Objectives

1. Understand the relationship between type 1 diabetes and female reproduction
2. Identify diabetes goals during pre-conception
3. Discuss management options for diabetes during pregnancy
4. Discuss postpartum care of patients with gestational diabetes
5. Gain an understanding of the relationship between diabetes and menopause

Type 1 Diabetes and Female Reproduction

- Up to 40% of females with type 1 diabetes will display irregularity in reproduction at a certain moment of their life
  - Menstrual disturbances
  - Hyperandrogenism
  - Early menopause

How does it happen?

- Neuroendocrine regulation of the Hypothalamic-Pituitary-Gonadal axis
Puberty and Type 1 Diabetes

- In the 1940s and 1950s, menarche occurred 2 years later in girls with DM1
- In the 1970s and 1980s, menarche occurred 1 year later in girls with DM1
- In the 1990s, menarche was delayed only mildly ~2-9 months
  - Coincides with advent of intensive insulin therapy

Adolescence and Type 1 Diabetes

- Excessive weight gain
- Deteriorating metabolic control
- Menstrual irregularities
- Unplanned pregnancies
- Appearance of microvascular complications

Metabolic control is the most important determinant of menstrual irregularities in adolescents with DM1

Young adult women and Type 1 Diabetes

- ~20-40% of adult women with DM1 have menstrual irregularities
- Glycemic control in the peri-menstrual period varies
  - 40-70% of pts may have hyperglycemia in the pre-menstrual and menstrual periods
  - Pathophysiology:
    - Diminished insulin sensitivity – from changes in estrogen and progesterone levels
    - Excessive craving for sweets as part of premenstrual syndrome
    - Some pts might have hypoglycemia during menses

Young adult women and Type 1 Diabetes

- Ovulation is usually preserved in DM1, particularly in those with optimal metabolic control
- BUT most studies have found fewer pregnancies and fewer live births in women with DM1
  - Due to diabetes-related complications/co-morbidities
  - Voluntary choice
PCOS and Hyperandrogenism in Type 1 Diabetes

- Pathophysiology:
  - Intensive conventional insulin therapy
  - Insulin resistance from glucose toxicity
  - Hyperinsulimic state → stimulates ovarian receptors → Hyperandrogenism
  - Consider screening for PCOS when a pt presents with menstrual irregularities

Premenopause and Menopause in Type 1 Diabetes

- 2 studies have looked at the age of menopause in DM1
  - one study found the age of menopause to be 8-10 years earlier than normal pts
  - another study found no difference in age of menopause
  - Main risk factors for earlier menopause:
    - Severe microvascular complications
    - ESRD
    - Proliferative retinopathy
  - Early menopause
    - † From decreased ovarian reserve
    - † Autoimmune oophoritis

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Pregestational Diabetes

- Pre-conception counseling is important!
  - Family planning and effective contraception should be prescribed until pt is ready to conceive
  - A1c goal of <6.5% to reduce the risk of congenital anomalies
  - Congenital anomalies seen with uncontrolled DM during the 1st 10 weeks of pregnancy:
    - Anencephaly
    - Microcephaly
    - Congenital heart disease
    - Caudal regression

Pregestational Diabetes

- Adverse outcomes associated with DM during pregnancy:
  - Pre-eclampsia
  - Hydramnios
  - Macrosomia and large for gestational age infant
  - Fetal organomegaly (hepatomegaly, cardiomegaly)
  - Maternal and infant birth trauma
  - Operative delivery
  - Perinatal mortality
  - Neonatal respiratory problems and metabolic complications
Pregestational Diabetes

- Review med list for potentially teratogenic medications
  - ACE-I/ARBs
  - Statins
- Counseling on risk of progression or development of DM retinopathy
- Eye exams before pregnancy or in 1st trimester and then once every trimester as indicated by the degree of retinopathy

Gestational Diabetes Mellitus

- When to screen?
  - Screen high-risk women at the first prenatal visit
    - BMI >30 kg/m²
    - Prior h/o GDM or pre-diabetes
    - PCOS
  - Universal screening at 24-28 weeks AOG

