

Pregnancy and Diabetes

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Session objectives

- Recognize the screening criteria and available testing for gestational diabetes
- Discuss the management of gestational diabetes during pregnancy and postpartum period
- Explain preconception care in patients with diabetes
- Describe the management of type 2 and type 1 diabetes in pregnancy

Case 1

- A 32-year-old lady presents in her 3rd month of pregnancy
- She had 2 previous pregnancies with no complications
- Family history is noncontributory
- Physical examination: only remarkable for a BMI of 28
- **Should she be screened for gestational diabetes ?**
- **If yes, why? how? when?**

Gestational Diabetes Mellitus (GDM) screening

Who to screen?

How to screen?

When to screen?

The guidelines

American Diabetes Association
Diabetes Care 2022;45 (suppl 1):S17

Endocrine Society
J Clin Endocrinol Metab 2013;98:4227

International Association of Diabetes and
Pregnancy Study Group
Diabetes Care 2010;33:676

**GDM:
Who to screen?**

Everybody

GDM: when to screen?

24-28 weeks gestation

GDM: How to screen?

There are 2 approaches:

1) One step approach

OR

2) Two step approach

1-step approach to screen for GDM

- Recommended by International Association of Diabetes and Pregnancy Study Group, American Diabetes Association & Endocrine Society
- Using the 75-gram oral glucose tolerance test
- Plasma glucose: fasting, 1,2 hours

75-gram OGTT

[0, 1, 2 hours]

Criteria for GDM

- ◆ Fasting : ≥ 92 mg (5.1 mmol)
- ◆ 1 hour : ≥ 180 mg (10 mmol)
- ◆ 2 hour : ≥ 153 mg (8.5 mmol)

GDM = any of the above

2-step approach to screen for GDM

- Recommended by the American College of Obstetrics & Gynecology
- Start with the 50-gram glucose loading test
 - No need for fasting
 - Plasma glucose after 1 hour
 - Abnormal if glucose ≥ 140 mg (7.8 mmol) [some use 130 mg (7.2 mmol)]
- If abnormal, do the 100-gram OGTT (0, 1, 2, 3 hours)

100-gram OGTT

[0, 1, 2,3 hours]

Criteria for GDM

- ◆ Fasting : ≥ 95 mg (5.1 mmol)
- ◆ 1 hour : ≥ 180 mg (10 mmol)
- ◆ 2 hour : ≥ 155 mg (8.6 mmol)
- ◆ 3 hour : ≥ 140 mg (7.8 mmol)

GDM = 2 of the above

Which approach to use?

- **1-step approach:**

- Recommended by the International Association of Diabetes and Pregnancy Study Group, American Diabetes Association & Endocrine Society
- Concern about “over-diagnosis”
- Increasingly adopted in many centers

Which approach to use?

- **2-step approach:**

- Recommended by American College of Obstetrics & Gynecology
- No need for fasting for 50-gram loading test
- Evidence that treatment using 100-g test values has benefit
- But, have to do the 100-g test if 50-g test is abnormal (2 tests)

Screening for GDM : professional guidelines

- **American Diabetes Association (ADA):**
 - The 1-step approach is associated with improved pregnancy outcomes
 - The 1-step approach is recommended
- **Endocrine Society:**
 - Recommends the 1-step approach
- **American College of Obstetrics & Gynecology (ACOG)**
 - Recommends the 2-step approach

American Diabetes Association. Diabetes Care 2022;45 (suppl 1):S17

American College of Obstetrics & Gynecology. Obstet Gynecol 2017; 130:e17

Endocrine Society. J Clin Endocrinol Metab 2013;98:4227

Screening for type 2 DM in pregnancy

ADA recommends screening

all women

for DM before 15th week of gestation

Screening for type 2 DM in pregnancy

Endocrine Society recommends
screening **all** women
for diabetes
before 13th week of gestation
Or ASAP thereafter

