PCOS Update 2020:
Common, Confusing and
More Serious Than Ever

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Mimi Secor, DNP, FNP-BC, FAANP, FAAN

• FNP for 43 years specializing in Women’s Health
• National Speaker, Educator, Author, Entrepreneur, Athlete
• 2020 Outstanding Alumnae Award from RMU, Provo, Utah

• DNP-2015, Rocky Mountain University, Provo, Utah
  Also became healthy and fit
• 2016 First Bodybuilding Competition
• 2018 Fourth Competition, 2nd Place in over 55 !!!

• #1 International Best-Selling Author of NEW Book,
• “Debut a New You: Transforming Your Life at Any Age”

• Passion for Helping NPs/PAs become Healthy and Fit
Disclosure

Speaker:
• Abbott, Nutrition/ Ensure products

PCOS Objectives for Session
Upon completion of this session attendees will be able to:

• Discuss epidemiology, pathophysiology, associated risks and complications. 15 mins

• List symptoms, signs & explain diagnostic work-up. 15 mins

• Describe “best practice” management approaches including pharmacologic treatments. 15 mins
PCOS: Overview

- Most common reproductive endocrine disorder
- 5 + million women in US
- 1 in 15 women (6-10%)
- Familial tendency
- Obesity (independent risk factor)
- Lean: ~10% (less well understood)

- Associated with serious sequelae:
  - Diabetes, CVD, MS, Infertility, Cancer, Mental Health Problems, etc. (list is ever-expanding)

PCOS Definition

- Androgen Excess Disorder
  (biosynthesis, utilization, metabolism)

- In Ovaries, Adrenal Glands

- With or Without Insulin Resistance

- Complex Differential
PCOS: What’s New?

• Leading cause of Menstrual Abnormalities
• Exact cause Unknown (GnRH, FSH, genetic)
  - In-utero, Environmental, Diet, Lifestyle, Stress
• Insulin Resistance 50-70%
• Insulin stimulates ovarian Testosterone !!!
  - causing hyperandrogenism symptoms, acne, hirsutism, etc.
• Correlation with Inflammatory Markers
  - CRP, TNF-a, IL-6, IL-18


PCOS: Symptoms and Risks

• Oligomenorrhea: Highly predictive!
• Hyperandrogenism: Hirsutism, Acne
• Obesity: esp. Central Obesity (30-70%)
• Infertility: (73-74%)
• Abnormal Uterine Bleeding (AWB)
• Uterine Cancer- (3x incr. risk), Breast, Ovarian
• MetS (6x Incr. risk), Diabetes Type 2 (3-5x risk)
• CVD, Dyslipidemia (70%)
• Mental Health: Depression, Anxiety, Bipolar, Eating Disorders, etc.
PCOS: Menstrual Irregularities
Classic Clinical Profile!

Oligomenorrhea to amenorrhea
• History since menarche (CLASSIC)
• 6 or fewer “menses” per year
• BUT may have regular cycles

Stein Leventhal 1935- singular entity/OVARY
Case Study
30 year old for Annual Exam

• ORAL CONTRACEPTIVES in past, side effects
• 3, 4 menses year
• Irregular menses since
  Menarche age 12
• Married in 1 year
• Pregnancy NOT desired yet
• Both Parents w Diabetes and Overweight

NEW PCOS:
Pathogenesis & Assoc. Risks

• Insulin Resistance (IR) and
  Hyperinsulinemia

• IR induces ovarian androgen production;
  Raising LH, incr. menstrual abnormalities
• Hyperandrogenism increases IR! (CYCLE)

• IR plays critical role in pathogenesis of
  Hyperandrogenism, Chronic Anovulation
  And Cardiometabolic risks!!!
NEW 2017: Abnormal Steroidogenesis

- Incr. Androgens and Estradiol leads to:
- malfunctioning of Hypothalamic-pituitary-ovarian axis (HPO)
- manifested by incr. LH, Anti-Mullerian Hormone (AMH),
- and higher frequency GnRH pulses; thickening ovary, incr T, lower FSH

PCOS: Complex Pathophysiology
Normal Cycle versus PCOS
Pathophysiology of PCOS: Ovary
Hyperinsulinemia, Hyperandrogenism

- Causes the Pituitary to hyper secrete LH (not All)
  TONIC levels of LH, FSH, Estrogen, Testosterone
- Estrogen/estrone, testosterone slightly elevated
- Estrogen/estrone blocks pituitary FSH, LH

- New follicles continuously stimulated,
  but don’t fully mature = RARE ovulation
- LH and Testosterone -thickens ovarian tissue (theca)
- Insulin suppresses apoptosis: programmed cell death
- Hence PCOS develops, vicious cycle!!!!

