

# PCOS

- U kursus Gynækologi 2
- 06.01-08.01 2010



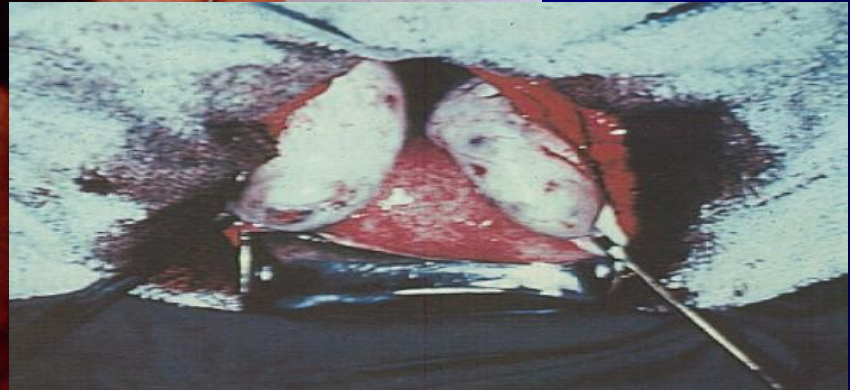
## PCOS:



- Lidt historie
- Livstidsperspektiv
- Kliniske fokusområder
- Diagnose
- Patofysiologi
- Behandling
- Prognostiske perspektiver (CVD)
- Klinisk resume

# PCO: Historie

Stein IF, Leventhal ML.  
Amenorrhoea  
associated with  
bilateral polycystic  
ovaries. Am J Obstet  
Gynecol;29:1818-191



# PCO: Historie

- Achard C, Thiers J. Le virilisme pileire et son association à l'insufficance glycolytique (diabète des femme à barbe). Bull Acad Natl Med 1921;86:51-71

# PCO: Historie

Mor-  
fologi

Syndro-  
met

Endo-  
krinologi

Ultralyd

Metabo-  
lisme

1935

1960

1970

1985

1990

# PCO: Livsperspektiv

Lav  
fødsels-  
vægt

Pubertas  
præcox  
Hirsu-  
tisme

Fed-  
me

Ureglmæssig  
cyklus  
Anovulation  
Infertilitet

Type-2  
diabetes  
Hjertekar-  
sygdom  
Cancer

Fødsel

Pubertet

Adolescens

Fertile  
periode

Senescens

# Definition på PCOS

ESHRE og ASRM Rotterdam 2003

- To af 3 følgende symptomer er til stede:
  - 1. Oligo- eller amenorre som følge af anovulation,
  - 2. Kliniske og/eller biokemiske tegn på hyperandrogenisme,
  - 3. Mindst et polycystisk ovarium
- Definition af PCO ved ultralyd:
  - Mindst 12 follikler 2 - 9 mm i diameter og/eller
  - ovarievolumen  $> 10$  ml.

[sos/pcos/2010](http://sos/pcos/2010)

# Definition på PCOS

ESHRE og ASRM Rotterdam 2003

- **Ad 2. Kliniske og/eller biokemiske tegn på hyperandrogenisme**
  - **Klinisk hirsutisme (Ferriman-Gallway score > 8**
  - **Akcne eller alopeci**
  - **Øget total testosteron**
  - **Øget frit testosteron**
  - **Lavt SHBG**

[sos/pcos/2010](http://sos/pcos/2010)

# Testosteron og SHBG (nmol/l)

	Middelværdi	Grænser
Total-t	1.0	0.6-1.8
Frit-t	0.014	0.006-0.034
SHBG	83	41-170

# Definition på PCOS

ESHRE og ASRM Rotterdam 2003

## Udelukke:

- Hyperprolaktinæmi
- Binyrebarkhyperplasi
- Cushing's syndrom
- Androgenproducerende tumor
- Akromegali

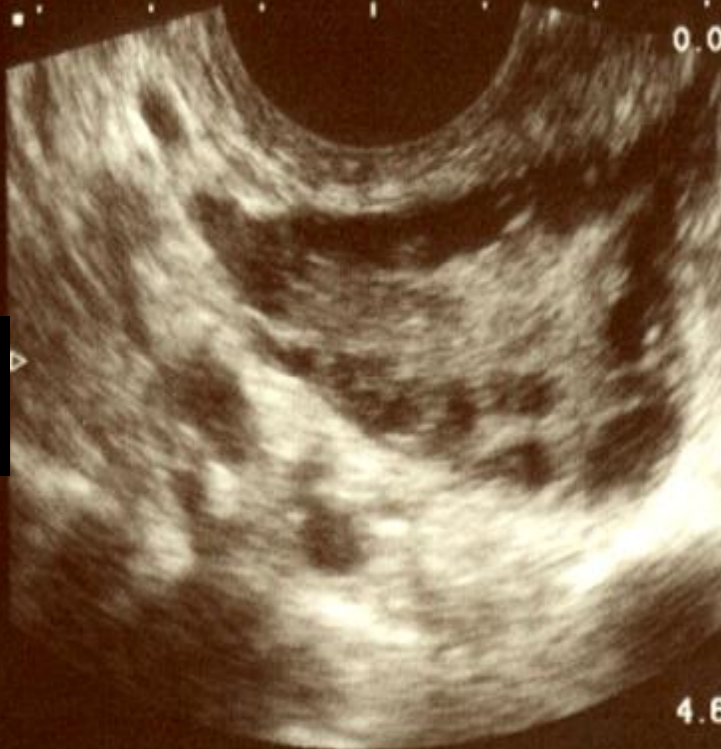
# Nogle differentialdiagnoser

	Hyperan- drogenisme	Oligo/a men- orrhoea	Klinik andet	Biokemi
Hyperpro- laktinæmi	- (+)	+	Galak- torrhoea	Prolaktin
Binyrebark hyperplasi	+	- (+)	Fam. androgenisme	21-hydroxy- progesteron
Cushing	+	+	Hypertension, ansigtstræk	24-h kortisol
Akrome- gali	- (+)	(+)	Akral fordtørrelse	IGF-1
Tumor	+	+	Clitoris hypertrofi o.a	Androgen

