This program is supported by an educational grant from Novo Nordisk Inc. It has been approved by the American Association of Diabetes Educators (AADE) for pharmacists, nurses, and dietitians.

*Diabetes & Pregnancy: A Management Guide* provides information on preconception care, treatment, and follow-up for women with type 1 or type 2 diabetes prior to pregnancy and for those who develop gestational diabetes during pregnancy.
The following program is a taped presentation by Carol Homko.

Dr. Homko is a nurse and certified diabetes educator, with almost 30 years of experience in diabetes education and management. She established the Diabetes and Pregnancy Program at Temple University Hospital in 1991 and continues to maintain an active clinical practice there. At the present time, Dr. Homko has a dual appointment as Assistant Research Professor in the Departments of Medicine and Obstetrics and Gynecology at the Temple University School of Medicine.

For the past fifteen years, her primary research has focused on GDM and pregnancies complicated by pre-existing diabetes. She has published widely in peer-reviewed journals and has authored multiple chapters on the management of pregnancies complicated by diabetes including AADE’s Core Curriculum for Diabetes Education (4th edition). Dr. Homko lectures frequently to local, national, and international audiences of health professionals. She is actively involved with the American Diabetes Association and the American Association of Diabetes Educators at both the local and national levels. Dr. Homko is current out-going chair of the Pregnancy/Reproductive Health AADE Specialty Practice Group.
The goal of this program is to provide information and guidance on the management of diabetes (both preexisting and gestational) before, during, and after pregnancy.

At the end of this program, the participant will be able to:

State the prevalence of preexisting and gestational diabetes mellitus (GDM) among pregnant women

Explain the purpose of preconception care in women with diabetes

Describe changes in metabolism during pregnancy

Define recommended screening and diagnosis guidelines for GDM

State goals common to the management of both preexisting diabetes and GDM during pregnancy

Identify differences in the management of preexisting diabetes and GDM in pregnancy

Identify potential fetal complications associated with preexisting diabetes and GDM
In general, 3 types of diabetes may complicate pregnancy; type 1, type 2, and gestational diabetes.

Type 1 diabetes is characterized by autoimmune destruction of β-cells resulting in virtually absolute insulin deficiency.

Type 2 diabetes is a heterogeneous metabolic disorder involving dual defects in insulin action and insulin secretion.

Gestational diabetes is defined as carbohydrate intolerance of varying degrees with onset or first recognition during pregnancy. This definition includes women who may have had undiagnosed type 2 diabetes prior to pregnancy but who are first diagnosed during pregnancy. Of the women diagnosed with GDM, 40% to 60% will develop type 2 diabetes later in life.

Pregnant women with diabetes have a significantly increased risk of both maternal and fetal morbidity and mortality if blood glucose levels are not well controlled. Therefore, the goal of therapy is to maintain euglycemia throughout gestation to minimize adverse pregnancy outcomes.

During pregnancy, maternal hypertension, dyslipidemia, and other comorbidities should also be managed.
Diabetes is the most prevalent chronic disease in pregnancy.

Preexisting type 1 or type 2 diabetes mellitus (DM) is estimated to complicate 2% to 5% of pregnancies in the United States.

Infant mortality rates due to complications from type 1 diabetes have decreased dramatically, from 25% in the 1960s to 2% since the 1980s and into the present. However, major congenital malformations remain the leading cause of mortality and morbidity in the offspring of mothers with diabetes. Congenital anomalies are associated with elevated blood glucose levels during the periconceptual period.

Moderate elevations in glycosylated hemoglobin (A1C) (7.0%–9.0%) are associated with a 2% to 5% risk of giving birth to a child with a major malformation whereas marked elevations in A1C (>10.0%–14.0%) increase that risk to between 20% and 40%.

Unplanned pregnancies still occur in about two thirds of women with preexisting diabetes, therefore, the American Diabetes Association (ADA) recommends counseling for all women of childbearing age.

GDM complicates 7% of all pregnancies in the United States, resulting in more than 200,000 cases annually. The prevalence of GDM may range from 1% to 14% of all pregnancies, depending on the population studied and the diagnostic tests employed. Macrosomia of the newborn is the most common complication, resulting in increased rates of surgical delivery.
Optimal metabolic control before and during pregnancy is essential for a successful outcome and to minimize the risk of fetal malformations and neonatal complications.

Advances in biochemical and electronic monitoring techniques have markedly improved maternal and fetal care and well-being in pregnancies complicated by diabetes. The reduction in fetal mortality is due in part to modern methods of fetal monitoring, introduction of neonatal intensive care units, and improved control of diabetes because of intensified insulin therapy protocols.

A team approach to care that reinforces the importance of planning future pregnancies, encourages optimal blood glucose control before and during pregnancy, manages other comorbidities such as hypertension and dyslipidemia, promotes healthy lifestyle behavior changes, and includes the patient in all aspects of care is more likely to achieve desired results and favorable outcomes for both mothers and their children.

Team members may include the following: the patient, primary care physician or endocrinologist, obstetrician/gynecologist knowledgeable about diabetes and pregnancy, registered nurse, registered dietitian, pharmacist specializing in diabetes, and social worker.
Preconception planning is required for all women with preexisting type 1 or type 2 diabetes. The woman’s health status should be evaluated, and the potential complications discussed prior to pregnancy.

Pregnancy is not recommended when certain conditions such as ischemic heart disease are present. Both the ADA and AADE recommend discussion of risks with the patient prior to conception. Some diabetes-related complications such as retinopathy and nephropathy can worsen during pregnancy. Women with diabetes require counseling regarding the effects of pregnancy on microvascular complications as well as the effects of these complications on pregnancy outcomes. The importance of achieving euglycemia prior to and early in pregnancy should be stressed to minimize complications.