Secor 2020 copyright
NEW 2017: CANCERS !!

- Chronic Hyperandrogenism
  - Incr. aromatization of Androgens to E2 (in Adipose Tissue)

- Anovulation also incr. risk of Endometrial Cancer: Hyperplasia --> Atypia --> Cancer

- INCREASING RISK of Endometrial, Breast, and Ovarian Cancer

Pathophysiology of PCOS: Hirsutism

- Hyperinsulinemia (50-70% of PCOS pts)
- Lowers SHBG = Sex Hormone Binding Globulin
  Resulting in…
- Higher Androgen production (Free T)
- Increases Alpha-reductase in skin cells
- Testosterone to Dihydrotestosterone = potent T
- Causing Acne, Hirsutism, etc.
NEW 2018: SHBG Biomarker for Predicting PCOS Risk

- **Systematic Review**: 675 studies, n 62
- **Lower SHBG, (incr.T)** incr. risk of PCOS
- Plays role in S/S of PCOS
- Incr. SHBG may reduce Complications
  - CHCs (Birth Control Pills) increase SHBG

- Ritu Deswal, Arun Yadav & Amita Suneja Dang (2018) Sex hormone binding globulin - an important biomarker for predicting PCOS risk: A systematic review and meta-analysis, Systems Biology in Reproductive Medicine, 64:1, 12-24, DOI: 10.1080/19396368.2017.1410591

PCOS and the “Gut” 2018: NEW Research!

- Androgens- affect Gut Microbiome
- > T = Less diverse GI microbiota !!!
- These changes may influence how the pathophysiology of PCOS develops!
- More research needed to determine effects of androgens on the gut microbiome

- Total N=163, PCOS N=73
PCOS Case Study
30 year old for Annual Exam

- OC in past, side effects
- 3, 4 menses year
- Irregular menses since
- Menarche age 12
- Married in 1 year
- Pregnancy NOT desired yet
- Both Parents w Diabetes

Diagnostic Workup/Labs?
PCOS Diagnostic Criteria: Varies by Organization

1. Oligomenorrhea or anovulation
2. Hyperandrogenism: Acne, hirsutism, central obesity
3. Ultrasound: Polycystic Ovaries
   • NEW: Rule out other conditions (Mimics)

Diagnostic Criteria by Organization:
• Rotterdam Criteria: 2 of 3 criteria (preferred)
• Androgen Excess Society: Hyperandrogenism PLUS 2 more criteria
• NIH: PCO morphology not included

Rotterdam consensus group. Revised 2004 consensus criteria. Fertil Steril 2004 Jan;81:19-25. 2 of 3 criteria plus Rule Out other conditions

PCOS Ovary
Classic “string of pearls”
PCOS: Initial Ultrasound

- Detected **PCOS in 83% of ADULT** pts
- **40%** of post-pubertal
- **3%** of pre/peri-pubertal girls with “Late-Onset Congenital Adrenal Hyperplasia (CAH)”
- **CAUTION**: Overdiagnosing PCOS in young teens !!!


Diagnosis of PCOS

- **Clinical presentation is sufficient!**
  - **If NO** virilizing symptoms **BUT**
- **Rule out associated conditions!** **AND**
- **Variable presentation is common**
- **Rapid Hirsutism Onset: Full Work-up!**

What Labs? PCOS Diagnostic Work-up and Differential: **Individualize**

- Body weight, BMI (>30), Waist (>35 inches),
- BP……………………………..>
- HCG…………………………...>
- CBC (at risk for anemia, or iron overload)
- TSH (abnormalities worsen PCOS or mimic it)………>•
- Lipids (Low HDL, High trigs/LDL)……………....>
- FBS, Random glucose, Hgb-A1c: DM= >6.4, At risk = >5.6-6.4 ….>•
- Oral GTT (most sensitive/specific-Preferred)

