

PCOS: A “Bear” of a Problem

**Satellite Conference and Live Webcast
Friday, November 15, 2013
9:00 – 11:00 a.m. Central Time**

**Produced by the Alabama Department of Public Health
Video Communications and Distance Learning Division**

Faculty

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Objectives

- **At the conclusion of this presentation the learner should be able to:**
 - **Define PCOS and Metabolic Syndrome**
 - **Identify the risk factors and implications associated with diagnosis of PCOS and Metabolic Syndrome**

Objectives

- **Explain and review the clinical significance of PCOS and Metabolic Syndrome**
- **Describe the management of PCOS and Metabolic Syndrome and relate to PHD protocol guidelines**



Definition of PCOS

- **Polycystic ovarian syndrome is a clinical syndrome characterized by obesity, irregular menses or amenorrhea, and signs of androgen excess like hirsutism and acne**
- **In most patients, the ovaries contain multiple cysts**

Rotterdam 2010 Definition PCOS

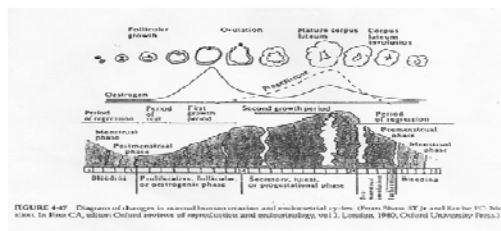
- **Oligo – ovulation / anovulation**
 - Menstrual irregularity
- **Hyperandrogenism**
 - Clinical or biochemical
- **Polycystic ovaries**
 - Greater than 10 – 12 follicles per ovary detected by pelvic ultrasonography, resembling “string of pearls”



PCOS

- **The most common cause of infertility in the United States**

Change in Cycles



PCOS – A Bear Of A Problem

- **Anovulation or ovulatory dysfunction**
 - Causing oligomenorrhea or amenorrhea
- **Androgen excess increasing risk of metabolic syndrome and causing hirsutism**

PCOS – A Bear Of A Problem

- **Hyperinsulinemia due to insulin resistance and may contribute to increased ovarian production of androgens**
 - **Becomes vicious cycle**
- **Over time, androgen excess increases risk of cardiovascular disorders, such as HTN**



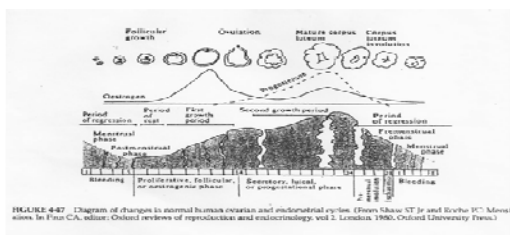
Menstrual Changes In PCOS

- **With anovulation:**
 - **Chronic follicular phase occurs secondary to constant estrogen stimulation**
 - **Endometrial proliferation or build up and vascularization of the endometrium results**

Menstrual Changes In PCOS

- **Thickened endometrium may become unstable and fragile eventually rupturing thus causing irregular and prolonged bleeding in anovulatory women**

Change in Cycles



Endometrial Hyperplasia and Cancer

- **Endometrial cancer arises from the inner layer (endometrium) of the uterus**
- **The endometrium gets thick in response to estrogen stimulation**

Endometrial Hyperplasia and Cancer

- **Chronic lack of progesterone causes unregulated growth of the endometrium or hyperplasia**
 - **A precursor to endometrial cancer**

Types of Endometrial Hyperplasia

- **Simple hyperplasia**
- **Complex hyperplasia**
- **Simple atypical hyperplasia**
- **Complex atypical hyperplasia**

Endometrial Hyperplasia

- **Simple hyperplasia**
 - **Thickening of the endometrium and increase number glands**
 - **No atypia and treated with progesterone supplementation**
 - **Less than 1% chance progression to cancer**

