POLYCYSTIC OVARY SYNDROME AND INSULIN RESISTANCE

Dr Maria Rosa Ranal
Department of Reproductive Biology
Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran
Mexico City

Dr François Pralong
Department of Endocrinology
Centre Hospitalier Universitaire Vaudois
Lausanne, Switzerland

Polycystic Ovary Syndrome

- Diagnostic Criteria:

  Clinical features

  Endocrine abnormalities

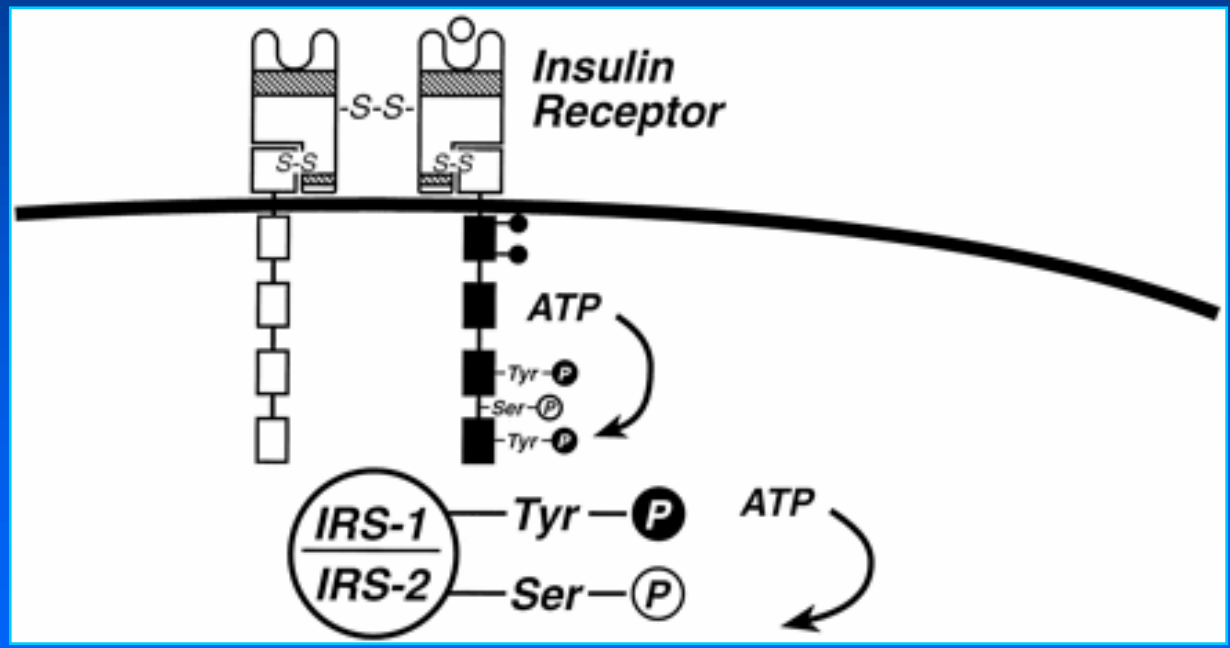
- Sequelae

Polycystic Ovary Syndrome

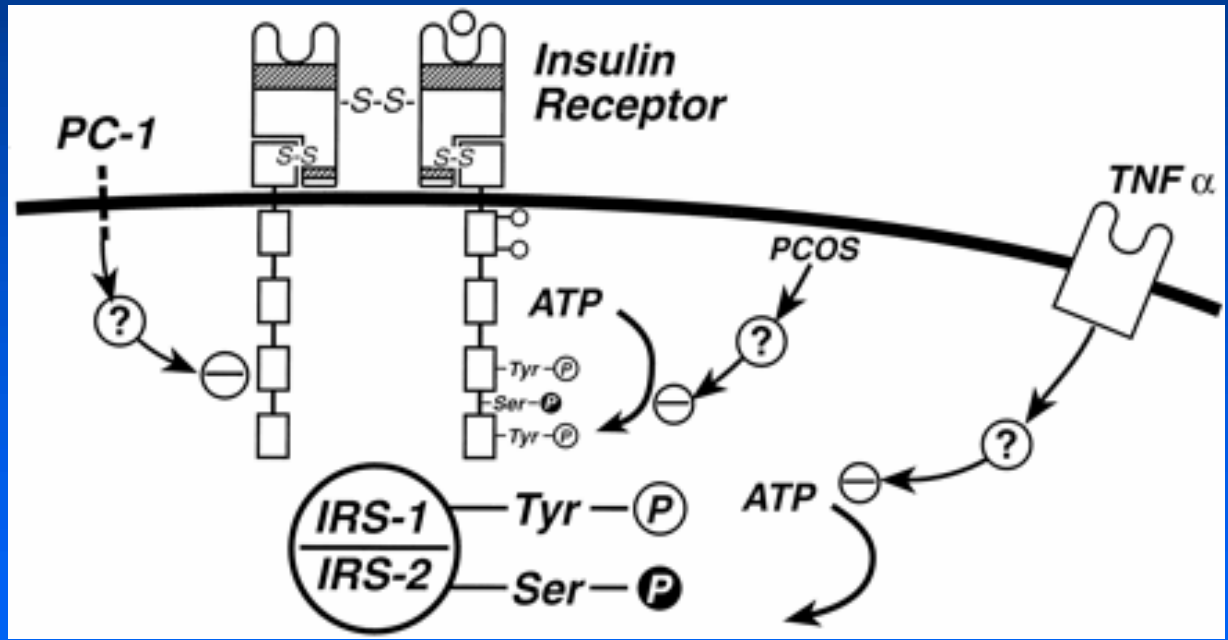
Etiology

- Androgens
- Insulin

Insulin Receptor



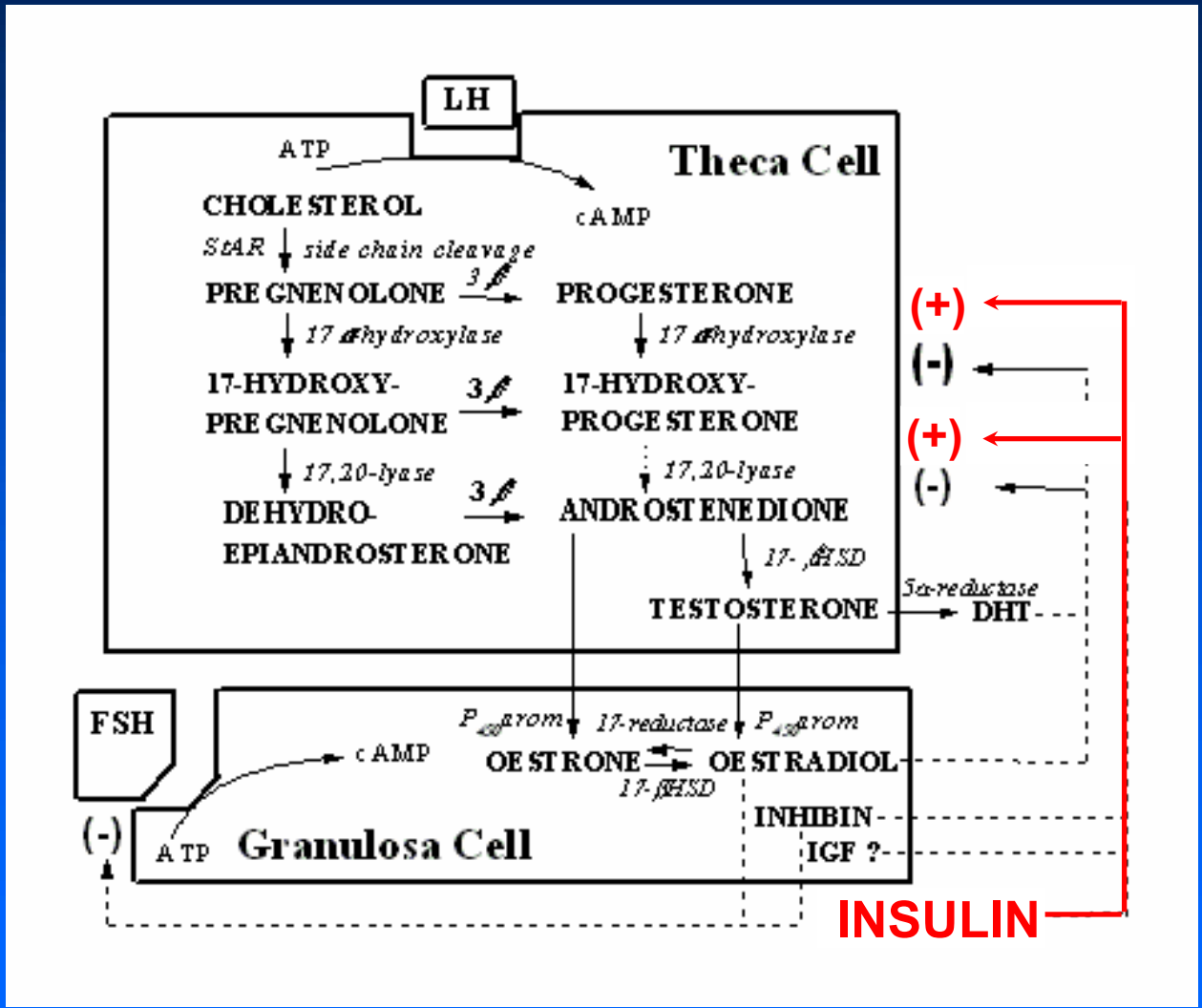
Insulin Resistance Mechanisms



Insulin effects related to ovarian function

Effect	Organ
Directly stimulates steroidogenesis	Ovary
Acts synergistically with LH/FSH to stimulate steroidogenesis	Ovary
Stimulates 17-hydroxylase	Ovary
Stimulates or inhibits aromatase	Ovary, adipose tissue
Up-regulates LH receptors	Ovary
Promotes ovarian growth and cyst formation synergistically with LH/hCG	Ovary
Up-regulates Type I IGF receptors or hybridinsulin/type I IGF receptors	Ovary
Inhibits IGFBP-1 production	Ovary, liver
Inhibits SHBG production	Liver
Potentiates the effect of GnRH on LH/FSH	Hypothalamus/pituitary