Patients with type 2 diabetes should transition from oral glucose-lowering agents to insulin prior to conception. Hypertension should be treated with medications not known to be teratogenic—angiotensin-converting enzyme (ACE) inhibitors are associated with neonatal renal failure and should be discontinued as soon as pregnancy is detected.

During pregnancy, management focuses on maintaining maternal euglycemia to maximize chances for a positive outcome. Management includes blood glucose monitoring, nutrition and weight management, insulin therapy, and fetal monitoring. Maternal surveillance is also required to monitor for potential complications such as hypertension and preeclampsia.

During labor and delivery, the goals are to provide adequate carbohydrate intake to meet energy requirements and maintain maternal euglycemia.

Postpartum, the woman’s glucose control should be followed closely to reestablish her insulin requirements.
Gestational diabetes care includes risk assessment, screening and diagnosis, as well as follow-up care.

Women who have had a previous pregnancy complicated by GDM require preconception planning for future pregnancies. A preconception glucose check is recommended for women with a history of GDM.

The ADA recommends that risk assessment for GDM be undertaken at the first prenatal visit and that women with high risk factors undergo glucose testing as soon as possible. Risk factors include the following: marked obesity, history of GDM, strong family history of diabetes, glycosuria, and membership in an ethnic group with high prevalence of type 2 diabetes.

It is recommended that women at average risk for GDM and women who have not been identified as having abnormal glucose tolerance prior to week 24 of gestation undergo a screening test for GDM between weeks 24 and 28 gestation.

The goals of management of GDM are to normalize metabolism and achieve euglycemia to improve pregnancy outcomes. These are achieved by monitoring of blood glucose, medical nutrition therapy (MNT), insulin therapy if needed, and close maternal and fetal monitoring.

In the postpartum period, the patient should be retested for glucose tolerance and counseled regarding lifestyle interventions to prevent and/or delay the development of diabetes. Even if there is normal glucose tolerance postpartum, women with previous GDM should be tested annually for diabetes.
Check Point

Infant mortality rates due to diabetes have declined since the 1960s in part because:

a) the prevalence of type 2 diabetes has declined.
b) the majority of pregnancies among diabetic women are now planned.
c) the risk of major congenital anomalies for an infant born to a diabetic mother is now the same as for an infant born to a nondiabetic mother.
d) better metabolic control during pregnancy has led to improved outcomes.

Infant mortality rates due to diabetes have declined since the 1960s in part because:

a) the prevalence of type 2 diabetes has declined.
b) the majority of pregnancies among diabetic women are now planned.
c) the risk of major congenital anomalies for an infant born to a diabetic mother is now the same as for an infant born to a nondiabetic mother.
d) better metabolic control during pregnancy has led to improved outcomes.
The answer is d.

Infant mortality rates due to diabetes have declined since the 1960s in part because better metabolic control has led to improved outcomes.

The correct answer is d.

Infant mortality rates have declined since the 1960s in part because better metabolic control has led to improved pregnancy outcomes.
As two thirds of pregnancies in women with type 1 or 2 diabetes are unplanned, the ADA suggests that preconception counseling ideally begin at the onset of puberty and continue until menopause. Preconception care should begin at least 3 to 6 months prior to conception to allow sufficient time to evaluate the mother's health status and to normalize glycemic control.

Poorly controlled diabetes during the early weeks of pregnancy significantly increases the risk of first trimester spontaneous abortions or of delivering an infant with a major anomaly.

Preconception care should include counseling regarding the potential risks of an unplanned pregnancy and appropriate contraception also needs to be emphasized and offered.

A thorough assessment is needed to detect any vascular complications, and women should be referred for an obstetric evaluation.

In addition, women should be seen by a diabetes educator and/or dietitian. An assessment of self-management skills, including blood glucose monitoring and insulin injection technique, should be performed and diabetes education provided as needed.

Nutrition counseling to meet nutritional needs in anticipation of pregnancy, including dietary intake of protein, folic acid, and multivitamin supplementation, is necessary.
A preconception assessment of a woman with preexisting diabetes should begin with a detailed medical history and physical examination that includes type of diabetes, age of onset, duration, and course of disease; history of acute and chronic complications; current treatment regimen; and obstetric history with attention to infertility problems and pregnancy complications.

A dilated retinal examination should be performed by an ophthalmologist. Laboratory evaluation should include urine for culture and sensitivity, a 24-hour urine collection for creatinine, creatinine clearance, and microalbumin, A1C, thyroid panel, and blood lipid profile. Additional studies such as EKG and/or testing for neuropathy may also be warranted in some women.
Possible Contraindications

Pregnancy is contraindicated when certain diabetes-related complications are present.

☐ Absolute
- Ischemic heart disease
- Active proliferative retinopathy

☐ Relative
- Renal insufficiency
  - Serum creatinine >2 mg/dL or creatinine clearance <50 mL/min
  - Blood pressure >130/80 mmHg despite treatment
- Severe gastroenteropathy

Women with ischemic cardiac disease should be counseled against becoming pregnant because the risks of maternal mortality are high.

If significant proliferative retinopathy is present, women should be counseled to delay pregnancy until treatment can stabilize the condition. Background retinopathy that occurs during pregnancy usually regresses after delivery.

