



# **Physical Activity and Health Promotion**

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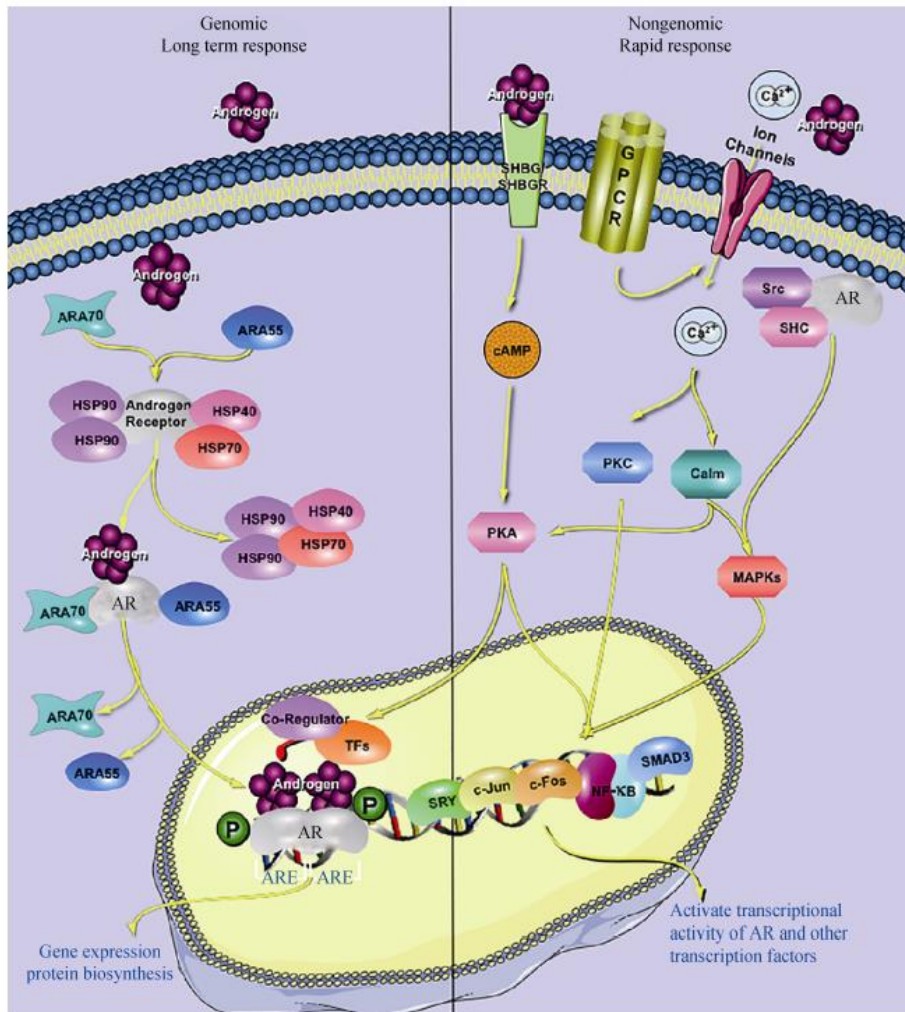
St John Calibita Hospital Tiber Island Rome