Endometrial Hyperplasia

- **Complex hyperplasia without atypia**
 - **Thicker than simple hyperplasia and demonstrates some abnormal architecture of the glands**
 - **Without treatment approximately 10% can progress to endometrial cancer**

Endometrial Hyperplasia

- **Treated usually with progesterone or if patient has completed childbearing may opt for hysterectomy**

Endometrial Hyperplasia

- **Complex hyperplasia with atypia**
 - **Similar abnormalities as complex hyperplasia without atypia, but the cells have bizarre appearance and can progress to endometrial cancer**

Endometrial Hyperplasia

– Increased risk of invasive endometrial cancer and is imperative the patient receive surgical staging by gynecologic oncologist

Endometrial Cancer

- Most common gynecologic malignancy in the United States
 - Estimated 41,000 women diagnosed this year with the disease
- Overall survival rate is excellent if disease confined to the uterus

Risk Factors: Endometrial Cancer

- Obesity
- Chronic anovulation
- Early menarche or late menopause
- Hypertension
- Exogenous estrogen use
 - No progestin

Symptoms of Endometrial Cancer

- Irregular, unusual or heavy vaginal bleeding
- ANY amount of bleeding or spotting after menopause
- Pain with intercourse
- Pain with urination
- Lower abdominal or pelvic pain



PCOS Signs and Symptoms

- Premature adrenarche
 - Characterized by excess dehydroepiandrosterone sulfate (DHEAS)
 - Early growth of axillary hair, body odor, and microcomedonal acne

PCOS Signs and Symptoms

- Typical symptoms
 - Obesity
 - Hirsutism
 - Body hair growth on upper lip, chin, around nipples, and the linea alba of lower abdomen
 - Irregular menses or amenorrhea

PCOS Signs and Symptoms

- Acne
- Balding
- Acanthosis nigricans of axillae, neck, and skin folds, knuckles, elbows
 - Secondary to high insulin levels
 - Insulin resistance

Diagnosis of PCOS (Rotterdam 2010)

- Oligo – ovulation / anovulation causing menstrual irregularity
- Clinical or biochemical evidence of hyperandrogenism
- Presence of polycystic ovaries
 - 10-12 follicles noted on pelvic u / s

Diagnosis PCOS (Biochemical)

- Some physicians may want:
 - Serum testosterone
 - Serum free testosterone
 - Better but more difficult to measure
 - Total testosterone
 - Usually normal to mildly elevated

Diagnosis PCOS (Biochemical)

- Follicle - stimulating hormone (FSH)
 - Normal to mildly decreased

Best Lab Information

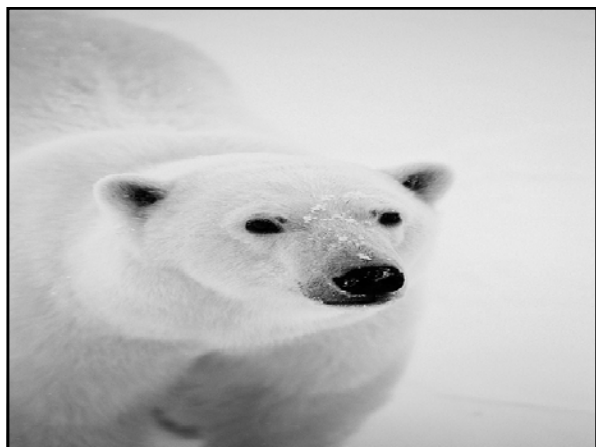
- Prolactin level
 - Greater than 20 ng / ml = hyperprolactinemia
- Thyroid-stimulating hormone (TSH)
 - Normal level = 0.5 – 4.5 mIU / L

To Rule Out Other – Some MDs May Want

- Evaluate serum cortisol levels to exclude Cushing's syndrome
- Early morning serum 17 - hydroxyprogesterone to evaluate congenital adrenal hyperplasia
- Serum DHEAS
 - If abnormal evaluate for amenorrhea