If significant renal disease is present, as validated by serum creatinine >2 mg/dL and/or creatinine clearance <50 mL/min, women must be warned about the high risk of infant morbidity and mortality associated with this particular complication. Significant proteinuria (>2 g/24 hr), when accompanied by hypertension, indicates significant risk.

During pregnancy and in the presence of renal insufficiency, it is recommended that blood pressure be maintained at <130/80 mmHg. Poorly controlled hypertension is considered a relative contraindication to pregnancy.

The use of ACE inhibitors should be discontinued and replaced with other antihypertensive medications since ACE inhibitors may cause anomalies of the genitourinary tract in the fetus.

Severe gastroenteropathy is also considered a relative contraindication to pregnancy, as metabolic control and nutrition for both the woman and her developing baby are very difficult to maintain with this particular complication.
Risk assessment for GDM should be undertaken at the first prenatal visit.

Characteristics that put women at high risk for GDM include a strong family history of diabetes in parents and siblings; obesity, defined as a body mass index >30 kg/m²; age, history of abnormal glucose metabolism; history of poor obstetric outcome or previous GDM; being a member of a high-risk ethnic group, which includes African American, American Indian, Hispanic/Latino, Asian Pacific Islander/Southeast Asian, Asian Indian, and indigenous Australian; and previous delivery of a large-for-gestational-age or macrosomic infant.

A large population-based retrospective study in the United States provided evidence that a woman’s own birth weight was inversely related to her risk of GDM, suggesting that early life factors may be important in the etiology of this disorder.

Polycystic ovary syndrome is common in women with type 2 diabetes and gestational diabetes.
According to ADA screening guidelines:

Risk assessment should be conducted at first prenatal visit to evaluate a woman’s risk for developing GDM. Women found to be at high risk should be screened as early as possible.

Women at average risk for GDM and those who have not been identified as having an abnormal glucose tolerance prior to the 24th week of gestation should have a screening test at 24 to 28 week’s gestation.

The glucose screening test, which is a random 50-gram 1-hour oral glucose challenge, can be administered without regard for time of day or interval since last meal.

If plasma glucose is <140 mg/dL, further testing is generally not required; however, high-risk individuals should be reevaluated later during pregnancy.

If plasma glucose is ≥140 mg/dL, further testing is required.

Women considered low risk do not require glucose testing. Low-risk women must meet all of the following criteria: age <25 years; weight normal prior to pregnancy; no known diabetes in first-degree relatives; no history of abnormal glucose tolerance; and no history of poor obstetric outcome.
If the 50-gram 1-hr oral glucose challenge screening value is $\geq 140$ mg/dL, the next step is to administer a diagnostic oral glucose tolerance test (OGTT). This 2-step approach identifies $\sim 80\%$ of women with GDM.

The OGTT is performed in the morning, after an overnight fast of between 8 and 14 hours. A 100-gram glucose load is given in a volume of at least 400 mL of fluid. The test should be preceded by at least 3 days of unrestricted activity and diet. Plasma glucose levels are measured fasting and at 1, 2, and 3 hours. Definitive diagnosis requires that 2 or more of the threshold values be met or exceeded:

A fasting plasma glucose $\geq 95$ mg/dL.
A 1-hour plasma glucose $\geq 180$ mg/dL.
A 2-hour plasma glucose $\geq 155$ mg/dL.
A 3-hour plasma glucose $\geq 140$ mg/dL.
A woman is considered at high risk for gestational diabetes if she:

a) is obese.
b) has a history of abnormal glucose metabolism.
c) belongs to a high-risk ethnic group.
d) all of the above.
The answer is d.

A woman is considered at high risk for gestational diabetes if she is obese, has a history of abnormal glucose metabolism, or belongs to a high-risk ethnic group.

The correct answer is d.

A woman is considered at high risk for gestational diabetes if she is obese, has a history of abnormal glucose metabolism, or belongs to a high-risk ethnic group.
Changes in metabolism that occur during the first trimester of pregnancy include a drop in fasting maternal glucose levels to 55 to 65 mg/dL, a level well below nonpregnant individuals; lower circulating concentrations of most amino acids; and, simultaneously, a rise in fasting plasma ketone concentrations and free fatty acid levels are observed. Thus, pregnancy simulates a state of “accelerated starvation,” leading to the increased use of alternate fuels for maternal metabolism while glucose is spared for fetal consumption.

During the second and third trimesters, circulating insulin levels are increased, in part because of accelerated hormonal activity counteracting insulin action. Hormone levels that are increased in late pregnancy include human placental lactogen (HPL), estrogen, progesterone, cortisol, and prolactin.

By the third trimester, insulin production can triple that of nonpregnancy levels to maintain euglycemia.
During late pregnancy, food ingestion results in higher and more prolonged plasma glucose concentrations. The sustained postprandial hyperglycemia enhances transplacental delivery of glucose to the fetus and promotes growth of the fetus. Insulin requirements increase 2- to 3-fold during late pregnancy.

Maternal insulin and glucagon do not cross the placenta.
The management of diabetes during pregnancy is best accomplished through the provision of multidisciplinary team care and targeted self-management education.

Women and their healthcare providers should work as a team to determine a management plan that includes nutrition, exercise, and medications.

Women may need to receive instruction on glucose and ketone monitoring for maintenance of glycemic control. Ketone monitoring can be useful for detection of insufficient carbohydrate and calorie intake, or metabolic changes caused by illness, infection, or stress. Ketone testing is recommended when there has been any illness or when blood glucose is >200 mg/dL.

Medical management should include counseling and resources for diabetes education.

Monitoring of maternal and fetal well-being is ongoing throughout gestation.