**Section of Reproductive Endocrinology**

## **Lesson 6**

# **Hypothesis on the action of androgens in promoting hypertension**





## The androgen signal pathways

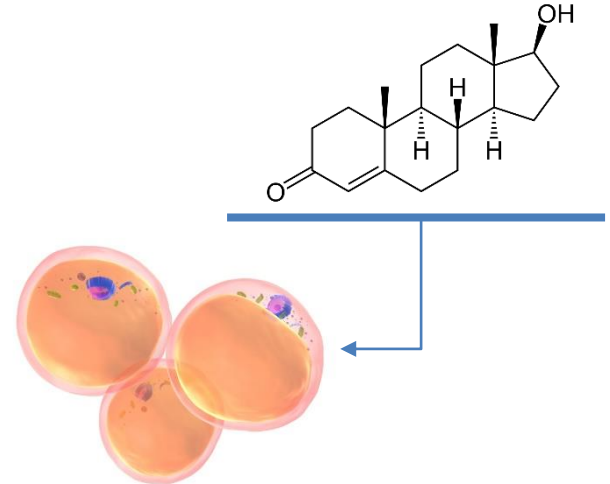
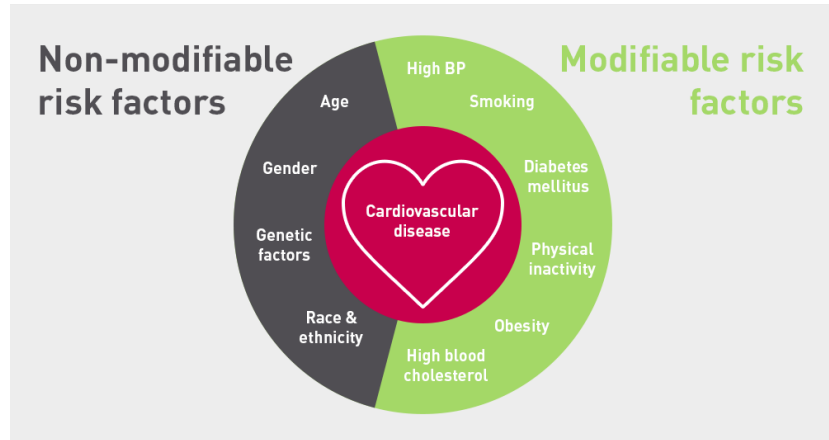
1.

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

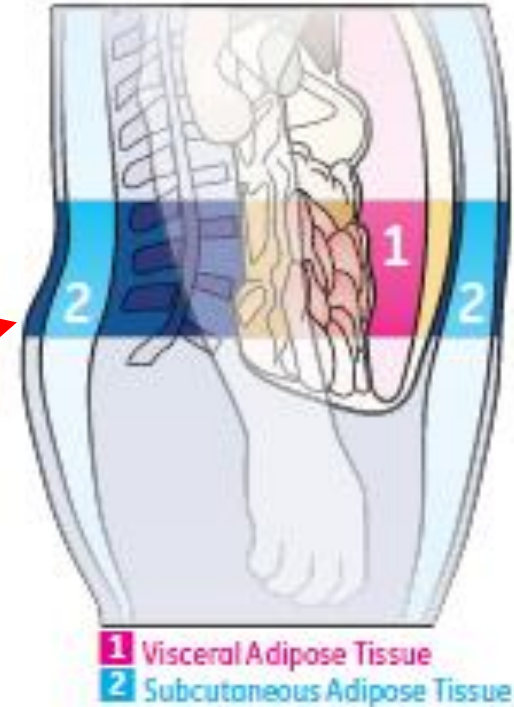
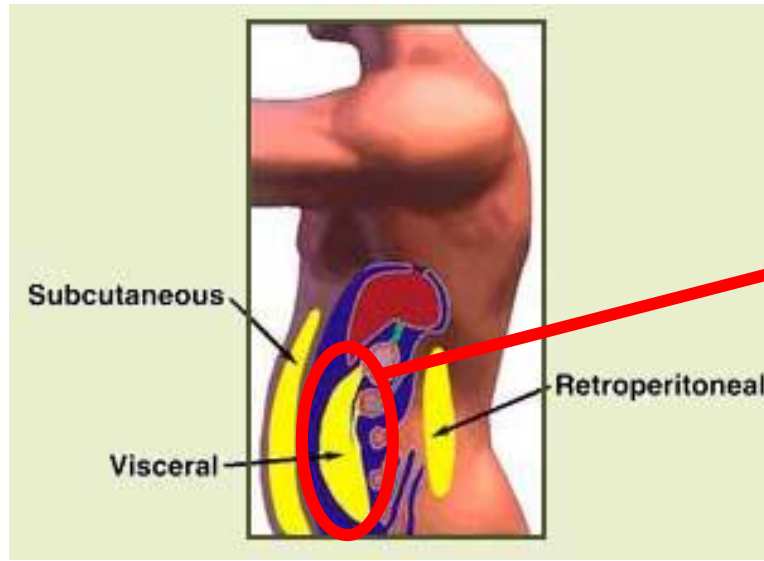
2.

