Pregestational diabetes mellitus: Obstetrical issues and management

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INTRODUCTION — The key elements in management of pregnancies complicated by diabetes are:

- Achieving and maintaining excellent glycemic control
- Screening, monitoring, and intervention for maternal medical complications (eg, retinopathy, nephropathy, hypertension, cardiovascular disease, ketoacidosis, thyroid disease)
- Monitoring of, and intervention for, fetal and obstetrical complications (eg, congenital anomalies, preeclampsia, macrosomia)

Most issues related to the obstetrical management of a pregnant diabetic woman (type 1 or type 2) will be reviewed here. The obstetrical management of these pregnancies is largely based upon clinical experience, data from observational studies, and expert opinion [1,2]. There is virtually no evidence from randomized trials.

Four important additional issues are discussed in detail separately: prepregnancy counseling, glycemic control, maternal medical complications, and neonatal issues:

- (See "Pregestational diabetes: Preconception counseling, evaluation, and management".)
- (See "Pregestational diabetes mellitus: Glycemic control during pregnancy".)
- (See "Infant of a diabetic mother".)

Gestational diabetes is also discussed separately:

- (See "Diabetes mellitus in pregnancy: Screening and diagnosis".)
- (See "Gestational diabetes mellitus: Glycemic control and maternal prognosis".)
- (See "Gestational diabetes mellitus: Obstetrical issues and management".)

FIRST TRIMESTER

First prenatal visit — Ideally, women with pregestational diabetes have received both (1) preconceptional counseling addressing maternal and fetal risks during pregnancy, and (2) management of diabetes to optimize their health status. (See "Pregestational diabetes: Preconception counseling, evaluation, and management".)

Unfortunately, many pregnancies are unplanned and many women do not receive or adhere to comprehensive management of their disease; thus, a prenatal visit may be the clinician's first opportunity to assess the patient's baseline medical status (retinopathy, nephropathy, hypertension, neuropathy, cardiovascular disease, thyroid dysfunction) and educate her about the management and potential complications of diabetes in pregnancy, as well as routine aspects of pregnancy care. (See "Prenatal care: Initial assessment".)

Classification — The severity of pregestational diabetes can be categorized according to the White classification (table 1) [3], which attempts to provide a standardized definition for describing pregnant women with diabetes and has some correlation with pregnancy outcome [4,5]. However, the White classes are not mutually exclusive, thus some have argued that the classification of diabetes should be reassessed [6]. We believe the presence/absence of vascular complications is a better predictor of adverse outcome than the specific White class [7].

To address the deficiencies in the White system, the following classification system for diabetes in pregnancy, based on the mechanism of disease, has been proposed [6]:

- Type 1 diabetes (ie, resulting from beta cell destruction, usually leading to absolute insulin deficiency)
  - a. without vascular complications
  - b. with vascular complications (specify nephropathy, retinopathy, hypertension, arteriosclerotic heart disease, transplant, etc)
- Type 2 diabetes (ie, resulting from inadequate insulin secretion in the setting of increased insulin resistance)

- a. without vascular complications
- b. with vascular complications (specify nephropathy, retinopathy, hypertension, arteriosclerotic heart disease, transplant, etc)

- Gestational diabetes (diabetes diagnosed during the second or third trimester of pregnancy and not clearly overt, eg, type 1 or type 2 diabetes)
- Other diabetes (eg, genetic origin, drug or chemical induced)

Testing

Routine — Routine prenatal laboratory evaluations are performed (table 2). Assessment for and treatment of asymptomatic bacteriuria is particularly important because there is a three- to five-fold greater propensity for asymptomatic bacteriuria in diabetic women. Rescreening among those who did not have bacteriuria on the initial test is generally not performed in low-risk women, but is reasonable in women at high risk for infection, such as women with diabetes mellitus. (See "Urinary tract infections and asymptomatic bacteriuria in pregnancy", section on 'Asymptomatic bacteriuria'.)