Maternal psychosocial and financial well-being should be assessed and used to guide development of the management plan.
Glycemic Goals in Pregnancy

**Plasma Blood Glucose**

- **Fasting/premeals**: 65–105 mg/dL
- **1-hr postprandial**: 110–135 mg/dL
- **2-hr postprandial**: <120 mg/dL
- **2 AM–6 AM**: 65–135 mg/dL

*These values are about 10% lower in whole blood.


In pregnant women without diabetes, maternal plasma glucose levels rarely exceed 120 mg/dL.

The following values are ADA-recommended therapeutic targets for pregnancies complicated by diabetes:

- Fasting/premeal plasma values of 65 to 105 mg/dL or whole blood values of 60 to 90 mg/dL
- 1-hr postprandial plasma values of 110 to 135 mg/dL or whole blood values of 100 to 120 mg/dL
- 2-hr postprandial plasma values of <120 mg/dL or whole blood values of <110 mg/dL

When middle-of-the-night monitoring is needed, plasma values should be between 65 and 135 mg/dL or whole blood values between 60 and 120 mg/dL.

Ideally, both premeal and postprandial blood glucose monitoring is recommended (6–8 times a day), as well as at bedtime, especially for those receiving multiple daily insulin injections or continuous subcutaneous insulin infusion (CSII) therapy. Middle-of-the-night monitoring is recommended if there is a suspicion of nighttime hypoglycemia. Precise monitoring schedules should be individualized.
Monitoring Glycemic Control

- **Self-monitoring of blood glucose (SMBG):**
  - Usually 4 or more times daily for women with preexisting diabetes
    - fasting
    - prelunch
    - predinner
    - bedtime
    - 1 or 2 hr postmeals (if needed)
  - At least 4 times daily for women with GDM not on insulin
    - fasting
    - 1-hr post: -breakfast, -lunch, -dinner

- **A1C measured monthly for women with preexisting diabetes**

- **Urine ketone monitoring when illness present or when blood glucose >200 mg/dL**

- **Food intake**

Maintaining close-to-normal blood glucose levels is essential to avoid complications. For women with preexisting diabetes, experts recommend self-monitoring of blood glucose (SMBG) at least 4 times daily and, if necessary, up to 8 times daily. In general, SMBG is needed before each meal and before the bedtime snack, if snacking. Postprandial measurements may be used to evaluate the effectiveness of short-acting insulin.

Women with GDM should monitor blood glucose at least 4 times daily: once in the morning (fasting) and 1 hr after each meal. It has been shown that for women with GDM, monitoring by 1-hr postprandial (vs 2-hr postprandial) glucose levels results in a lower incidence of fetal macrosomia.

A1C should be measured monthly in women with preexisting diabetes. Mild elevations of A1C have been associated with increased fetal morbidity. The use of measuring A1C in women with GDM has not been established.

Ketone monitoring for women with preexisting diabetes is recommended during illness, when blood glucose levels exceed 200 mg/dL, or when the woman is unable to eat as a result of nausea or vomiting. Ketones cross the placenta, and there is some evidence that they may be harmful to the fetus. Studies have demonstrated an association between elevated plasma ketone levels and lower IQ scores in offspring. Although ketone monitoring can be used as a management tool for women with GDM, its effectiveness in improving fetal outcomes is not established.

Recording food intake along with results of SMBG provide data to determine the cause of hyperglycemia: inadequate insulin dosing or extra carbohydrate intake. Recording 2 to 3 days of food intake just prior to follow-up visits is suggested.
The ADA recommends that women receive nutritional counseling by a registered dietitian for individualized Medical Nutrition Therapy (MNT).

Unless a woman is underweight, energy intake does not need to increase in the first trimester. However, energy requirements increase by 300 kcal/d during the second and third trimesters.

Weight-gain goals are based on the woman’s prepregnancy BMI, and are as follows: a 25- to 35-lb weight gain for women with a normal BMI, 35 to 45 lb for underweight women, 15 and 25 lb for overweight women, and 15 lb for women with a BMI $\geq 30$ kg/m$^2$.

Protein requirements increase during the second and third trimesters to support expansion of blood volume, uterus, and breasts, and synthesis of fetal and placental proteins. The Dietary Reference Intake (DRI) for protein is an additional 25 g/d.

The DRI/RDA for carbohydrate intake is 175 g/d.
Pregnant women with inadequate dietary intakes or who are cigarette smokers may need a daily vitamin-mineral supplement.

The requirement for folic acid in pregnancy is 600 mg/d. Folate supplementation is associated with a decreased incidence of small-for-date births and neural tube defects.

The DRI for calcium in pregnancy is 1000 mg/d.

Pregnant women should be counseled to avoid alcohol and smoking, and to limit caffeine intake to <300 mg/d (about 2 cups of coffee).

Artificial sweeteners approved by the US Food and Drug Administration are considered safe for use during pregnancy when they are used within the acceptable daily intakes. Artificial sweeteners should be limited to three to four portions per day.

Pregnant women are advised to avoid or limit their intake of certain fish that may be high in mercury. These may include shark, swordfish, mackerel, and others. State health department recommendations should be consulted.
Pregnant women with preexisting diabetes need to balance food intake with insulin to maintain euglycemia.

During the first trimester, hormonal changes can cause blood glucose levels to be erratic. The increased risk for hypoglycemia during this time may necessitate adjustments in insulin or in food intake. Frequent, smaller meals and snacks may be helpful. The nausea and vomiting of morning sickness may also require adjustments in medication and diet.