Nongenomic stimulation of second messenger cascades

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



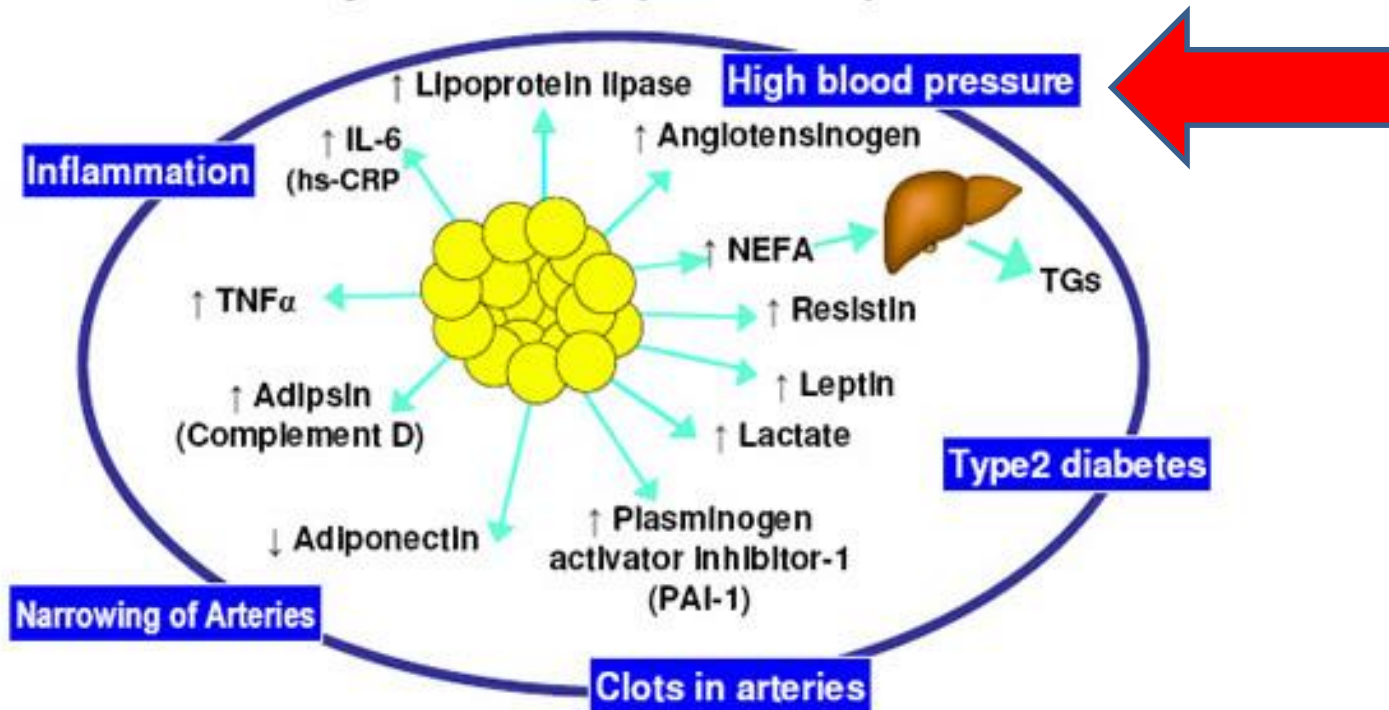
# Involvement of androgens in the development of metabolic syndrome and hypertension: gender-specific regulation of the visceral adipose cell