Case 2

- A 29-year-old lady presents in her 7th month of pregnancy
- This is her first pregnancy
- A 75-gram oral glucose tolerance test done yesterday revealed gestational diabetes
- She has no complaints
- Physical examination is unremarkable
- **How to approach?**

GDM: effects on the mother

- Preeclampsia
- Need for cesarean section
- Long term:
 - GDM in future pregnancies
 - Type 2 DM

GDM: effects on the fetus

- Macrosomia
- Birth trauma
- Shoulder dystocia
- Neonatal hypoglycemia and hyperbilirubinemia
- Long term: obesity, type 2 DM

Benefits of treatment of GDM

- U.S. Preventive Services Task Force and National Institutes of Health
- Systematic review and meta-analysis showed:
 - ↓ Risk of preeclampsia
 - ↓ Risk of macrosomia
 - ↓ Risk of shoulder dystocia

Management of GDM

- Lifestyle modifications including:
 - Nutritional therapy
 - Physical activity
 - Weight management
- Monitor home glucose:
 - Before meals & postprandial
- A trial for **1-2 weeks**

GDM: Dietary intervention

- The optimum dietary plan is not known
- Reduced carbohydrate intake (to 35-45%) of total calories is recommended, distributed in 3 small- to moderate-sized meals & 2 to 4 snacks
- The food plan should provide adequate calorie intake to promote fetal and maternal health, achieve glycemic goals, and promote weight gain according to Institute of Medicine recommendations (next slide)

Weight gain during pregnancy

Prepregnancy BMI	<u>Rates of weight gain in 2nd & 3rd trimesters</u>	
	Range, kg/week	Range, lb/week
Underweight (<18)	0.44-0.58	1-3
Normal weight (18.5-24.9)	0.35-0.5	0.8-1
Overweight (25-29.9)	0.23-0.33	0.5-0.7
Obesity (≥ 30)	0.17-0.27	0.4-0.6

GDM: the role of exercise

- A program of moderate exercise is recommended if no medical or obstetrical contraindications
- Exercise led to improvement in glucose and reductions in need to start insulin or insulin dose
- Aim for 30 minutes of moderate-intensity aerobic exercise at least 5 days a week or a minimum of 150 minutes per week
- Simple exercise such as walking for 10–15 minutes after each meal can lead to improved glycemic control

Glucose targets in GDM

- **Capillary glucose of:**

- Fasting <95 mg (5.3 mmol)

and either

- One-hour postprandial <140 mg (7.8 mmol)

or

- Two-hour postprandial <120 mg (6.7 mmol)

**For postmeal monitoring:
when does the timing start?**

From the start of the meal

When to start medications in GDM?

- Start medications if >20 % of home glucose values are above target after lifestyle modifications
- 70-85% of women achieve control with lifestyle modifications alone (western studies)

Metformin

- Less hypoglycemia compared to insulin
- Less maternal weight gain compared to insulin
- Less effective compared to insulin (25-45% were uncontrolled)
- Possibly associated with prematurity
- Intrauterine growth restriction and higher BMI in childhood
- Crosses placenta (umbilical cord levels as or higher than maternal levels)
- Not approved by US-FDA for GDM

American Diabetes Association. Diabetes Care 2022;45 (suppl 1):S232

JA, et al. BMJ Open Diabetes Res Care 2018;6:e000456

Balsells M, et al. BMJ 2015;350:h102; Jiang Y-F, et al. J Clin Endocrinol Metab 2015;100:2071

Glyburide (Glibenclamide)

- Effective (only 5-15% required addition of insulin)
- ↑ risk of macrosomia, neonatal hypoglycemia and increased neonatal abdominal circumference compared to insulin or metformin
- Crosses placenta
- No long-term safety data
- Not approved by US-FDA for GDM

American Diabetes Association. Diabetes Care 2022;45 (suppl 1):S232

Balsells M, et al. BMJ 2015;350:h102; Castillo W, et al. JAMA Pediatr 2015;169:452

