

Saturday, April 18<sup>th</sup>, 2015

PCOS Awareness Symposium 2015  
Philadelphia

# Polycystic Ovary Syndrome: Creating a Treatment Plan

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# The Canary in the Coalmine

- PCOS seems to accelerate the aging process
- It is possible to reverse the aging process
- Be scrupulous in your commitment to be healthy

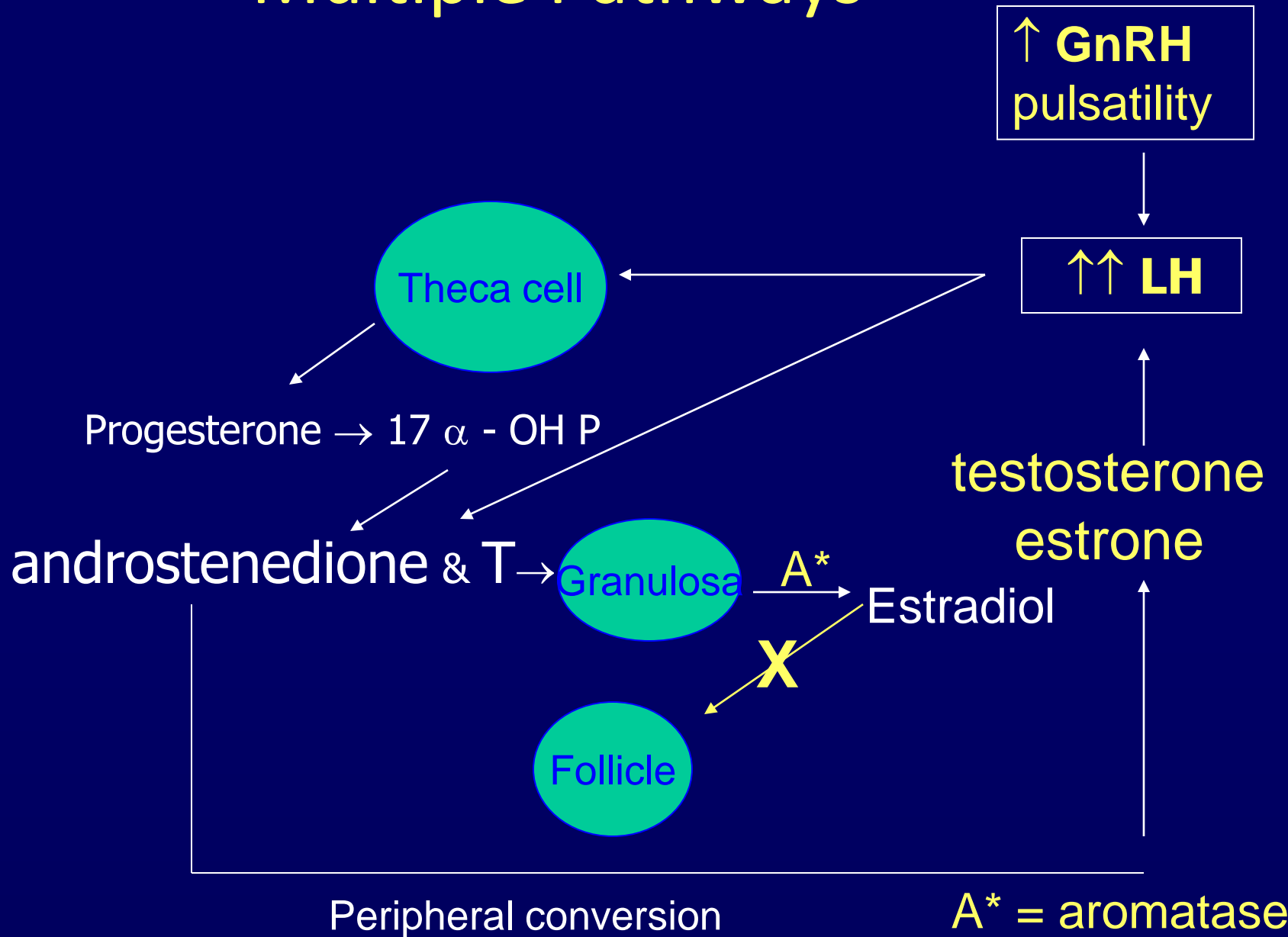
# Multiple Systems

- Reproductive
- Endocrinologic
- Cardiac
- Renal (kidney)
- Hepatic (liver)
- Brain (mood)
- Dermatologic