SVEN SKOUBY

2002-03-27 8561  
18:34:56 6.5MHz

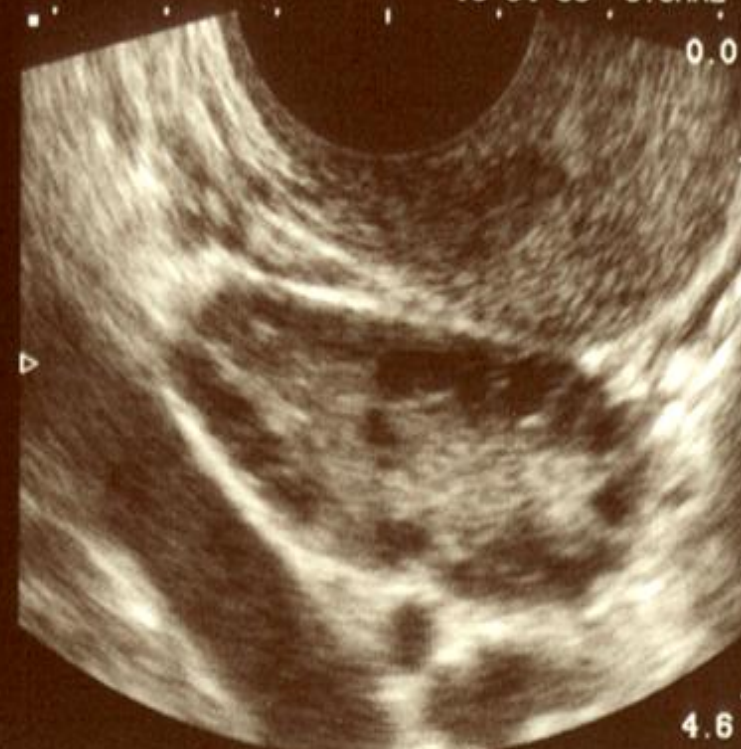
G:54%  
FR:14  
MI:0.9



SVEN SKOUBY

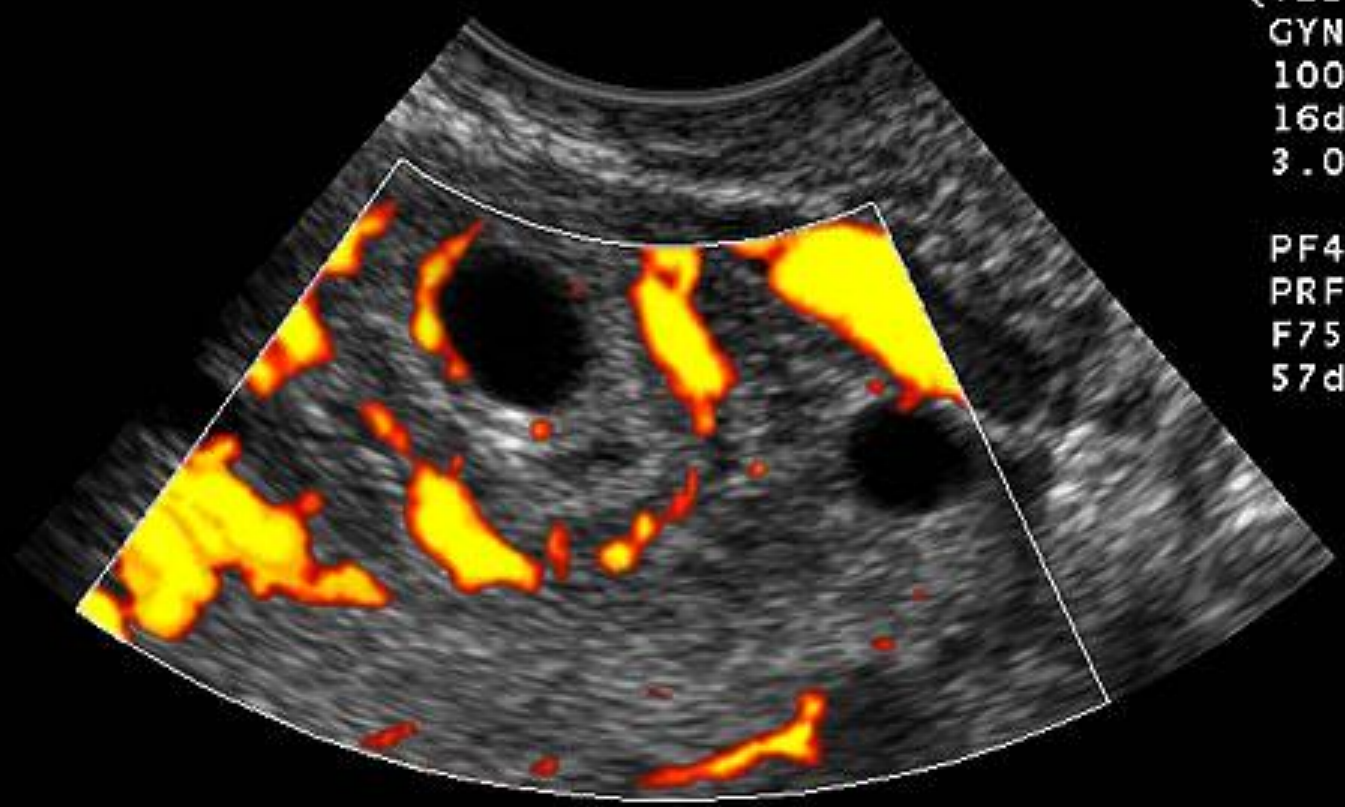
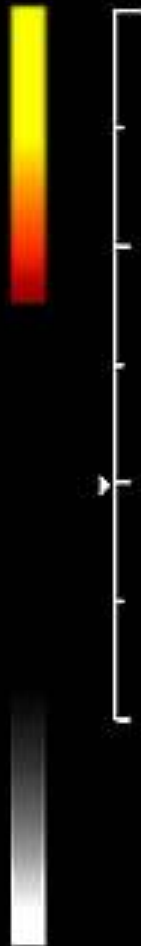
2002-03-27 8561  
18:34:39 6.5MHz

G:54%  
FR:14  
MI:0.9



6.5EV13/6.00  
TIB 0.4  
(TIS 0.4)  
GYN Infert  
100%  
16dB RS5  
3.0cm 9fps

PF4.80MHz  
PRF750Hz  
F75Hz  
57dB RS6



# PCOS: Hyppighed

- Prævalens 5-8% af kvinder i fertil alder

# PCOS og BMI

- 60% er overvægtige. 40-60% BMI > 30

# PCOS. Klinisk manifestationer

Infertilitet	74%
Hirsutisme	69%
Amenorrhoe	51%
Fedme	41%

# Årsager til sekundær anovulation

	Amenoré	Oligomenoré/ Anovulatoriske blødninger
• Hypothalamisk	50%	< 5%
• Ovariel defekt	5%	< 5%
• Hyperprolaktinæmi	15%	< 5%
• PCOs	25%	85%
• Andre	10%	< 5%

# PCOS: Genetics

	Group I	Group II	P
Ovarian volume	2,8	1,7	0,016
Follicles	5,4	0,8	<0,01
PI (uterine artery)	3,2	4,2	0,031

Battaglia C et al. Human Reproduction 2002

# PCOS: Developmental origin

Genetic predisposition  
(Insulin resistance)

Prenatal exposure to androgen?

