

Polycystic Ovarian Syndrome

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Outline

- Definition
- Symptoms
- Causal factors
- Diagnosis
- Complications
- Treatment

Why are we talking about it?

- Affects ~ 10% of women, only 50% diagnosed
- Average of 2 years and 3 providers to diagnose
- Only 16 % are satisfied with information provided
- Multiple potential etiologies
- Variable clinical presentations

Why are we talking about it?

PCOS. Ladies, please
enjoy the libido of a 19
year old male
while having the
facial hair of a 16
year old boy.



your  cards
someecards.com

Why are we talking about it?

- Cosmetic issue – hair growth, acne and obesity affecting self esteem
- Menstrual issue – unpredictable, spaced and/or prolonged menses
- Fertility issue – oligo-ovulatory
- Cancer issue – unopposed estrogen
- Health issues – cardiovascular, diabetes, sleep apnea, dyslipidemia, depression, etc.

Who has PCOS?

	1990 US NIH criteria		2006 AE-PCOS criteria	
	2003 Rotterdam criteria			
	Phenotype A	Phenotype B	Phenotype C	Phenotype D
Hyperandrogenism and hirsutism	Present	Present	Present	Absent
Ovulatory dysfunction	Present	Present	Absent	Present
Polycystic ovarian morphology	Present	Absent	Present	Present

Definition – most commonly used

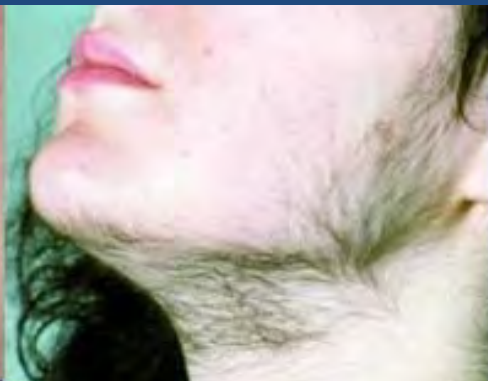
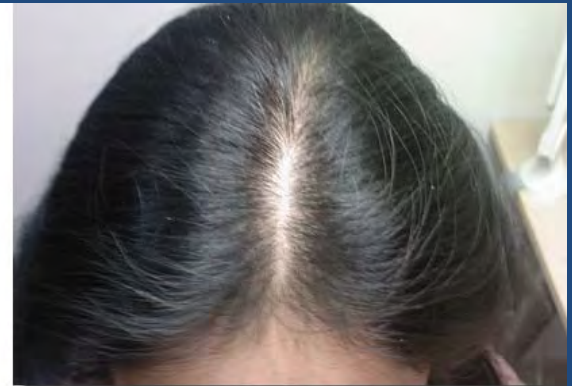
- First described in 1935 by Stein and Leventhal
- **Rotterdam criteria 2003 (2 of 3):**
 - **Infrequent** (<9/year) or prolonged **menses**
 - Physical exam findings of **excess androgen**
 - Ultrasound finding of 12 + **follicles** between 2 and 9 mm
- **Diagnosis of exclusion**
 - (CAH, Cushing, Meds, Thyroid, Prolactinoma, etc)

Definition – more inclusive

- Androgen excess society, 2006 PCOS:
- **Hyperandrogenism**, clinical or biochemical in combination with **ovarian dysfunction**, including both functional and ultrasound abnormalities

Symptoms

- Menstrual irregularity, usually infrequent
- Facial and body hair, excess thick pigmented hair on the lip, chin, peri-areolar, mid sternum and linea alba, toes and fingers
- Male pattern hair loss
- Acne
- Skin darkening in creases, groin, under breasts and skin tags around arm and neck
- Weight gain



How do we get PCOS?

- Unknown, however...it has to do with AMH
 - Anti mullerian hormone
- AMH is a growth factor, regulates follicles
- In the ovary, it inhibits follicle recruitment and inhibits how follicles grow in response to FSH

How do we get PCOS?

