

# Diabetes in Pregnancy

BERRY CAMPBELL, M.D.  
University of South Carolina  
School of Medicine  
Division of Maternal Fetal Medicine

## GESTATIONAL DIABETES: DIAGNOSIS AND MANAGEMENT

### LEARNING OBJECTIVES:

- To identify risk factors for gestational diabetes.
- To discuss methods of screening and diagnosis of gestational diabetes.
- To discuss the complications of gestational diabetes and pregestational DM.
- To discuss the management of diabetes in pregnancy.

## GESTATIONAL DIABETES

“ Any degree of glucose intolerance with onset or first recognition during pregnancy...”

*Fourth International Workshop-Conference on GDM 1997*

## GESTATIONAL DIABETES MELLITUS

Type II DM (Adult onset DM)

- Long associated with poor obstetrical history, i.e. large babies, stillbirth.
- Gestational DM considered since 1965.

## *Glucose Intolerance in Pregnancy*

- 15 % Abnormal 1 hour screen
- 15% Abnormal 3 hour OGTT
- 15 % Fail diet therapy

## GESTATIONAL DIABETES MELLITUS CLASSIFICATION

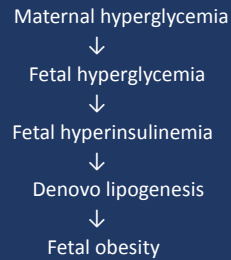
### • White's Classification

Class A1: diet controlled, blood sugar normal  
Class A2: insulin required to normalize blood sugar

## GDM-WHY DO WE CARE?

- Increased risk for fetal macrosomia (16-45% of GDM fetuses)
- Fetal macrosomia associated with risk of:
  - Maternal trauma at delivery and c-section
  - Neonatal birth injuries
  - Neonatal metabolic changes
  - Childhood obesity
  - DM, questionable decreased IQ
- Insulin requirement in 15% with ↑ PNM risk

## Macrosomia *Pathophysiology*



## Gestational Diabetes Mellitus *Significance*

- ↑ **Long Term Morbidity**
- Childhood obesity
  - Type 2 Diabetes

## Gestational Diabetes Mellitus *Significance*

- ↑ **Subsequent Glucose Intolerance**
- Up to 50-70% develop Type 2 diabetes mellitus

## Diabetes Mellitus

### Fetal Complications

## Macrosomia

- >4,000 - 4,500 gm
- 50% of GDM
- 40% of pre-gestational DM
  - fetal hyperglycemia results in excessive fetal growth
- increased risk of birth trauma, fetal loss, childhood/life-long obesity, development of Type 2 diabetes

## Shoulder Dystocia

- Brachial plexus injury
  - Erb's palsy: upper arm paralysis (C5,6)
  - Klumpke: lower arm paralysis (C8,T1)
- Fractured clavicle
- Fractured humerus
- Fetal hypoxemia
- Know maneuvers to treat shoulder dystocia

## Respiratory Distress Syndrome

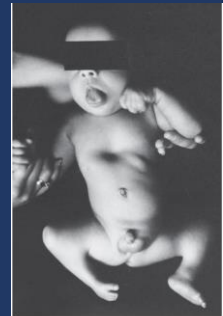
- Exact mechanism unknown
- Decreased with improved control
- Rare after 39 weeks

## Congenital Malformations: Pregestational DM

- Insult that causes malformations generally prior to 7 weeks
- A1C < 8.5%--3.4% major anomalies; ≥ 8.5—22.4% major anomalies (Miller et al)
- CNS malformations: 10-fold increase
  - Anencephaly, ONTD, Holoprosencephaly
- Cardiac anomalies: 5-fold increase
  - VSD, Transposition of the Great Vessels

## Congenital Malformations

- Sacral agenesis or caudal dysplasia
  - 200 – 400 x more common



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## Congenital Malformations: Pregestational DM