Weight should be monitored at each visit to ensure that weight gain goals are met. For a woman of normal weight, gains of <2 lb per month or >6.5 lb per month may require further evaluation.

In general, nutritional guidelines for pregnant women with type 1 or type 2 diabetes are similar to recommendations for pregnant women who do not have diabetes. Good nutrition should include the following: 2–3 servings of fruit, 3–5 servings of vegetables, 2–3 servings of calcium-rich foods, and 2 servings of meat per day.
Medical Nutrition Therapy
GDM

- Control carbohydrate intake
  - 3 small to moderate meals with 2–4 snacks
  - Avoid foods with high carbohydrate content such as regular soft drinks, juice, and desserts
- Monitor blood glucose postmeal to assess glucose control
- If undereating, check for starvation ketones
- Add glyburide or insulin if unable to achieve glucose control with meal plan and appropriate weight gain

MNT is the primary treatment for the management of GDM.

MNT for GDM involves a carbohydrate-controlled food/meal plan. It is recommended that carbohydrate intake be distributed throughout the day into 3 meals and 2 to 4 snacks. Foods high in total carbohydrate and other sugars such as soft drinks, juice, and desserts are not recommended.

The ADA and the American College of Obstetrics and Gynecology support the use of SMBG in women with GDM. Women should monitor fasting and postmeal blood glucose levels to improve glycemic control and infant outcomes. The usual frequency of testing is 4 times a day—fasting and 1 hour after each meal.

If there is insufficient food intake, there may be a shift from carbohydrate to fat metabolism, resulting in a rise in plasma and urinary ketones. Urine or blood ketones should be monitored if the woman is undereating.

Insulin or glyburide therapy should be initiated if blood glucose targets are not consistently met with MNT and appropriate weight gain.
Physical Activity
Preexisting Diabetes and GDM

- Physician clearance
- Physical activity
  - Cardiovascular, strength, flexibility
- Identification of appropriate exercises
  - Individualized program with realistic goals
  - Certain exercises contraindicated during pregnancy (eg, supine after 1st trimester)
- Education on monitoring well-being during activity
- Explanation of risks and contraindications
  - Hypoglycemia

Exercise can be broadly divided into 3 categories: cardiovascular (aerobic), resistance (strength), and flexibility (stretching) activities. In the absence of contraindications, a pregnant woman can maintain a moderate activity level. However, physician clearance is recommended.

Discussion with a professional is recommended for identification of appropriate exercises and development of an individualized program with realistic goals. Certain exercises may not be appropriate because they may place stress on the fetus (eg, supine after first trimester).

Exercise can lead to hypoglycemia. Women should be instructed to test blood glucose before and after exercise and to consume 15 grams of carbohydrate if blood glucose is low.

Women should be taught to monitor breathing (talk test), heart rate, temperature, and muscle fatigue during activity.
As described earlier, the metabolic changes in early pregnancy include a loss of glucose and gluconeogenic substrates to the developing fetus, which diminish insulin requirements.

In the second and third trimesters, insulin requirements gradually increase because of the increased placental production of the “contrainsulin” hormones of pregnancy (HPL, prolactin, estrogen, progesterone). Insulin requirements increase to as much as 2 to 3 times usual levels.

Insulin requirements are estimated based on weight, gestational age, blood glucose monitoring results, and caloric intake. In general, insulin requirements increase throughout pregnancy as follows:
0.7 unit/kg of body weight between weeks 1 to 18 of gestation, 0.8 unit/kg of body weight weeks 18 through 26 of gestation, 0.9 unit/kg of body weight weeks 26 through 36 of gestation, and 1.0 unit/kg of body weight weeks 36 through 40 of gestation.

SMBG is used to determine whether glycemic goals are met and to adjust the timing and amount of insulin. For women with GDM, results of SMBG will also help to determine whether insulin therapy should be initiated.

The insulin regimen will be individualized to achieve target blood glucose goals and frequent insulin adjustments are usually required.

Rapid-acting insulin analogs with peak hypoglycemic action 1 to 2 hours after injection offer improved postprandial glucose control compared with regular human insulin and are therefore preferred in pregnancy.
Insulin Therapy
Preexisting Diabetes (Types 1 and 2)

- Women with type 2 diabetes convert from oral antidiabetic therapy to insulin
- Short- or rapid-acting insulins are administered before meals to reduce glucose elevations associated with eating
- Longer-acting (basal) insulins restrain hepatic glucose production between meals and in fasting state
- Insulin pumps are well tolerated in women with type 1 or type 2 diabetes who need large amounts of insulin and who have difficulty achieving euglycemia
  - Advantages: flexibility, decreased incidence of hypoglycemia
  - Disadvantages: cost, extensive patient education, mechanical problems may cause hypo- and hyperglycemia

In pregnant women with preexisting type 1 or type 2 diabetes, insulin is considered the mainstay of therapy. Women with type 2 diabetes who are on oral antidiabetic medications should convert to insulin since they will invariably require insulin for glycemic control during the pregnancy.

Short- or rapid-acting insulins (prandial insulins) are administered before meals to reduce the glucose elevations associated with eating and allow utilization of consumed fuels. Longer-acting (basal) insulins are used to restrain hepatic glucose production between meals and in the fasting state.

CSII or insulin pump therapy is used to deliver insulin in a pattern that more closely resembles normal physiologic insulin release to both women with type 1 and type 2 diabetes. Other advantages of pump therapy during pregnancy include more rapid and predictable insulin absorption, enhanced lifestyle flexibility, and simplified morning sickness management.