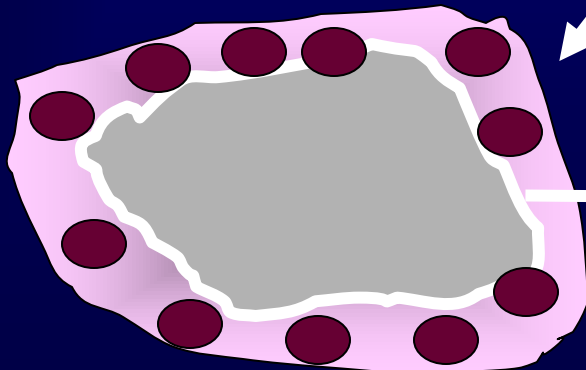
Central obesity  
Abnormal LH secretion

High LH

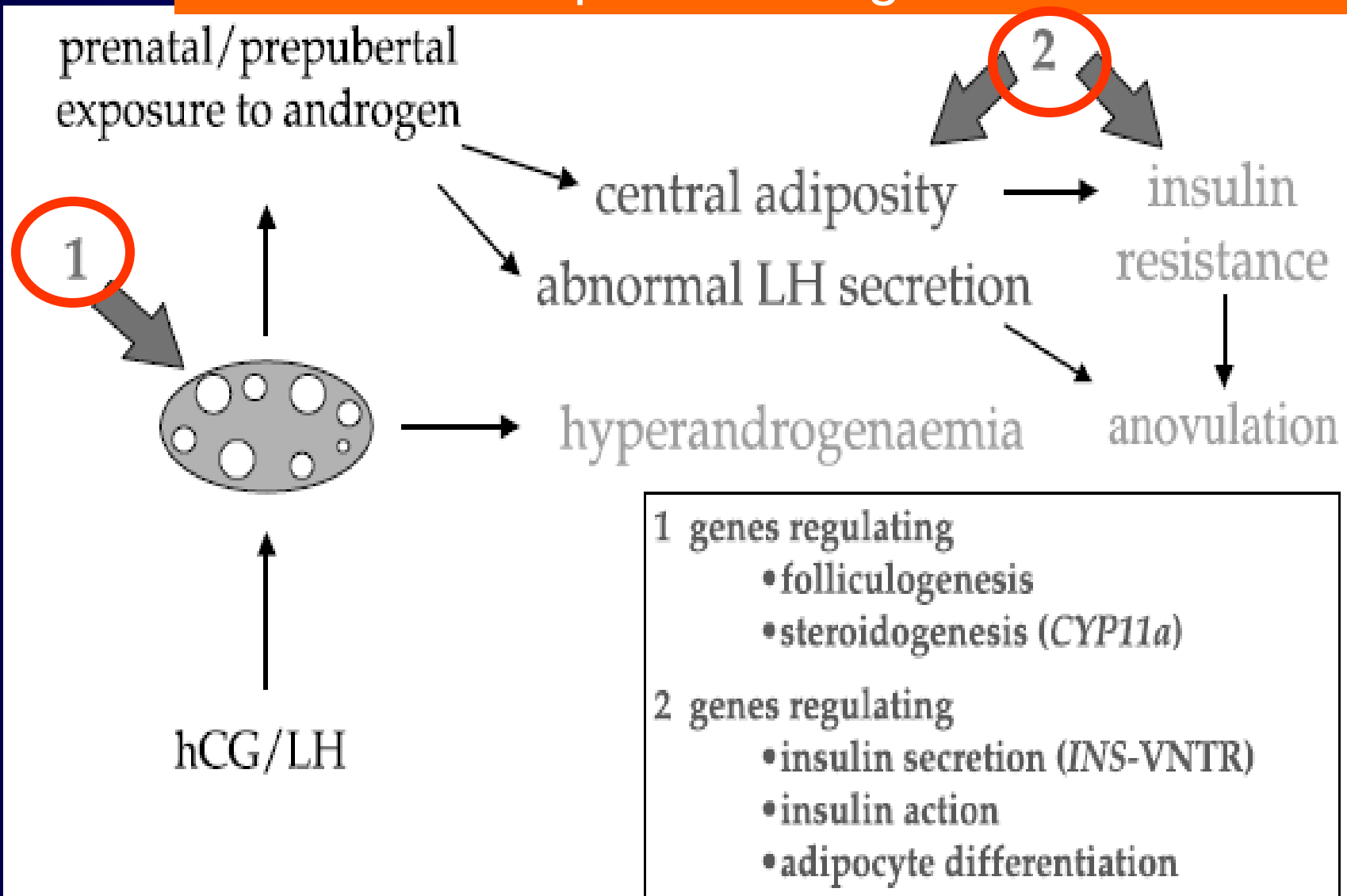
Insulin resistance

Hyperandrogenism

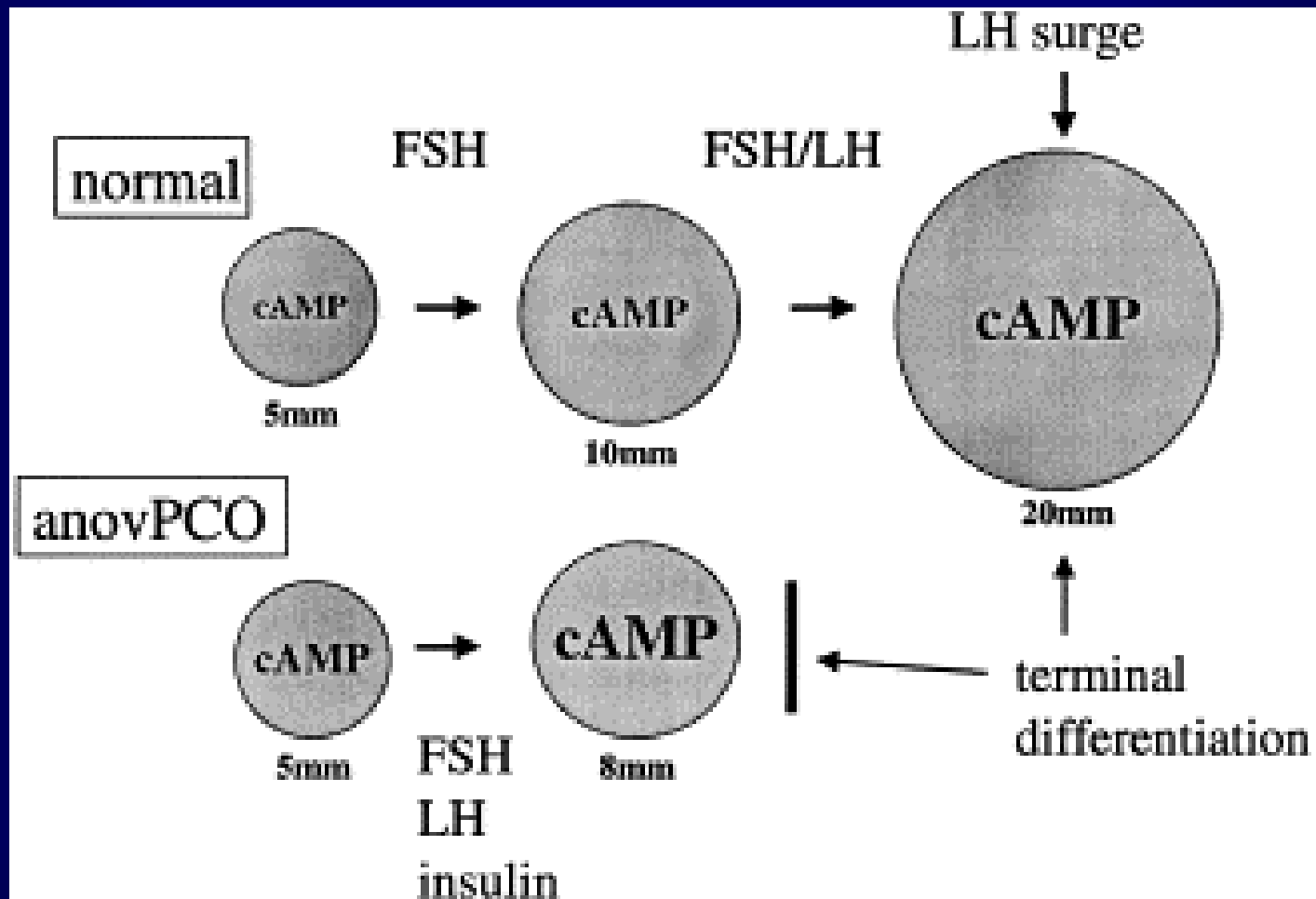
Anovulation



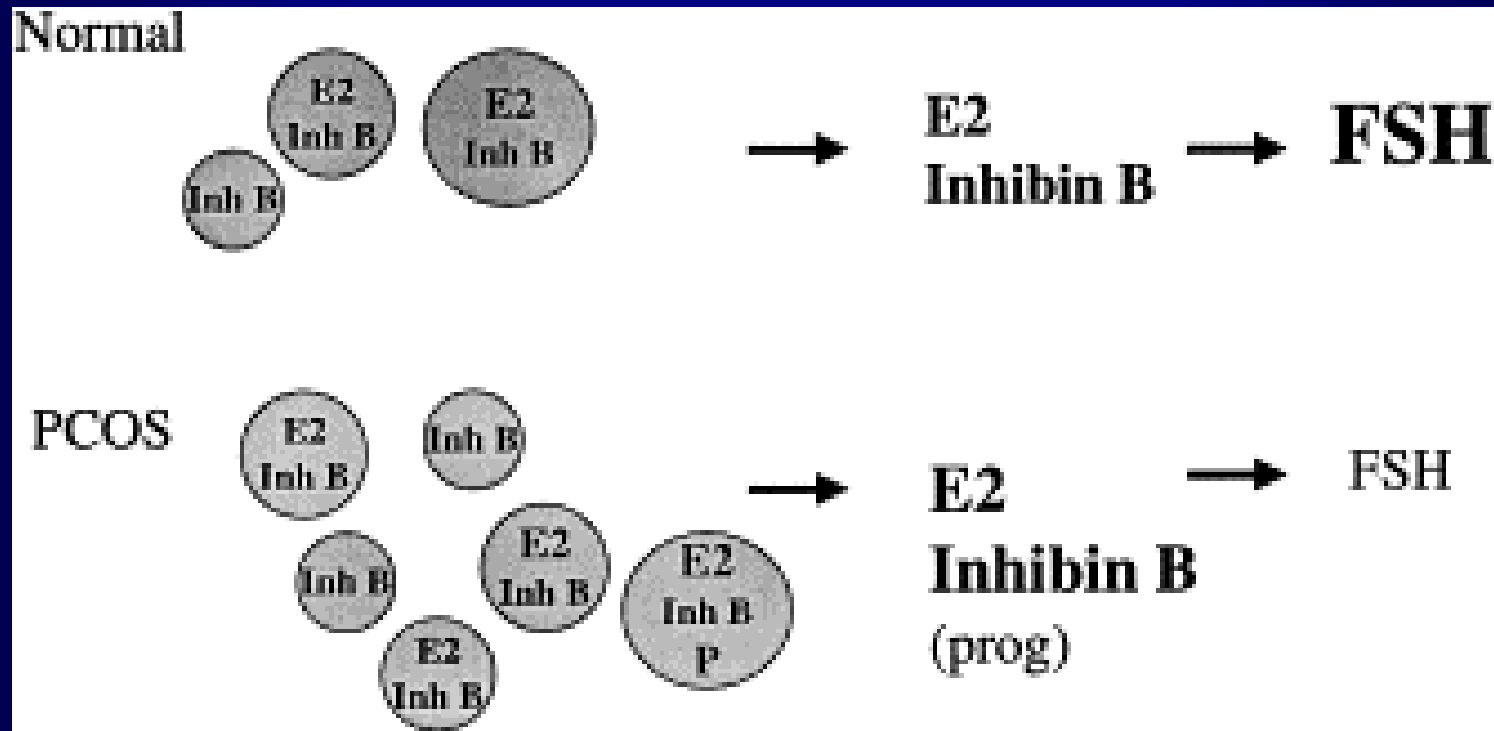
# PCOS: Developmental origin?

