PRE PREGNANCY
You are called about a patient recently seen by her Primary care physician. Her Pt is desirous of Pregnancy.

She has been diagnosed with Polycystic Ovary Syndrome and her doctor was concerned because: the patient is 5’ 4” tall, she weighs 256lbs. Her BMI is 43.6.

She is 28 years old G2P0Ab2. She has not had a menses in 2 years and reports always irregular.

Her waist is 43”. She is Hispanic. Triglycerides are 256 mg/dL. LDL Cholesterol is 196. HDL Cholesterol is 30 mg/dL. Fasting glucose is 104 mg/dL. 2 hour glucose post 75 gm challenge is 156 mg/dL. BP is 143/92.

Her Dr wants to put her on Clomiphene Citrate to help her ovulate because she read that the Reproductive Medicine Network found that Clomiphene is superior to Metformin for ovulation as a first line therapy.

Her Dr. is concerned about her lipids because she knows that Pregnancy is a state of insulin resistance and she wants to avoid pancreatitis...
1. What intervention(s) is/are optimum for this patient?

2. What are the interventions that you can/should prescribe?

3. What is the likelihood that she will ovulate with Clomiphene?

4. What are normal Cholesterol and Triglycerides in Pregnancy?

5. At what levels of Cholesterol and Triglycerides should she initiate medical therapy during pregnancy?
Women with Polycystic Ovary Syndrome (PCOS) are Highly Likely to Develop Risk Factors for CVD

Patients with Polycystic Ovary Syndrome (PCOS):

- 5-fold risk of developing Type 2 diabetes compared to age- and weight-matched control
- Up to 70% have dyslipidemia
- Metabolic syndrome is present in about 40%
- Metabolic manifestations less common in non-obese PCOS patients

Boudreaux 2006, Wild 2010
Pre-pregnancy cardiometabolic and inflammatory risk factors and subsequent odds of a hypertensive disorder in pregnancy

Monique M. 2012
# Obesity-related complications

**n=8,092**

<table>
<thead>
<tr>
<th>BMI</th>
<th>Diabetes</th>
<th>Hypertension</th>
<th>Toxemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI&lt;25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI 25-9</td>
<td>3.4(1.7,6.1)</td>
<td>1.9(.97,3.7)</td>
<td>1.7(1.2,1.4)</td>
</tr>
<tr>
<td>BMI &gt;30</td>
<td>15.3(8.2,29.6)</td>
<td>4.8(2.3,9.9)</td>
<td>2.7(1.7,4.4)</td>
</tr>
</tbody>
</table>

**Obesity-Related Complications in Danish Single Cephalic Term Pregnancies 2005**
Obesity adversely affects reproduction, is associated with anovulation, pregnancy loss & late pregnancy complications.

Obesity within PCOS is associated with failure of infertility treatment.

Weight loss prior to infertility treatment improves ovulation in women with PCOS.

Pre-Pregnancy Counseling is a window of Opportunity for Prevention!

Smoking, alcohol, Folic acid, diet, exercise
Lifestyle Interventions for PCOS

- Treatment of adverse lifestyles, including obesity and physical inactivity, should precede ovulation induction – heart healthy

- The ideal amount of weight loss is unknown, but a 5% decrease of body weight might be clinically meaningful

- 5-10% wt loss - 50% chance of return of regular ovulation!
Lifestyle Interventions for PCOS

• Caution is recommended about conceiving during
  – hypo-caloric diets
  – excessive physical exertion
  – pharmacological intervention after bariatric surgery
  – Vitamin deficiency post bariatric surgery
Risk of atherosclerotic outcomes by Hx of pregnancy loss

1, 031, 279 women followed 15 years

<table>
<thead>
<tr>
<th>Event</th>
<th>RR MI</th>
<th>RR Stroke</th>
<th>RR Hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stillbirth</td>
<td>2.69</td>
<td>1.74</td>
<td>2.42</td>
</tr>
<tr>
<td>Miscarriages(4)</td>
<td>2.98</td>
<td>1.89</td>
<td>3.78</td>
</tr>
<tr>
<td>Miscarriage trend (1)</td>
<td>1.09</td>
<td>1.13</td>
<td>1.19</td>
</tr>
</tbody>
</table>