- Rule out Obesity
- Rule out Hypertension
- Rule out Pregnancy
- Rule out Anemia/ Iron overload
- Rule out Hypothyroidism
- Rule out Abn. Lipids
- Rule out Glucose Abn.
- Rule out Diabetes

PCOS Diagnostic Work-up and Differential: **Individualize**

- Total Testosterone: -PCOS = > 60, Tumor > 150-200
- Free T: PCOS= 2- 3%
- Prolactin 3-27ng/ml: ...................>
  -If headache, vision changes, galactorrhea
  -May be abnormal in PCOS
- LH/FSH Ratio >3, .......................>
  BUT may normal in PCOS
- 17-hydroxyprogesterone ...........>
  (am, early follicular)
  <200 ng/dl rules out NCAH = Non-classical adrenal hyperplasia (in teens)
- **Ultrasound:** OPTIONAL .....................>
  - Rule out a Virulizing Tumor
  - Rule out Prolactinoma
  - Non-specific, expensive
  - Rule out Non-classical Adrenal Hyperplasia (NCAH)
  - PCOS (Diagnostic criteria)
PCOS: Diagnosis of Exclusion

- Thyroid disease (TSH)
- Hyperprolactinaemia (Prolactin)
- Non-classic Congenital Adrenal Hyperplasia (CAH) --> REFER
- Cushings --> REFER


PCOS: NEW 2017

Thyroid Disorders More Common

- Primary Hypothyroidism associated with:
- Increase risk of Ovarian Cysts:
  - Resolve with treatment
- Decreased SHBG*
  *Sex Hormone Binding Globulin
- Increased Free Testosterone

NEW - PCOS: **Prolactin (3-27ng/ml)**

- 20% with PCOS have elevated Prolactin levels!
  - suggests abnormal ovarian response
  - to altered gonadotrophin signaling
- Adrenals have prolactin receptors
- Prolactin excess may be integral to PCOS !!!

- **If Hyperprolactinaemia:**
  - Associated Hirsutism 56% (higher T levels)
  - Associated PCOS 50-67%


**NEW 2017: OBESITY and PCOS**

Risk of **ANEMIA** or OVERLOAD

**ANEMIA:** Proinflammatory cytokines can increase **Hepcidin** inhibiting absorption of iron from enterocytes

**OR**

**IRON OVERLOAD:**
- In Obese with PCOS
- Measured by Ferritin, Iron, Hepcidin
- Risk for Insulin Resistance, DM, CVD
PCOS **Exclude**: Late Onset, Non-classic (CAH)
Congenital Adrenal Hyperplasia

- Mild enzymatic defect - form
- ** Presents in adolescence or later** (late-onset CAH)
- Prevalence 1-10%
- Most common cause in Caucasians (1:500-1000)
- Hyperandrogenism (acne, hirsutism)
- **More regular menses/ovulation C/o to PCOS**
- **Diagnosis:** REFER
- Early follicular 17-hydroxyprogesterone (17 OH-PG)
- If borderline 17 OH-PG:
  - Check ACTH-stimulation test

PCOS Differential: Cushings?

- **Cushing's Disease** (Pituitary)
- **Cushing's Syndrome** (Adrenal)
- **Symptoms/Signs:** Slow-insidious onset similar to PCOS
  - Central adiposity or obesity in general, hirsutism, absent menses, acne, male pattern hair loss.
  - Hypertension, hyperglycemia, dyslipidemia
  - **Differences**: Wide purple striae, easy bruisability, posterior cervical fat pad (buffalo hump), red round/puffy face, muscle wasting of extremities
- **Labs:** May Order or REFER (based on your expertise)
  1. Overnight Dexamethasone (1 mg) Suppression test
  2. Late night Salivary Cortisol
  3. (24 hour urine) for free cortisol and creatinine
NEW 2017: CANCER REMINDER SLIDE

• Chronic Hyperandrogenism
  - Incret aromatization of Androgens to E2 (in Adipose Tissue)

• Anovulation also incr. risk of Endometrial Cancer: Hyperplasia --> Atypia --> Cancer