- Teratogenic factors
  - Maternal hyperglycemia
  - Ketone excess
  - Excess free oxygen radicals
- Typical patient profile
  - Poor periconceptional control
  - Long-standing diabetes
  - Vascular disease

## Intrauterine Growth Restriction: DM

- Vascular disease causing decreased uterine blood flow
- Pre-eclampsia/CHTN
- Pregestational DM
- Not usually found in GDM

## Fetal Death: DM

- More common after 36 weeks with
  - Vascular disease
  - Poor glycemic control
  - Polyhydramnios
  - Fetal macrosomia
  - Pre-eclampsia

## Neonatal Complications-DM

- Hypoglycemia
  - Maternal/fetal hyperglycemia
  - 50% of macrosomic babies
- Hypocalcemia
  - Failure of PTH production at birth
- Magnesium deficiency
- Hyperbilirubinemia
  - 25-50% have neonatal jaundice
- Polycythemia
  - Increased erythropoietin

## Maternal Complications-DM

- Spontaneous abortion
- Pre-eclampsia
- Cesarean section
- Birth trauma
- DKA
- Hypoglycemic coma
- Infections (UTI, pyelo)
- Postpartum hemorrhage

## Screening for Diabetes Mellitus

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## Glucose Metabolism

- Human placental lactogen (HPL)
  - Produced by the placenta
  - Promotes lipolysis
  - Decreased glucose uptake
    - "anti-insulin"
  - Peaks 24 – 28 weeks

## Testing for Gestational DM

### Screening Test

1 hour glucose challenge

### Diagnostic Tests

3 hour 100g glucose tolerance test

2 hour 75g GTT

## Glucose Challenge Test

**Performed at 24-28 weeks**  
**Oral glucose load = 50 grams**  
**Normal < 140 mg %**

## Oral Glucose Challenge

- 140 mg% ~ 90% sensitivity, 15% positive
- 130 mg% ~ 100% sensitivity, 23% positive

## Oral Glucose Challenge *Fasting or Fed*

- **No difference in normals**
- **GDM, higher if fasting ( $173.9 \pm 28.8$ ) vs. post-meal ( $154.8 \pm 24.1$ )**
- **Consider lowering cutoff to 130 mg % if fed**

Coustan et al, 1986

## High Risk for GDM (early testing): >25 BMI + one or more--

- Physical inactivity
- 1<sup>st</sup> degree relative with DM
- HR race/ethnicity (AA, Asian, Latino, native American)
- Prior baby >4000g
- Prior GDM
- HTN
- PCOS
- A1C > 5.6
- CV disease; low HDL; high TG
- BMI > 40 alone

• \*\*\*repeat 24-28 weeks if normal\*\*\*

ACOG # 180, 2017

## Early Screening Tests

**1 hr 50 g GTT/3 hr 100g GTT**  
**Positive screen, neg 3 hr—**  
**repeat 3 hr at 24-28**  
**Hb A1C-poor sensitivity**

## 3 hour GTT

Group	Fasting	1hr	2hr	3hr
NDDG	105	190	165	145
Carpenter	95	180	155	140

**\*\*no data to suggest which is superior\*\***

## Management

- **Dietary**
- **Glucose monitoring**
- **Medical therapy**
- **Fetal assessment**
- **Labor & Delivery**
- **Postpartum**

## DIETARY MANAGEMENT

- Enables normalization of glycemia in 80-90% of GDM patients [Class A1]
- Meal plans and caloric requirements individualized based on weight and height -1800-2400 kcal/day [30-35 kcal/kg/day]
- Usually 3 main meals and 2 to 3 snacks
- 35-40% CHO, 20% protein and 40% fat
- Refer diabetic education

## DIET MANAGEMENT

- Diet achieves euglycemia in most patients.
- "Low CHO" diet [35-40%] is most beneficial.
- Diet should be individualized according to each patient's response to food ingestion.
- Caloric restriction may be option in motivated patient ie: 1800 cal/day.