Ranthe, M. AHA 2012
First trimester outcomes and Lipids
ABCD study Netherlands

<table>
<thead>
<tr>
<th></th>
<th>Triglycerides</th>
<th>Cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PIH</strong></td>
<td>1.6 (1.10, 2.3)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>PET</strong></td>
<td>1.7 (1.10, 2.6)</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>LGA</strong></td>
<td>1.5 (1.23, 1.78)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

**Preterm delivery and born small for gestational age (SGA) or large for gestational age (LGA) are associated with increased risk for cardiac structural defects, type 2 diabetes, cardiovascular diseases, hypertension later in life!**

When does metabolic syndrome begin?
Cardiometabolic outcomes of Offspring at age 32 by quartile of maternal PRE - Pg weight and weight gain both during Pg

• BMI\Waist
• TG
• Blood Pressure
• Insulin

Hochner 2012
Common Diagnoses In Ob/Gyn That Increase Lifetime Cardiovascular Disease (CVD) Risk

• Pregnancy-induced Hypertension, Gestational Diabetes (GDM), Polycystic Ovary Syndrome (PCOS), premature delivery
• Hypertension (HTN), Diabetes, Hyperlipidemia
• Smoking, Overweight/Obesity, Unhealthy Diet, Lack of Exercise

Source: Mosca 2011, Wild 2010
Excursions into Metabolic Syndrome During Pregnancy

Source: Sattar & Greer, 2002; Adapted from Deborah Ehrenthal, MD, FACP

Population with complicated pregnancies
Healthy population
Threshold for vascular or metabolic disease

Vascular Risk Factors

Pregnancies
Middle Age

Age
PREGNANCY
Pregnancy = Diabetogenic Lipogenic?

• Insulin Resistance
• Placental secretion of diabetogenic hormones
• Increased adipose deposition
• Decreased exercise
• Increased caloric intake
• ...endocrine metabolic changes insure fetus with ample fuel and nutrients
Effects of Pg on Diabetes

• Increased Diabetogenic hormones
  – HPL
  – Estrogen
  – Progesterone
  – Prolactin
  – TNF-alpha

• Long term (pre-gestational DM)
  – Renal disease
  – Retinal disease
  – Transition to overt DM with frequent Pg
Effects of Diabetes on PG

Maternal
- Increase risk of SAB
- Increased risk of PTL, PTD
- RR preeclampsia 2.3
- More infections
- Operative delivery
- Birth trauma

Fetal
- Anomalies
- Growth retardation
  - Macrosomia RR 1.3
  - IUGR
  - Stillbirth
  - Polyhydramnios
  - PMROM
    - RR 3.1
Infant Consequences

- Obesity and diabetes in childhood
- Impaired fine and gross motor functions
- Higher rates of inattention &/or hyperactivity
Insulin Sensitizing Medication

- Metformin, Glyburide - Class B
- Pioglitazone, Rosiglitazone - Class C
- No advantage over lifestyle modification for ovulation
- Metformin Restricted to pts with glucose intolerance
- DC in early Pg?
- No advantage of adding Metformin to Clomiphene for first line ovulation induction
Metformin In Pg

- 197 Infertile PCOS women
- Cohort study no randomization
- Metformin throughout vs. D/C when PG or spontaneously conceived
- Continuation 8.8% Pg loss vs. 29.4%
- Recurrent AB 12.5% vs. 49.4%
- Confirms Khattab, S. 2006
  odds of loss .23(.011,0.42) with Metformin

Nawaz, F.H 2009
Lipids in PG

• Pg is a stress test for mother fetus and later life
• Nature focuses on fetal well being for nutrition
• Poorly controlled maternal nutrition affects the infant
  – How much, within what homeostatic boundaries and with what effect later in life is under intense scrutiny
### Developmental programming of cardiovascular disease

![Diagram showing the developmental programming of cardiovascular disease across mother, pregnancy, lactation, child, and adult stages.]