A study comparing the use of CSII (insulin pump) with multiple daily injections in women with type 1 diabetes found that achieving good metabolic control was the critical factor in avoiding risk of fetal malformation, regardless of whether multiple daily injections or CSII were used.

A study in women with type 2 diabetes showed that use of a pump was well tolerated, especially in those taking large amounts of insulin; however, use of a pump was associated with weight gain.
For women with GDM, insulin is the pharmacologic therapy that has most consistently been shown to reduce fetal morbidities when added to MNT. Insulin therapy is recommended when MNT fails to maintain fasting plasma glucose (FPG) at levels ≤105 mg/dL.

If only postprandial glucose levels are abnormal, a rapid-acting insulin may suffice.

If FPG is also elevated, intermediate- or long-acting insulin may also be required.

Twice-daily or intensive therapy may be needed.
Glyburide Therapy
GDM

- The first randomized controlled trial comparing glyburide to insulin in women with GDM was published in 2000
- Glyburide not found in umbilical cord blood
- Similar levels of glycemic control
- No difference in neonatal outcomes
- Acceptable alternative to insulin if woman is not able to meet glycemic goals with MNT

Oral antidiabetic agents have generally not been recommended during pregnancy because of possible teratogenic effects and neonatal hypoglycemia. The first-generation sulfonylureas were found to cross the placenta and stimulate neonatal insulin secretion, causing fetal hyperinsulinemia.

However, newer medications, such as second-generation sulfonylureas, do not significantly cross the placenta. One randomized controlled trial compared the use of insulin and glyburide in women with GDM who were not able to meet glycemic goals with MNT.

Treatment with either agent resulted in similar levels of glycemic control and similar neonatal outcomes. No detectable levels of glyburide were found in umbilical cord blood samples. The researchers concluded that glyburide can be safely used as an alternative to insulin therapy in GDM.
The goals of a successful pregnancy are to produce a healthy term infant and a healthy mother. The medical, physical, and mental needs of the woman must be met throughout the pregnancy and the postpartum period.

Using a team approach with the woman as the center of the team enhances the achievement of outcome goals. Regular visits to a team member throughout the pregnancy are needed. The woman should be monitored for weight gain goals and the maintenance of euglycemia, including adjustments to meal plan and insulin as needed.

Monitoring of maternal health and fetal development are other important steps of successful management of a pregnancy complicated by diabetes.
All women go through emotional adjustments during their pregnancy; however, emotions are often magnified in women with diabetes because of the demands associated with the optimization of glycemic control throughout pregnancy.

Increased anxiety about the effects of diabetes on herself and on the fetus, as well as doubts about her ability to manage both pregnancy and diabetes may play a role in her willingness to undertake the added responsibility of a demanding treatment plan.

The intensity of following a strict protocol “emotionally lengthens” the pregnancy time span for even the most willing patient. Emotional support is an essential part of a woman’s emotional well-being and may include support from her spouse, other family members, healthcare professionals, peers, or support groups.

A psychosocial assessment can provide valuable information about lifestyle, family, job, and economic situation and helps to individualize the management plan thereby maximizing the woman’s adaptation to a diabetic pregnancy.

Adequate follow-up visits during the postpartum period are also essential to assist the woman to balance her own self-care needs with the needs of her infant.
Metabolic control is an important predictor of perinatal outcome.

The glucose value at which a woman will spill ketones is lower during pregnancy; therefore, the risk of diabetic ketoacidosis (DKA) is greater. Ketones cross the placenta and may be harmful to the fetus. A fetal loss rate of 30% has been reported with maternal DKA and coma. In addition, elevated maternal serum ketones are associated with lower IQ scores in offspring.

Major congenital anomalies are most common in those with poor blood glucose control in early pregnancy.

Vascular complications, especially hypertension and preeclampsia, also influence outcome.

The greater the degree of hypertension, the greater the likelihood of a poor outcome for mother and child.

Patients with nephropathy are at increased risk for preeclampsia, fetal-growth restriction, and preterm delivery, and have a 3-fold increase in the rate of stillbirth over women who have diabetes but who do not have nephropathy.
In addition to an increased risk of hypoglycemia and ketoacidosis during pregnancy, the risk for developing certain complications is increased by diabetes. These include hypertensive complications (including pregnancy-associated hypertension, chronic hypertension, and preeclampsia/eclampsia; progression of retinopathy and/or nephropathy; polyhydramnios (excessive amniotic fluid); urinary tract infections; premature labor; and an increased rate of cesarean-section delivery.
Poorly controlled diabetes in the early weeks of pregnancy significantly increases the risk of spontaneous abortion or congenital anomalies; several studies have shown an association between A1C values (at 8–12 weeks) and an increased risk of anomalies.

The types of birth defects that occur in infants of women with poorly controlled diabetes are varied but most often involve the cardiovascular, central nervous, and skeletal systems as seen on this slide. They include:

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Ratio of Incidence*</th>
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<tbody>
<tr>
<td>Caudal regression</td>
<td>252</td>
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<tr>
<td>Situs inversus</td>
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<tr>
<td>Renal anomalies (total)</td>
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<td>Heart anomalies</td>
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<td>Anal/rectal atresia</td>
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<tr>
<td>Spina bifida or other central nervous system</td>
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*Ratio of incidence is in comparison to the general population.
Fetal surveillance is done at the discretion of the physician(s), based on individual needs.

Ultrasound testing is commonly performed during the first trimester to estimate date of delivery, during the second trimester to identify structural abnormalities, and during the third trimester to assess fetal growth and development as well as to measure amniotic fluid levels.