Glycated hemoglobin — In addition to the standard prenatal laboratory panel, a glycated hemoglobin concentration is obtained. It reflects the woman's average level of glycemic control over the prior few weeks, and thus assists in counseling her regarding the risks of miscarriage, congenital malformations (see 'Risk of congenital anomalies' below), and preeclampsia.

Assessment of comorbidities — Additional tests that should be obtained early in pregnancy in diabetic gravidae [8], if not assessed preconceptionally, include:

- Baseline renal function, initial quantification of urinary proteinuria is performed on a random urine sample using the urinary protein-to-creatinine ratio. This method is both reproducible and more convenient for the patient than a 24-hour collection. (See "Proteinuria in pregnancy: Evaluation and management" and "Assessment of urinary protein excretion and evaluation of isolated non-nephrotic proteinuria in adults".)
- Thyroid stimulating hormone (TSH) and thyroid peroxidase status if unknown, as the incidence of thyroid dysfunction in women with type 1 diabetes is as high as 40 percent.
- Electrocardiogram, as a screen for ischemic heart disease, especially in women with cardiovascular symptoms, hypertension, or evidence of diabetic vasculopathy.
- Dilated, comprehensive eye examination by an ophthalmologist to detect retinopathy [9,10]. Close follow-up is indicated during pregnancy, with the frequency determined by baseline findings. The American Diabetes Association suggests eye examinations every trimester and for one year postpartum, as indicated by degree of retinopathy [10]. (See "Diabetic retinopathy: Prevention and treatment", section on 'Pregnancy'.)

Ultrasound — Ultrasound examination is obtained for the usual obstetrical indications (table 3).

First trimester ultrasound examination is often obtained to document viability, as the rate of miscarriage is higher in women with diabetes, especially those with poor glycemic control, and to assist in estimation of gestational age. Accurate estimation of gestational age is critical since many of these pregnancies undergo scheduled delivery. (See "Prenatal assessment of gestational age and estimated date of delivery".)

Some major congenital abnormalities (eg, anencephaly) can be detected in the late first trimester by detailed fetal anatomic survey using a transvaginal transducer. Sensitivity is lower earlier in gestation because of difficulty in visualizing small structures and because some abnormalities of organs such as the gastrointestinal tract, brain, and kidney can be visualized better in the more physiologically advanced fetus. In particular, the fetal heart, which is a common site of diabetic embryopathy, is optimally visualized in the second trimester. (See "Fetal cardiac abnormalities: Screening, evaluation, and pregnancy management".)

Early fetal growth delay (biometric measurements smaller than expected for predicted gestational age) in pregnancies complicated by pregestational diabetes was thought to be predictive of the development of congenital anomalies and low birth weight [11]; however, this assumption has been refuted by subsequent analyses [12-14]. (See "Prenatal assessment of gestational age and estimated date of delivery".)

Screening for aneuploidy — Maternal diabetes mellitus is not a risk factor for aneuploidy. Women who have diabetes are offered prenatal screening and diagnosis for Down syndrome according to practices in use for the general obstetrical population.

First trimester serum and ultrasound markers of Down syndrome are not affected by maternal diabetes, but if second trimester testing is performed (eg, quadruple test), then adjustments need to be made since serum alpha fetoprotein (AFP) and unconjugated estriol (uE3) levels are reduced in women with diabetes. It is presumed that noninvasive screening using cell-free DNA is not affected by maternal diabetes, but this has not been specifically studied. (See 'Screening for aneuploidy' below.)

Counseling and management

General principles — The clinician should emphasize the importance of strict adherence to diet, exercise and medication; meticulous self-monitoring of blood glucose; and the need for frequent prenatal visits and intensive fetal surveillance later in

pregnancy. Information on diet, insulin therapy, and glucose monitoring should be provided by clinicians with experience in management of diabetes during pregnancy. A team approach is efficient and is usually required to provide the necessary expertise. In addition to the obstetrical providers (physician, nurse, and/or midwife), the team may include an endocrinologist, endocrinology nurse, nutritionist, and the patient's primary care provider. (See "Pregestational diabetes mellitus: Glycemic control during pregnancy".)