• INCREASING RISK of Endometrial, Breast, and Ovarian Cancer

Abnormal Uterine Bleeding (AUB)
PCOS & Uterine Cancer = Incr Risk

• Anovulation related !!!
• Comprehensive, focused history
• Many causes: PALM-COEIN classification
• Consider DIFFERENTIAL by AGE and HISTORY

• Post-menopause AUB:
  - Any bleeding beyond 12 months since LMP
  - Even “1 drop of blood” is concerning
  - Must REFER to OBGYN to R/o Cancer 9% risk!
Abnormal Uterine Bleeding (AUB)
Classification/Differential: PALM-COEIN

<table>
<thead>
<tr>
<th>DIAGNOSIS:</th>
<th>CAUSE:</th>
<th>Consider by AGE:</th>
</tr>
</thead>
<tbody>
<tr>
<td>P</td>
<td>Polyps:</td>
<td>&gt; 30 years</td>
</tr>
<tr>
<td>A</td>
<td>Adenomyosis:</td>
<td>&gt; 30</td>
</tr>
<tr>
<td>L</td>
<td>Leiomyoma/ Fibroids:</td>
<td>&gt; 30</td>
</tr>
<tr>
<td>M</td>
<td>Malignancy/Hyperplasia:</td>
<td>&gt; 40 (Obesity, DM, PCOS, &gt;50 yr)</td>
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Non Structural

| C          | Coagulopathy:        | Any age          |
| O          | Ovulatory Dysfunction:| Any age          |
| E          | Endometrial Disorders:| Any age          |
| I          | Iatrogenic, Medications:| Any age          |
| N          | Not Classified       |                  |

EMB: When to Perform?

NOT Based on Age

- Duration of exposure to unopposed estrogen?
- If long standing anovulation then…
  Risk of Hyperplasia, Atypia, Cancer!!!
- **PCOS: HIGH RISK due to Anovulation**

When in doubt:

- Transvaginal US & endometrial biopsy!
  - “Low threshold” regardless of age
  - Do NOT trust JUST an ultrasound
# Ovulatory vs Anovulatory Bleeding: 

**KEY**

<table>
<thead>
<tr>
<th>Ovulatory</th>
<th>Anovulatory</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Premenstrual symptoms</td>
<td>• No premenstrual symptoms</td>
</tr>
<tr>
<td>• Pattern for each patient</td>
<td>• No pattern</td>
</tr>
<tr>
<td>• Bleeding pattern</td>
<td>• Each bleeding event differs</td>
</tr>
<tr>
<td>• From episode to episode</td>
<td></td>
</tr>
</tbody>
</table>
Ultrasound: NOT BASED ON AGE
Reproductive Age: Endometrial Stripe >10 mm
Menopause: Endom. stripe ≥ 5 mm = abnormal
Endometrial Biopsy needed

Abnormal Uterine Bleeding:

• Amenorrhea (>6 months)
  – Progestin challenge
  – Medroxyprogesterone acetate 10 mg orally x 10-12 days
  – Withdrawal bleed, then OK
  – No withdrawal bleed
  – Give Combination OC (COC) x 1 month, if bleed, OK
  – If no bleed, REFER to Endocrinologist (reproductive)
Case Study
30 year old for Annual Exam

- OC in past, side effects
- 3, 4 menses year
- Irregular menses since
- Menarche age 12
- Married in 1 year
- Pregnancy NOT desired
- Both Parents w Diabetes

Work-up/ Labs:
- BMI 32
- Waist 38 inches
- COC withdrawal bleed
- HDL 35 mg/dl
- LDL 130
- Triglycerides 210 mg/dl
- Fasting glucose 102 mg/dl

Management plan:
- More labs/tests?
- Metformin?
- Contraceptive?
- Pregnancy?
- Folic acid 400 mcg!
PCOS Management: Symptom Relief, Prevention of Complications

• Menstrual disturbances
• Hyperandrogenic symptoms
• Obesity management
• Infertility management
• Mental health
• Prevention of complications

Team Approach to PCOS and Individualized Management

• Primary care
• ObGyn
• Infertility
• Cardiovascular
• Diabetes/Endocrine
• Mental health
• Nutritionist
• Wellness coach?

