Objectives

- To understand the implications of common medical conditions on pregnancy
- To define differences in disease management goals in pregnancy
- To be able to appropriately change medical management of patients prior to pregnancy

Common Complicating Medical Conditions that Precede Pregnancy

- Hypertension ~5%
- Diabetes Mellitus ~1-2%
- Thyroid Disease ~5%
  - Leading causes of hospitalization in pregnancy
    - Preterm labor
    - Hypertension
    - Diabetes Mellitus
    - Bleeding

Hypertensive Disorders in Pregnancy

**Chronic Hypertension:** Hypertension before 20 weeks gestation

**Preeclampsia:** Hypertension with proteinuria after 20 weeks gestation

**Gestational Hypertension:** Hypertension after 20 weeks gestation, without signs of preeclampsia (termed transient hypertension if BP normalizes postpartum)

**Superimposed Preeclampsia:**
- Preeclampsia in woman with pre-existing hypertension

### Risks of Hypertension in Pregnancy

- **Fetus/Neonate**
  - Intrauterine growth restriction
  - Small for gestational age infant
  - Prematurity (induced)

- **Mother**
  - Exacerbation of hypertension and risk of stroke, MI, renal failure
  - Superimposed preeclampsia

### Chronic Hypertension and Preeclampsia Rates

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>General population</td>
<td>4-5%</td>
</tr>
<tr>
<td>Preexisting hypertension</td>
<td>25%</td>
</tr>
<tr>
<td>&lt; 4 y duration</td>
<td>22%</td>
</tr>
<tr>
<td>≥ 4 y duration</td>
<td>31%</td>
</tr>
<tr>
<td>DBP &lt;100 mm Hg</td>
<td>24%</td>
</tr>
<tr>
<td>DBP 100-110 mm Hg</td>
<td>42%</td>
</tr>
</tbody>
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Based on BP at visit regardless of antihypertensive Rx

Adapted from Sibai Am Obstet Gyn 2002;100:369

### Preexisting Hypertension in Pregnancy

- Pregnancies do well unless superimposed preeclampsia develops
- Goal SBP < 150-160; DBP <100-110 mm Hg
- Antihypertensives generally can be tapered during pregnancy to lower fetal exposure

### Pharmacologic Treatment of Preexisting Hypertension in Pregnancy

- CEIs and ARBs prior to conception (CD)
  - Fetal anuria and oligohydramnios (2nd & 3rd trimester)
  - Neonatal renal failure (2nd & 3rd trimester)

- Methyldopa (B)
  - Recommended 1st line
  - National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy
  - Used since 1960s
  - Infant F/U up to 7.5 yrs (Cockburn J et al. Lancet 1982;1(8273):647)

### Alternatives to Methyldopa

- Beta-blockers (C)
  - Labetolol alternative first line
- Calcium channel blockers (C)
  - Only long acting ones
  - Attention with magnesium sulfate
- Diuretics (B)

### Summary: Chronic Hypertension and Pregnancy

- Importance of family planning with all women with hypertension
- Awareness re need to switch from certain antihypertensives prior to conception (ACEIs, ARBs)
- Knowledge that BP goals differ during pregnancy
- Awareness of hypertensive complications of pregnancy
Diabetes Mellitus

- Birth defect risk rises related to level of HbA1C at conception- as high as 20%
- Preconception glucose control can reduce birth defects to ~1% over general population

Prepregnancy Planning for Women with Diabetes

- Discuss family planning at least yearly and stress the importance of prepregnancy glucose control
- If HbA1C not in normal range, plan with patient 6 months to achieve glucose control prior to conception
- Counseling re risks
- Prepregnancy determination of retinopathy, nephropathy and other complications (i.e. gastroparesis)
- Adjustment of diabetes medications (including BP meds)

Optimal Diabetes Control for Conception

American Diabetes Association control goals:
- HbA1C < 7%
- Preprandial plasma blood glucose 80-110 mg/dl
- 2-hour postprandial plasma blood glucose < 155 mg/dl

Risks of Diabetes Mellitus in Pregnancy

- Fetus/Neonate
  - Birth defects
  - Macrosomia
  - Prematurity (induced)
  - Birth Trauma
  - Neonatal Hypoglycemia
- Mother
  - Progression of diabetic complications: retinopathy, nephropathy, preeclampsia
  - Increased chance for C-section

Management of Diabetes Mellitus Preconception and During Pregnancy

- Diet and home glucose monitoring remain the mainstay of management
- If on other agents, change to insulin- insulin remains the gold standard for treatment of diabetes during pregnancy
- Ongoing studies on use of oral agents for Type 2 DM but the jury is out.