Even in early pregnancy, women with pregestational diabetes are often seen more frequently than women with uncomplicated pregnancies. These extra visits can be used to review monitored blood glucose values and results from the ophthalmologic and laboratory examination (eg, renal function, glycated hemoglobin, thyroid function). In addition, the telephone, e-mail, or facsimile machine can be used to exchange information about glucose values and adjustments in insulin therapy.

Management of hypertension — Women receiving angiotensin converting enzyme (ACE) inhibitors or receptor blockers (ARBs) for hypertension or nephropathy should have been taken off these medications prior to pregnancy because of their teratogenic potential. If not discontinued prior to pregnancy, use of these drugs should be suspended during pregnancy. (See "Angiotensin converting enzyme inhibitors and receptor blockers in pregnancy".)

In pregnant patients with diabetes and chronic hypertension, the American Diabetes Association suggests blood pressure targets of 120 to 160/80 to 105 mmHg as this target range likely achieves a reasonable balance between long-term maternal health and avoidance of impaired fetal growth [10].

Similarly, the American College of Obstetricians and Gynecologists' (ACOG) guideline for management of chronic hypertension in pregnancy emphasizes the importance of antihypertensive therapy for women with blood pressures >160/105 mmHg and no evidence of end organ damage and suggests maintaining blood pressure at a higher target (120 to 160 mmHg systolic and 80 to 105 mmHg) in women on medication; for women with end organ damage, a group which would include many who have long-standing diabetes, they suggest maintaining blood pressure <140/90 mmHg to avoid progression of disease during pregnancy [15]. A detailed discussion of antihypertensive therapy for pregnant women can be found separately. (See "Management of hypertension in pregnant and postpartum women".)

Management of comorbidities — Treatment of comorbid medical complications, if present, is also reviewed separately. (See "Pregestational diabetes: Preconception counseling, evaluation, and management" and "Pregnancy in women with diabetic kidney disease".)

Although obesity is common in diabetic women, obesity is associated with many pregnancy risks independent of diabetes (see "Obesity in pregnancy: Complications and maternal management"). Whether obesity adds to the risks associated with diabetes in pregnancy is an area of ongoing investigation. A 2013 study of New York City maternal mortality data from 1995 to 2003 found that maternal obesity and pregestational diabetes were each associated with an increased risk of death during a delivery hospitalization (adjusted OR 2.9 and 3.3, respectively), but how concurrence of these two conditions influenced mortality risk was not reported [16]. A second study using New York City birth data argued that diabetes and obesity were independent risk factors for the outcomes of cesarean and preterm delivery [17], in agreement with other studies that showed obesity adds to the risk of pregnancy-associated maternal and neonatal morbidity in diabetic women [18,19]. Clinicians caring for women who are both obese and diabetic should be mindful of the potential morbidities of both conditions.

Prevention of preeclampsia — Pregestational diabetes is a risk factor for preeclampsia (pooled rate 11 percent, 95% CI 8.4-13.8 percent; pooled relative risk 3.7, 95% CI 3.1-4.3 [20]). The United States Preventive Services Task Force recommends that women at high risk for preeclampsia, including all those with type 1 and 2 diabetes, begin 81 mg/day of aspirin after 12 weeks of gestation. This is our practice, and we often begin low-dose aspirin earlier in the first trimester to ensure that treatment has been initiated by 12 weeks of gestation [21]. (See "Preeclampsia: Prevention".)

Risk of congenital anomalies — Data from multiple studies have consistently shown a higher risk of major congenital malformations and miscarriage associated with increasing first trimester glycated hemoglobin values (figure 1) [22-24]. Although glycated hemoglobin values from different laboratories may not be comparable because of differences in methodology and a lack of standardization among laboratories, a value >1 percent above the upper limit of the normal range is associated with an increased risk of congenital anomalies. The relationship between glycated hemoglobin and congenital anomalies/miscarriage is discussed in detail separately. (See "Pregestational diabetes: Preconception counseling, evaluation, and management" and "Estimation of blood glucose control in diabetes mellitus".)