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

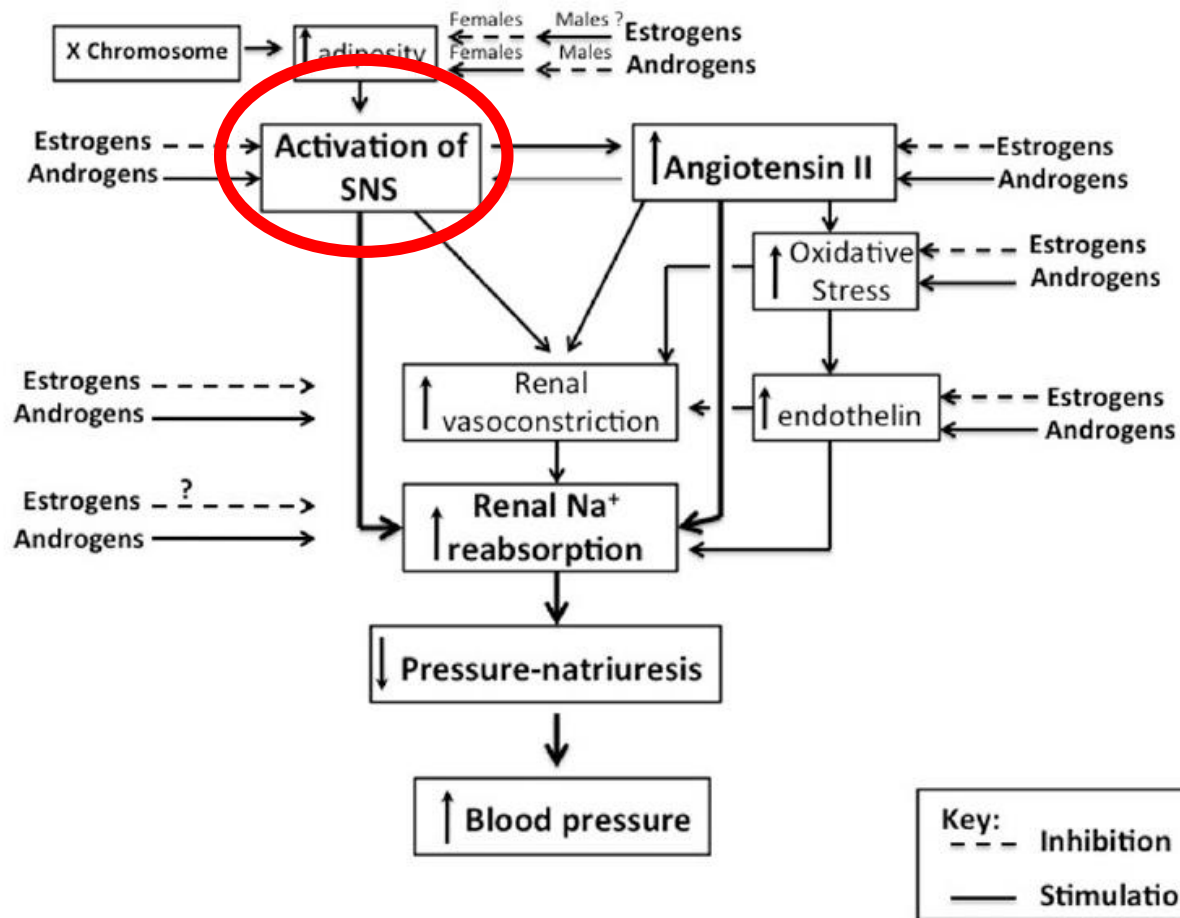
# Internal fat as a “hormone factory”

Internal high-risk fat is highly metabolically active





# **Androgens and hypertensive risk in males**

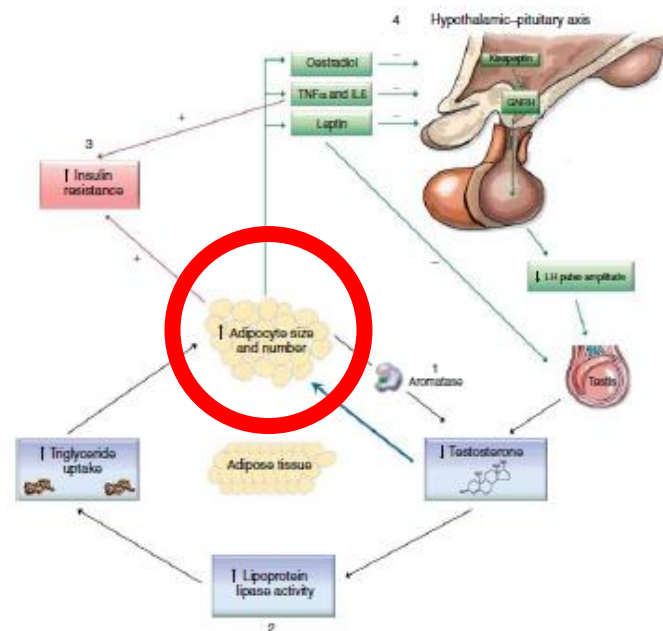


Men with free testosterone levels in the lowest quartile have a 24% greater risk for all-cause mortality due to ischemic heart disease

