Preexisting Diabetes

Type 1 diabetes mellitus (T1DM): caused by lack of insulin production by pancreas due to autoimmune causes; patients must take insulin daily; diagnosis during pregnancy unlikely

Type 2 diabetes mellitus (T2DM): caused by combination of insulin resistance and inability of pancreas to increase insulin production and release; patients who present with elevated blood glucose in early pregnancy may have preexisting T2DM (test pregnant women believed at high risk); testing — fasting blood glucose (FBG) ≥126 mg/dL; hemoglobin A1c (HbA1c) ≥6.5%; random blood glucose >200 mg/dL (T2DM likely, but confirmed with one of other tests); 

Risks to infant: congenital malformations — rate 7% to 10% in infants of diabetic mothers; risk increases with poor diabetic control during first 10 wk of pregnancy; risk ≈20% if HbA1c 8% to 10%; American Diabetes Association recommends delaying conception until HbA1c <7%; fetal hyperglycemia — fetus produces insulin in response to hyperglycemia; fetal insulin acts as growth hormone, and fetus may become macromacronic (>4 kg); above 90th percentile for gestational age [GA]); good glycemic control in mother can reduce risk for macrosomia; stillbirth — reassure patient that risk decreases considerably with good glycemic control and fetal evaluation; prematurity — infants at greater risk for complications of prematurity

Risks to mother: some evidence of transient worsening of vascular disease; worsening of diabetic nephropathy — increased proteinuria; lack of normal increase in creatinine clearance during pregnancy; diabetic retinopathy — some studies show greater likelihood of progression of retinopathy during pregnancy; preeclampsia — important to evaluate proteinuria during first half of pregnancy

Weight control: weight reduction for obese women recommended prior to becoming pregnant; obesity associated with increased risk for congenital malformations and other pregnancy complications

Contraception: recommended for diabetic patients not contemplating pregnancy, and patients with less than optimal diabetic control

Preconception visit: evaluate for vascular disease (electrocardiography appropriate in patients at risk for heart disease; echocardiography may be useful); refer to ophthalmologist for retinal examination (dilation of pupils not contraindicated during pregnancy); perform 24-hr urine collection (useful as baseline for proteinuria); evaluate thyroid function; evaluate list of medications (discontinue potentially teratogenic angiotensin-converting enzyme inhibitors and angiotensin receptor blockers); prescribe multivitamins with folate (≥400 μg/day) to lower risk for neural tube defects

Early pregnancy evaluation: ultrasonography (US) important for assessment of GA; team approach (with, eg, patient, nurse educators, dietitians, social workers) important; switch to insulin if patient taking oral agents

Screening: first trimester — patients should be counseled about screening for trisomies and neural tube defects; second trimester — continue screening for trisomies and neural tube defects; perform level 2 US to evaluate fetal anatomy; risk for birth defects (eg, renal, cardiac, skeletal) higher in diabetic pregnancies; perform fetal echocardiography to screen for congenital heart defects

Glycemic management: registered dietitian can make recommendations about carbohydrate and protein intake and weight goals; artificial sweeteners pose no increased risk to fetus; goals — FBG <95 mg/dL; 1-hr postprandial glucose <140 mg/dL; 2-hr postprandial glucose <120 mg/dL; patients with T2DM become more insulin resistant as pregnancy progresses (dose of insulin may need to be increased); patients with T1DM more prone to hypoglycemia (adjust insulin dose carefully)

Metformin: effective; does not cause significant weight gain or hypoglycemia; spontaneous abortion — case series suggest reduction of risk in patients with polycystic ovary (PCO); many endocrinologists recommend continuing metformin throughout first trimester or entire pregnancy; randomized placebo-controlled trials from Italy suggest increased risk for spontaneous abortions (but metformin discontinued as soon as pregnancy diagnosed); another large randomized trial compared metformin to clomiphene, and did not see reduced risk with metformin; treatment during pregnancy — randomized trial did not show prevention of gestational diabetes in patients with PCO or insulin resistance syndrome; speaker suggests no benefit of continuing metformin after conception; in patients with preexisting diabetes, unlikely that metformin sufficient to control blood sugar; randomized trial suggested that metformin equally as effective as insulin in gestational diabetes (insulin added to metformin in nearly 50% of patients); placental transfer — study saw that metformin concentrated on fetal side of placenta, and fetal levels higher than maternal levels; no adverse effects on fetus shown; no long-term studies; counsel patients and document