We typically inform patients with a markedly elevated glycated hemoglobin value of the increased risk of congenital anomalies, particularly neural tube and cardiac defects [25]. We tell them that more information about fetal development will be obtained from first and second trimester sonographic examinations and maternal serum analyte results.

The American College of Obstetricians and Gynecologists (ACOG) recommends preconception and first trimester pregnancy supplementation with 4 mg of folic acid for "women at high risk for neural tube defects" and we encourage this level of supplementation for our patients with diabetes, although it is possible that the pathophysiology of increased risk in these patients is unrelated to folate deficiency. Some guidelines recommend 5 mg folic acid [8]. (See "Folic acid supplementation in pregnancy", section on 'Pregestational diabetes'.)

Risk of macrosomia — Women should be counseled that weight gain across pregnancy should not exceed Institute of Medicine recommendations (table 4), which are stratified and inversely related to starting body mass index. Gestational weight

gain above these recommendations increases the risk for large for gestational age and macrosomic infants [26-30]. Prepregnancy obesity and hyperglycemia also contribute to this risk. (See "Weight gain and loss in pregnancy", section on 'Recommendations for weight gain during pregnancy' and "Pregestational diabetes mellitus: Glycemic control during pregnancy", section on 'Calorie requirements'.)

SECOND TRIMESTER

General principles — Women are seen by the obstetrical provider every two to four weeks through the second trimester, but more frequently if complications arise or glycemic control is suboptimal. This schedule of visits should be individualized based upon the severity of the diabetes, the degree of glycemic control, and the presence of other pregnancy complications. As discussed above, blood glucose values can also be reviewed via telephone, e-mail, or facsimile machine.

If a first trimester ultrasound examination has not been obtained, biometric measurements from a second trimester ultrasound examination may be used to confirm or revise the estimated date of delivery (EDD).

Screening for aneuploidy — As discussed above (see 'Screening for aneuploidy' above), screening for aneuploidy is offered, according to routine obstetrical practice. Diabetes does not increase the risk of fetal aneuploidy. However, levels of maternal serum alpha-fetoprotein (MSAFP), unconjugated estriol (uE3), and inhibin A, which are components of some second trimester Down syndrome screening tests, are significantly reduced in women with diabetes, thereby mimicking the pattern suggestive of Down syndrome. Therefore, MoM values should be adjusted in women with diabetes. (See "Laboratory issues related to maternal serum screening for Down syndrome", section on 'Diabetes mellitus'.)

Screening for neural tube defects — The prevalence of neural tube defects (NTDs) is higher in women with pregestational diabetes mellitus. As an example, in a study from 1982 (before recommendations for folate supplementation and food fortification), NTDs occurred in 2 percent of pregnancies complicated by diabetes versus 0.1 to 0.2 percent of the general population [31]. In a study from 2004, NTDs occurred in 0.19 percent of pregnancies complicated by diabetes versus 0.07 percent of pregnancies in women without diabetes [32]. The lower prevalence in 2004 likely reflect trends in better periconceptional glucose control, as well as increased periconceptional folate exposure.

Either ultrasound alone or in combination with measurement of MSAFP may be used to screen for neural tube defects. We use ultrasound alone. Since the median MSAFP level is 15 percent lower and the prevalence of NTDs is higher in women with diabetes than in those without diabetes, a lower threshold MSAFP value (eg, approximately 1.5 MoM [multiples of the median]) has typically been used in women with diabetes to obtain the same negative predictive value for NTDs as in women without diabetes. Laboratory requisitions for MSAFP typically ask providers to indicate if the patient has diabetes; however, the need for correction for diabetes independent of maternal weight has been challenged [33]. (See "Open neural tube defects: Risk factors, prenatal screening and diagnosis, and pregnancy management".)