Insulin in Management of Diabetes Mellitus Preconception and During Pregnancy

- Human insulin recommended
- Most experience with NPH and regular (Category B)
- Now increasing experience with shorter acting i.e. lispro and aspart (both Category B) and both are commonly used
- Use of glargine insulin controversial (Category C)
  - increased IGF-1-receptor affinity and mitogenic potency in human osteosarcoma cell-culture model
- Pumps can be used
Insulin during pregnancy

- Insulin resistance increases as pregnancy progresses
- Insulin requirements typically increase in pregnancy but may decrease just before delivery therefore doses needed to be adjusted throughout pregnancy

Gestational Diabetes Mellitus and the Primary Care Physician

- GDM: Diabetes first diagnosed in pregnancy after the 1st trimester, resolves with delivery
- Risk of future Type 2 DM as high as 60%
- ADA recommends regular screening of all women with a hx of GDM for Type 2 DM

Gestational diabetes and the incidence of type 2 diabetes

Summary: DM and Pregnancy

- Need for pregnancy planning to normalize HbA1c
- May need to switch medications (both glycemic and antihypertensive meds) before conception
- Insulin doses require adjustment throughout pregnancy
- Women with a history of GDM should receive regular screening for Type 2 DM

Thyroid Disease

- Hyperthyroidism
- Hypothyroidism

CLINICAL PRACTICE GUIDELINE
Management of Thyroid Dysfunction during Pregnancy and Postpartum: An Endocrine Society Clinical Practice Guideline

J Clin Endocrinol Metab 92: 2007

Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and Postpartum

Thyroid October 2013, 25(10):1083-1125
Hyperthyroidism: Diagnosis In Pregnancy

- Diagnosis often complicated by the changes in thyroid function that take place in normal pregnancy.
- Early pregnancy, rise in HCG (has thyroid stimulatory activity), leads to compensatory fall in TSH.
- TSH concentration is usually within the normal range; in some women falls into the suppressed range.

Hyperthyroidism: Diagnosis In Pregnancy

- Diagnosis of hyperthyroidism should not be based solely on a low TSH level but also on symptoms of hyperthyroidism and elevated T4.
- Symptoms: weight loss or absence of weight gain, anxiety, and palpitations.
- Exam: an enlarged thyroid (is not part of normal pregnancy)

Hyperthyroidism: Risks to Pregnancy

- Fetal/Infant
  - Intrauterine growth restriction (IUGR)
  - Small for gestational age (SGA) infant
- Maternal
  - Preterm Labor

Subclinical hyperthyroidism (TSH < 2.5th % for GA and fT4 < 1.75 ng/dl) is not associated with these risks

Casey et al Obstet Gyn 2006

Hyperthyroidism: Treatment In Pregnancy

- Do not treat based on lab numbers alone
- Treat for symptoms or pregnancy issues (i.e. IUGR)
- Antithyroid drugs can be used in pregnancy
- Use the lowest dose possible to achieve improvement in sx
- Goal is NOT to normalize TSH; aim for upper limit of normal total or freeT4
- Remember: the course of Graves' disease in pregnancy: exacerbation in the 1st trimester then improvement/remission in 3rd (can flare postpartum)

Antithyroid Drugs In Pregnancy

- PTU had been recommended as 1st line since no association with aplasia cutis
- Black box warning on PTU June 2009 updated April 2010 to use PTU (liver damage) only when other treatments not an option
- PTU in first trimester; after 1st trimester, use methimazole

Bahn RS, Burch HS, Cooper DS et al. Thyroid 2009; 19: 673-674.
Hypothyroidism: Diagnosis In Pregnancy

- Diagnosis made by elevated TSH
- Symptoms: weight gain, constipation (typical of normal pregnancy), cold intolerance (not typical of pregnancy).

Hypothyroidism: Risks to Pregnancy

- Fetal/Infant
  - Poor growth
  - Possible decrease in IQ
- Maternal
  - Increases risk for preeclampsia, placental abruption (preterm delivery)

Hypothyroidism: Treatment Prior to and During Pregnancy

- Aim for TSH <2.5 at conception
- Check TSH as soon as pregnancy test positive
- Requirement for thyroid hormone characteristically increases in pregnancy and returns to prepregnancy requirement postpartum
- Titrate thyroid hormone dose to maintain TSH <2.5 1st and 2nd trimesters, <3.5 3rd
- Reduce thyroid hormone dose to prepregnancy dose at delivery and check TSH at 6 wk pp visit

Summary Thyroid Disease and Pregnancy

- Goals for treatment differ than outside pregnancy
- Pregnancy may alter the course of the condition- ie Grave’s disease

Overall Summary

- Women with medical problems should receive regular family planning counseling
- Adjustment of medications is often necessary prior and during to pregnancy
- Goals for treatment of medical problems may differ during pregnancy

Question 1

You see a 34 yo women with Type 2 diabetes and hypertension who has recently stopped using contraception. She is taking glyburide and lisinopril. Her last HbA1c was 9%.

Your recommendations include all of the following except:
1. Aim for HbA1c<7%.
2. D/C lisinopril and substitute labetolol before she tries to become pregnant
3. D/C lisinopril and substitute an angiotensin 2 receptor blocker (ARB) to help protect her kidneys during pregnancy
4. Eye exam for retinopathy assessment
Question 2

A 24 yo women with Graves disease is on methimazole 10 mg/dy and is in her 3rd trimester of pregnancy. She feels well with good weight gain. BP 100/60 P 100. Her TSH returns <0.01. You should

1) Increase her methimazole
2) Decrease her methimazole
3) Order a T4
4) Add a B-blocker for tachycardia

FDA Classification System for Drugs in Pregnancy

- A – Adequate and well-controlled studies have failed to show a risk to the fetus in the 1st trimester and there is no evidence for risk in the latter trimesters
- B – Animal reproduction studies have failed to show a risk to the fetus and there are no adequate and well-controlled studies in humans
- C – Animal reproduction studies have shown adverse effect on the fetus and there are no adequate and well-controlled studies in humans but potential benefits may outweigh risk
- D – Evidence of adverse human fetal risk but potential benefits may outweigh risk


General References