<table>
<thead>
<tr>
<th>Mother Pathology</th>
<th>Pregnancy Pathology</th>
<th>Lactation Early Outcome Parameters</th>
<th>Child Predictors of Cardiovascular Risk</th>
<th>Adult Late Outcome Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under- or dysnutrition</td>
<td>Hypoxia</td>
<td>Birthweight</td>
<td>Endothelial function</td>
<td>Clinically manifest</td>
</tr>
<tr>
<td>Corticosteroid treatment</td>
<td>Hypertension</td>
<td>Early changes in glucose metabolism</td>
<td>Vascular reactivity</td>
<td>- CHD</td>
</tr>
<tr>
<td>Mechanical obstruction of uterine artery</td>
<td>Hyperinsulinemia</td>
<td>Oxidative stress markers</td>
<td>Fatty streaks</td>
<td>- Hypertension</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>Hyperglycemia</td>
<td>Intimal thickening</td>
<td>Selective immune responses</td>
<td>- Diabetes</td>
</tr>
<tr>
<td>Obesity</td>
<td>Hypercholesterolemia</td>
<td>Antigen-specific B or T cell populations</td>
<td>Conditions assessed by NCS:</td>
<td>Acute events</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>Oxidative stress</td>
<td>IgM</td>
<td>- Obesity</td>
<td>- Insulin resistance</td>
</tr>
<tr>
<td>Diabetes</td>
<td>B and T cell cytokines</td>
<td>Transplacental</td>
<td>- Diabetes</td>
<td>- Infections</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>antibodies</td>
<td>Pathogenic or Beneficial Programming Mechanisms</td>
<td>- Allergy</td>
<td>- and others</td>
</tr>
<tr>
<td>Bacterial &amp; viral infections</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Allergies</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>...and others</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


The National Children’s Study
Gestation and Lipids

• During the first 2/3 gestation the mother is in an anaerobic state, increasing her fat depots thanks to hyper-phagia and enhanced lipogenesis.

• During the last 1/3 the mother switches to a catabolic state. Glucose is the most abundant nutrient crossing the placenta, which causes maternal hypoglycemia despite an increase in gluconeogenesis.

• Adipose tissue lipolytic activity increases raising plasma fatty acids and glycerol that reach the liver, leading to an increase in hepatic production of TG, that return to the circulation in VLDLs.

• Enhanced CETP enriched LDL and HDL with TG.

Herrera E. Eur J Clin Nutr 2000;54:Suppl 1 S47-S51
Gestation and Lipids

• Glycerol is also used as a gluconeogenic substrate saving other more essential molecules like amino acids for the fetus.

• Under fasting conditions, FA, via beta-oxidation are converted into ketone bodies which easily cross the placenta and are metabolized by the fetus.

• Enhanced liver production of VLDL-TG together with a decrease in adipocyte LPL, increased plasma CETP & hepatic lipase cause both an increment in particles and particle TG.

• Maternal TG do not cross the placenta, but are hydrolyzed by LPL releasing FA to the fetus.
Gestation and Lipids

• Changes in lipid metabolism during Pg promote accumulation of fat stores in early and mid Pg and enhance mobilization in late Pg

• Cholesterol is used by placenta for steroid synthesis, and fatty acids for placental oxidation and membrane formation

• Anabolic phase in preparation for rapid fetal growth in late PG

Basaran 2009
Effect of Pregnancy on adipose lipolysis; metabolic fate of the lipolytic products & liver production of glucose, VLDL and ketone bodies and availability of substrates to the fetus

TG = triglycerides

Herrera E. Eur J Clin Nutr 2000;54:Suppl 1 S47-S51
VLDL Lipolysis During Pregnancy

Lipoprotein Lipase activity is diminished in adipose tissue and throughout the body in late pregnancy delaying lipolysis of the TG-rich VLDLs.

TG levels will rise

Adapted from Herrera E. Eur J Clin Nutr 2000;54:Suppl 1 S47-S51
Lipoprotein Particle Composition Changes During Pregnancy

Overproduction of TG-rich VLDL

Lipoprotein Lipase activity is diminished in adipose tissue and throughout the body in late pregnancy delaying lipolysis of the TG-rich VLDLs.