Glyburide: sulfonylurea; stimulates pancreas to produce and release more insulin; randomized trial compared glyburide to insulin in patients with gestational diabetes, and results similar in terms of adverse outcomes (eg, macrosomia, cesarean delivery, neonatal hypoglycemia); placental transfer — glyburide

Educational Objectives

The goal of this program is to improve management of diabetes and gestational diabetes in pregnant women. After hearing and assimilating this program, the clinician will be better able to:

1. Describe maternal and fetal risks associated with diabetes.
2. Review effects of oral agents used for glycemic control.
3. Counsel patients about reducing risk for maternal and perinatal complications.
4. Identify and treat gestational diabetes.
5. Discuss antepartum fetal testing in patients with well-controlled gestational diabetes.

Faculty Disclosure

In adherence to ACCME Standards for Commercial Support, Audio-Digest requires all faculty and members of the planning committee to disclose relevant financial relationships within the past 12 months that might create any personal conflicts of interest. Any identified conflicts were resolved to ensure that this educational activity promotes quality in health care and not a proprietary business or commercial interest. For this program, Dr. Coston and the planning committee reported nothing to disclose.
did not appear in cord blood; subsequent studies demonstrate that glyburide levels in cord blood at time of delivery ≥70% of maternal levels (mother not in therapeutic range); no adverse effects demonstrated; placental transfer raises concerns; counsel patients and document

**Insulin:** treatment of choice for pregnant diabetic patients; does not appear to cross placenta; current insulins do not seem to evoke antibody response; regular insulin or crystalline zinc insulin — onset of action 30 to 60 min after injection; peak onset at 2 to 4 hr; duration 6 to 8 hr; regular insulin used 20 to 30 min before breakfast; often combined with neutral protamine Hagedorn (NPH) insulin (intermediate-acting insulin; onset 1-3 hr; peak at 6 hr; duration 12-18 hr); split-mix regimen for insulin — combination of regular and NPH insulin at breakfast to cover breakfast and lunch; combination of regular insulin and NPH at dinner to cover through next morning (can use NPH insulin at bedtime if insulin wears off during night)

**Insulin analogues:** insulin lispro and insulin aspart — formulated for rapid absorption; onset of action within 15 min after injection; peak onset at 1 to 2 hr; duration 4 hr; convenient and more flexible for use by patients; demonstrated not to appear in cord blood of exposed neonates; insulin glargine and insulin detemir (Levemir) — long-acting; no peak; duration 24 hr; insulin glargine shown not to cross placenta; insulin detemir more widely studied, and shows outcomes similar to those of NPH insulin (control of FBG slightly better with insulin detemir); insulin detemir moved from category C to B (no data about appearance in cord blood; unclear whether placental transfer occurs); speaker continues long-acting insulins in patients who become pregnant during use; but does not start long-acting insulins during pregnancy; if NPH insulin not sufficient, add insulin glargine

**Self-monitoring of blood glucose:** check FBG and 2-hr postprandial glucose levels; FBG goal <95 mg/dL; 2-hr postprandial glucose goal <120 mg/dL; many patients check 1-hr postprandial glucose (<140 mg/dL or <130 mg/dL goal); no good evidence about whether checking 1-hr or 2-hr postprandial glucose level superior; studies show that postprandial glucose levels more predictive of adverse fetal outcomes than preprandial testing

**Insulin use:** patients with T1DM usually on much lower doses than patients with T2DM; as pregnancy progresses, some patients (particularly obese patients) with T2DM may need more than patients with T1DM; high fetal mortality rate; evaluate risk for maternal death; managing patients with T1DM usually on much lower doses than patients with T2DM; patients should visit ophthalmologist at least once every trimester; during pregnancy, renal plasma flow increases markedly in gastrointestinal tract with increased nausea and vomiting; metoclopramide useful; coronary artery disease — evaluate patients; diabetic women with history of myocardial infarction within 6 mo to 1 yr of becoming pregnant at increased risk for maternal death; diabetic ketoacidosis (DKA) — particularly in women with T1DM; high fetal mortality rate; evaluate and treat; if abnormal fetal heart rate tracings detected, do not perform immediate cesarean delivery (surgery during DKA risky; correcting DKA can correct nonreassuring fetal tracing); give adequate fluids