α-Fetoprotein is a maternal blood test that can identify a fetus at risk for neural tube defect. The risk of having a child with a neural tube defect is 10 to 20 times greater in women with diabetes than in the general population.

Amniocentesis is routinely performed during the late first trimester for women over 35 years of age to diagnose chromosomal abnormalities and may also be performed in late pregnancy to assess fetal lung maturity.
A reactive nonstress test (NST) evaluates the absence or presence of fetal compromise; however, a nonreactive stress test may be seen in sleep states or other conditions not necessarily adverse.

A biophysical profile, which is a combination of NST and ultrasound evaluation, may be done if NST results are questionable, although this is not always routinely performed in women with GDM.

These tests may be done biweekly, weekly, or daily depending on individual circumstances.

Fetal activity is a simple, inexpensive method of monitoring fetal well-being and is generally instituted at 30 to 32 weeks of gestation. Several protocols (eg, kick counting) can be used for instructing the patient to measure and record perceived fetal movements in a given time period.
Fetal and neonatal complications related to uncontrolled diabetes can be prevented or reduced if the patient can establish and maintain near-normal blood glucose levels throughout pregnancy.

Hypoglycemia in the newborn, which is defined as a glucose level <35 mg/dL for both term and preterm infants, is the most common neonatal metabolic complication; it is seen in 10% to 25% of all infants born to mothers with diabetes.

If maternal diabetes is poorly controlled, the fetus receives more glucose and alternate fuel sources than it requires for normal growth, and must therefore secrete additional amounts of insulin to use this excess glucose.

At delivery, the glucose supply decreases but the baby continues to secrete high amounts of insulin. This results in neonatal hypoglycemia which is usually treated by early feeding or intravenous (IV) glucose if necessary.

Hypocalcemia (about 50% of newborns) and hypomagnesemia (about 33%) are neonatal complications that should be promptly diagnosed and treated; they are probably related to the severity of maternal diabetes which can cause secondary transient hypoparathyroidism during the first 2 to 4 days of life.

Hypomagnesemia may be the result of blunted secretion of parathyroid hormone; hypocalcemia may be secondary to hypomagnesemia.
Possible Fetal/Neonatal Complications

- Polycythemia
- Cardiomyopathy
- Hyperbilirubinemia
- Stillbirth and respiratory distress syndrome

Fetal polycythemia is associated with increased levels of erythropoietin and is probably secondary to chronic intrauterine hypoxia caused by the effects of hyperglycemia and hyperinsulinemia. Venous hematocrits >65% to 70% have been observed in 20% to 40% of newborns during the first days of life. The anabolic effect of fetal hyperinsulinemia can also lead to the development of cardiomyopathy.

The cause of hyperbilirubinemia is multifactorial. Potential causes include increased hemolysis and ineffective erythropoiesis, increased bruising and trauma, or a delay in liver enzyme maturation.

Stillbirth and respiratory distress syndrome are now less common, due to sophisticated monitoring techniques, prolongation of pregnancy beyond 38 weeks’ gestation, and demonstrated evidence that glycemic control is critical.
Macrosomia is typically defined as a fetus weighing >4000 grams (8.8 lb), or one that is >90th percentile for gestational age.

Macrosomia is one of the most common complications of GDM. The incidence of macrosomia is increasing in the United States, possibly because of rising rates of obesity and diabetes; it occurs in 10% of all pregnancies in the general population; with diabetes, however, the incidence is between 20% and 32%, according to the AADE.

The development of macrosomia is highly correlated with maternal glycemia control. Maternal hyperglycemia leads to fetal hyperglycemia, which in turn stimulates the fetal pancreas to produce excessive amounts of insulin, which is a growth factor for fetal tissue.

Macrosomia mainly affects fetal heart, liver, and subcutaneous fat. These infants tend to have twice as much body fat as infants of nondiabetic mothers.

Macrosomia increases the risk for operative delivery and potential complications for infants include shoulder dystocia, fractured clavicles, brachial plexus injury, and asphyxia.

Macrosomia has been associated with an increased risk for childhood and adolescent obesity as well as type 2 diabetes.
Possible fetal complications related to uncontrolled types 1 and 2 diabetes include:

a) hypocalcemia
b) macrosomia
c) cardiomyopathy
d) all of the above
The answer is d.

Possible fetal complications related to uncontrolled types 1 and 2 diabetes include hypocalcemia, macrosomia, or cardiomyopathy.

The correct answer is d.

Possible fetal complications related to uncontrolled types 1 and 2 diabetes include hypocalcemia, macrosomia, or cardiomyopathy.
The fetal heart rate should be continuously monitored during labor and delivery in pregnancies complicated by diabetes.

Maternal blood glucose levels are measured hourly and the goal is to maintain levels between 70 to 100 mg/dL.

Patients with preexisting diabetes should be managed with an IV glucose/insulin infusion during labor and delivery.

Women with GDM usually do not require insulin but can be managed with an IV glucose/insulin infusion if needed.

There are numerous intrapartum insulin management regimens recommending the initiation of IV insulin therapy at blood glucose levels ranging from 90 to 140 mg/dL. A useful protocol is:

- If the plasma blood glucose value is between 100 to 150 mg/dL, then insulin is added to IV saline solution and administered at the rate of 1.0 unit/hr.
- If the plasma blood glucose value is >150 mg/dL, insulin is infused at the rate of 2.0 units/hr.
- If blood glucose remains >100 mg/dL for 2 hours after initiation of insulin, the rate is increased by 0.5 unit/hr, repeated every 2 hours if blood glucose remains elevated.
- Insulin is discontinued when blood glucose levels fall to <100 mg/dL.
- If blood glucose level falls <70 mg/dL, infusion solution is changed to 5% dextrose.
- Women with uncontrolled diabetes may need 0.5–2.5 units/hr during active labor.