## CARBOHYDRATE RESTRICTION

- RCT N=21 per group
- low CHO < 42%  
high CHO > 45%
- low CHO group had
  - lower post-prandial BS
  - lower insulin requirement
  - lower LGA and C/s

## EXERCISE EFFECTS

- Reduces insulin requirements by up to 50%
- Increases insulin sensitivity in Type 2 DM
- Acutely lowers glucose levels, particularly post-breakfast.
- Exact mechanism is unknown
- 30 minutes 5 days weekly aerobic exercise (ACOG, 2017)

Mullford et al, Clin Perinatal, 20 (3):619, 1997

## Glucose Monitoring

- **Home monitoring**  
**Fasting, 1-2 hour post-prandial daily**
- **Intermittent weekly monitoring**  
**Fasting, one post prandial weekly**
- **A1C each trimester (pre-gestational DM)**

## TARGET PLASMA GLUCOSE PREGNANCY

<b>FASTING</b>	<b>&lt; 95 MG %</b>
<b>1 HOUR POST-MEAL</b>	<b>&lt; 140 MG %</b>
<b>2 HOUR POST-MEAL</b>	<b>&lt; 120 MG %</b>

## Why Check Post-Prandial Values?

- Post-prandial BS become abnormal before fasting and pre-meal BS
- Several authors have correlated post-prandial hyperglycemia in GDMs with macrosomia
- Postprandial-SBGM leads to better glycemic control through more aggressive management → less macrosomia & CS

## THRESHOLDS FOR STARTING INSULIN

- Failure to achieve euglycemia
  - FBS > 95 mg/dl
  - 2 hr post-prandial > 120 ; 1 hr >140  
[10-15% values elevated]
- Evidence of developing macrosomia by U/S screening at 29-33 weeks gestation.

## Insulin Types

	<b>Onset</b>	<b>Duration</b>	<b>Peak</b>
Regular	1 hour	6 hours	2-3 hours
NPH	2 hours	24 hours	8 hours
Log	1-10 min	4-5 hours	1-2 hours
Levemir	1-3 hours	18-26 hrs	Min at 8-10 hr
Lantus	1-2 hours	24 hours	none

## INSULIN LISPRO [Humalog]

- A newer insulin analogue, rDNA
- More rapid onset than Regular, more convenient
- Peaks at 1 hour vs. 2 hours with Regular
- Shorter duration of action
- May benefit GDMs by specifically reducing post-prandial hyperglycemia

## INSULIN DOSING

**0.5-1.0 UNITS/KG divided doses**  
(0.5 < 20 weeks; 1.0 > 20 weeks)

**20 N/10 LOG AM; 10 LOG SUPPER; 10 N**  
**@HS**

**Target elevated BS**

## Insulin Therapy

AM 2/3	PM 1/3
↓	↓
NPH /Reg or Humalog	R or H / NPH
2/3 1/3	1/2 1/2

## Glucose Control and Fetal Size

N=246

- Mean glucose > 105 mg %, 24% LGA
- Mean glucose < 105 mg %, 9% LGA

Langer and Mazze, AJOG, 1988;159

## Antepartum Assessment

Serial growth every 4 weeks.  
 No antenatal testing for A1 well controlled.  
 BPP or NSTs for A2 well controlled weekly starting at 32 weeks  
**BPP and/or NSTs twice weekly poorly controlled, vascular disease, etc.**

## Delivery

- Gestational, pregestational well controlled: 39-40 week delivery
- Poorly controlled gestational or pregestational: individualize-late preterm vs early term (34w-36w6d; 37w0d-38w6d)

## Gestational Diabetes

*Mode of Delivery*

- Vaginal preferred
- Cesarean considered if Efw > 4500 grams
- Individualize each case

## Labor Management

- Blood glucose every 1-2 hours
- BS > 120 mg %, consider insulin drip vs slide scale with log
- Maintain glucose < 120 mg %
- IV Fluid D5 0.45% NS at 125 cc/hour