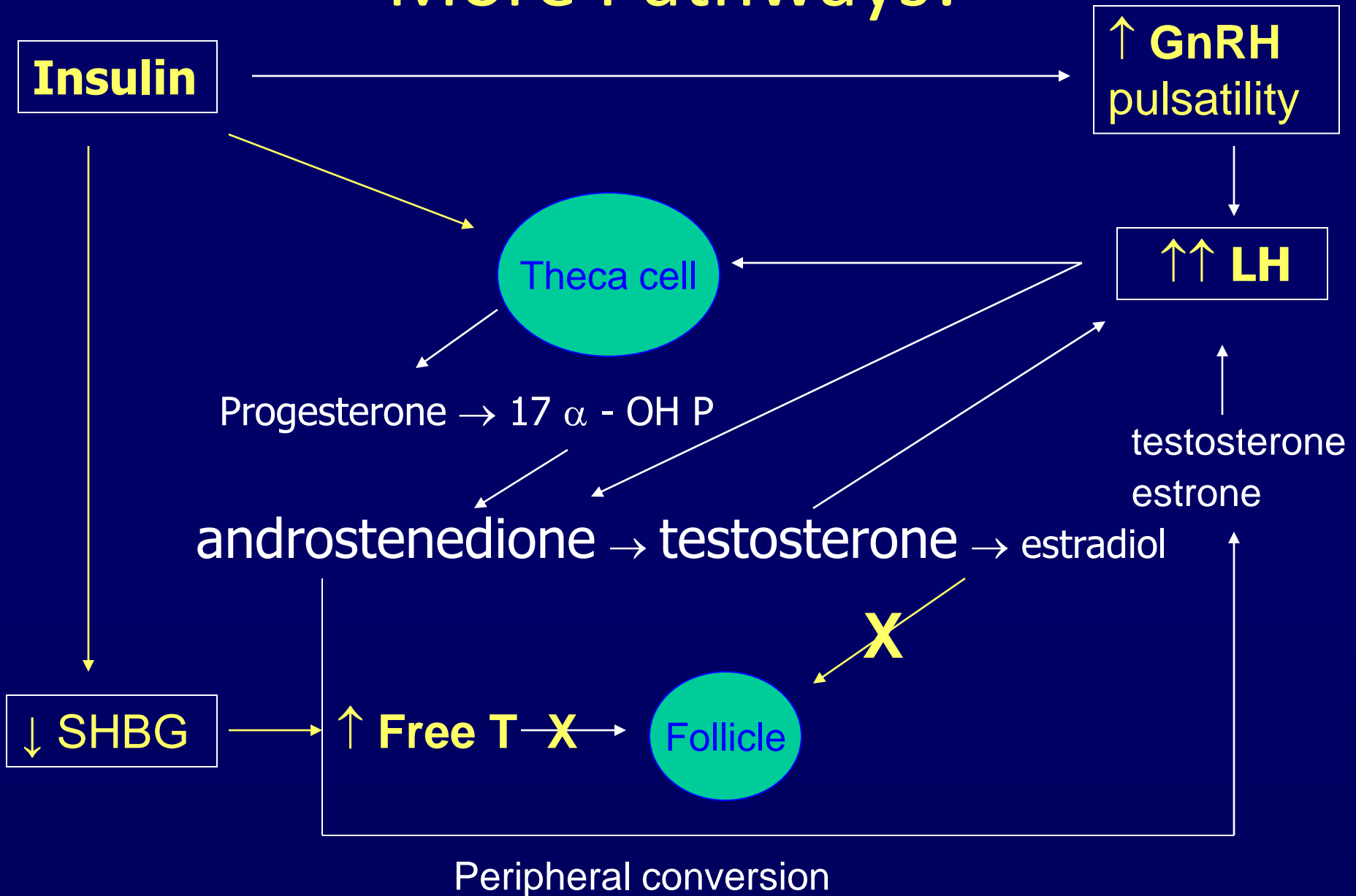
# Multiple Signs & Symptoms

Irregular periods, Bleeding too much, Bleeding too little, Anxiety, Depression, Eating disorders, Weight gain, Acanthosis nigricans, Skin tags, Follicular keratitis, Hirsutism, Acne, Alopecia, Excess sweating, Seborrheic dermatitis, Hidradenitis suppurativa, Fatty liver, High triglycerides, low HDL-cholesterol, Elevated glucose, Infertility, Breastfeeding problems, Poor sleep, Miscarriages, Fatigue, Endometrial cancer

# Multiple Pathways



# More Pathways!



# The Magic Bullet

## The oral contraceptive pill

- High doses of estrogen (ethinyl estradiol)
- Increase SHBG and lower free testosterone\*
- Improve skin symptoms in most:
  - Alopecia
  - Hirsutism
  - Acne
- Regulate bleeding (in most)