- PCOS is a d/o of follicular growth due to a granulosa cell defect in the synthesis of AMH
- AMH inhibitory action on FSH induced aromatase production likely contributes to hyperandrogenism and enhances insulin resistance
- Androgens → (Aromatase) → Estrogen

How do we get PCOS?

- Elevated serum AMH predicts poor response to various PCOS treatments
- Improvement in clinical parameters after treatment is a/w serum AMH decline

How do we get PCOS?

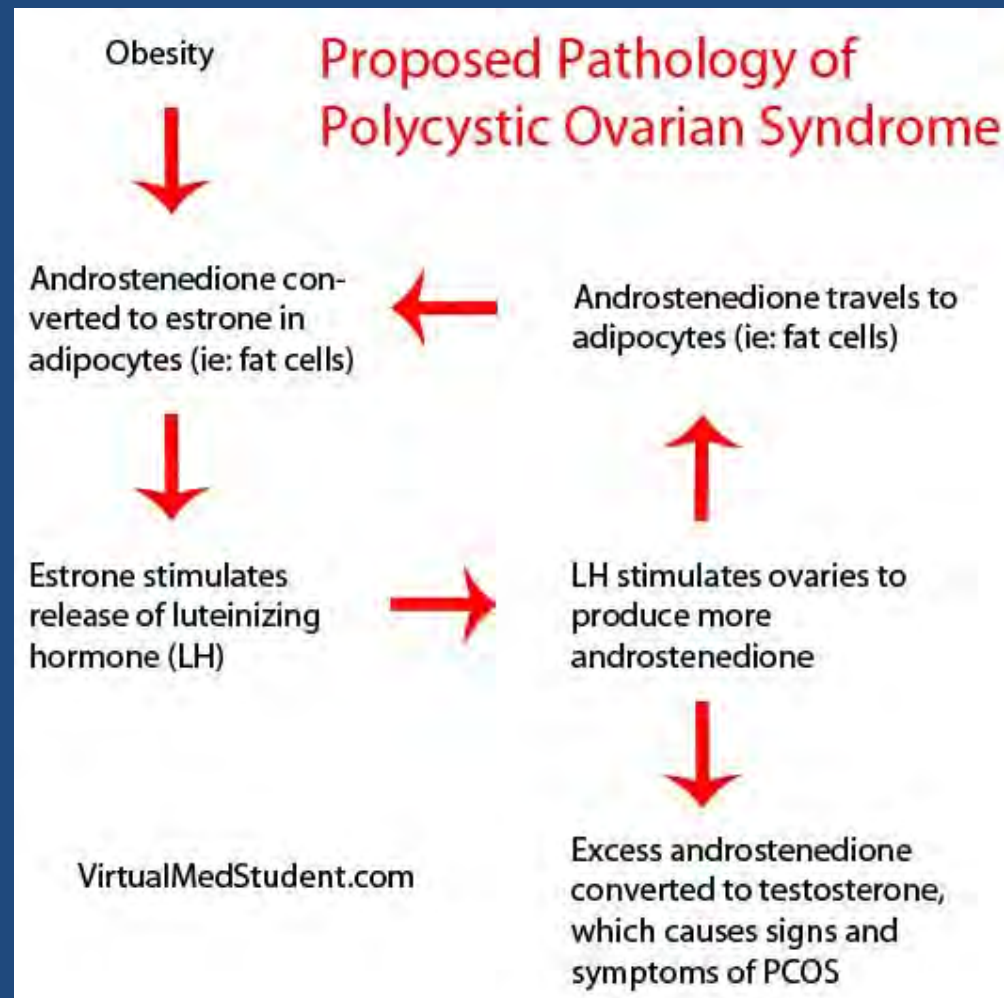
French NIH 5 days ago!!!:

- AMH higher in pregnancy of women with PCOS by ~ 30%
- Dosed pregnant mice with AMH and it caused irregular menses, fertility issues and late puberty in offspring
- Excess AMH promoted cells in the fetal brain to cause excess testosterone production