• Contraception vs Conception?
• Revisit regularly

• Fast track fertility!!!
PCOS: Prevention is KEY

- Exclude other conditions
- Symptom relief
- Lifestyle changes
- Medical management
- Obesity control
- Nutritional plan
- Mental health
- Prevention of complications

PCOS and Pregnancy Risks: Ticking Time Bomb **

- Infertility: 40% female/PCOS
- Spontaneous Abortion /SAB, (25-73%)
- Gestational Diabetes (3 x increased risk)
- Preeclampsia/Hypertension

** (esp. with associated Obesity)
Before PCOS Management: Contraception or Conception?

• Discuss plans for future pregnancy

• **DO NOT** wait until age 35 for 1st baby!
NOT Desiring Pregnancy: 
PCOS Treatment Approaches

• **Life Style Changes:** Weight loss, Diet, Exercise!
  50% reduction in IR (WOW!)

• **Combination Hormonal Contraceptives (CHC)**
  NEW; Low-androgen safer progestins;
  Levonorgestrel (LNG), Norethindrone (NE),
  Norgestimate (NGM)
  (http://dx.doi.org/10.1136/bmj.h2135)

• **Insulin sensitizers:** Metformin (XR, low/slow
  30% reduction in IR

• **Combination therapy:** Metformin and CHC?

Weight Loss: KEY

• **5% loss:** improves insulin sensitivity!
• Reduces Testosterone levels
• Improving Acne, Hirsutism, etc.

• Lowers BP, improves labs
• Enhances fertility!

• Return of regular menses (withdrawal bleed)
• Reduces Uterine Cancer risk!
Weight Loss

• Bariatric surgery
• Metformin combination therapy with incretin agents/GLP-1 (liraglutide, exenatide, etc.)
  – Promotes weight loss, lowers insulin resistance, improves reproductive function
  – Unclear safety for women of reproductive age

PCOS and Nutrition: Systematic Review 2013

• Low-carb, low-glycemic index diet = Greater reductions in insulin resistance, fibrinogen, total, and high-density lipoprotein cholesterol
• Low-glycemic index diet = Impr. quality of life
• High-protein diet = Improved depression and self esteem.

Dietary composition in the treatment of polycystic ovary syndrome: a systematic review to inform evidence-based guidelines.
NOT Desiring Pregnancy: Combination Therapy for PCOS

- **Contraceptives**: First line
  - Combination hormonal contraceptives (CHC)
  - Progestin only: Caution w DMPA (insulin resistance?)
  - Intrauterine Contraceptives (IUC)

**Plus:**

- **Insulin Sensitizers**:
  - Metformin XR 500-2250 mg oral daily @ hs (start low, go slow)

NOT Desiring Pregnancy: Combination Hormonal Methods

- For Oligomenorrhea, Acne & Hirsutism
- Induces Withdrawal Bleed (pt thinks is menses)
- Prevents Uterine Cancer
- Suppresses T, (ovarian androgen production)
- Improved BMI, Glucose Tolerance & Basal Insulin
- **NEW:** Possible increased risk of CV events
  - Lower E2, safer progestins: LNG, NE, NGM*
  
  *LNG= Levonorgestrel, NE= Norethindrone, NGM= Norgestimate

  ([http://dx.doi.org/10.1136/bmj.h2135](http://dx.doi.org/10.1136/bmj.h2135)).

- If BMI >30, VTE risk increased by x 3.5 fold !!!

Progestin Only Methods and PCOS

- **Medroxyprogesterone Acetate (MPA):**
  - An option esp. if estrogen is contraindicated
  - May be associated with weight gain
  - Possible impact of high-dose progestin on IR?

- **Levonorgestrel IUC:**
  - Local endometrial effects- so probably OK
  - Minimal systemic levels

- **Etonogestrel Implant:**
  - Low systemic levels, so probably OK
NEW 2017: Metformin Effects

- Restores Ovulatory Cycles and Menses
- Improves Insulin Resistance, BP, Lipids
- Raises SHBG: improves Hyperandrogenism
- Protects vascular endothelium (Pleiotropic effect*)
- Reduces cancer risks: (dose-dependent)
  Endometrial, Breast, Colon, Hepatic, Ovarian
- Redistribution of Visceral Fat to Subcutan. Fat
  *vascular dilation, suppression of inflam, <CRP