\*Sherif K, *Metabolism*, 1996

# Oral Contraceptive Pills

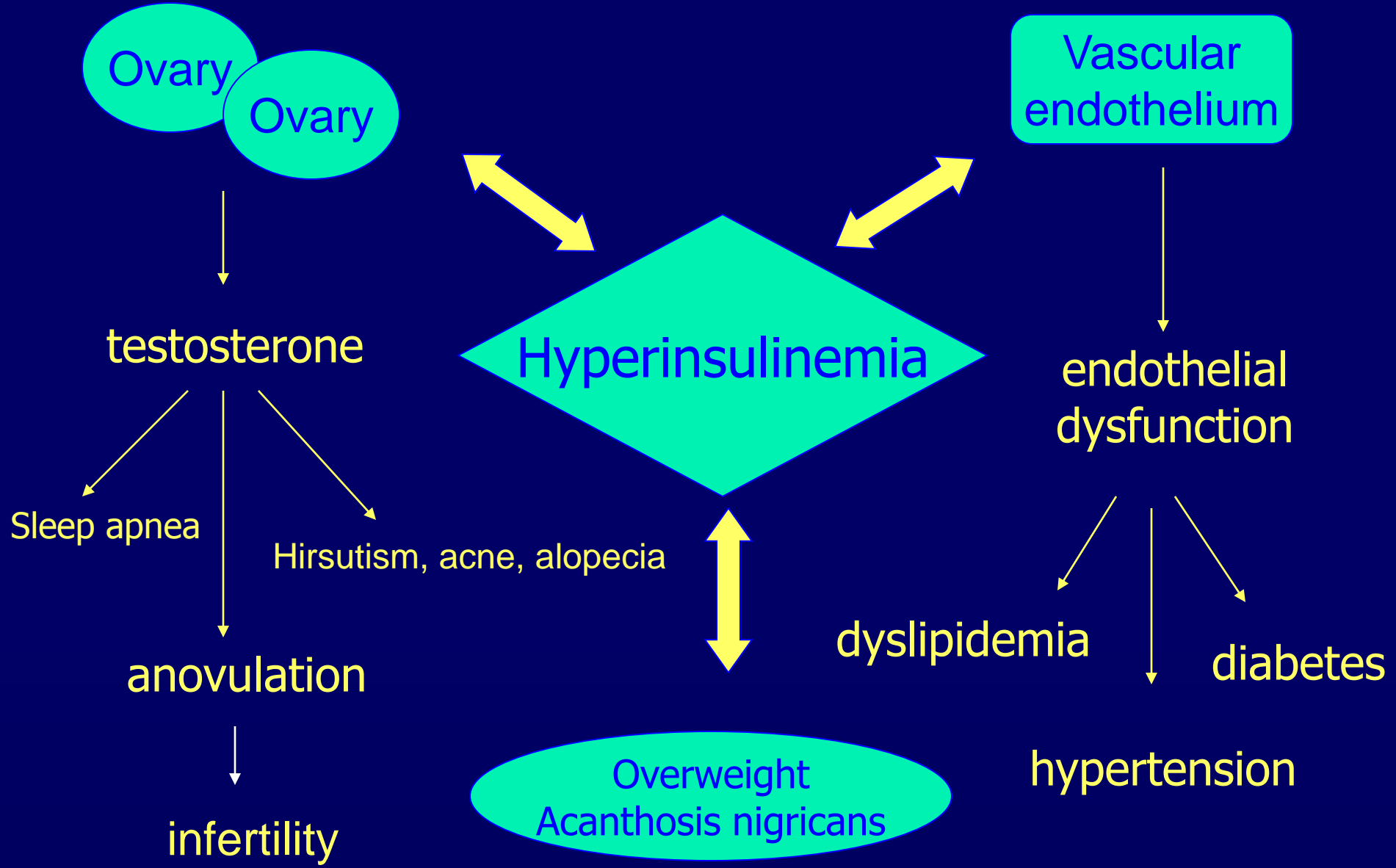
- Risks:
  - Worsen insulin sensitivity – cause glucose intolerance
  - Increase triglycerides
  - Microalbuminuria
  - Unmask thrombophilias – more common in PCOS?
  - Double relative risk of MI/stroke in high-risk group
  - May gain weight
  - May affect mood
- Advantages of some formulations?