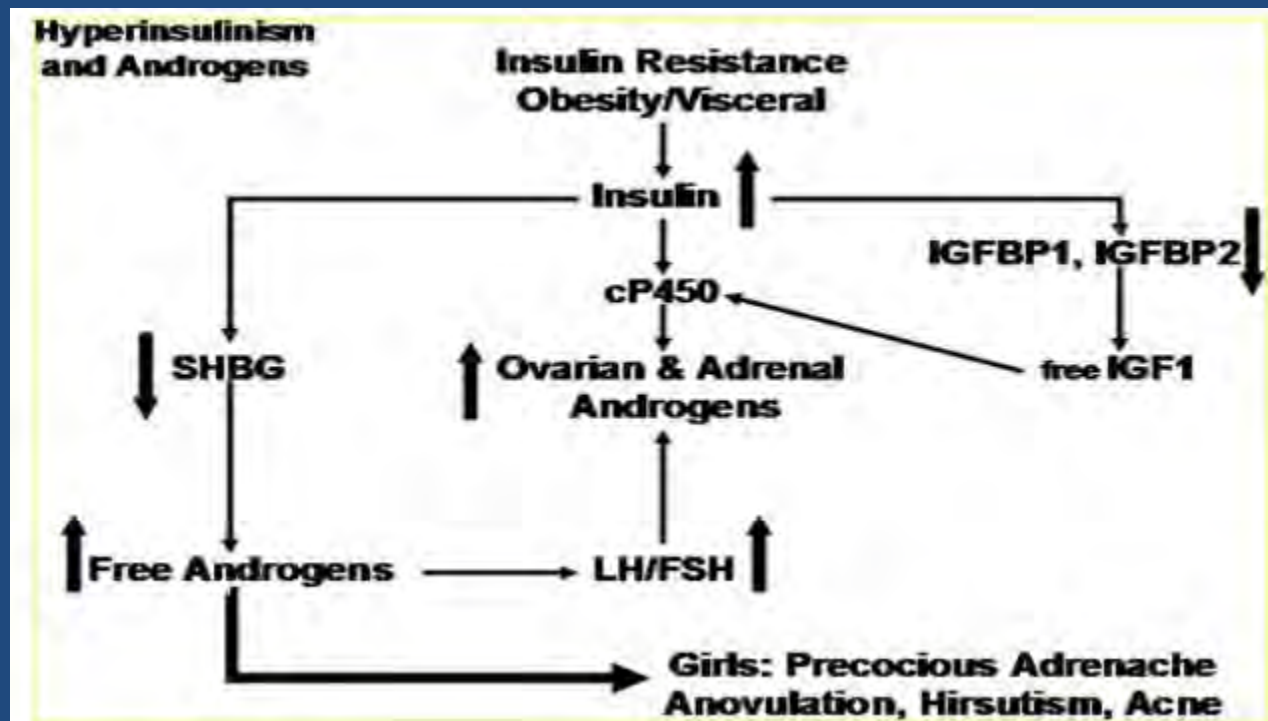
Causal factors - Genes

- Heredity – genes linked to PCOS
 - Prevalence in mothers and sisters 20 – 40%
- Genetic trait influenced by:
 - environmental factors (diet and obesity)
 - a number of genetic variants of genes that regulate:
 - Androgen biosynthesis and action
 - Gonadotropin secretion and action
 - Ovarian folliculogenesis
 - Insulin secretion and action
 - Weight and energy regulation

How else do we get PCOS?



How does insulin resistance fit in ?



Contributing factors - Insulin

- Cells become resistant to insulin, blood sugar increases and insulin increases
- Increased insulin causes stimulation of biosynthesis of androgens
- This causes difficulty with ovulation
- Etiology for this process is unclear
- This is not causative, must have genetic predisposition for hyperandrogens.

