The Infant of the Diabetic Mother
Maternal Diabetes

- Harmful effects on the fetus recognized over 100 years ago
- GDM----3 to 10 %
- IDM --0.1 to 0.3 %
Introduction

- Discovery of insulin
- Understanding of pathophysiology of diabetes
- Improved preconception counseling

<table>
<thead>
<tr>
<th></th>
<th>1964</th>
<th>1984</th>
</tr>
</thead>
<tbody>
<tr>
<td>maternal mortality</td>
<td>50%</td>
<td>9%</td>
</tr>
<tr>
<td>fetal mortality</td>
<td>21%</td>
<td>2%</td>
</tr>
</tbody>
</table>
Introduction

- ↓ morbidity not as striking
- 4 to 5 fold decrease morbidity
  - fetal growth and birth trauma
  - intrauterine and perinatal asphyxia
  - polycythemia
  - hyperbilirubinemia
  - cardiomyopathy
  - postnatal metabolic disturbances
What is the etiology of congenital malformations associated with diabetes?
Congenital Malformations

- Overall incidence---5 to 9%
  - 2-3 fold higher than general population
  - Predominantly with IDM
- Malformations of CNS seen most often
- Diversity-No malformation considered pathognomonic
Congenital Malformations

- No increase in major congenital malformations among of
  - Diabetic fathers
  - Prediabetic women
  - GDM after first trimester
Suggests that glycemic control during embryogenesis is the main factor in the origin of malformations
Incidence of major malformations among women without preconception counseling

<table>
<thead>
<tr>
<th>SOURCE</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993 Willhoite</td>
<td>8/123</td>
<td>6.4</td>
</tr>
<tr>
<td>1991 Kitzmiller</td>
<td>12/110</td>
<td>10.9</td>
</tr>
<tr>
<td>1991 Greene</td>
<td>23/432</td>
<td>7.4</td>
</tr>
<tr>
<td>1984 Ballard</td>
<td>19/196</td>
<td>9.7</td>
</tr>
<tr>
<td>1983 Simpson</td>
<td>11/142</td>
<td>7.7</td>
</tr>
<tr>
<td>1978 Kitzmiller</td>
<td>13/137</td>
<td>9.5</td>
</tr>
<tr>
<td>1977 Gabbe</td>
<td>19/260</td>
<td>7.3</td>
</tr>
</tbody>
</table>
Congenital Malformations

Impact of Pre-conception Counseling

- Kitzmiller (1991)
  - Pre-conception counseling: 1.2%
  - Referred at 6-30 weeks EGA: 10.9%

- Willhoite (1993)
  - Pre-conception counseling: 1.6%
  - No pre-conception counseling: 6.5%
Congenital Malformations

• Freinkel 1980

Fuel Mediated Teratogenesis--exposure of the embryo to an abnormal metabolic environment during the initial stages of embryogenesis results in abnormal development of the embryo.
Congenital Malformations

- Hyperglycemia
- Hyperketonemia
- Oxygen-Free Radicals
Hyperglycemia

Specific ultrastructural changes

- Decreased embryo size
- Yolk sac malformations
  - sparse, patchy, non-uniform capillaries
  - abnormal transport of nutrients
Hyperglycemia

Other consequences:
- Arachadonic acid deficiency
- Accumulation of sorbitol
- Deficiency of myo-inositol associated with CNS malformations
Hyperketonemia

- $\beta$-hydroxybutyrate
  - Dose related
  - Time-of-exposure related
  - Synergism with glucose
    - minimally teratogenic doses of both metabolites

- Long-term neurodevelopmental abnormalities
Fetal Hyperglycemia

- 1-2 hours of fetal hyperglycemia can have detrimental effects
- ↑ insulin secretion
  - Storage of excess nutrients → macrosomia
  - Post natal hypoglycemia
Fetal Hyperglycemia

- Drives catabolism of the oversupply of nutrients
  - depletes fetal O2 stores → episodic fetal hypoxia
    - hypertension, cardiac remodeling and hypertrophy

- ↑ erythropoiesis → polycythemia
  - poor circulation and hyperbilirubinemia
Oxygen-Free Radicals

- Result of glucose metabolism
- Increased lipid peroxidation
  - direct effect on DNA
  - imbalance between prostaglandins and prostacyclins
Congenital Malformations: The Laundry List
Congenital Malformations

Skeletal/CNS

- Caudal regression syndrome
  not considered pathognomonic
  occurs 600x more frequently among IDM

- Neural tube defects

- Microcephaly
Caudal Regression Syndrome

- **Spectrum of malformation**
  - cessation of growth of rostral portion of spinal cord
  - abnormal neural, muscular, skeletal and vascular components