An increase in CETP activity is found at mid gestation. The increase in VLDL-TG and its delayed lipolysis during pregnancy in the presence of increased CETP activity facilitates enrichment of LDL and HDL with TG.

LDL-TG & HDL-TG

Large LDL

Large HDL

TG-enriched particles

Overproduction of TG-rich VLDL

Lipoprotein Lipase activity is diminished in adipose tissue and throughout the body in late pregnancy delaying lipolysis of the TG-rich VLDLs.
Plasma lipoprotein TG in women at the 3rd trimester of pregnancy (red) and at post-lactation.

Under non-pregnant conditions the TG content in HDL and LDL are low compared to VLDL. In Pg women there is a significant increase in TG in all lipoprotein fractions.

Herrera E. Eur J Clin Nutr 2000;54:Suppl 1 S47-S51
Gestation and Lipids

• A third mechanism by which maternal hypertriglyceridemia benefits offspring is its contribution to milk synthesis in preparation for lactation

• With decreased adipocyte LPL, TG are more available to the breasts. Around parturition there is rapid increases in LPL expression and activity in mammary glands. This is due to both increased prolactin and insulin levels and a specific enhancement in mammary gland insulin sensitivity

• Thus mammary induction of LPL facilitates clearing of maternal TG for milk synthesis. Essential FA from the diet become available to the nursing infant.
# Lipid Changes in Pg

<table>
<thead>
<tr>
<th></th>
<th>Controls(mg/dL) Pre-Pg</th>
<th>1&lt;sup&gt;st&lt;/sup&gt; Trimester</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; Trimester</th>
<th>Third Trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cholesterol</strong></td>
<td>183±25</td>
<td>173±18</td>
<td>243±53</td>
<td>267±30</td>
</tr>
<tr>
<td><strong>LDL Cholesterol</strong></td>
<td>99±23</td>
<td>90±17</td>
<td>130±46</td>
<td>136±33</td>
</tr>
<tr>
<td><strong>Non HDL Chol</strong></td>
<td>114±16</td>
<td>106±16</td>
<td>160±35</td>
<td>186±23</td>
</tr>
<tr>
<td><strong>Triglycerides</strong></td>
<td>77±34</td>
<td>79±27</td>
<td>151±80</td>
<td>245±73</td>
</tr>
</tbody>
</table>

Basaran, A. 2009
Dietary Treatment of Hypercholesterolemia in PG

14 PG Patients -12 nl, 1 juvenile diabetic, one type II familial hypercholesterolemia

Cholesterol free diet vs. 600 -1000 mg daily (eggs)
Adjusted calories for 1.4 Kg/mo wt gain

Cholesterol varied 234-187mg/dL
From -47+37 mg vs. +36 mg/dL +12

Change primarily in LDL cholesterol
Change in nl, diabetic and type II familial hypercholesterolemia

TG increased steadily in spite of diet to 198+43 mg/dL
Striking decrease 1 week post partum

Mc Murry, M. 1981
Lipid Changes in Pg

- Trig and Cholesterol usually not > 332 and 337 mg/dL
- Extreme values can occur (Trig>1000 mg/dL)
- Pre-existing, coexistent medical disorders,
- Co-existent Pg disorders, limited to gestational period (DM,PET), supra-physiologic, dysbetalipoproteinemia, partial LPL deficiency and Apo E3/3 phenotype

Basaran 2009
Gestational Diabetes...Any degree of glucose intolerance with onset of first recognition during pregnancy

• Most with GDM have glucose intolerance that begins in pregnancy

Some have Type 2 DM unrecognized prior

• 10% with GDM have circulating islet-cell antibodies &/or HLADR3 or DR4....increase risk for Type 1 post delivery (exact risk unknown)*

Gestational Diabetes
Prevalence

• Varies worldwide & among racial/ethnic groups
• US: 2-5% (1.4-14%)
• NA & Hispanic>AA>Caucasian
• Increasing in all groups*
• Increased maternal age
• Obesity

Diabetes in Pregnancy Dietary Care

- Nutritional counseling ideal
- 30 kcal/kg/day
- Pre-pregnant weight
- Most appropriate diet not established...
- Carbohydrate 60%
- Protein 20%
- Fat 20%
- Saturated 10%
- Unsaturated 10%
Gestational Diabetes
Oral Hypoglycemic Agents