**Sherif, *Am J Obstet Gyn* 1999**

**Nestler, *JCEM* 2005**



# Traditional treatment does not address insulin resistance



# Prescription for Treatment Goals

- ❑ Dermatologic symptoms caused by androgens
  - ❑ Hirsutism
  - ❑ Acne
  - ❑ Alopecia
  - ❑ Excess sweating
  - ❑ Seborrheic dermatitis
  - ❑ Hidradenitis supparativa

# Prescription for Treatment Goals

- ❑ Symptoms directly related to insulin resistance
  - ❑ Weight gain
  - ❑ Acanthosis nigricans
  - ❑ Skin tags
  - ❑ Follicular keratitis

# Prescription for Treatment Goals

- ❑ Psychologic/psychiatric symptoms
  - ❑ Anxiety
  - ❑ Depression
  - ❑ Eating Disorders

# Prescription for Treatment Goals

- ❑ Metabolic problems
  - ❑ Fatty liver
  - ❑ High triglycerides and low HDL-cholesterol
  - ❑ Elevated A1c (3-month sugar)

# Prescription for Treatment Goals

- ❑ Infertility
- ❑ Sleep apnea
- ❑ Difficulty breastfeeding

# Key: decrease insulin resistance

- Nutrition
  - Decrease simple carbohydrates
  - Decrease calories
- Increase physical activity
- Sleep
- Insulin-sensitizing medications
- Insulin-sensitizing supplements

# Prescription for Treatment



# Improve Insulin Sensitivity

- ❑ Nutrition
- ❑ Physical Activity
- ❑ Sleep
- ❑ Insulin-Sensitizing Supplements & Alternative Therapies
- ❑ Medications

# Improve Insulin Sensitivity: Nutrition

- Decrease calories
- Improve type of calories
  - Decrease simple carbohydrates
  - Stay low on glycemic index (GI)
  - If gluten free, watch other grains

## Improve Insulin Sensitivity: Physical Activity

- Build muscle mass\*\*
- You shouldn't have to be in the gym 5 days/week

# Sleep

- Adequate sleep is essential to insulin sensitivity
- Sleep deprivation shortens life
- Need progesterone to sleep, but progesterone is low in PCOS

# Improve Insulin Sensitivity

## Medications that may decrease weight

- Insulin Sensitizers
  - Metformin
  - TZD's – thiazolidinediones (Actos, Avandia)
- Incretins – derived from the Gila Monster
  - Byetta → Bydureon (weekly)
  - Victoza → Saxenda (weekly)
  - Trulicity
  - Symlin

## Improve Insulin Sensitivity:

Weight Loss Medications that *do not* improve insulin sensitivity.....but when you lose weight, you are more insulin sensitive

- Phentermine
- Topamax
- Qsymia = phentermine and Topamax
- Belviq – affects brain serotonin
- Contrave = naltrexone and bupropion
  
- Alli (Xenical)

# Metformin

- Benefits:
  - Weight loss (minimal)
  - Improved lipid profile
  - Improved acne, hirsutism and alopecia
  - Normalization of transaminases
  - Ovulation & pregnancy
    - Cochrane meta-analysis: first-line agent for anovulation
- Side effects
  - Gastrointestinal: diarrhea, nausea
  - Decreased B-12 absorption and ↑ homocysteine

# Treatment

- Metformin ER: 500mg titrated up to 2000mg/day
- Pioglitazone and rosiglitazone
  - Associated with fluid retention
- Byetta, Symlin, Victoza
- Spironolactone: dose-dependent



# Thiazolidinediones

- May be more effective in thin PCOS
- Thiazolidinediones (TZD's or glitazones)
  - Troglitazone – most studied
  - Pioglitazone
  - Rosiglitazone
  - Both associated with fluid retention
- Check liver function tests in 4 weeks

# Anti-androgens

- Spironolactone 100mg twice a day\*\*
- May take as long as 3-6 months to see improvement, especially in alopecia
- Alpha-reductase inhibitors: saw palmetto, flutamide, finasteride
  - Transaminase elevations
- Ornithine decarboxylase inhibitors: eflornithine
  - 30% “response” rate at six months

# Treatment with insulin sensitizers improves fertility & CVD risk factors

Decrease hyperinsulinemia

↓ testosterone

↑ ovulation

fertility    endometrial ca

↓ hyperandrogenemia

Hirsutism, Acne, Alopecia

improve endothelial function

BP, lipids, glucose

↓ Cardiovascular risk

# Treatment

- Ovulation occurs in most within 3 months
  - May be as early as 1 month or prior to first menses
  - Must discuss risk of pregnancy within the first month
- If pregnancy desired
  - Discuss use of metformin during pregnancy
  - Most obstetricians ok with metformin during pregnancy
  - Stop pioglitazone and rosiglitazone asap

# Supplements with insulin-sensitizing properties

- Omega-3 fatty acids
- Cinnamon
- Vitamin D
- Chromium
- N-acetyl cysteine\*\*
- Resveratrol
- Alpha lipoic acid
- Magnesium\*\*
- D - chiro inositol & Myo-inositol

# Prescription Plan

- Address the basics that improve insulin sensitivity
  - Nutrition
  - Physical activity
  - Sleep
- Are your symptoms due to high testosterone or high insulin or both?
- Think about what direction you want to go in when you're 50 years old: commit now to live

# Divide your symptoms into three compartments