Women with GDM usually do not require insulin during labor; however, the protocol above can be used if blood glucose values are not between 70 to 100 mg/dL.
Euglycemia remains the goal of therapy during the postpartum period, which is characterized by an immediate reduction in insulin requirements.

Women with preexisting diabetes may not need insulin for 24 to 48 hours or longer after delivery.

In general, insulin requirements are recalculated at 0.6 unit/kg current weight for nonlactating women and 0.4 unit/kg current weight for lactating women.

Breastfeeding should be strongly encouraged for all women with diabetes.

Nutrition requirements for a women with preexisting diabetes should focus on maintaining blood glucose control and meeting the nutritional needs of lactation.

The same meal plan as that of the third trimester is usually appropriate during lactation; addition of a bedtime or middle-of-the-night snack may be needed.

Women with type 2 diabetes whose glucose value cannot be maintained with MNT may need to continue to take insulin while breastfeeding; oral glucose-lowering agents are not recommended during lactation.
Women with GDM should be evaluated for glucose tolerance in the postpartum period. The recommended test is a 2-hr, 75-gram OGTT performed at the 6 to 8 week postpartum visit, or after lactation and, if normal, annually thereafter.

Normoglycemia is defined as FPG values $<100 \text{ mg/dL}$ or a 2-hr plasma value $<140 \text{ mg/dL}$.

Abnormal OGTT values are classified into 2 categories: impaired glucose tolerance (IGT) or type 2 diabetes.

Diabetes is diagnosed if the FPG value is $\geq 126 \text{ mg/dL}$, or if the 2-hr plasma value is $\geq 200 \text{ mg/dL}$; prediabetes is FPG 100 to 125 mg/dL or 2-hr postprandial blood glucose $\geq 140 \text{ mg/dL}$ and $\leq 200 \text{ mg/dL}$.

Women who test positive for diabetes or IGT should be referred to a healthcare provider familiar with the treatment/management of diabetes.

Patients that are not diagnosed with type 2 diabetes should be advised of their increased risk for developing gestational diabetes with subsequent pregnancies, as well as for developing type 2 diabetes later in life.

Screening and preconception counseling should be planned before the next pregnancy is considered.

Infants of mothers with diabetes have an increased risk of obesity and glucose intolerance in childhood and adolescence and, therefore, monitoring of growth and development is recommended.
Women who have had GDM have a 60% to 70% chance of developing GDM in subsequent pregnancies.

As many as 20% of women with GDM tested in the early postpartum period will have an abnormal OGTT.

Women who have had gestational diabetes are at increased risk (40%–60%) of developing type 2 diabetes compared with the general population, usually within 5 to 15 years.

Obese women have a 50% to 75% risk of developing type 2 diabetes.

A fasting blood glucose (FBG) value on the 75-g OGTT of ≥130 mg/dL increases the risk of developing type 2 diabetes to 95%.

The postpartum period is an opportune time to emphasize risk and advise of lifestyle modifications to reduce or delay the onset of diabetes and its related complications.
Recommendations
Preexisting Diabetes (Types 1 and 2)

- Education from early adolescence
- Preconception counseling and pregnancy planning
- Maintain healthy lifestyle: eating and activity
- Establish most effective treatment regimen for maintaining glycemic control
- Appropriate postpartum follow-up

The ADA recommends education about preconception care for all women of childbearing age who have preexisting diabetes. Ideally, education should begin in early adolescence. Women not planning a pregnancy within the next year should be given general information regarding the risks of pregnancy and the importance of contraception and prepregnancy planning.

Those planning a pregnancy within the next year should be given more detailed preconception counseling.

During pregnancy, a healthy lifestyle should be maintained, including a nutritious diet and physical activity.

The most effective treatment for maintaining glycemic control, with avoidance of hypoglycemia, should be used throughout pregnancy to maximize outcomes.

Appropriate postpartum follow-up to reestablish insulin requirements is important.
Every pregnant woman should be assessed for risk of GDM at her first prenatal visit. Women at high risk should be screened as early as possible for abnormal glucose tolerance.

Women at average risk and those who have not been identified earlier as having abnormal glucose tolerance should be screened for GDM at 24 to 28 weeks’ gestation.

Glycemic control should be maintained by a combination of MNT and exercise, adding insulin or alternatively, glyburide, if needed.

Appropriate postpartum follow-up to reevaluate glucose tolerance is critical and the woman with GDM should be educated to request annual testing for diabetes.
Summary

- Diabetes increases risk of most common complications of pregnancy and birth defects.
- Advances in screening, diagnosis, and care have lowered infant mortality substantially.
- Attentive care and glycemic control before, during, and after pregnancy can reduce major complications.
- The most effective therapy for controlling fasting and postprandial blood glucose should be identified and used.

In summary, diabetes is associated with an increased risk for adverse pregnancy outcomes.

Advances in screening, diagnosis, and care have lowered infant mortality from 25% in 1960s to 2% since the 1980s.

Attentive care before, during, and after pregnancy can reduce the major complications of diabetes for both mother and fetus.

The most effective therapy for controlling fasting and postprandial blood glucose should be identified and used since good glycemic control is critical in the management of pregnancies complicated by diabetes.
Thank you for participating in this program.