Screening for other congenital anomalies — A detailed ultrasound examination of fetal anatomy is performed at approximately 18 weeks of gestation in pregnancies complicated by pregestational diabetes because of the increased prevalence of congenital anomalies in this group. If those performing the ultrasound are aware of the diagnosis of diabetes, they can be particularly mindful of evaluating for anomalies common to such pregnancies. Early detection of congenital anomalies allows parents and clinicians to prepare for the birth of neonate who may require specialized care. Alternatively, some parents may choose pregnancy termination; such procedures are more easily and safely undertaken at earlier gestational ages.

The second trimester ultrasound examination should encompass a detailed survey of fetal anatomy. As noted above, fetuses of women with diabetes are at risk for neural tube defects and evidence of such anomalies is often apparent on ultrasound (see "Ultrasound diagnosis of neural tube defects"). The second trimester ultrasound in pregnancies complicated by diabetes should also focus on cardiac anatomy, including a four-chamber view of the heart and visualization of the outflow tracts. Detailed examination of the fetal heart is important because congenital heart disease occurs more frequently in the offspring of women with diabetes than in the general population and accounts for about one-half of diabetes-related major congenital anomalies [25,34]. As an example, in a series of 535 pregnant women with preexisting diabetes, 30 (5.6 percent) delivered an infant with confirmed congenital heart disease; the risk was 8.3 percent in women with A1C ≥8.5 percent versus 3.9 percent of those with an A1C below this level [35]. Some centers refer all women with diabetes for fetal echocardiograms, while others restrict fetal echocardiography to fetuses with an abnormal detailed anatomic survey or women with marked glucose abnormalities. A selective approach is acceptable given routine echocardiography has a low yield in centers with high volume, skilled comprehensive ultrasound services [36,37]. Conotruncal and ventricular septal defects are the most common cardiac defects found in these fetuses. (See "Fetal cardiac abnormalities: Screening, evaluation, and pregnancy management".)

Significant augmentation of interventricular septal thickness may be noted in midtrimester fetuses of diabetic women and often progresses during the course of pregnancy [38]. The hypertrophy primarily occurs in women with poor glycemic control. Although this condition is usually mild and asymptomatic, congestive cardiomyopathy, which is a more diffuse process of hypertrophy and hyperplasia of the myocardial cells, can also occur. Both disorders are transient and managed with supportive care. (See "Infant of a diabetic mother", section on 'Cardiomyopathy'.)

Test performance — The utility of sonographic examination was illustrated by the following large series:

- In one series of 432 pregestational diabetic gravidas evaluated at 12 to 23 weeks of gestation, the prevalence of major congenital abnormalities at delivery was 7 percent [39]. Sonographic identification of major birth defects before 24 weeks had

sensitivity, specificity, and positive and negative predictive values of 56, 99.5, 90, and 97 percent, respectively [39]. The lesions most commonly missed were ventricular septal defect, an abnormal hand or foot, unilateral renal abnormality, and cleft palate without cleft lip.

- In another report, 289 gravid women with pregestational diabetes underwent comprehensive prenatal diagnostic testing including glycated hemoglobin, maternal serum AFP, comprehensive fetal ultrasonography with a standard four-chamber cardiac view at 18 weeks, and detailed multi-image echocardiography at 22 weeks of gestation [40]. Sensitivity, specificity, and positive and negative predictive values for the diagnosis of major noncardiac fetal abnormalities were 59, 100, 100, and 98 percent, respectively. Sensitivity, specificity, and positive and negative predictive values of the standard four-chamber view were 33, 100, 100, and 97 percent; the majorities of missed cardiac defects were septal and outflow tract lesions. The addition of echocardiography improved the detection of cardiac defects.

THIRD TRIMESTER

General principles — In the third trimester, diabetic gravida are seen frequently, as often as every one to two weeks until 36 weeks of gestation, and then weekly until delivery. The major concerns of the third trimester are:

- Continued close monitoring of maternal blood glucose levels
- Fetal testing and monitoring to minimize the risk of intrauterine fetal demise
- Monitoring for obstetrical or medical complications necessitating premature delivery
- Evaluation for excessive or insufficient growth.