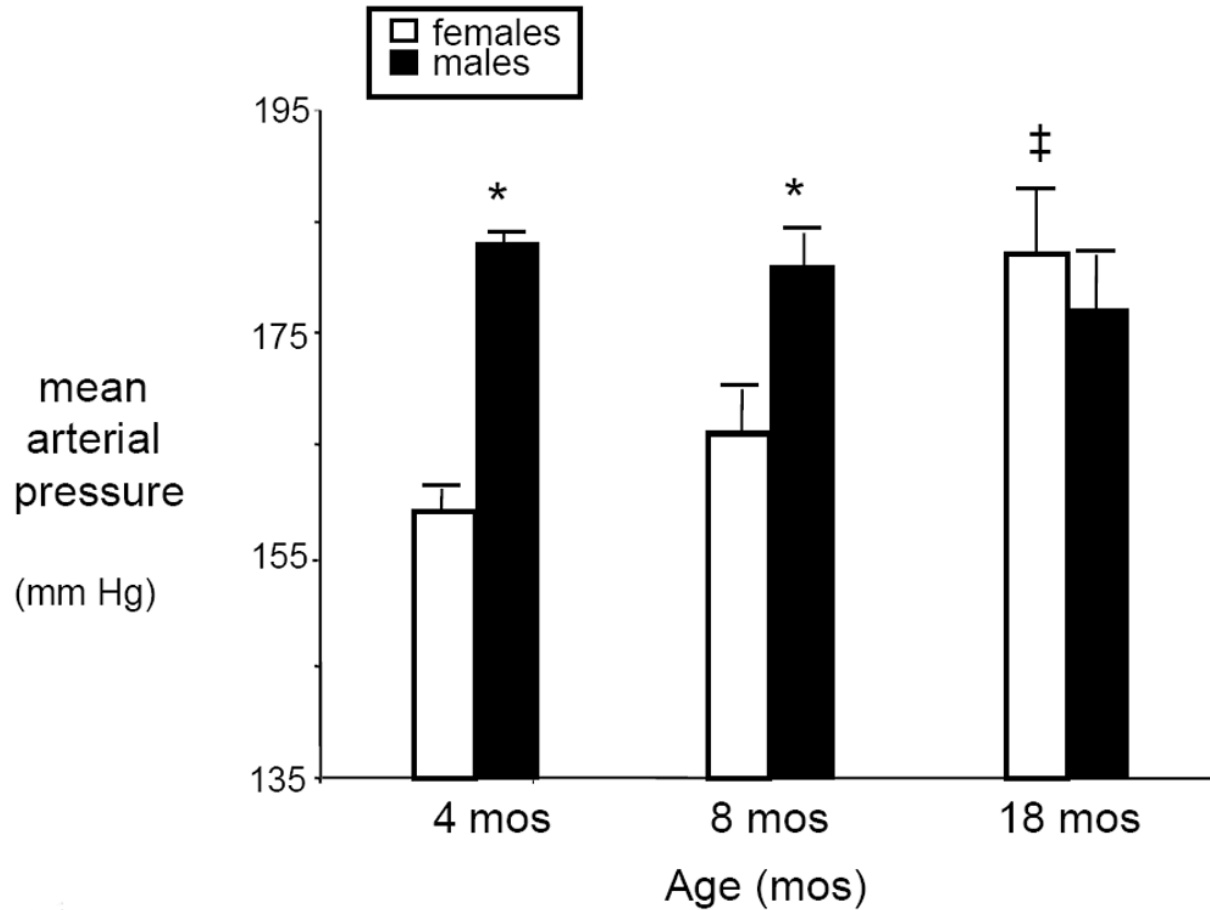
Hormone	Events (n)	Mean hormone level	Model 1 <sup>a</sup> HR (95% CI)	Model 2 <sup>b</sup> HR (95% CI)
Testosterone (nmol/l)				
Q1 (<9.7)	104	8.0	1.0 (ref)	1.0 (ref)
Q2 (9.7–12.7)	108	11.3	0.99 (0.76–1.30)	1.06 (0.81–1.40)
Q3 (12.7–16.0)	85	14.3	0.84 (0.63–1.12)	0.85 (0.64–1.15)
Q4 (>16.0)	98	19.2	1.01 (0.77–1.33)	1.09 (0.81–1.46)
Free testosterone (pmol/l)				
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)