*Caudal Regression* with limbs intact but malformed

*Sirenomelia*
Absence of hind limbs, external genitalia, anus and rectum; Potter sequence secondary renal agenesis
Congenital Malformations

Cardiac

- Transposition + VSD
- Ventricular septal defect
- Coarctation + VSD or PDA
- Atrial septal defect
- Hypertrophic Cardiomyopathy
Congenital Malformations

Renal

- Hydronephrosis
- Renal agenesis
- Ureteral duplication
Congenital Malformations

**GI**
- Duodenal atresia
- Anorectal atresia
- Small left colon syndrome
Mrs. J is 32 YO, G1P0 who is currently in labor and has been pushing for two hours. You are called to the delivery secondary to fetal distress. While waiting in the DR you learn that the prenatal tests were unremarkable except for glucose testing that led to the dx of GDM. Maternal glucose control was poor during the past few weeks with average glucoses > 120 and insulin was rx.
Delivery of the body is delayed secondary to shoulder dystocia. Your initial assessment of the infant includes poor resp effort, cyanosis, and HR 80. After the initial steps of resuscitation including 45 sec. of FM PPV the infant responds and is transferred to the baby suite for further evaluation.
Which baby is the infant of the diabetic mother?

A

B
What perinatal and neonatal complications should you anticipate?
Perinatal and Neonatal Complications

- Disorders of fetal growth
- Intrauterine and perinatal asphyxia
- Hypoglycemia
- Respiratory distress syndrome
Perinatal and Neonatal Complications

- Hypertrophic Cardiomyopathy
- Polycythemia
- Hyperbilirubinemia
- Hypocalcemia
Disorders of Fetal Growth
Macrosomia

- Birth Weight > 4000 g or > 90th %-ile
- Increased rate of C-section
- Birth Trauma
  - shoulder and body dystocia
  - brachial plexus injury
  - facial nerve injury
  - asphyxia
  - abdominal trauma
Macrosomia

- Insulin and insulin-like growth factors
  - Primary growth factors for the fetus
  - Abnormal adipose deposition
  - Visceral organ hypertrophy and hyperplasia
  - Acceleration of skeletal growth

- Increased levels of lipids, ketones, and amino acids also stimulate insulin secretion
Intrauterine Growth Restriction

- Incidence reported as high as 20 %
- **Contributing factors:**
  - Maternal vascular disease
  - Hypertension
  - Intrauterine infection
  - Chromosomomal abnormalities
Intrauterine Growth Restriction

- Oligohydramnios
- Hypoxia
- Fetal distress
- Asphyxia
- Intrauterine and neonatal death
Birth Asphyxia

● Incidence
  - 20 TO 30%

● Primary Risk factors:
  - Prematurity
  - Fetal growth disorders
  - Maternal vascular disease
  - Peripartum maternal hyperglycemia
    - Drives catabolism of the oversupply of nutrients
      - depletes fetal O2 stores → episodic fetal hypoxia
Hypoglycemia

- Risk Factors
  - Prematurity
  - Birth asphyxia
  - Cesarean section
  - Disorders of fetal growth
  - Stimulation of the fetal pancreas
    - Pedersen Hypothesis
Respiratory Distress Syndrome

- **Risk:**
  - 3 to 5 times the risk in the non-diabetic population

- **Contributing Factors:**
  - Prematurity
  - Maternal glycemic control
Hypertrophic Cardiomyopathy

- IDDM and GDM with poor glycemic control
- Incidence 20 to 30%
- Manifestation of generalized organomegally
- ↑ catecholamines
  - hypertension, cardiac remodeling and hypertrophy
Hypertrophic Cardiomyopathy

- LV and RV hypertrophy
- Asymmetric ventricular septal hypertrophy
- Valves and great vessels normal
Polycythemia

- Respiratory distress
- Cardiac failure
- Decreased renal function
- Renal vein thrombosis
- Necrotizing enterocolitis

- CNS damage
- Hypoglycemia
- Hypocalcemia
- Hypomagnesemia
- Hyperbilirubinemia
Hyperbilirubinemia

- Prematurity
- Polycythemia
- Birth trauma
  - Injuries to abdominal viscera
  - Cephalhematoma
  - Bruising
Summary

- Diabetes in pregnancy poses significant risk to both mother and fetus
- Overpowering effects that extend from the time of conception through postnatal development
Summary

- Biochemical basis for teratogenicity
- Disorders of growth and metabolism lead to considerable morbidity and mortality
- Role of the obstetrician
  - significantly reduce morbidity and mortality
    - preconception counseling
    - attention to maternal glucose control
Role of the Pediatrician

- Understand the fetal metabolic consequences of maternal diabetes
- Anticipate and treat complications
“A man with a watch knows what time it is. A man with two watches is never sure.”

Thank you for your attention. I hope it was interesting. Please give your feedback, you may not write your name.