Obstetrical management consists of reinforcement of good glycemic control, electronic and sonographic fetal monitoring, estimation of fetal size, surveillance for pregnancy complications such as preeclampsia or polyhydramnios, and, in some cases, determination of fetal pulmonary maturity.

During the second trimester, generally only small changes in insulin doses are needed in women whose glucose control was stable by the end of the first trimester. In contrast, during the third trimester, insulin resistance due to the hormones produced by the placenta increases rapidly, and changes in insulin dose are commonly required to maintain euglycemia.

Assessment of fetal well-being — Intrauterine fetal demise is now a rare complication of diabetic pregnancy, primarily due to achievement of good glycemic control. The fetus of the diabetic mother is at risk for hypoxia primarily from two mechanisms: (1) fetal hyperglycemia and hyperinsulinemia increase fetal oxygen consumption, which may induce fetal hypoxemia and acidosis if the oxygen needs of the fetus are not met [41-45], and (2) maternal vasculopathy and hyperglycemia can lead to reduced uteroplacental perfusion, which may be associated with reduced fetal growth [46].

The American College of Obstetricians and Gynecologists (ACOG) recommends antepartum fetal testing for pregnancies complicated by pregestational diabetes [47]. There are no data from large or randomized trials on which to make an evidenced-based recommendation as to which pregnancies complicated by diabetes should undergo fetal surveillance, when to start, what test to order, or how often to perform it [48]. As a result, management is largely based upon clinical experience and expert opinion. ACOG has suggested antepartum monitoring using fetal movement counting, biophysical profile, nonstress test (NST), and/or contraction stress test at "appropriate intervals," with initiation of testing generally at 32 to 34 weeks of gestation [47]. At least one study, however, has questioned the reassurance provided by a normal amniotic fluid volume in diabetic pregnancies, finding that the NST, but not the amniotic fluid index, was predictive of a nonreassuring fetal heart rate tracing in labor requiring cesarean delivery [49]. A 2009 NIH workshop recognized the limitations of available data and concluded that, in managing diabetic pregnancies, it was “not clear which method [of antenatal testing], if any, is superior” [50].

We begin antepartum surveillance around 32 weeks of gestation, increasing the frequency of testing to two times per week from 36 weeks until delivery [51]. In complicated patients with intrauterine growth restriction, oligohydramnios, preeclampsia, or poorly controlled blood glucose concentrations, testing may start as early as 26 weeks of gestation and is performed more frequently. Any significant deterioration in maternal status necessitates reevaluation of the fetus. The frequency of intrauterine fetal death (excluding congenital malformations) with such protocols is approximately 3 per 1000 pregnancies in women with type 1 diabetes [52].

If non-reassuring fetal testing is related to a potentially reversible problem such as hyperglycemia or ketoacidosis, it is advisable to resuscitate the fetus in utero by treating the medical disorder. Pathologic fetal heart rate patterns will often revert to normal when the mother's metabolic status is corrected.

If non-reassuring fetal testing appears to be related to a non-reversible problem, the gestational age and the associated risk for sequelae of prematurity strongly influence management. In premature fetuses, we try to delay delivery, at least long enough to treat the mother with glucocorticoids to accelerate fetal lung maturation (see 'Antenatal glucocorticoids' below). This can be done while monitoring the fetus more intensively, or even continuously. The degree of compromise indicated by fetal surveillance is used to weigh the relative risks and benefits of delaying delivery.

Assessment of fetal growth — Evaluation of fetal growth is a particularly important component of third trimester obstetrical care, as pregnancies complicated by maternal diabetes are commonly associated with accelerated growth [53], but are also at increased risk of impaired fetal growth. We obtain an ultrasound examination at 28 to 32 weeks of gestation to assess fetal growth. We repeat the examination at three- to four-week intervals if the examination or maternal conditions raise continued concern of

insufficient fetal growth. We typically perform the last sonogram at approximately 38 weeks of gestation to estimate fetal weight and assist with delivery plans. Alternatively, some obstetricians only obtain an early third trimester evaluation of fetal growth in those diabetic patients with hypertension or nephropathy and wait until 38 weeks of gestation for evaluation of others.