To Rule Out Other – Some MDs May Want

- Rule out Metabolic Syndrome
 - Evaluate BP and serum glucose levels and lipid profile



Definition of Metabolic Syndrome

- Metabolic syndrome is characterized by a group of risk factors for cardiovascular disease, dyslipidemia, and Type 2 Diabetes Mellitus
- Clinically patients may have:
 - Excess intra - abdominal fat
 - Waist size greater than or equal to 35" in women, 40" in men

Definition of Metabolic Syndrome

- Insulin resistance
 - Acne, hirsutism, androgenic alopecia, acanthosis nigricans
- Elevated serum triglyceride levels
 - Greater than or equal to 150 mg / dL
- Decreased HDL cholesterol level
 - Less than or equal to 50 mg / dL

Definition of Metabolic Syndrome

- HTN
 - 130 / 85 mmHg
- Elevated fasting glucose
 - Greater than or equal to 100 mg / dL

Metabolic Syndrome

- Insulin resistance has been reported in about 50 - 75% of the women with PCOS
 - Regardless of BMI
- The risk for insulin resistance is higher in women who have chronic anovulation, polycystic ovaries, hirsutism, and family history

Metabolic Syndrome

- Dyslipidemia with elevated LDL, elevated cholesterol, and decreased HDL, is usually associated with PCOS
 - Can be correlated with the level of insulin resistance



Clinical Significance

- Insulin resistance
 - The body is resistant to the effects of insulin resulting in hyperglycemic state
- Pancreas overcompensates by producing more insulin, causing the ovaries to produce more androgens
 - Hirsutism, acne, oligo-ovulation / anovulation

Clinical Significance

- Hyperglycemic state secondary to increased insulin production = Type 2 Diabetes Mellitus

Cardiovascular Disease Risk

- Low serum sex hormone - binding globulin (SHBG) found in most women with PCOS is linked to decreased levels of serum high-density lipoprotein cholesterol (HDL - C)
 - The most cardio protective lipid in the body

Cardiovascular Disease Risk

- **Decreased levels of HDL – C are associated with increased risk for cardiovascular disease**
- **Increased serum - free testosterone is associated with elevated systolic and diastolic blood pressure levels leading to hypertension**

Additional Factors

- **Elevated C - Reactive Protein (CRP) levels**
 - **Directly linked to coronary inflammation and other cardiovascular related risks are elevated in PCOS**
 - **Increases the risks of cardiovascular disease**

Dyslipidemia

- **Atherothrombotic cardiovascular disease is the leading cause of death in men and women and is the underlying reason for:**
 - **Angina**
 - **Unstable angina**
 - **Acute myocardial infarction**
 - **Sudden cardiac death**

Dyslipidemia

- **Ischemic stroke**
- **Risk factors include:**
 - **Elevated levels of atherogenic lipoproteins – LDL**
 - **Elevated triglycerides**
 - **Low levels of HDL**

Cardiovascular Disease

- **Accounts for approximately \$448 billion of direct and indirect health care costs annually**
- **More women die from cardiovascular disease than men**
 - **Framington Heart Study**

Cardiovascular Disease

- **More women die from cardiovascular disease than from cancer, stroke, chronic lung disease, Alzheimers disease, unintentional injuries, diabetes, and influenza pneumonia combined**

Total Cholesterol

- A large meta - analysis study has shown that a total cholesterol level greater than 240mg / dL confers almost a two and one - half increased risk for cardiovascular disease in women less than 65 years of age

Low - Density Lipoprotein Cholesterol

- Increasing levels of LDL - C are associated with increased risk of cardiovascular disease
 - Per the American Diabetes Association (ADA) and the National Cholesterol Education Program (NCEP) Third Adult Treatment Panel (ATP III)

Low - Density Lipoprotein Cholesterol

- LDL - pattern B phenotype often accompanies insulin resistance and other features of metabolic syndrome, and are implicated in cardiovascular disease