PCOS: Metformin vs CHC*? 2016

- NEW 2016: Systematic review and meta-analysis
- 172 studies, 4 studies w 231 participants met criteria
- Based on very-low to low quality data

Findings:
- OC: Superior for regulation of Menses, and Acne
- Metformin: greater reduction in BMI, decreased dysglycemia, lower LDL
- Neither superior for Hirsutism, lowering TG, or incr HDL

- CHC = combination hormonal contraceptive
  Al Khalifah, et al. PCOS, Teens. Pediatrics 2016 May; 137:e20154089
Hirsutism and PCOS: REFER if Severe or Persistent

- Combined hormonal contraceptives (CHC)
- Insulin sensitizers!
- **Spironolactone**: (Cat C): 25-100 mg orally bid ($)
  - Inhibits 5α-reductase, preventing T to DHT*
  - Incr. SHBG, decreasing free T
- **Finasteride**: (Cat D), 1mg oral daily (same as above)
- **Eflornithine HCL**: (Cat C): topically ($$$)
- Various hair removal techniques

* DHT = Dihydrotestosterone (potent form of testosterone)
NEW 2019: Vitamin D, PCOS, +/-Obesity Systematic Review, n=1558

- Vitamin D Supplementation
- especially for Autumn and Winter symptoms
- Reduces Insulin Resistance in PCOS
- and Improves Mental Health !!!!


- Association between Vit D Receptor AND VDR Fok1 polymorphisms & PCOS risk

Vitamin D: NEW 2018 Cardiometabolic Benefits

- Study supports:
- 50,000 IU vitamin D supplementation every other week for 8 weeks
- Beneficial effects on insulin and lipid metabolism
- Infertile women with PCOS who are candidate for IVF (n = 40)

The effects of vitamin D supplementation on metabolic profiles and gene expression of insulin and lipid metabolism in infertile polycystic ovary syndrome candidates for in vitro fertilization.
Dastorani M1, Aghadavod E2, Mirhosseini N1, Foroozanfard F3, Zadeh Modarres S1, Amiri Siavashani M4, Asemi Z5.
PCOS: Menopause (NAMs)

- **Systemic Estrogen** for Hot Flashes: Within 10 y of FMP
  
  **Caution**: Subclinical Cardiovascular Disease

- **Estrogen Transdermal** (Evamist): SAFER than Oral

- **Progesterone Oral** (Prometrium) 100mg at hs
  
  sleep, hot flashes, fewer side effects than MPA*, may be safer than synthetic progestins (Breast ca risk)

- **Estradiol, Progesterone combo Oral** (NEW Bijuva)

- **Vaginal symptoms:**
  
  - **Estrogen Vaginal**: cream, tablets, ring (Estring), inserts (Imvexxy)
    
    • **NEW**: NO NEED TO PROTECT UTERUS WITH PROGESTOGEN OR IUC !!!
  
  - **SERM Oral Ospemifene** (Osphena), **Prasterone DHEA** (Intrarosa) PV
    
    • Laser (Mona Lisa Touch) (NEW FDA Warning, AVOID Laser procedures)
  
  - **Pelvic PT** (APTA.org)
    
    • if superficial or deep dyspareunia doesn’t resolve w meds above

PCOS: Prevention is KEY

- Exclude other conditions
- Symptom relief
- Lifestyle changes
- Medical management
- Obesity control
- Nutritional plan
- Mental health
- Prevention of complications
PCOS Summary
Upon completion of this session attendees will be able to:

• Discuss epidemiology, pathophysiology, associated risks and complications. 20 mins

• List symptoms, signs & explain diagnostic work-up. 20 mins

• Describe “best practice” management approaches including pharmacologic treatments. 20 mins

Addendum Slides
Thank you

Thanks to Carol Lesser NP, Boston IVF
Patty Duprey NP, Tom Bartol NP

R. Mimi Secor, DNP, FNP-BC,
FAANP, FAAN

My App: text “DrMimi” to 36260

Resources

- www.PCOSsupport.org
- www.Soulcysters.org
- www.pcosstrategies.org

Patient Education:
- WWW.nih.gov
- www.acog.org

Weight Loss Ap:
- MyFitnessPal
References


References


References

• Mcluskie, I. PCOS. BMJ 2017; 357: doi: https://doi.org/10.1136/bmj.i6456
• Moran, LJ, Hutchison, SK, Norman, RJ. Lifestyle changes in women with polycystic ovary syndrome. Cochrane Database Syst Rev 2011; (7): CD007506.
• Pasquali, R. Contemporary approaches to the management of PCOS. Therap Adv Endo/Metab 2018;9(4):123-134. https://doi.org/10.1177/2042018818756790