• Primary effect is to enhance insulin secretion
• As of 2000, ACOG has not supported use of oral agents over insulin in pregnancy
• In US major objection to use is/was the theoretical risk of:
  – Congenital fetal anomalies
  – Fetal macrosomia
  – Neonatal hypoglycemia
• Emergence of a new generation of agents has lead to a reexamination of this issue: Glyburide & Metformin
Gestational Diabetes
Glyburide

- A second generation sulfonylurea
- MOA: Increases insulin secretion & decreases insulin resistance by lowering glucose toxicity
- Onset of action 4 hrs, duration of action 10 hrs.
- Shown to not cross the placenta (minimal?)
- Category B drug
Glyburide & Gestational Diabetes

• Langer 2000: only RCT of 404 patients, demonstrated similar efficacy of glyburide & insulin in glucose control & pregnancy outcome

• Conway 2004: retrospective study of 75 patients, found glyburide was useful in achieving glycemic control.

• Jacobson 2005: retrospective study of 584 patients found similar efficacy between glyburide & insulin, but higher rates of preeclampsia and phototherapy in the glyburide group.
Metformin & GDMA2

- Safety profile of metformin (class B) in the first trimester and apparent lack of teratogenicity has been well documented.

- Prematurity?...single trial with insulin

- Does cross placenta ...Clinical trials only?

- Metformin treatment of GDM appears to be safe, and is effective in many women, however 1/3 or ½ will need insulin to achieve glycemic targets.

- A randomized trial that directly compared Metformin and Glyburide in treatment of GDM found use of Glyburide was more likely to result in adequate glycemic control.
  - Insulin was eventually required in only 16 percent of those randomized to glyburide compared with about 35 percent of patients randomized to metformin.

Moore 2010, Metzger 2007
Glyburide or Metformin vs Insulin for GDMA2

- Advantages for oral treatment of GDMA2
- Lower cost and Improved Compliance
- 1 vial of 10cc of Regular insulin=$37.99
- 1 vial of 10cc of NPH insulin=$37.99
- A box of 100 syringes=$19.00
- 30 day supply of glyburide or metformin (max dose)=$4.00 at Walmart
- or $43.99 at Walgreen’s
Hypertensive Disorders in Pregnancy

**Categories**

- Those with HTN who become pregnant
- Those who develop HTN disorders during pregnancy

**Classes**

- Chronic hypertension
- CHTN with superimposed preeclampsia
- Gestational hypertension
- Preeclampsia
- Eclampsia
- Transient hypertension
• Methyldopa (Aldomet) 250-1000 mg qid
• Labetolol (Nomodyne) 100-1200 mg bid
• Nifedipine (Procardia) 10-30 mg tid
• Nifedipine (Procardia XL) 30-60 mg qd
• Hydralazine (Apresoline) 10-75 mg qid
• Minoxidil (Loniten) 5-10 mg qd
• Clonidine (Catapres) 0.1-0.2 mg bid
MEDICATIONS THAT CAUSE HYPERTENSION

- Corticosteroids
- Cyclosporine
- Contraceptives
- Amphetamines
- Sympathomimetics
- Ephedrine
- Cocaine!
Lipid levels with medical conditions

- Obesity, weight gain, hypothyroidism, gestational and non gestational diabetes, Preeclampsia, OH consumption, LMW Heparin, glucocorticoids, psychotropic meds, kidney disease, lipodystrophy
- Effects not well characterized
- Observed hyperlipidemia is independent of Diabetic status ....

