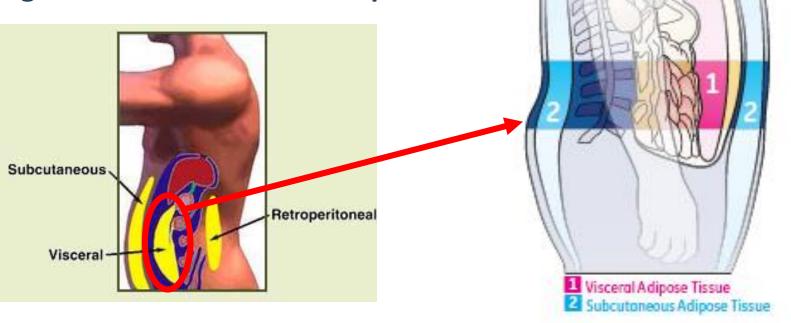
There is a gender-specific regulation exerted by androgens on metabolism, adipose cell function and cardiovascular risk





Involvement of androgens in the development of metabolic syndrome and hypertension: gender-specific

regulation of the visceral adipose cell

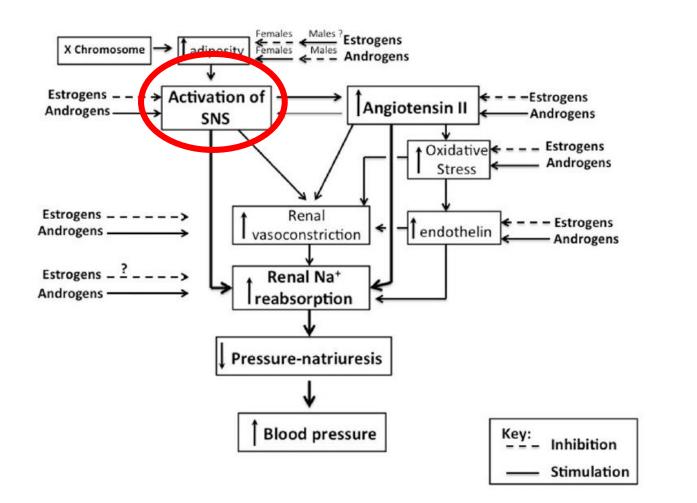


The amount of central adipose fat and the related adipokine dysregulation is related to higher insulin resistance and increased risk of hypertension

Internal fat as a "hormone factory"

Internal high-risk fat is highly metabolically active High blood pressure Lipoprotein lipase Anglotensinogen IL-6 Inflammation (hs-CRP NEFA TGs TNFα Resistin Leptin Adipsin (Complement D) Lactate Type2 diabetes Plasminogen Adiponectin activator inhibitor-1 (PAI-1) **Narrowing of Arteries** Clots in arteries

Androgens and hypertensive risk in males



Men with free testosterone levels in the lowest quartile have a 24% greater risk for all-cause mortality due to ischemic hearth disease

Hormone	Events (n)	Mean hormone level	Model 1a HR (95% CI)	Model 2 ^b HR (95% CI)
Testosterone (nmol/l)				
Q1 (<9.7)	104	8.0	1.0 (ref)	1.0 (ref)
Q2 (9.7-12.7)	108	11.3	0.99 (0.76-1.30)	1.06 (0.81-1.40)
Q3 (12.7–16.0)	85	14.3	0.84 (0.63-1.12)	0.85 (0.64-1.15)
Q4 (>16.0)	98	19.2	1.01 (0.77–1.33)	1.09 (0.81-1.46)
Free testosterone (pmoVI)				
Q1 (<158)	143	130	1.0 (ref)	1.0 (ref)
Q2 (158–197)	102	178	0.78 (0.61-1.01)	0.80 (0.62-1.04)
Q3 (197-242)	78	219	0.72 (0.55-0.96)	0.73 (0.55-0.97)
Q4 (>242)	72	285	0.97 (0.72–1.30)	0.92 (0.68–1.24)
Estradiol (nmol/l)				
Q1 (<0.04)	86	0.03	1.0 (ref)	1.0 (ref)
Q2 (0.04-0.06)	47	0.05	0.82 (0.57-1.17)	0.81 (0.56-1.16)
Q3 (0.06-0.08)	131	0.06	1.48 (1.12-1.94)	1.32 (0.99-1.75)
Q4 (>0.080)	116	0.09	0.98 (0.74-1.30)	0.98 (0.73-1.30)

^aAdjusted for age.

bAdjusted for age, systolic blood pressure, HDL/cholesterol ratio, self-reported diabetes, current smoking, and waist/hip ratio.