Addendum Slides
Rotterdam Criteria 2004
2 of 3 required

- Oligomenorrhea (esp. >3 months) or anovulation
- Hyperandrogenism:
  - Acne, hirsutism, central obesity

- NEW - Ultrasound: Polycystic Ovaries
  - 12 follicles 2-9 mm
  - or increased volume >10ml in >1 ovary
  - 25% of NORMAL women have ovarian cysts!

Rotterdam consensus group. Revised 2004 consensus criteria.

Diagnosis of Metabolic Syndrome
Requires 3 Criteria

- B/P >130/85
- Abdominal obesity: >35 inches (women), >40 inches (men)
- Triglycerides >150 mg/dl
- HDL Cholesterol: < 50 mg/dl (women), < 40 (Men)
- Fasting Glucose > 100 mg/dL
- 2 hr GTT (75 gm load) 140-199 mg/dl
Glucose Testing
OGTT for ALL abnormal values

• Random elevations suggest a trend
• Fasting & Oral GTT required

• Fast 8 hours: 65-99 mg/dl = normal
  • 100-125 = Impaired fasting glucose
    • > 95 suspicious
  • > 126, suspect DM, retest different day
  • >140 mg/dl x 2 = Probable diabetes

Hgb A1C Guidelines per ADA for Diabetes Diagnosis:

• Predictive screening tool!

• 5.7-6.4 = “At risk”
• ≥ 6.5 = Diabetes

Oral Glucose Tolerance Test (OGTT) Preferred for PCOS (ACOG)

- 2-hour Oral Glucose Tolerance Test (75 gm load)
  - $\geq 140$, $< 200$ mg/dl = Impaired Glucose Tolerance
  - $> 200$ mg/dl = Non-insulin-dependent DM

- GTT abnormal: 2-8 years before DM develops!
  - Better than FBS

Treatment Options: Metformin

- Biguanide 4+ decades worldwide
- Not FDA approved for PCOS
- BUT widely used for PCOS, and well studied
- Side effects & toxicity well studied
- Must check liver, renal function before use
- Insulin sensitizing effect
- Menses induction: 90% in 6 months
- Increases ovulation esp. w/ clomiphene/ letrozole
  - 75% w Combo Rx
- NOT- Teratogenic: Cat B in pregnancy & lactation
**Metformin XR: Preferred**

- Less side effects
- Improved lipid profile: Triglycerides, HDL, LDL
- Weight loss especially with higher doses!

**Easy dosing at HS/ bedtime**
- Start low, go slow…
- Start 500 mg orally at HS
- Increase 500 mg weekly
- 2000-2250 mg daily maximum dose

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**Hirsutism and PCOS: Cont’d**

- **Eflornithine** HCL (Vaniqa) topical cream: $$$
  - “Hair growth retardant”
  - Cat C
  - Apply thin film BID, rub in thoroughly
  - Do NOT wash area for 4 hours

- **Finasteride** (Propecia, Proscar): Effective, Off-label
  - Anti-androgenic, inhibits 5a-reductase, T to DHT
  - Cat D
  - Side effects: Depression, anxiety
  - 1 mg oral daily: Reduces side effects (2.5-5 mg daily)
Infertility and PCOS
Ovulation Doesn’t Equal Pregnancy!

• Easy to stimulate ovulation with various meds

• Referral to Reproductive Endocrinology is KEY
  Early esp. with PCOS
  And if “Older”
  30-35 and esp. if >40 years old

Clomiphene versus Letrozole for Subfertile w/ PCOS: 2017

• N = 159
• Participants receiving Letrozole as a primary treatment
  - achieved a significantly higher (P = 0.022) clinical pregnancy rate (61.2%)
  - compared to Clomiphene (43.0%).

• Live Birth Rates were NOT statistically different