Toescu 2004
## Effects of Selected Drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>OH</td>
<td>INCREASED</td>
</tr>
<tr>
<td>ESTROGEN</td>
<td></td>
</tr>
<tr>
<td>GLUCOCORTICOIDES</td>
<td></td>
</tr>
<tr>
<td>BBLOCKERS</td>
<td></td>
</tr>
<tr>
<td>VALPROATE</td>
<td></td>
</tr>
<tr>
<td>SERTALINE</td>
<td></td>
</tr>
<tr>
<td>ISORETENOID</td>
<td></td>
</tr>
<tr>
<td>CYCLOSPORIN, TACROLIMUS, ETC</td>
<td></td>
</tr>
</tbody>
</table>
Lipoprotein Changes in T2DM

• Triglyceride–rich lipoproteins
  – Increased particle number
  – Increased postprandial concentrations
  – Triglyceride enriched and cholesterol enriched particles

• LDL
  – Increased particle number
  – Small dense particles

• HDL
  – Decreased particle number
  – Changes in particle composition

Mazzone 2008
Chylomicronemia

- Hi VLDL & Chylomicrons (V)
- TG > 1000 (usually > 2000 mg/dL)
- Risk for pancreatitis

Clinical features
- Eruptive xanthoma
- Hepatosplenomegaly
- Lipemia retinalis
- Abdominal pain without pancreatitis

- Peripheral neuropathy
- Dyspnea
- Memory loss/dementia
Severe Hypertriglyceridermia

• Reduce fat calories (15%)
• Insulin therapy (acute insulin infusion NPO) if hyperglycemia
• Omega 3 – fatty acids (4-10g/d) - 20-45% reduction
  – Lovaza (840 mg/1 gram capsule) TG> 500 mg/dL
    • FDA anticoagulant monitoring periodically
• Gemfibrozil
• Goal:
  – Trigs < 400 mg/dL to prevent pancreatitis
Hypertriglyceridemia

Low fat diet <20% calories from fat
Admission, NPO, iv D5/0.45 until TG levels fall by half, or TPN as per dietician
MCTG 10-30g/day
Omega 3 (3-4g/d)
Topical sunflower oil 1tblsp subcut
Gemfibrozil 600mg bid or Fenofibrate 145-200
Niacin
Gene therapy

Goldberg JCEM 2012
## Lipid Changes During Pregnancy

<table>
<thead>
<tr>
<th>Type of hyperlipidemia</th>
<th>Key Feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>Increased chylomicrons</td>
</tr>
<tr>
<td>Type 2a</td>
<td>Raised LDL</td>
</tr>
<tr>
<td>Type 2b</td>
<td>Raised VLDL+LDL</td>
</tr>
<tr>
<td>Type 3</td>
<td>Raised LDL (dysbetalipo proteinemia)</td>
</tr>
<tr>
<td>Type 4</td>
<td>Hi VLDL</td>
</tr>
<tr>
<td>Type 5</td>
<td>Hi Chylomicrons + VLDL</td>
</tr>
</tbody>
</table>

Basaran A, ( ) 2009
## Lipid Lowering Agents and Pregnancy Class

<table>
<thead>
<tr>
<th>Lipid Lowering Agent</th>
<th>Pregnancy Class</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Statins</strong></td>
<td>X</td>
</tr>
<tr>
<td><strong>Fibrates</strong></td>
<td>C</td>
</tr>
<tr>
<td><strong>Ezetimibe</strong></td>
<td>C</td>
</tr>
<tr>
<td><strong>Niacin</strong></td>
<td>C</td>
</tr>
<tr>
<td><strong>Cholestyramine</strong></td>
<td>C</td>
</tr>
<tr>
<td><strong>Colesevelam</strong></td>
<td>B</td>
</tr>
</tbody>
</table>

*Eapen et al Familial hypercholesterolemia and pregnancy Journal Clinical Lipidology 2012 6, 88-91*
4.7 Treatment options during pregnancy

4.7.1 Statins, ezetimibe, and niacin should not be used during pregnancy. Use of other lipid lowering medications (e.g., colesevelam) may be considered under the guidance of the healthcare practitioner.

4.7.2 Consider LDL apheresis during pregnancy if there is significant atherosclerotic disease or if the patient has homozygous FH.
## Preeclampsia vs. no – 1 yr P. Partum!