Testosterone: a metabolic hormone in health and disease

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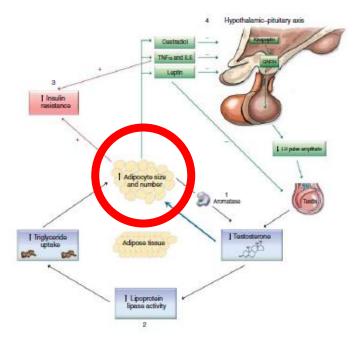
HORMONES 2015, 14(4):569-578



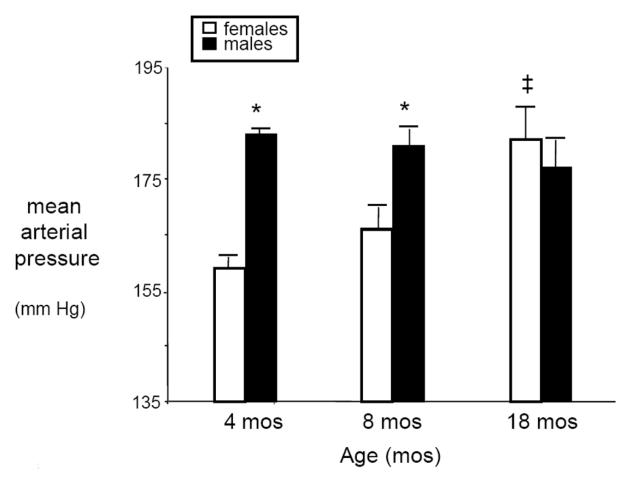
Hypogonadism as a possible link between metabolic diseases and erectile dysfunction in aging men

Giovanni Corona, 1 Silvia Bianchini, 1 Alessandra Sforza, 1 Linda Vignozzi, 2 Mario Maggi²

¹Endocrinology Unit, Maggiore-Bellaria Hospital, Medical Department, Azienda-Usl Bologna, Bologna; ²Sexual Medicine and Andrology Unit, Department of Experimental, Clinical and Biomedical Sciences, University of Florence, Florence; Italy

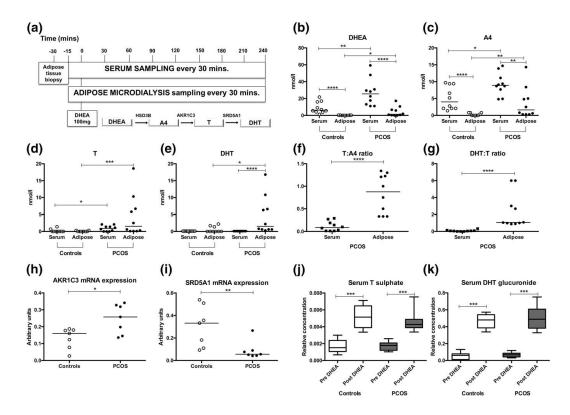


Androgens and hypertensive risk in young women with PCOS

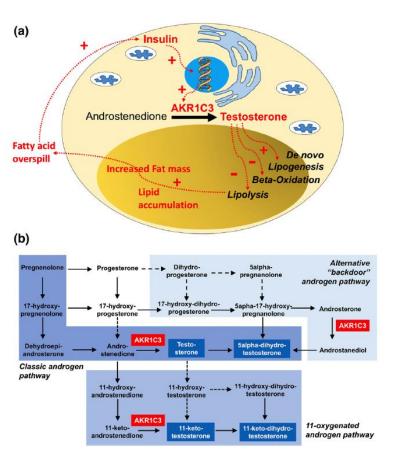


Yanes LL Am J Hypertens. 2011 July; 24(7)

PCOS women have increased expression of the androgen-activating enzyme aldo-ketoreductase type 1 C3 (AKR1C3) in adipose tissue



In PCOS women increased risk of hypertension is linked to the metabolic dysfunction



Androgens and hypertension in post-

menopausal women



Estrogen NEKB Hypertrophied **P38MAPI** adipocytes MEK/ER Enricthelial cells IL-6 MCP-1 TNFG AGT FFAs ICAM-1 VCAM-1 TNF-0 IL-18 IL-6 MIP-1 MCP-1 Paracrine cross-talk Endothelial damage macrophages Atherosclerosis Hypertension Proinflammatory cytokine Insulin-Resistance **Metabolic Syndrome and** Glucose intolerance Cardiovascular disease **Atherotrombosis** associated Insulin and Leptin-signalling Insulin-signalling disruption disruption IL-6 and JNKs pathway IKKB constitutive expression

Androgens and Hypertension in Men and Women: a Unifying View

Costanzo Moretti¹ · Giulia Lanzolla² · Marta Moretti³ · Lucio Gnessi² · Enrico Carmina⁴

- Androgen deficiency may promote inflammatory and immune responses inside the adipose tissue
- NF-kB may play an important role in the inflammatory activation and progression of adypocyte dysfunction and dysregulation in CNS and liver
- IKKβ one of the most important activator of NF-kB rises in its central expression in high fat diet, reducing leptin sensitivity and promoting IL-6 secretion
- NF-kB proinflammatory pathway takes part to endothelial dysfunction and vascular diseases associated with metabolic syndrome

Summary

Androgen deficiency, mainly increasing visceral obesity and determining adipocyte and endothelian dysfunction, seems to be the main responsible of increased prevalence of hypertension in man but also in women particularly in the post manopause when the protective action of estrogens is over