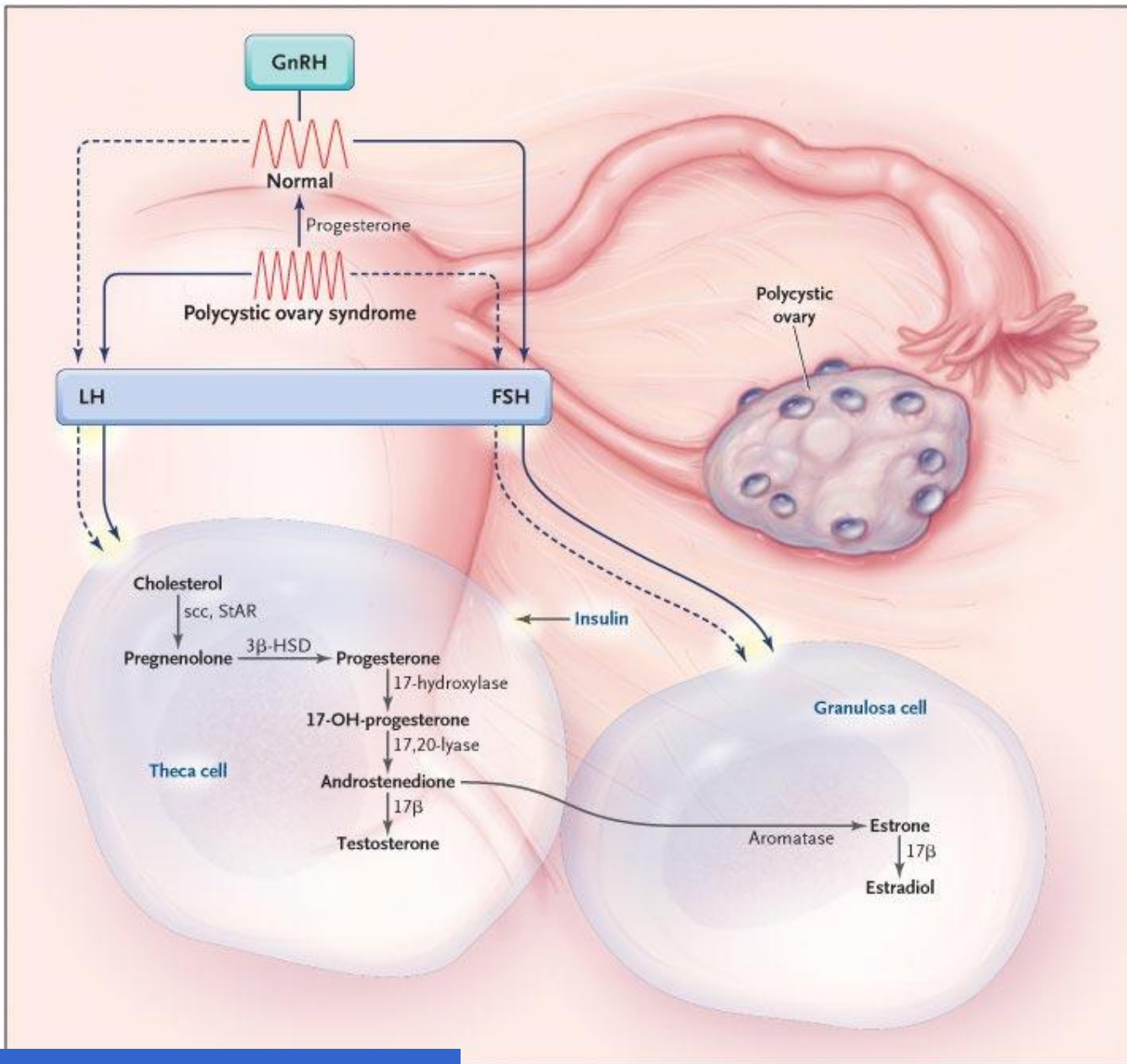


# PCOS vs Controls



# PCOS vs Controls

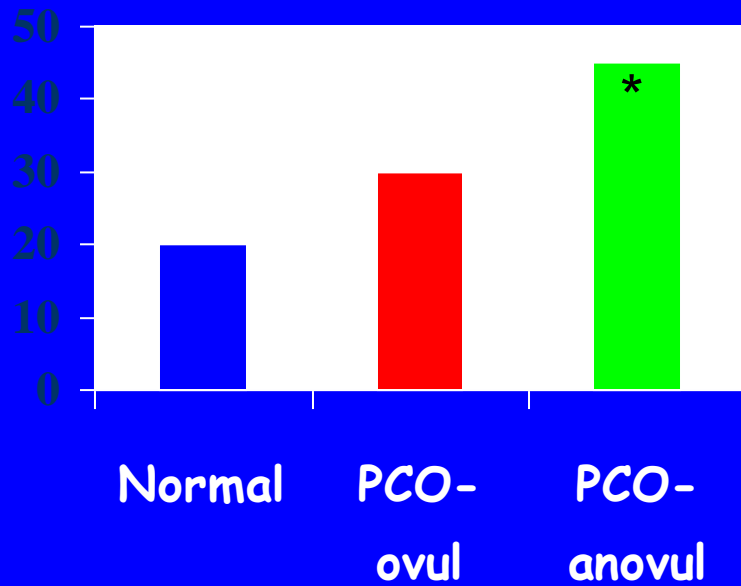




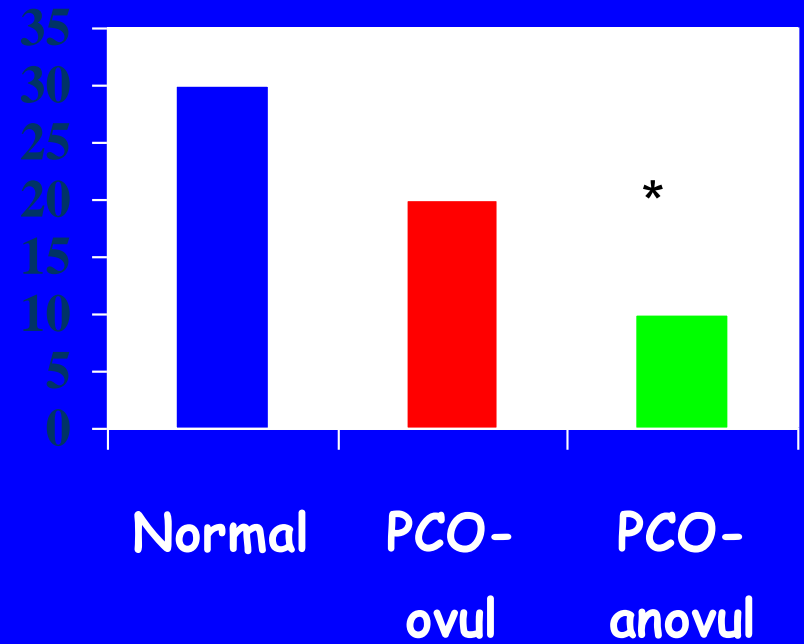
# PCOS: Kliniske metaboliske aspekter

# PCOS vs Controls

## Insulin area

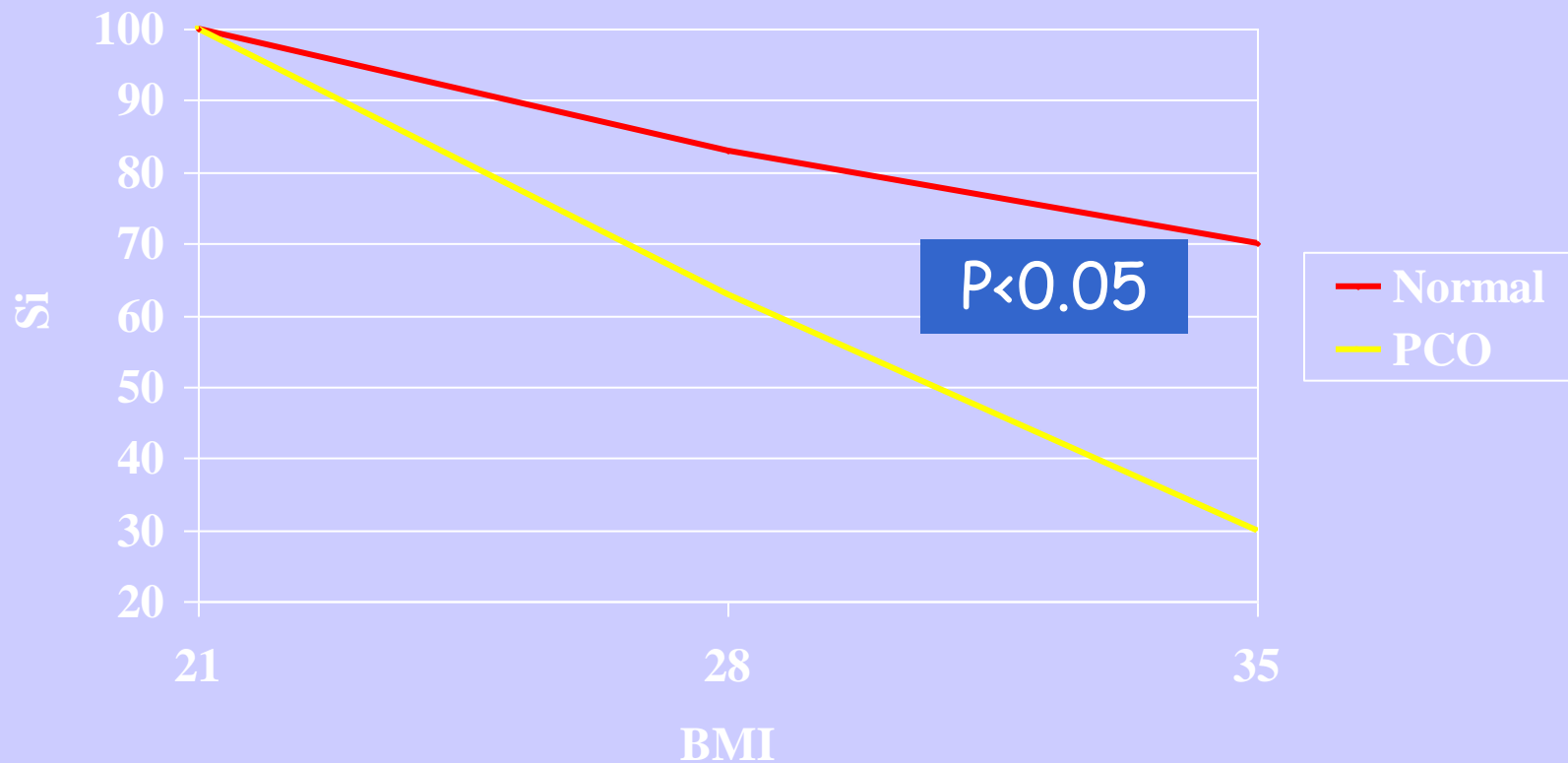