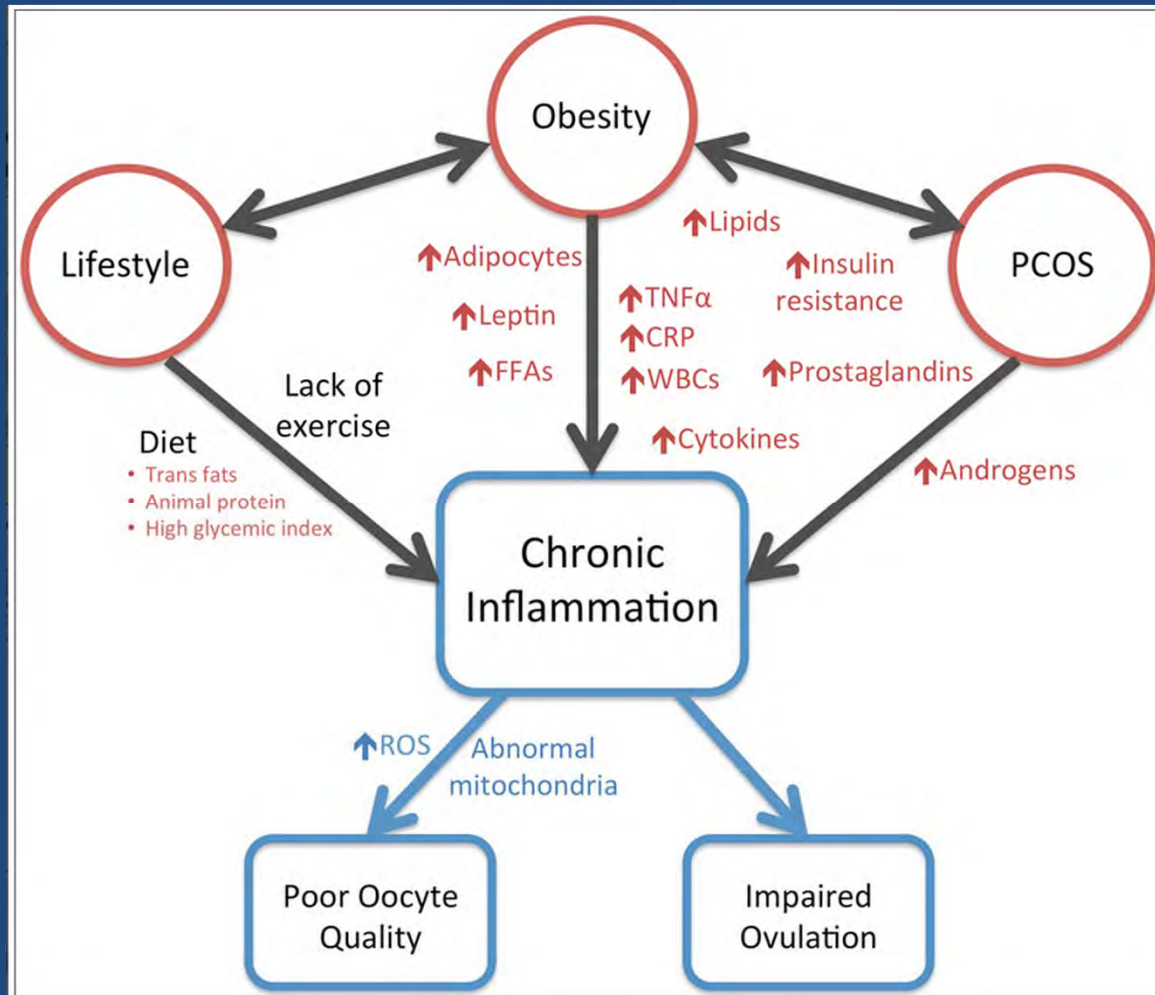
Contributing factors - Inflammation

- Low grade inflammation stimulates polycystic ovaries to produce androgens
- Increased CRP in PCOS > 5 mg/L
 - (BMI matched controls, 37% v. 10%)
 - Worsens in pregnancy and may contribute to worse pregnancy outcomes

Contributing factors - obesity

- 40 – 80 % pts with PCOS are obese
- Increases androgens but not clear if this is causative
- Symptom onset is often with weight gain