Jiang Y-F, et al. J Clin Endocrinol Metab 2015;100:2071

Guidelines on the use of medications for GDM

- ADA & ACOG recommend insulin as first line
- Metformin may be considered for:
 - Patients who cannot use insulin due to cost, language barriers or comprehension
 - Patients who refuse insulin
 - Patients who are unable to use insulin safely or effectively
- Since Metformin can cause growth retardation/acidosis it should not be used in women with hypertension, preeclampsia, or at risk for intrauterine growth restriction

Insulin in GDM

◆ Meal insulin:

- Regular insulin: FDA-approved (category B)
- Rapid-acting: Lispro & Aspart: FDA-approved (category B)
- No difference in outcomes using regular or above rapid insulins
- Endocrine society recommends rapid-acting insulin over regular insulin
- Glulisine: not FDA-approved (category C)

Insulin in GDM

◆ Basal insulin:

- NPH & Detemir: FDA-approved (category B)
- Detemir led to less hypoglycemia compared to NPH
- NPH costs less than Detemir
- Glargine: not FDA-approved (category C)
- Glargine appears to be safe (uncontrolled studies)

Choice of insulin regimen in GDM

- The choice depends on home glucose values
- If only postprandial glucose is high, use only meal insulin
- If only fasting glucose is high, use basal insulin
- If both fasting and postprandial glucose are high, use both basal & meal insulin
- Adjust insulin regimen and doses accordingly

Case 3

- A 33-year-old lady with history of gestational diabetes that was managed with insulin
- She had an uneventful vaginal delivery
- She is to be discharged from the hospital
- She has no complaints
- Fasting capillary glucose is normal
- **How would you approach?**
- **What is the future plan?**

GDM: care after delivery

- Stop glucose-lowering medications immediately after delivery
- Monitor glucose 1-3 days after delivery to rule out
- Counseling on lifestyle measures to reduce the risk of type 2 diabetes, the need for future pregnancies to be planned and the need for regular diabetes screening, especially before any future pregnancies

Breastfeeding

- Breastfeeding decreased the incidence of maternal diabetes among women with a history of GDM
- Breastfeeding is recommended for women with history of GDM

American Diabetes Association. Diabetes Care 2022;45 (suppl 1):S232

Endocrine Society guidelines. J Clin Endocrinol Metab 2013;98:4227

Gunderson EP, et al. Ann Intern Med 2015; 163:889.

Ziegler AG, et al. Diabetes 2012; 61:3167.