## Si



# Insulin sensitivity and BMI

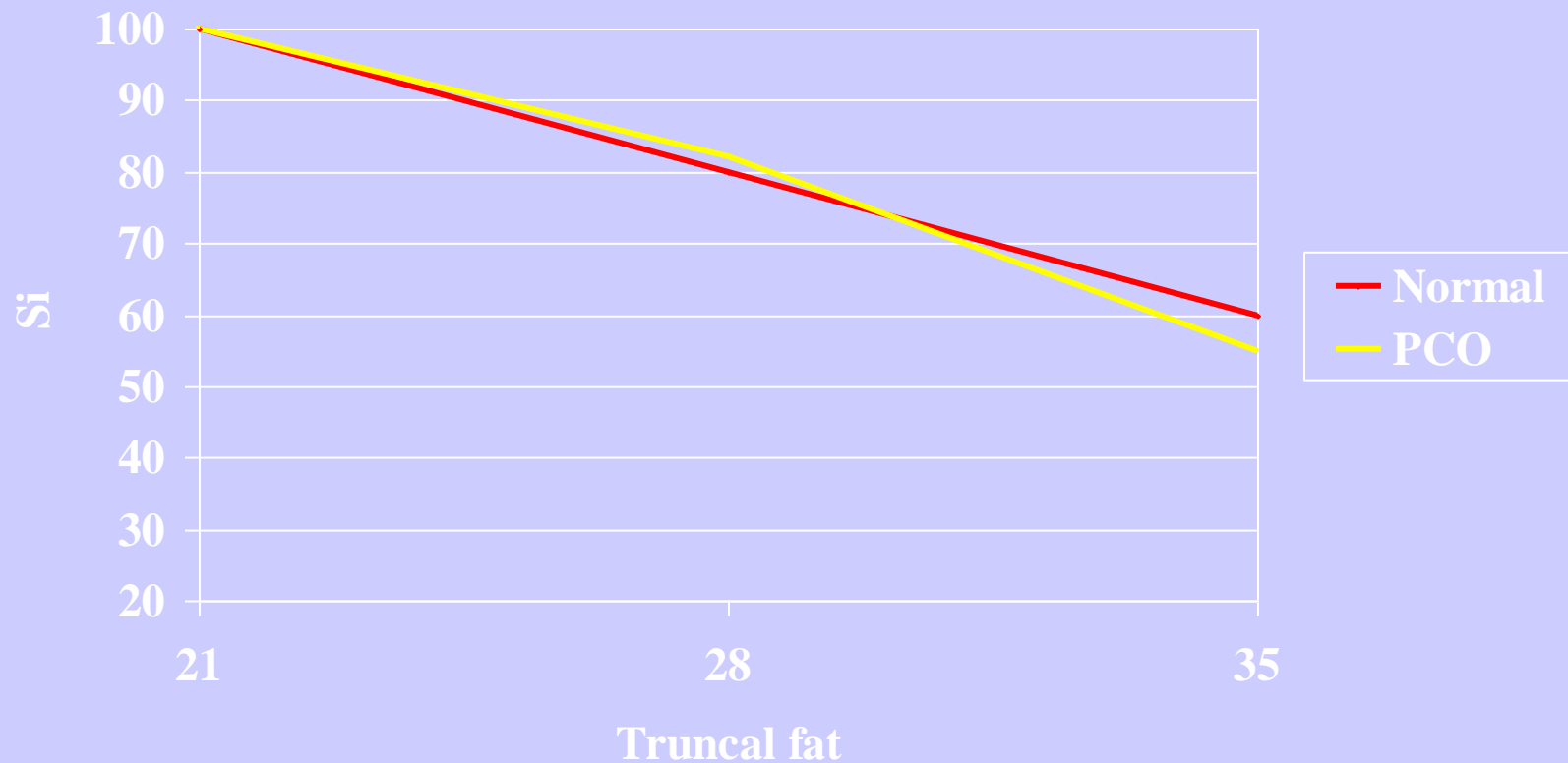
% change in glucose disposal rate (Si)



Holte J et al, J Clin Endocrinol Metab 1994

# Insulin sensitivity and truncal fat in normal and PCO women

% change in glucose disposal rate ( $S_i$ )