**Perinatal complications:** congenital malformations; perinatal mortality; prevention of stillbirth predicated on antepartum fetal testing and good metabolic control of diabetes; antepartum fetal testing recommended by American Congress of Obstetricians and Gynecologists (ACOG) between 32 and 34 wk GA in most patients (testing earlier [eg, 26-28 wk GA] may be important in patients with vascular disease, growth restriction, and other complications); shoulder dystocia more likely in infants of diabetic mothers than nondiabetic mothers; no good evidence that early delivery effective in preventing macrosomia; neonatal hypoglycemia, hyperbilirubinemia, plethora, and hypocalcemia more common in infants of diabetic mothers

**Management during third trimester:** in mother notes decreased fetal movement, then perform evaluation; umbilical Doppler US shown helpful only in intranatal growth restriction; monitoring fetal growth with US — useful; in patients with preexisting diabetes, monitor every 3 to 4 wk beginning at 26 wk GA; if estimated fetal weight ≥4500 g, recommend cesarean delivery without trial of labor; if estimated fetal weight 4000 to 4500 g, individualize management based on patient’s history, glucose control, morphology of fetus, and labor progression; avoid operative delivery (associated with shoulder dystocia)

**Management during labor:** avoid neonatal hypoglycemia; maintain maternal blood glucose (70-120 mg/dL); labor induction — start early in morning; patient should take normal insulin dose night before, and not take any insulin on morning of induction; start intravenous (IV) line with constant infusion of 5% dextrose in 50% normal saline; monitor blood glucose every hour; if glucose increases, add insulin (infuse 1.00-1.25 units/hr; can be titrated up or down, based on blood glucose level); takes 4 to 6 hr to reach steady state with constant insulin infusion; planned cesarean delivery — start early in morning; if patient in good control and FBG normal, then maintain blood glucose during procedure; after birth of infant, IV glucose acceptable; rapid infusion of IV glucose before delivery can cause fetal acidemia

**Management after delivery:** patient should no longer receive high doses of insulin; if glycemic control prior to pregnancy good, resume prepregnancy regimen (if glycemic control previously poor, titrate insulin dose [50% of dose often suggested]); breast-feeding — should be encouraged; some evidence (contraversial) that breast-feeding infants at lower risk for diabetes; family planning — avoid estrogen-containing contraception in women with vascular disease

**Gestational Diabetes**

**Background:** gestational diabetes defined as glucose intolerance of varying severity first diagnosed or recognized during pregnancy; O’Sullivan criteria — recommended by ACOG; FBG, 1-hr 100-g oral glucose tolerance test (OGTT), 2-hr 100-g OGTT, or 3-hr 100-g OGTT (any 2 elevated values diagnose gestational diabetes); using plasma or serum results in glucose values ≥14% higher than those of whole blood; earlier method of glucose analysis detected other reducing substances that resulted in glucose values ≥5 mg higher than those of current methodology (enzymes specific for glucose)

**Interpretations of O’Sullivan criteria:** National Diabetes Data Group (NDGG) increased rounded-off O’Sullivan numbers by 15%; Carpenter and Coustan criteria lowered O’Sullivan numbers by 5 mg to correct for methodology, and then raised them by 14% to correct for use of plasma; ACOG recommends either interpretation; study showed that NDGG criteria above 95% confidence limits, whereas Carpenter and Coustan numbers within 95% confidence intervals; Hyperglycemia and Adverse Pregnancy Outcome study — showed that relationship between 75-g OGTT and adverse outcomes (eg, macrosomia, high cord C-peptide level, cesarean delivery,
neonatal hypoglycemia, overweight infants, preeclampsia, shoulder dystocia, birth injury); 2013 consensus conference at National Institutes of Health recommended 50-g 1-hr OGTT (elevated value indicates 3- to 100-g OGTT); ACOG currently recommends 2-step approach

**Treatment:** self-monitoring of glucose; FBG <95 mg/dL; 1-hr postprandial glucose <130 mg/dL or <140 mg/dL; 2-hr postprandial glucose <120 mg/dL; if one-third of values above criteria during period of 1 wk, or one-third of values at any one time of day, then start or increase insulin; most patients with mild gestational diabetes can be managed with diet alone; *oral agents* — agents that cross placenta may affect fetus and neonate (no harm demonstrated); insulin usually used when needed