<sup>a</sup>Adjusted for age.

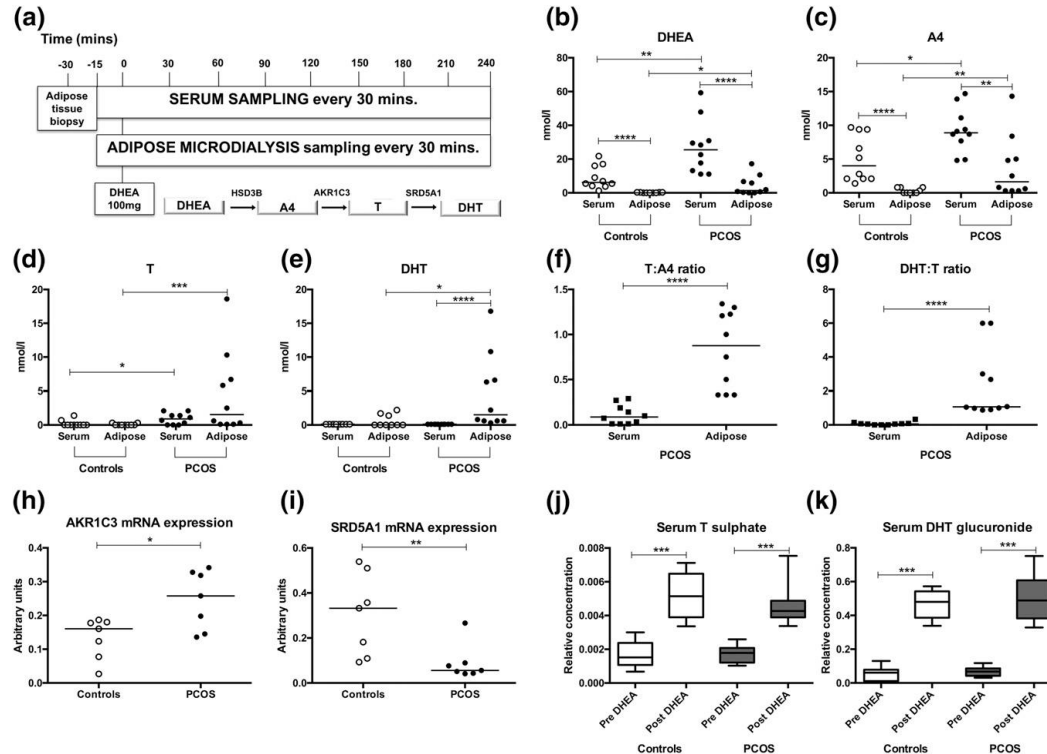
<sup>b</sup>Adjusted for age, systolic blood pressure, HDL/cholesterol ratio, self-reported diabetes, current smoking, and waist/hip ratio.