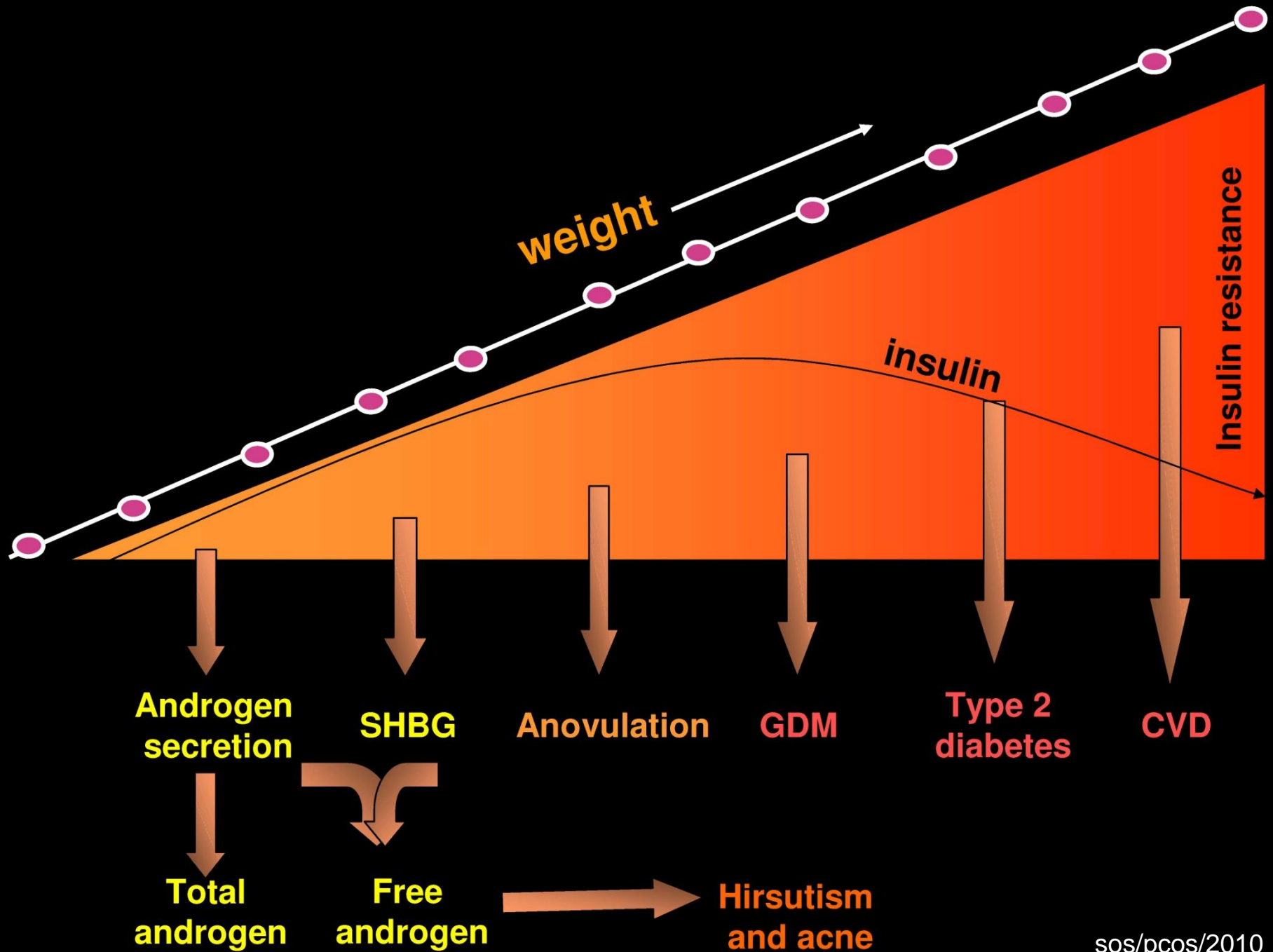


Holte J et al, J Clin Endocrinol Metab 1994

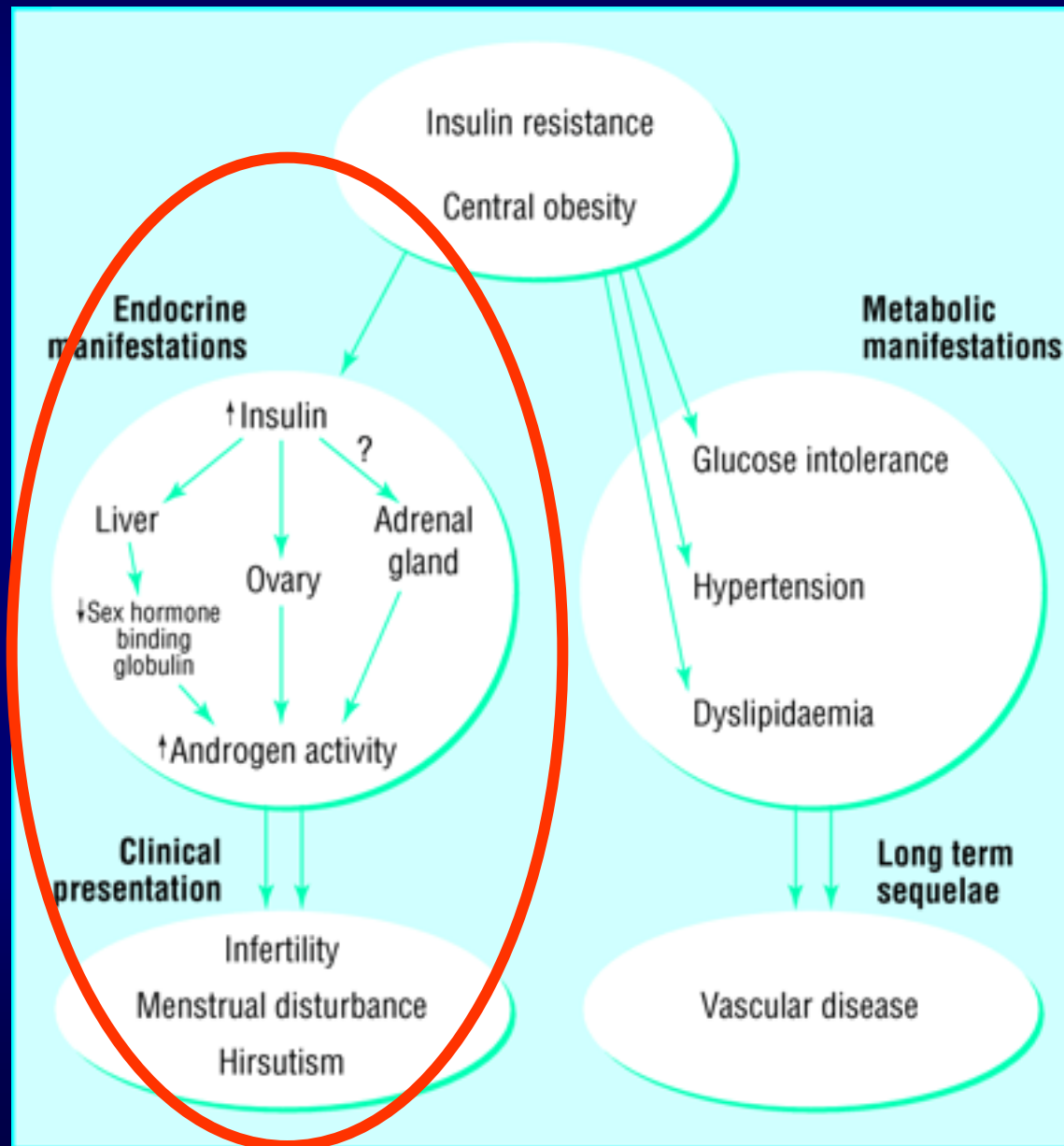
sos/pcos/2010

# PCOS: Prævalens af insulin resistance

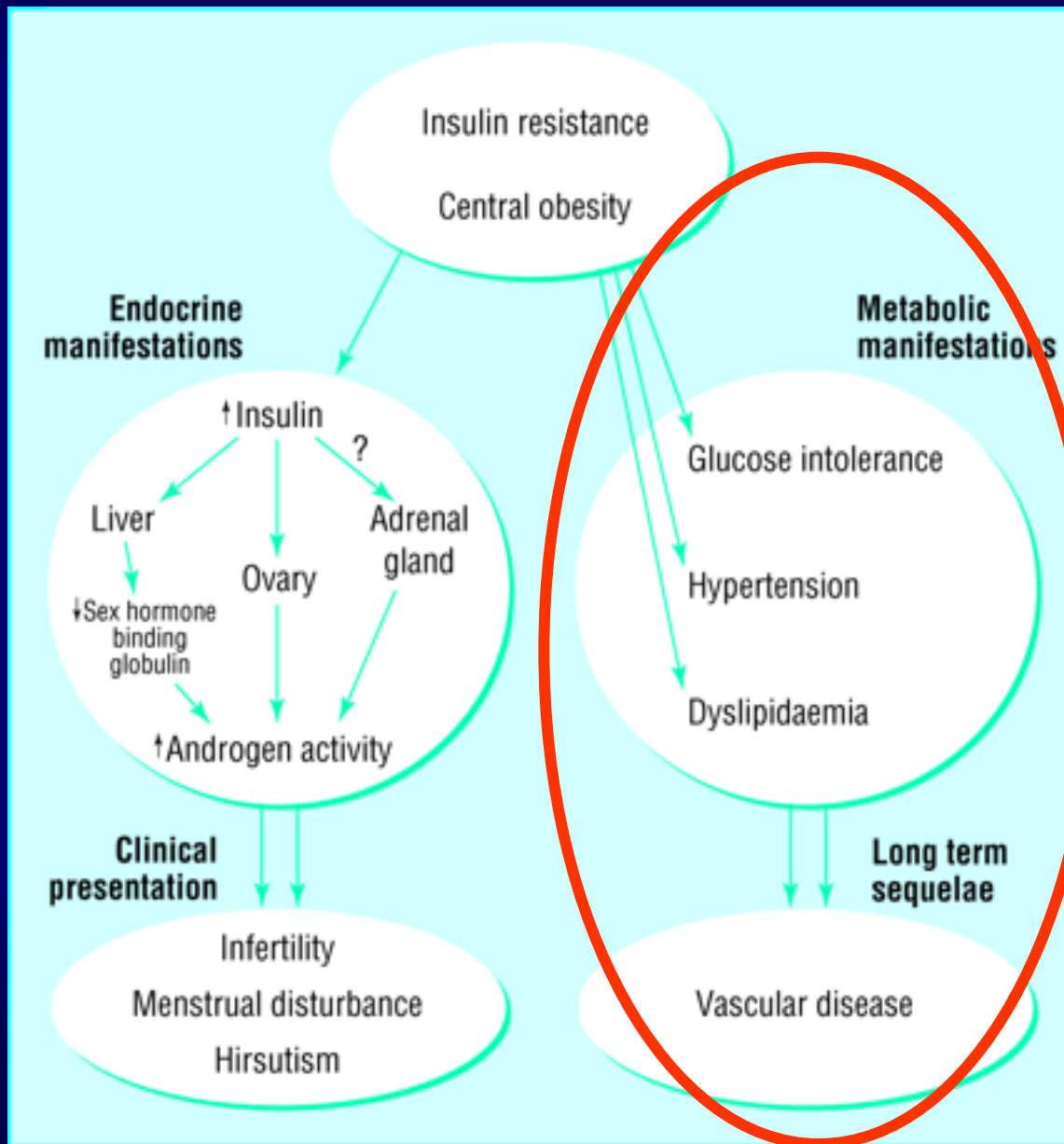