Gestational Diabetes – Making the Diagnosis

<table>
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<tr>
<th>Approach</th>
<th>Criteria</th>
<th>Fasting mg/dL</th>
<th>1H postprandial mg/dL</th>
<th>2H postprandial mg/dL</th>
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<td>75-gm (2-hr)</td>
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<td>75-gm (1-hr)</td>
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<td>NDDG</td>
<td>&lt; 100</td>
<td>140-190</td>
<td>150-190</td>
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</table>

These thresholds are for diagnosis of gestational diabetes. Diagnosis of overt diabetes and diabetes in pregnancy are based on different criteria (e.g., NDDG): fasting plasma glucose (120 mg/dL, 20 minutes) or 2-hour plasma glucose (200 mg/dL, 75 minutes) in accordance with current guidelines. NDDG: two-hour glucose (130 mg/dL, 120 minutes) following a 75-gm oral glucose load is consistent with diabetes in pregnancy.

Gestational Diabetes – Glucose Goals

- Targets:
  - Fasting ≤ 90 mg/dL
  - 1H postprandial ≤ 130-140 mg/dL
  - 2H postprandial ≤ 120 mg/dL

- A1c targets
  - 1st trimester: <6% - <7%
  - 2nd-3rd trimesters: 6-6.5% but <6% may be optimal as pregnancy progresses

- Hypoglycemia
  - Increases risk of low birth weight

Less stringent goals may be appropriate for those with frequent hypoglycemia
Gestational Diabetes – Oral Agents

- **Glyburide**
  - Usually effective as monotherapy
  - Increases neonatal hypoglycemia
  - Increases macrosomia
  - Use was deemphasized in 2016 guidelines compared to previous years

- **Metformin**
  - Lower risk of hypoglycemia
  - May lower weight gain
  - May be used if it is adequate to attain glycemic goals
  - Not usually effective as monotherapy
  - May slightly increase risk of prematurity
  - Metformin and glyburide (pregnancy category B)
  - Both cross placenta
  - Long-term safety data are not available

Gestational Diabetes – Insulin

- **Preferred agent for pregestational**
  - Type 1 and type 2 not adequately controlled with diet, exercise, and metformin

- **Metformin**
  - All insulins are category B except for glargine, glulisine, and degludec
  - Starting dose: 0.7-2 units/kg current pregnant weight

Gestational Diabetes – Labor and Delivery

- **1st trimester**
  - Characterized by insulin sensitivity and lower insulin requirements
  - Risk of hypoglycemia, especially in type 1 pts

- **2nd trimester**
  - Rapidly increasing insulin resistance
  - Weekly or biweekly insulin adjustments

- **Late 3rd trimester**
  - Leveling off or small decrease in insulin requirements

Gestational Diabetes – Postpartum Care

- **Insulin requirements drop dramatically postpartum**
  - DM Type 1 – typically go back to pre-pregnancy doses
  - Pre-existing DM Type 2 – insulin, metformin, glyburide enter breastmilk in small amounts and are unlikely to cause hypoglycemia in infant
  - GDM – typically will not need medications post partum

- **Breastfeeding**
  - May decrease long-term risk of developing DM2

- **Screen for postpartum depression**
  - More common than in non-diabetics

- **Contraception counseling**
Women with GDM are at high risk for:
- Recurrent GDM (1/3 to 2/3)
- Prediabetes (20% of women)
- Overt type 2 diabetes (19% in 9 years)
- Type 1 diabetes
- Cardiovascular disease

Women with GDM need 75g OGTT at 6-12 weeks postpartum.
- A1c is not recommended due to increased red cell turnover from pregnancy or blood loss at delivery.
- Repeat testing every 1-3 years with any of:
  - A1c
  - Fasting glucose
  - 75g OGTT

Estrogen and progesterone affect insulin sensitivity:
- Higher estrogen = better insulin sensitivity
- Higher progesterone = more insulin resistance

Perimenopausal period is characterized by flux in estrogen and progesterone levels → unstable glucose.
- Weight can increase with menopause → higher insulin requirements or need for more oral meds
- Those with pre-diabetes might worsen to overt DM2

Hot flashes and night sweats
- Might be mistaken for symptoms of hypoglycemia
- Always check glucose to differentiate between the two
- Can cause insomnia - leads to stress which can worsen diabetes control

References:
- www.UpToDate.com
Questions?

Thank you.

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