PCOS relationships

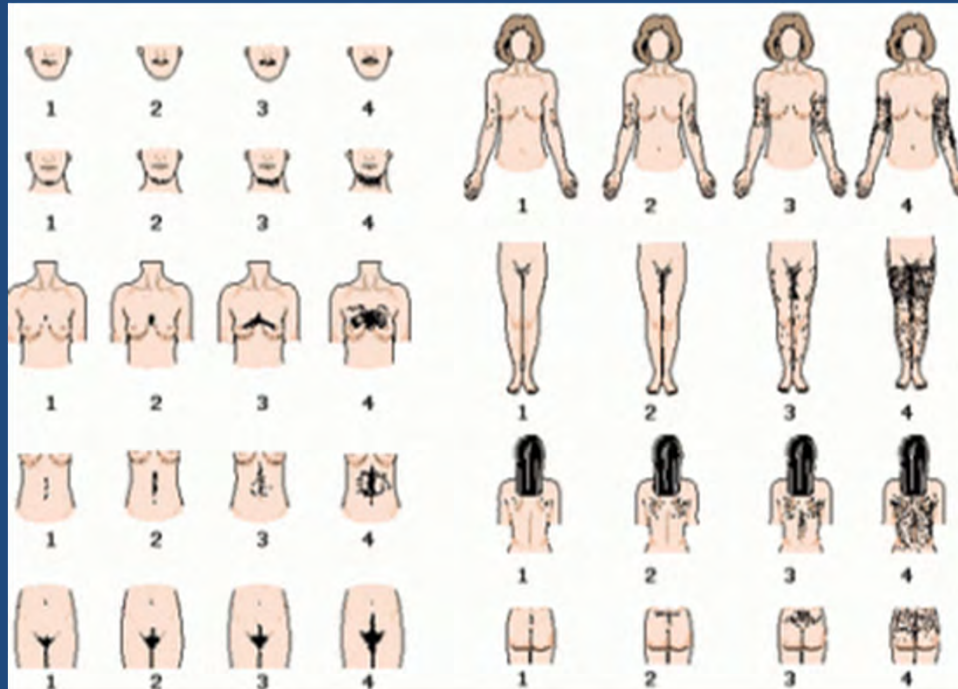


Diagnosis

- No test
- History and Physical exam
- Transvaginal ultrasound
 - If hirsutism alone
 - 12 follicles in at least 1 ovary



Hirsutism scale



Sites recommended - 9

Face- upper lip
chin

Body- chest
arms
upper back
lower back
upper abdomen
lower abdomen
thighs

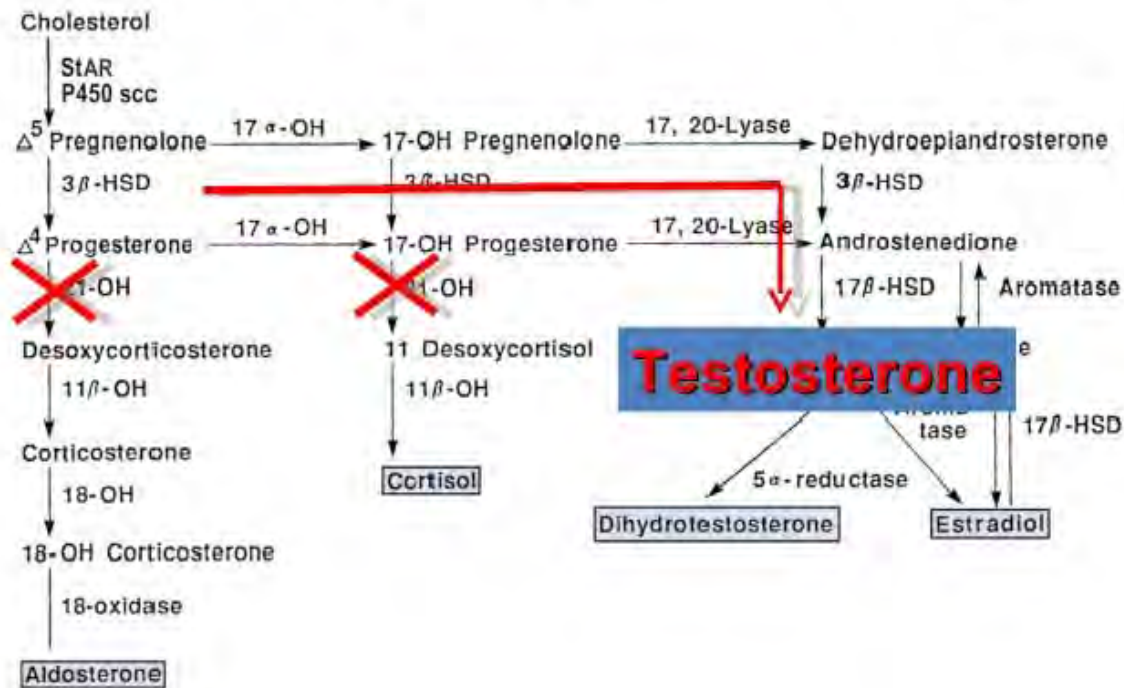
Score for density of terminal hairs each site (0-4)
Hirsutism >8