- Overvægtige: 60%
- Normalvægtige: 30%



# Metabolisk syndrom



# Metabolisk syndrom

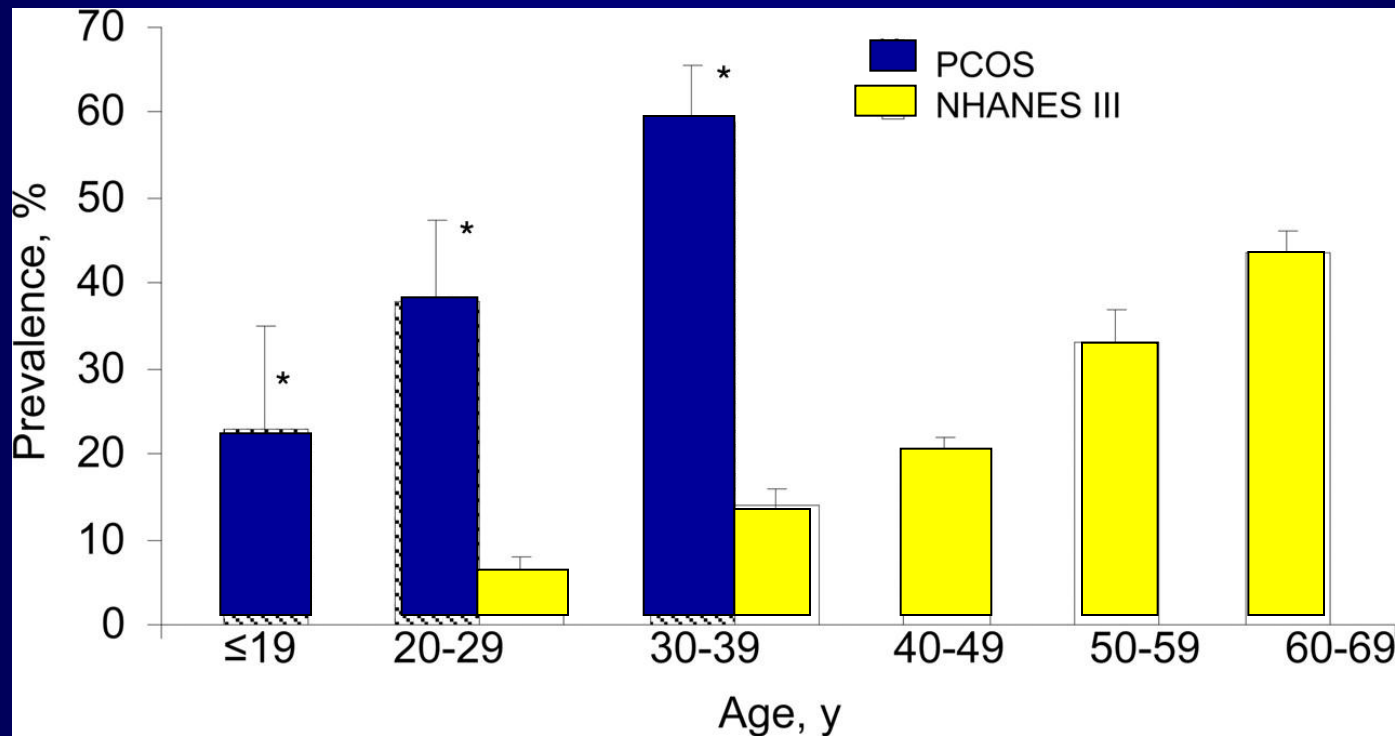


# Metabolisk syndrom

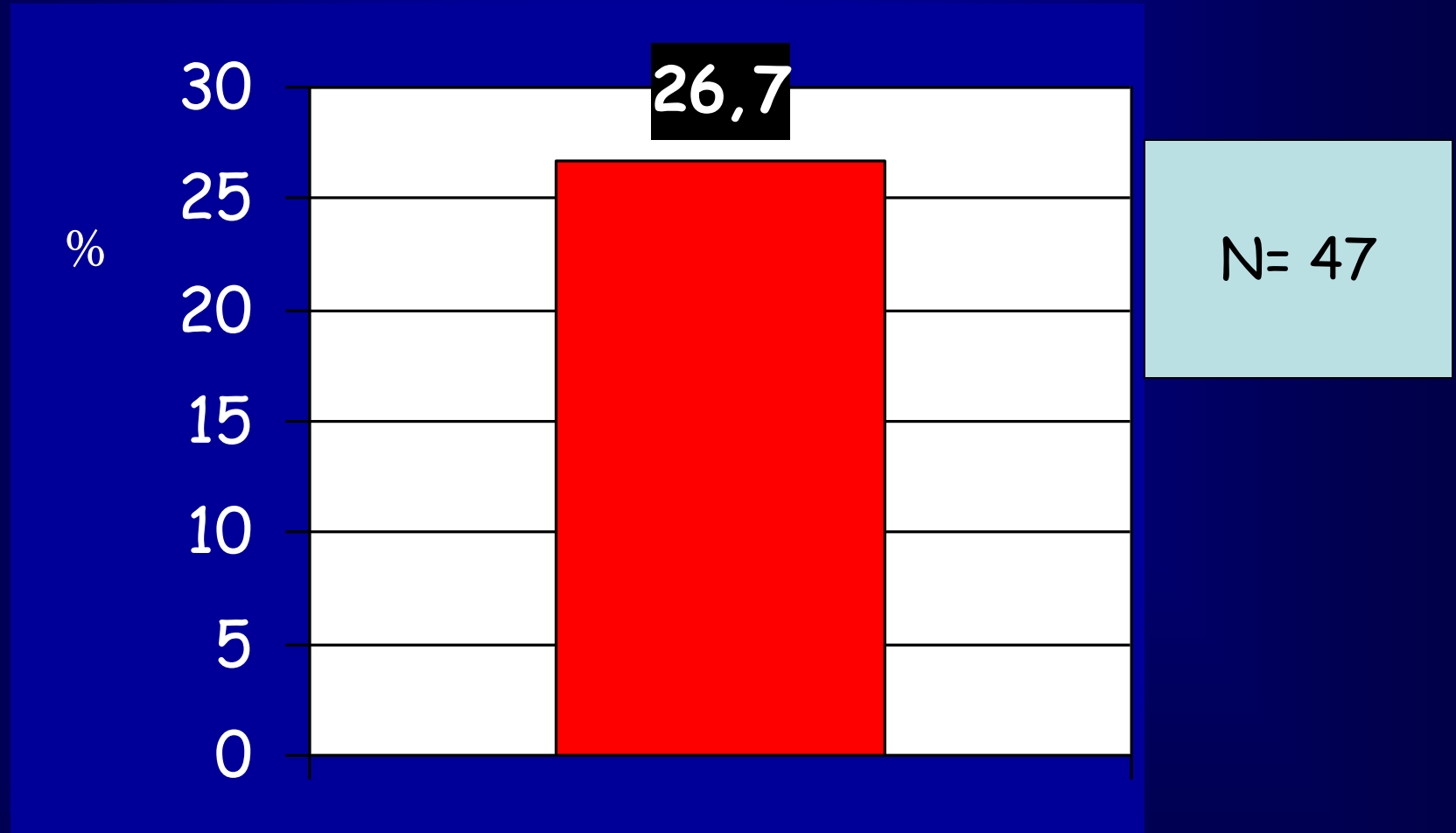
## WHO:

- Nedsat glukosetolerans eller diabetes
- Insulinresistens
- Forhøjet blodtryk 140/90 mmHg
- Forhøjede plasmatriglycerider og/eller lav HDL-kolesterol
- Central adipositas (talje hofte-ratio), og/eller BMI >30 kg/m<sup>2</sup>
- Mikroalbuminuri

# Prevalence of the MBS among women with PCOS compared with non-PCOS



# Type-2 DM and prevalence of PCOS :



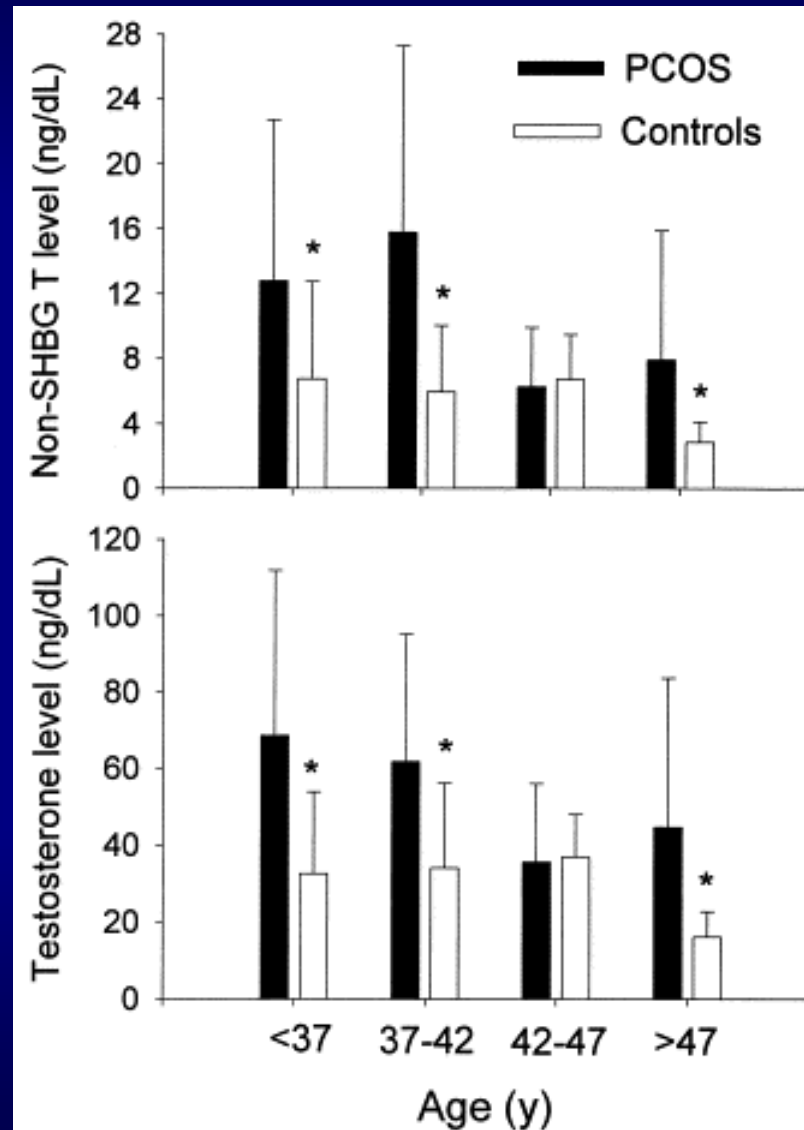
Peppard HR et al Diabetes Care 2001

# PCOS and OR of CVD and diabetes:

N=319	OR	95%CI
CHD	1,5	0,5-2,9
Cerebrovascular disease	2,8*	1,1-7,1
Hypertension	1,4*	1,0-2,0
Diabetes	2,8*	1,5-5,5

Wild, S et al. Clin Endocrinol, 2000

# Testosterone levels in PCOS



# PCOS: Endometrie cancer

Authors	Study design	Participants	Findings	Comments
Speert 1949 <sup>2</sup>	Case series	14 women under 40 years with endometrial carcinoma	8 with cystic and 1 with sclerotic ovaries	No controls
Dockerty et al 1951 <sup>4</sup>	Case series	36 women under 40 years with endometrial carcinoma	14 with cystic ovaries (no histology in 8)	No controls
Jackson and Dockerty 1957 <sup>5</sup>	a) Case series b) Cross-sectional	a) "many thousands" of endometrial cancer cases b) 27 women with PCOS on biopsy	a) 16 women with PCOS b) None had endometrial carcinoma	No evidence of association
Ramzy and Nisker 1978 <sup>6</sup>	Case-control	15 ovaries from cases of endometrial cancer, 25 from women with PCOS, 21 from controls	Ovaries from endometrial carcinoma cases more similar to the normal than to PCO	No evidence of association
Coulam et al 1983 <sup>7</sup>	Retrospective cohort	1270 women with chronic anovulation	SMR for endometrial carcinoma 3.1	No data for women with PCOS
Gallup and Stock 1984 <sup>8</sup>	Case series	111 cases of endometrial cancer	PCOS in 31.2% of women under 40, 2.3% over 40	No controls
Escobedo et al 1991 <sup>9</sup>	Case-control	399 cases of endometrial carcinoma; 3040 controls	Odds ratio for endometrial carcinoma 4.2 for "ovarian factor" infertility	No data for women with PCOS
Dahlgren et al 1991 <sup>2</sup>	Case-control	147 cases of endometrial cancer; 409 controls	Increased hirsutism in cases with endometrial cancer	No data for PCOS
Ho et al 1997 <sup>10</sup>	Retrospective cohort	116 patients with endometrial hyperplasia	Prevalence of endometrial carcinoma not increased in cases with PCOS	No evidence of association
Pierpoint et al 1998 <sup>11</sup>	Retrospective cohort	786 women with PCOS	Mortality from "miscellaneous cancers" not increased	No data for endometrial cancer
Wild et al 2000 <sup>12</sup>	Retrospective cohort	345 surviving women from Pierpoint cohort	Odds ratio for endometrial cancer 5.3	Obesity a possible confounder

sos/pcos/2010

# PCOS: klinisk resume

- Reproduktion
  - PCO
  - Hyperandrogenisme
  - Anovulation
  - Øget LH sekretion
  - Øget abortrisiko
- Metabolisme
  - Insulinresistens
  - dyslipedemi
- Almen klinisk ekspression
  - Fedme
  - Hjertekarsygdom
  - Diabetes
  - Cancer

# PCOS: behandling

	Insulin resistens	Ovulationsrate	Hirsutisme	Akne	BMI	TG	LDL-C
Livsstil	↓	↑	→	→ ↓	↓	↓	↓
OC	↓	↓	↓	→ ↓	→ ↓	→ ↓	→ ↓
Metformin	↓	↑	↓	→	→	↓	→ ↓
Glitazon	↓	↑	↓	→	↓	↓	→ ↑
Spiro-lacton	↓	?	↓	↓	→	→	→