Accelerated fetal growth — Accelerated growth is most common among women whose diabetes is marked by insulin resistance; high insulin requirements are associated with accelerated fetal growth even in euglycemic pregnancies [54].

The term "large for gestational age" (LGA) usually refers to a fetus or newborn that is greater than the 90th centile for fetuses or infants of that gestational age (possibly including adjustments for fetal gender and ethnicity). At 40 weeks of gestation, the 90th percentile for birth weight in the United States is about 4060 grams [55]. The term "macrosomia" refers to a fetus or infant that is greater than some defined weight regardless of gestational age, gender, or ethnicity. Various authors and professional organizations have defined macrosomia as greater than 4000, greater than 4250, and greater than 4500 grams. The American College of Obstetricians suggests a threshold of 4500 grams because maternal and infant morbidity increases sharply above this level [56].

Maternal diabetes mellitus may double the incidence of LGA infants; it also changes the anthropometric measurements of infants of diabetic mothers (IDMs) compared with offspring of women without diabetes [57]. Specifically, the chest-to-head and shoulder-to-head ratios are increased in IDMs [58].

LGA fetuses are at increased risk for a prolonged second stage of labor, shoulder dystocia, operative delivery, maternal and infant birth trauma, and perinatal death [59]. Maternal diabetes mellitus increases the likelihood of shoulder dystocia two- to six-fold compared to the population without diabetes [60] and increases the likelihood of dystocia-associated fetal morbidity, such as brachial plexus injury [61]. The correlation between shoulder dystocia and birth weight in gravida with and without diabetes is shown in the table (table 5) [62]. (See "Shoulder dystocia: Risk factors and planning delivery of at risk pregnancies".)

Accelerated fetal growth is also associated with an increased risk of neonatal metabolic and physiologic disturbances. Continued control of blood glucose concentration during the third trimester is important to minimize the risk of these complications. (See "Infant of a diabetic mother", section on 'Neonatal effects'.)

If present, accelerated fetal growth in fetuses of pregnancies of women with diabetes often becomes apparent at 26 to 28 weeks of gestation, which is the rationale behind an early third trimester ultrasound examination [34,63,64]. A possible explanation for this observation is that insulin is the major regulatory hormone of fetal growth and fetal insulin receptors are maximally expressed at 19 to 25 weeks of gestation. In spite of this physiology, ultrasound examination at 29 to 34 weeks is not highly predictive of later LGA births in these pregnancies [65].

Although neonatal weight is an important predictor of neonatal morbidity and estimation of fetal weight at term is an important variable in delivery planning, there is no highly reliable method for identifying LGA fetuses before delivery [34,66,67]. This was illustrated in a review of studies of ultrasound for predicting EFW >4000 g in women with diabetes [34]. Sensitivity ranged from 33 to 83 percent and specificity ranged from 77 to 98 percent. (See "Fetal macrosomia", section on 'Women with diabetes'.)

Given the limitations of fetal weight estimates, some investigators have used other measurements for predicting LGA and shoulder dystocia. LGA is most apparent in the liver and abdomen and occurs in approximately 88 percent of fetuses in whom the abdominal circumference and estimated fetal weight both exceed the 90th percentile [68]. Enlarged biparietal diameter and head circumference are less predictive of LGA than enlarged abdominal measurements. Fetal fat thickness or body habitus and a variety of equations (eg, chest minus biparietal diameter ≥1.4 cm) have also been used to predict LGA and risk of shoulder dystocia. These assessments have yielded sensitivities of 83 to 96 percent in pregnancies complicated by diabetes [69]. Although these assessments can be somewhat predictive of LGA and shoulder dystocia, many of the measurements are difficult to obtain and reproduce accurately and these formulas have not been validated in large studies or at a variety of sites.