Major Steroid Biosynthetic Pathways



Treatments for PCOS

* Oral Contraceptives

- Clomiphene
- Ovarian diathermy/laser tx
- ART

* Cyproterone acetate+ EE
  Spironolactone

*

★ Weight loss

★ Insulin sensitizing agents

Insulin sensitizing agents

* Biguanides (metformin)

* Thiazolidinediones (troglitazone)

Numerous placebo-controlled trials

Similar benefficial effects

Role of Insulin in Central Nervous System

* NIRKO mice : disruption of IR in neurons

*Mice lacking IRS-2

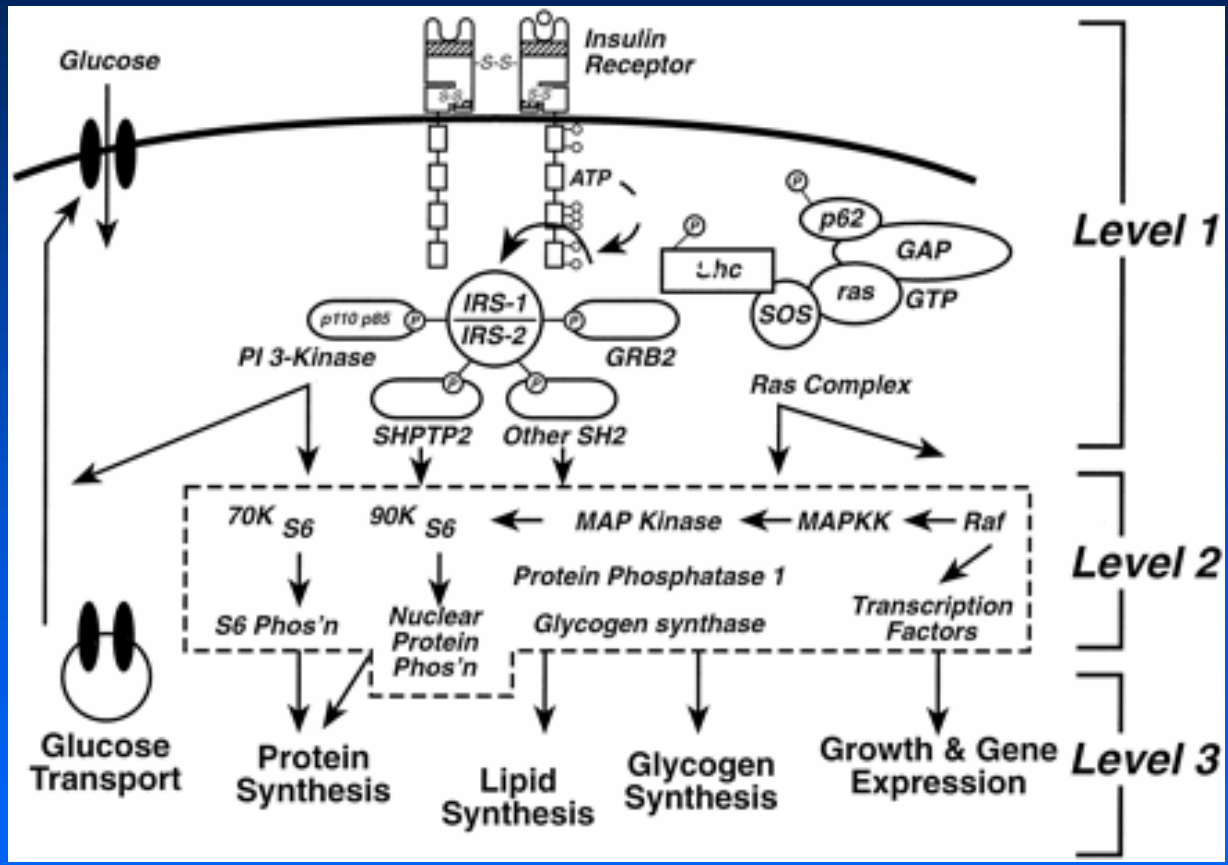
Conclusions

1. PCOS is a metabolic and reproductive disease

2. Insulin resistance has a central role in its pathogenesis

3. Numerous defects in insulin signaling may be involved

4. Probably polygenic disease. Problem of the wide range of phenotypic expression


Glucose
Insulin Receptor
S-S
ATP
p62
GAP
Shc
ras
GTP
SOS
p110 p85
IRS-1
IRS-2
GRB2
PI 3-Kinase
Ras Complex
SHPTP2
Other SH2
70K S6
90K S6
MAP Kinase
MAPKK
Raf
Protein Phosphatase 1
S6 Phos'n
Nuclear Protein Phos'n
Glycogen synthase
Transcription Factors
Glucose Transport
Protein Synthesis
Lipid Synthesis
Glycogen Synthesis
Growth & Gene Expression
Level 1
Level 2
Level 3