Additional Factors

- CVD is the primary clinical outcome of metabolic syndrome
 - American Heart Association
- Diabetes is the major risk factor for development of CVD (ATP III)
- Excess abdominal fat leads to increased free fatty acids in the portal vein, increasing fat accumulation in the liver

Additional Factors

- Fatty liver - cirrhosis
- Prothrombic state with increased levels of fibrinogen and plasminogen activator inhibitor - 1 and inflammatory process = increased risk for thrombosis

More Risk Factors

- Prolonged anovulatory cycles leads to endometrial hyperplasia and increased risk of uterine cancer
- Increased serum uric acid levels, resulting in chronic renal disease
- Lipoprotein (a) is an independent risk factor for coronary heart disease



Treatment Guidelines

- **Per ACOG recommendation:**
 - **Healthy diet and exercise**
 - **Weight loss**
 - **Use of Metformin**
 - **Decreases body’s resistance to insulin, decreases blood sugar and circulating androgens**

Treatment Guidelines

- **In combination with clomid to improve ovulation for those seeking pregnancy**
- **Management of cardiovascular risk factors**

Combined Hormonal Contraception

- **If not seeking pregnancy:**
 - **Combination low - dose hormonal contraceptives recommended by ACOG for management of menstrual disorders if not contraindicated by other health concerns**
 - **BMI greater than 34, smoking, migraines, HTN, etc.**

Progestin Contraceptives

- **If combined hormonal contraception is contraindicated, ACOG recommends**
 - **Progestin only contraceptives**
 - **Progestin containing intrauterine devices as an alternative for endometrial protection from uterine hyperplasia**

Progestin Contraceptives

- **No studies address the long term use of DepoProvera or oral Provera use**

Treatment Options – Public Health

- **Public Health – page 66 Clinic Protocol Manual under Family Planning Contraceptive Management of Patients with Risk Factors:**
 - **Phone consult REQUIRED to initiate and annual consult thereafter for combined method use**

Treatment Options – Public Health

- **Phone consult REQUIRED to initiate and annual consult thereafter to continue progestin only**

Health Department Protocol

- **Menstrual history compatible with suspected PCOS necessitates endometrial assessment and evaluation to rule out endometrial hyperplasia PRIOR to initiating hormonal methods**

Health Department Protocol

- **Metabolic Syndrome pre - disposes to cardiovascular disease, stroke, Type 2 Diabetes Mellitus**
 - **Therefore patient needs medical work - up and ongoing medical management**

Conclusion

- **PCOS and Metabolic Syndrome is a “bear of a problem”**
- **We see more patients who are overweight or obese with irregular menstrual cycles and hyperandrogenic characteristics**

Conclusion

- **Current health risks associated with PCOS and Metabolic Syndrome need assessment and treatment to prevent significant FUTURE health conditions**
 - **Important in Family Planning**

Take Home Message

- PCOS is significant because it is associated with:
 - Infertility
 - Uterine cancer
 - Insulin Resistance/Metabolic Syndrome/Diabetes
 - Dyslipidemia/Cardiovascular Disease

Going To Be A Bear

- In this life I am a woman
- In my next life I would like to come back as a bear
- When you are a bear, you get to hibernate
- You do nothing but sleep for six months
 - I could deal with that

Going To Be A Bear

- Before you hibernate, you are supposed to eat yourself stupid
 - I could deal with that
- When you are a girl bear, you birth your children (who are the size of walnuts) while you are sleeping and wake to partially grown cute, cuddly cubs
 - I could definitely deal with that

Going To Be A Bear

- If you are a mama bear, everyone knows you mean business
- You swat anyone who bothers your cubs
- If your cubs get out of line, you swat them too
 - I could deal with that

Going To Be A Bear

- If you are a bear, your mate EXPECTS you to wake up growling
- He EXPECTS that you will have hairy legs and excess body fat
 - Yup, going to be a bear!