## Glucoregulation during L&D

- Usual dose of PM insulin
- Hold AM insulin, patient is NPO
- If C-section, schedule first case
- If laboring, check every 1 (IDDM)-2 (GDM) hours and maintain glucose 70 – 120 mg/dl
- May need insulin drip to control
- Slide scale SQ is also acceptable

## Slide Scale Insulin (log)

### • Low dose SQ

- 121-149 1 unit
- 150-199 2 units
- 200-249 3 units
- 250-299 4 units
- ≥ 300 Call

### • High dose SQ

- 121-149 3 units
- 150-199 6 units
- 200-249 9 units
- 250-299 12 units
- ≥ 300 Call

## METFORMIN

- Biguanide
- Inhibits liver gluconeogenesis, absorption of glc and stimulates glc uptake in peripheral tissues
- Crosses placenta near maternal levels
- GI upset/diarrhea
- Similar outcomes as insulin
- BUT--- slight increase PTB but lower GHTN (vs insulin)
- 25-45% fail and require insulin

## Metformin

- Used in pregestational DM and may be continued in pregnancy
- Frequently used in PCOS patients to improve ovulation and decrease insulin resistance
- Often continued in pregnancy to decrease spontaneous abortion in the first trimester
- Some recommend continued use throughout to reduce the risk of GDM
- Can be used for treatment of GDM

## Metformin

- Start 500mg qHS
- Increase up to 3000mg / day divided
- INSULIN IS 1<sup>ST</sup> LINE THERAPY (ACOG, 2017)

## Glyburide

- Oral hypoglycemic – 2<sup>nd</sup> Generation Sulfonylurea
- Outpatient management
- Check LFT's
- Same diet and therapeutic goals
- Starting dose: 2.5 mg daily
- Maximum dose: 20 mg daily – divided
- Better side effect panel than metformin
- Better patient acceptance
- Associated with larger birthweights; more failures

## Glyburide

- Sulfonylurea-avoid with sulfa allergy
- Increases insulin secretion from beta cells
- Increases peripheral tissue insulin sensitivity

## Insulin Therapy

- Insulin is initiated when therapeutic goals are exceeded with diet/exercise/oral agent
  - Usually started inpatient; outpatient reasonable with reliable, educated patient
  - Divided AM and PM dosing
  - Mixture of short- and long-acting insulin to achieve therapeutic goals
  - May target dosing for specific elevations
- FIRST LINE THERAPY FOR MEDICAL MANAGEMENT

## Pregestational Diabetes

- Ideally done preconception, but usually done in the first trimester
  - Folic acid supplementation
  - HgbA1C
  - 24 hour urine – protein and creatinine cl
  - Renal function
  - Eye exam
  - EKG if vascular disease or CHTN
  - Nutrition consult
  - ASA low dose

## Pregestational Diabetes

- Early ultrasound for accurate dating
- Offer prenatal diagnosis (1<sup>st</sup> and 2<sup>nd</sup> tri)
- Anatomy survey at 18 – 20 weeks
- Fetal echo at 22 weeks

## Postpartum Management

- Pregestational diabetics: resume insulin at 50% of the prepregnancy dose and adjust as needed
- GDM resolves following delivery
- GDM check BS while pp in hospital
- Diabetes screening 6 – 12 weeks following delivery
- Increased lifetime risk of Type 2 Diabetes (~50%)

## Insulin Drip

**50 units regular/500 cc NS**

**10 cc/hr equals 1 unit/hour**

## General pregnancy issues

- AMA: NST/BPP from 36 weeks
- BMI>35: serial growth every 6 weeks, testing from 36 weeks
- Hyperthyroid: growth, testing as with CHTN. Serial growth only with hypothyroid (no testing)

- 25 yo G1 at 36w 4d (Thursday)
- A1C 7.3 second trimester, 8.3 at 34 weeks
- US at 32 weeks normal fluid, EFW 50%tile
- Repeat US poly at 38cm, EFW 98%tile (9#12)
- BPP, NST normal
  
- Plan?