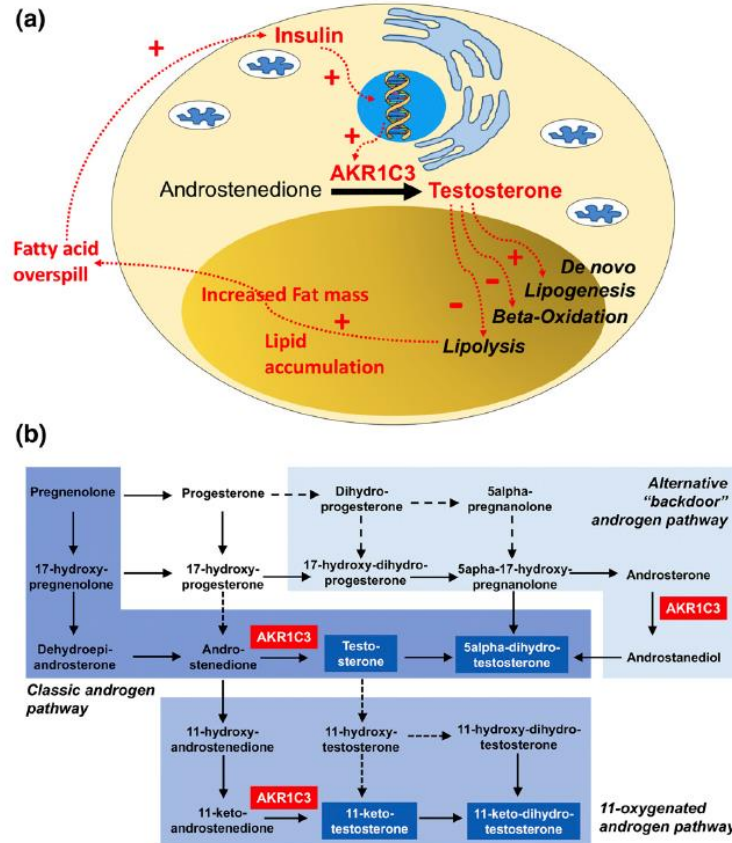
# **Androgens and hypertensive risk in young women with PCOS**



# 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

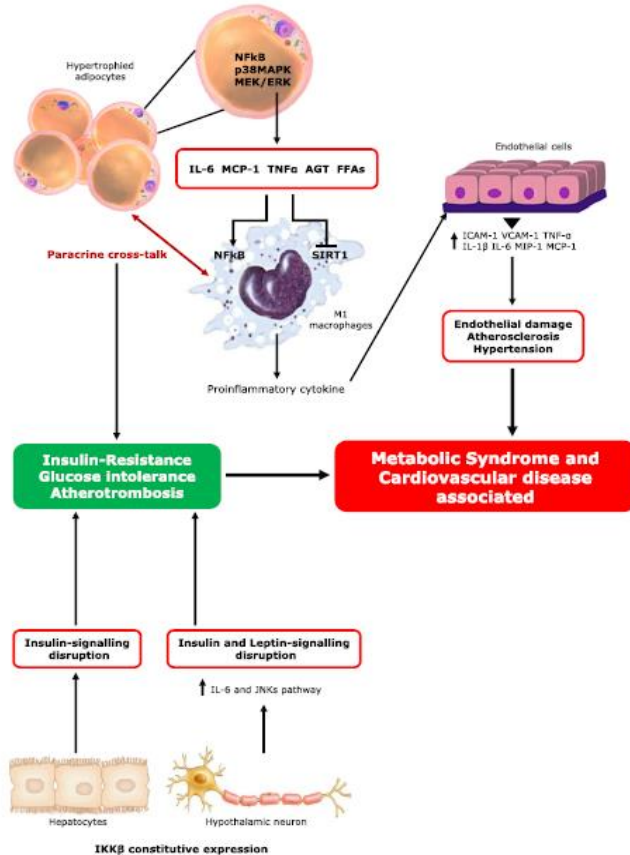




# **Androgens and hypertension in post-menopausal women**

## "Apple" vs. "Pear"





## Androgens and Hypertension in Men and Women: a Unifying View

Costanzo Moretti<sup>1</sup> · Giulia Lanzolla<sup>2</sup> · Marta Moretti<sup>3</sup> · Lucio Gnassi<sup>2</sup> · Enrico Carmina<sup>4</sup>

- Androgen deficiency may promote inflammatory and immune responses inside the adipose tissue
- NF-κB may play an important role in the inflammatory activation and progression of adipocyte dysfunction and dysregulation in CNS and liver
- IKKβ one of the most important activator of NF-κB rises in its central expression in high fat diet, reducing leptin sensitivity and promoting IL-6 secretion
- NF-κB 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 endothelium dysfunction, seems to be the main responsible of increased prevalence of hypertension in man but also in women particularly in the post menopause when the protective action of estrogens is over