Screening for diabetes after GDM

75-gram OGTT

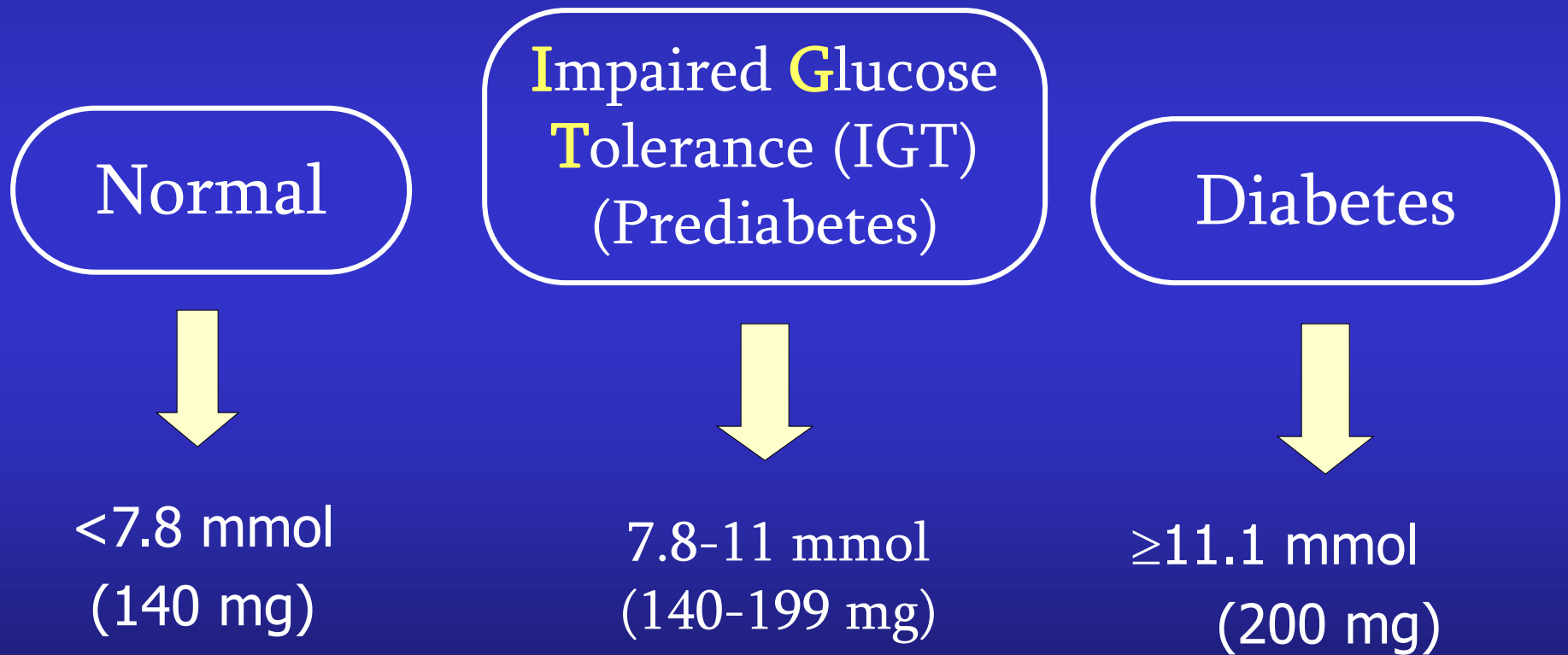
- To be done 4-12 weeks after delivery
- Fasting and 2-hour plasma glucose
- A1c is not recommended

Fasting plasma glucose

- **Normal:**
 - <5.6 mmol (100 mg)
- **Diabetes:**
 - ≥ 7 mmol (126 mg)
- **Impaired fasting glucose (IFG) [Prediabetes]:**
 - 5.6 to 6.9 mmol (100-125 mg)

75-gram OGTT

2-hour plasma glucose interpretation



GDM: long term f/u

- Future risk of type 2 DM: 50-60%
- Lifelong screening for the development of diabetes or prediabetes **every 1-3 years** using fasting glucose, A1c or 75-gram OGTT
- Lifestyle changes (healthy weight, physical activity)
- Women found to have prediabetes should receive intensive lifestyle interventions and/or Metformin to prevent diabetes

Case 4

- A 33-year-old lady with type 2 DM and hypertension for 3 years
- On Metformin, Sitagliptin, Enalapril, Simvastatin
- BP is controlled
- A1c 6.7, kidney function is normal
- **She is asking for an advice for contraception**
- **What is the plan if she is planning for pregnancy?**

Diabetes before pregnancy: Preconception counseling

- Should be part of diabetes care for women during reproductive age
- Family planning and effective contraception should be used until treatment regimen and glucose control are optimized for pregnancy
- Any form of contraception is acceptable (not different from persons who do not have DM)

Preconception care: glycemic targets

- ◆ Preprandial glucose: <95 mg (5.3 mmol)
- ◆ Postprandial glucose:
 - 1-hour <120 mg (6.7 mmol)
 - or
 - 2-hour <140 mg (7.8 mmol)
- ◆ A1c <6.5%

Preconception care: glucose-lowering drugs

- Stop non-insulin glucose-lowering medications (not well studied)
- Switch to insulin (Basal + Meal)
- Regular, Aspart, Lispro, NPH, Detemir can be used
- Endocrine Society recommends rapid-acting insulin over regular insulin