Antepartum fetal testing: according to ACOG, no consensus on benefit of antepartum fetal testing in patients with well-controlled gestational diabetes; at speaker’s center, patients with well-controlled gestational diabetes who require insulin undergo antepartum testing twice weekly starting between 34 and 36 GA, depending on other factors; in patients well-controlled with diet, starting weekly testing at 36 GA reasonable

Delivery decisions: *route of delivery* — similar to patients with preexisting diabetes; make decision with patient; *timing* — with potential for various medical complications between 34 and 39 wk GA, individualize based on level of control and other factors

Postpartum management: obtain OGTT at 6 to 8 wk to determine whether patient had preexisting diabetes or prediabetes; test patients with previous gestational diabetes or high risk for diabetes at least every 3 yr; diabetes can be diagnosed if FBG ≥126 mg/dL or 2-hr 75-g OGTT ≥200 mg/dL; *prediabetes* — impaired fasting glucose (100-125 mg/dL); impaired glucose tolerance (2-hr value 140-199 mg/dL); counsel about lifestyle modifications; test annually

Other ways to diagnose diabetes and prediabetes: HbA1c 5.7% to 6.4%; FBG; OGTT more sensitive (2-hr 75-g OGTT ideal)

Family planning: all forms acceptable; some data suggest that Hispanic women with previous gestational diabetes who breast-feed may have higher likelihood of T2DM when taking progesterin-only oral contraceptives

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Dr. Coustan’s lecture is from Audio-Digest Obstetrics and Gynecology Board Review Course, a comprehensive review with approximately 60 hours of lectures presented by faculty from a variety of prominent teaching institutions across the country. For more information, please visit www.audiodigest.org. The Audio-Digest Foundation thanks Dr. Coustan for his cooperation in the production of this program.

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**Suggested Reading**


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**Estimated time to complete the educational process:**

- **Review Educational Objectives on page 1:** 5 minutes
- **Take pretest:** 10 minutes
- **Listen to audio program:** 60 minutes
- **Review written summary and suggested readings:** 35 minutes
- **Take posttest:** 10 minutes
1. The American Diabetes Association recommends that women with diabetes delay conception until their hemoglobin A\textsubscript{1c} is:
   (A) <8.0%  (B) <7.5%  (C) <7.0%  (D) <6.5%

2. Dilation of pupils is contraindicated in diabetic women who are pregnant.
   (A) True  (B) False

3. Metformin is known to cause which of the following conditions?
   (A) Significant weight gain  (B) Significant hypoglycemia  (C) Spontaneous abortions  (D) None of the above

4. Which of the following statements is true about glyburide?
   (A) Stimulates pancreas to produce and release more insulin
   (B) Associated with higher risk for adverse outcomes than insulin in patients with gestational diabetes
   (C) Contraindicated in pregnant women
   (D) Has never been shown to appear in cord blood

5. Which of the following insulins has the longest duration of action?
   (A) Crystalline zinc insulin  (B) Insulin lispro  (C) Insulin aspart  (D) Insulin glargine

6. Choose the correct statement about hypoglycemia.
   (A) Usually occurs in patients with gestational diabetes
   (B) Commonly seen in patients with type 2 diabetes mellitus (T2DM)
   (C) Snacks comprised of a mix of protein and carbohydrate recommended

7. Which of the following should be avoided when treating diabetic women for hypertension?
   (A) β-blockers  (B) Angiotensin receptor blockers  (C) Calcium channel blockers  (D) Methyldopa

8. Most patients with mild gestational diabetes can be managed with diet alone.
   (A) True  (B) False

9. According to the American Congress of Obstetricians and Gynecologists, which of the following is correct about antepartum fetal testing?
   (A) No consensus on benefit in patients with well-controlled gestational diabetes
   (B) Should be performed twice weekly starting at 32 wk gestational age (GA) in all patients with gestational diabetes
   (C) Should be performed weekly starting at 36 wk in all patients with well-controlled gestational diabetes
   (D) Should be performed weekly starting at 32 wk GA in all patients

10. Some data suggest that Hispanic women with previous gestational diabetes who are breast-feeding may have a higher likelihood of T2DM when taking:
    (A) Calcium channel blockers  (B) β-blockers  (C) Progestin-only contraceptives  (D) Estrogen-containing contraceptives

Answers to Audio-Digest Family Practice Volume 62, Issue 28: 1-C, 2-A, 3-B, 4-B, 5-D, 6-D, 7-C, 8-A, 9-A, 10-A