<table>
<thead>
<tr>
<th></th>
<th>Preeclampsia (n = 70)</th>
<th>Normo tensive (n = 70)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>77.3 (20.2)</td>
<td>71.8 (14.7)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.0 (7.0)</td>
<td>26.0 (5.0)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>&lt; 25 (healthy)</td>
<td>23 (32.9)</td>
<td>34 (48.6)</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>25-30 (overweight)</td>
<td>20 (28.6)</td>
<td>23 (32.9)</td>
<td></td>
</tr>
<tr>
<td>&gt; 30 (obese)</td>
<td>27 (38.6)</td>
<td>13 (18.6)</td>
<td></td>
</tr>
<tr>
<td>Wt gain – pre to Post</td>
<td>1.83 (3.58)</td>
<td>0.59 (2.18)</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Systolic</td>
<td>120.0 (11.9)</td>
<td>111.3 (9.3)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Diastolic</td>
<td>81.5 (10.3)</td>
<td>72.7 (8.1)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Insulin (pmol/L)</td>
<td>63.6 (55.2)</td>
<td>44.7 (27.9)</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>HOMA</td>
<td>1.18 (1.02)</td>
<td>0.83 (0.52)</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>4.69 (0.85)</td>
<td>4.30 (0.76)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.10 (0.69)</td>
<td>0.96 (0.53)</td>
<td>NS</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>1.47 (0.36)</td>
<td>1.50 (0.30)</td>
<td>NS</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>2.71 (0.81)</td>
<td>2.37 (0.67)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>NonHDL cholesterol</td>
<td>3.22</td>
<td>2.80</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Microalbumin/creatinine</td>
<td>0.80 (0.40, 2.68)</td>
<td>0.51 (0.40, 0.90)</td>
<td>&lt; .01</td>
</tr>
</tbody>
</table>

Smith 2009
POST PARTUM

There seems to be no structured follow-up of women after a hypertensive disorder of pregnancy; guidelines on cardiovascular risk management after a hypertensive disorder of pregnancy are lacking!

Currently used 10-y risk prediction models for cardiovascular disease are likely to underestimate the risk of cardiovascular disease in this group of young women.

Any physician performing cardiovascular risk counseling in women should be aware of the importance of obstetric risk factors for later cardiovascular health.

A postpartum cardiovascular risk screening should be based on guidelines for cardiovascular risk assessment in asymptomatic people.

Lifestyle interventions in the reproductive age may reduce prolonged exposure to cardiovascular risk factors, may positively influence the next pregnancy, and contribute to a healthy lifestyle for the partner and children.
PREVENTION
Contraception should always be addressed regardless of whether pregnancy is desired!!!
Statin Rx for Women of Child Bearing age

HMG-CoA Reductase Inhibitor—Informed Consent Form for Women of Childbearing Age

I have reviewed the information on HMG-CoA Reductase Inhibitors and listened to my healthcare practitioner and understand all of the following:

- HMG-CoA Reductase Inhibitors can cause severe birth defects to the developing fetus of pregnant females if taken during pregnancy.
- I must NOT take HMG-CoA Reductase Inhibitors if I am pregnant and/or think of becoming pregnant.
- I am not pregnant now and do not plan to become pregnant during treatment with HMG-CoA Reductase Inhibitors.
- I must use two forms of effective birth control one month prior and during my treatment with HMG-CoA Reductase Inhibitors.
- Birth control methods may fail. No birth control is absolutely safe.
- I must stop taking my HMG-CoA Reductase Inhibitors and contact my physician if:
  - My menstrual period is delayed while on HMG-CoA Reductase Inhibitor treatment.
  - I become pregnant while on HMG-CoA Reductase Inhibitor treatment.

I acknowledge that all the above points have been fully explained to me by my healthcare practitioner and that I understand these points fully.

Patient Signature _____________________________ Date 01/16/2007

Block Scheduling

Clinician Signature _____________________________ Date 01/16/2007

James A. Underberg, MD
Dyslipidemia in Pregnancy
Take Home Message(s)

• Mother’s metabolism adapts for fetal efficiency – no need to overload the system - Excess affects the fetus
• Pre-conception is best window of opportunity for Prevention
• Triglycerides increase with insulin resistance – Pg is a stress test
• Accumulating evidence that preeclampsia & gestational diabetes portend IH Disease later
• Metabolic complications happen in those at risk prior to Pregnancy and should be assessed BEFORE PREGNANCY
• AND POST PARTUM!
• Don’t let these people fall through the cracks in our health care system!