Preconception care: screening for complications

- **Dilated eye examination:**
 - Before pregnancy or in first trimester
 - In every trimester
 - For 1 year postpartum as recommended by the eye care provider
- **Kidney function:**
 - Serum creatinine, eGFR, UACR

Preconception care: Folic acid

- Start 3 months before stopping contraception
- Dose:
 - Endocrine Society: 5 mg daily
 - ADA: at least 400 micrograms daily

Preconception care: Managing comorbidities

- **Hypertension:**

- Target B.P. <130/80
- Stop ACEI & ARB
- Can use: Methyldopa, Labetalol, Hydralazine, Clonidine,
Long-acting Nifedipine, Diltiazem

- **Lipid-lowering agents:**

- Stop statins & fibrates

Case 5

- A 35-year-old lady with type 2 DM is on Metformin, Glyburide and Sitagliptin
- She has no reported diabetes complications
- She missed her last menstrual period by 2 weeks
- A pregnancy test done yesterday was positive
- Physical examination is normal
- A1c 6.8%, kidney and liver function tests are normal
- **How would you approach?**

Management of type 2 diabetes in pregnancy

- Stop non-insulin glucose-lowering medications (not well studied, not FDA-approved, lack of safety data)
- Follow up with educator and dietitian
- Recommended weight gain:
 - For overweight women: 6.8-11.3 kg (15-25 lb)
 - For obese women: 4.5-9 kg (10-20 lb)
 - No data on optimal weight gain versus weight maintenance in women with BMI >35

Glucose management of type 2 diabetes in pregnancy

- Initial insulin dose: 0.5-0.7 units/kg/day
- Insulin requirement increases as pregnancy advances
- Basal + meal regimen is recommended
- Regular, Aspart, Lispro, NPH, Detemir can be used
- Endocrine society: **“Glargine may be continued in pregnancy”**

Type 1 diabetes in pregnancy

- Enhanced insulin sensitivity occurs in early pregnancy and leads to lower insulin requirements and higher risk of hypoglycemia
- Around 16 weeks, insulin resistance increases and total daily insulin doses will need to be increased as pregnancy advances
- Insulin requirement increases significantly (can reach doubling of pre-pregnancy insulin doses by 3rd trimester)

Glucose targets for DM 1 & DM 2 in pregnancy

- Preprandial glucose: <95 mg (5.3 mmol)
- Postprandial glucose:
 - 1-hour : <140 mg (7.8 mmol)
 - or** 2-hour: <120 mg (6.7 mmol)
- HbA1c:
 - < 6% if it can an be achieved without significant hypoglycemia
 - Can be relaxed to <7% if necessary to avoid hypoglycemia

Management of type 1 diabetes in pregnancy

- Continuous glucose monitoring (CGM) can be used with blood glucose monitoring
- The following targets are recommended:
 - Target range 63-140 mg (3.5-7.8 mmol): TIR, goal >70%
 - Time above range [>140 mg (10 mmol)], goal <25%
 - Time below range [<63 mg (3.5 mmol)], goal <4%
 - Time below range [<54 mg (3.5 mmol)], goal <1%

Diabetes in pregnancy: screening for complications

- **Dilated eye examination:**
 - In first trimester
 - Then in every trimester
 - For 1 year postpartum as recommended by the eye care provider
- **Kidney function (serum creatinine, UACR, eGFR)**

Diabetes: post-delivery care

- Monitor glucose
- Insulin requirements decrease (reduce dose initially by ~ 25%)
then adjust according to home glucose monitoring
- Encourage breastfeeding
- Medications during breastfeeding:
 - Insulin is safe
 - Endocrine society: “Metformin & Glyburide can be used”
 - But both are not approved by the FDA

Summary: key points

- Universal screening for GDM, at 24-28 weeks gestation
- Most centers use 1 step 75-g OGTT (0, 1, 2 hours)
- If GDM is uncontrolled on lifestyle changes, use insulin
- Preconception care for DM is important
- Diabetes in pregnancy: insulin, eye and kidney care