Diagnosis - Labs

- Normal cycles: Only serum total testosterone
- Oligomenorrhea: Serum androgens
 - Total testosterone (> 60 ng/dL)
 - 17 hydroxyprogesterone at 8 am in early follicular phase to r/o 21 hydroxylase deficiency (NCCAH) preferred or random draw if infrequent menses (> 200 ng/dL)
 - FSH, TSH, PRL, hCG

NCCAH

21-Hydroxylase deficiency



Screening Labs for Comorbidities

- Fasting lipid panel
- 2 hour gtt when possible
- If gtt not possible:
 - Fasting glucose
 - A1c

Labs not to order

- Free testosterone (not accurate)
- DHEAS unless testosterone > 150 ng/dL
- LH (LH/FSH ratio was an old idea)
- Insulin resistance

COMPLICATIONS

Complications – Metabolic syndrome

PCOS

- Irregular menses
- Hirsutism
- Acne

- HTN
- Dyslipidemia
- Risk of T2DM
- Obesity
- Insulin resistance

Metabolic syndrome

- HTN
- Dyslipidemia
- Risk of T2DM
- Obesity
- Insulin resistance

43% with PCOS have metabolic syndrome

Metabolic syndrome risk assessment

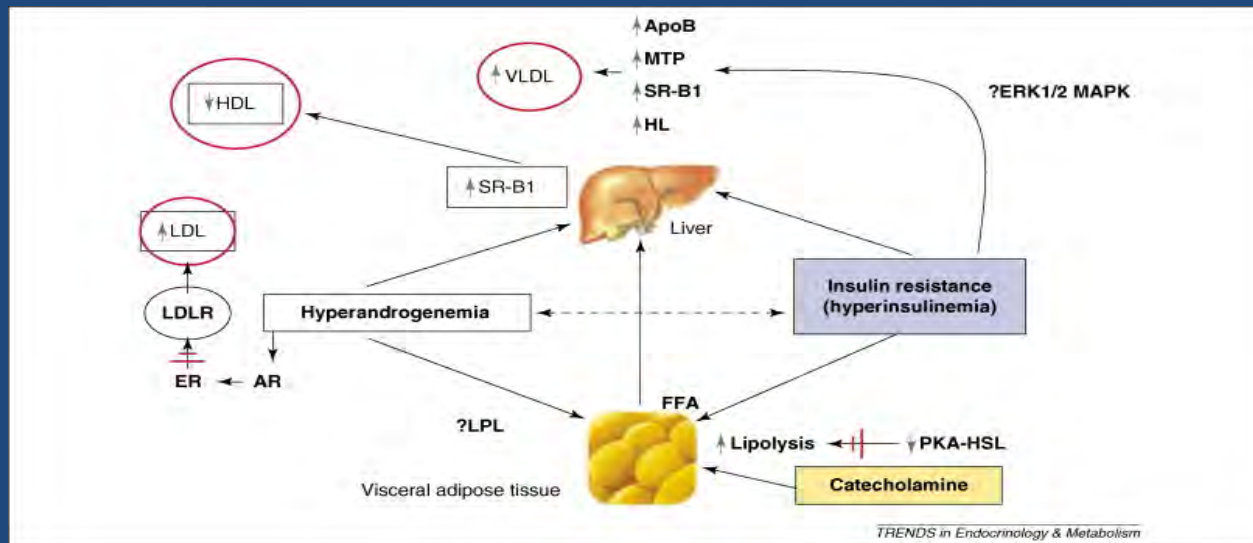
- Blood pressure
- BMI
- fasting lipid profile
- 2 hour gtt
 - Normal, repeat every 2 years
 - Impaired, repeat every 1 year

Complications - CHD

- PCOS is not a well established independent risk factor
- Impact on obesity, insulin resistance, type II diabetes, and dyslipidemia predispose to heart disease.

Complications -Dyslipidemia

- Low HDL < 35 (30%)
 - High LDL > 130 (15%)
 - High TG > 200 (15%)
-
- Again independent of weight



Complications

Non alcoholic fatty liver disease

- Severe liver inflammation cause by fat accumulation in the liver
- Routine screening not suggested
 - Uncertainty of which test to use
 - Uncertainty of how to treat it
 - Uncertainty of cost effectiveness to screen

Complications – sleep apnea

- Snoring, daytime fatigue, AM headache
- Present even when controlling for BMI
- Important determinant of insulin resistance, glucose intolerance and type II diabetes in PCOS pts

Complications - Eating disorders, Depression, Anxiety

- Matched BMI still have an increased risk
- Screen with PHQ-9 and GAD-7

Complications - Obstetric

- Increased risk of miscarriage (unclear etiol)
- Increased risk of:
 - premature birth
 - macrosomia
 - cesarean birth
 - GDM (independent of BMI)
 - Gestational HTN
 - pre-eclampsia

Complications - Gynecologic

- Infertility due to anovulation
 - Can measure serum progesterone day 21
 - If not cycling, can draw progesterone 7 -10 days before menses
 - Can use US to determine ovulation
- Endometrial hyperplasia or cancer
 - Excessive estrogen
 - Inadequate progesterone
 - 1.3/10,000 per year < 50 yo
 - No consensus but oligomenorrhea EMS 7mm ok

Treatment

Treatment Goals for PCOS

- Improve hyperandrogenic symptoms
- Reduce risk factors for type II DM and heart disease
- Prevent endometrial hyperplasia and cancer
- Provide contraception
- Ovulation induction

Treatment

- Education
- Focus first on diet and exercise
- Calorie awareness, 5 – 10% loss
- Avoid advanced glycated end products (AGEs). They are pro-inflammatory and pro-atherogenic

Treatment

- Estrogen/Progesterone birth control pill
 - Improves menstrual irregularity
 - Provides contraception
 - Decreases available androgen
 - Protects the endometrium
- Ideal: 20 mcg Est and low androgen progesterone like Norgestimate (or Desogestrel or Drospirinone)

Treatment

- Androgen excess
 - If suboptimal cosmetic response after 6 months on OCP, add anti-androgen like Spironolactone 50 – 100mg twice a day
 - GNRH (too costly and complex)
 - Wax, electrolysis, laser
 - Vaniqua 13.9% topical cream

Treatment

- Endometrial protection
 - OCP, cyclic or continuous progesterone or IUD
 - Metformin is second line because it can restore menstrual cyclicity as it restores ovulatory menses in 30 – 50% with PCOS

Treatment

- Infertility
 - Ovulation induction with Clomid or Letrozole (both reduce estrogen neg feedback)
 - Metformin only if glucose intolerant
 - Surgery (wedge resection or drilling) rare



Treatment

- Non alcoholic steatohepatitis
 - Weight loss and Metformin
- Sleep apnea
 - CPAP improved insulin sensitivity and reduced diastolic blood pressure

Future

- Urine presence of proteins related to PCOS may allow for earlier diagnosis
- More utilization of AMH knowledge
- Cetrorelix (IVF drug) to reverse induced symptoms of PCOS and help with fertility, used to stimulate the development of multiple eggs

Thank you for your invitation
and attention!