Growth restriction — Impaired growth is more common among women with diabetic vasculopathy and/or superimposed preeclampsia. It is associated with increased fetal and neonatal morbidity and mortality, and has long-term health implications. (See "Infants with fetal (intrauterine) growth restriction".)

If there is evidence of intrauterine growth restriction, which is uncommon, but often related to preeclampsia or preexisting maternal vasculopathy, tests of fetal well-being are initiated. (See "Fetal growth restriction: Evaluation and management", section on 'Pregnancy management'.)

Preeclampsia — The incidences of hypertension and preeclampsia are increased in pregnant women with diabetes and are related to pregestational hypertension and vascular and renal disease. Poor glycemic control also appears to play a role [70].

- In one review, the incidence of preeclampsia in diabetic women with and without vascular disease was 17 and 8 percent, respectively, compared to a rate of 5 to 8 percent in women without diabetes [57].
- In another series of 462 women with pregestational diabetes, the rate of preeclampsia in women with White classification B, C, D, and F/R (table 1) was 11, 22, 21, and 36 percent, respectively [71].
- In a third study, the risk of preeclampsia increased significantly with increasing A1C values above optimal levels [70]. Compared to women with A1C <6.1 percent at 26 weeks of gestation, the odds of preeclampsia for women with A1C 6.1 to 6.9

percent, 7.0 to 7.9 percent, and ≥8 percent were 2.1, 3.2, and 3.8, respectively. At 34 weeks of gestation, the odds of preeclampsia with A1C values ≥7.0 percent and ≥8 percent were 3.3 and 8.0, respectively.

The increased risk of preeclampsia is concordant with the observation that insulin resistance appears to increase the risk of developing preeclampsia, even in the absence of overt diabetes [72,73]. Impaired endothelium-dependent vasodilation appears to be related to the duration of diabetes [74].

Diagnosis and management of preeclampsia are similar to that in women without diabetes, except among those who enter pregnancy with preexisting nephropathy. In these women, diagnosing preeclampsia can be difficult and requires relying on deterioration of other markers. (See "Preeclampsia: Management and prognosis" and "Preeclampsia: Clinical features and diagnosis", section on 'Differential diagnosis'.)

Polyhydramnios — Maternal diabetes is a common etiology of polyhydramnios, although the mechanism for the increased amniotic fluid volume has not been clearly defined. Possibilities include fetal polyuria secondary to maternal and fetal hyperglycemia, decreased fetal swallowing, or an imbalance in water movement between the maternal and fetal compartments [75]. Polyhydramnios is frequently associated with accelerated fetal growth.

Fetal outcomes in pregnancies with diabetes-associated polyhydramnios may not be as poor as outcomes in pregnancies in which polyhydramnios is associated with fetal neurologic disease, twin to twin transfusion, or other syndromes. For this reason, and because interventions for polyhydramnios are limited, diabetes-associated polyhydramnios rarely requires special management [76]. (See "Physiology of amniotic fluid volume regulation" and "Polyhydramnios".)

Preterm labor — Compared with controls without diabetes or hypertension, women with pregestational diabetes have higher rates of both indicated preterm delivery (22 versus 3 percent; OR 8.1; 95% CI 6.0-10.9) and spontaneous preterm delivery (16 versus 11 percent; OR 1.6; 95% CI 1.2-2.2) [77]. Indicated preterm delivery is primarily initiated because of preeclampsia [77,78], but both gestational and pregestational diabetes have been associated with indicated preterm delivery independent of preeclampsia. The reasons for an increased risk of spontaneous preterm delivery are not clear [79,80].

The indications for inhibition of preterm labor are similar to those in the general obstetrical population. Our preferences for tocolytic therapy are nifedipine or indomethacin. We avoid beta-adrenergic receptor agonist therapy, as these drugs can cause severe hyperglycemia in women with diabetes. (See "Inhibition of acute preterm labor".)

Antenatal glucocorticoids — If preterm birth between 23 and 34 weeks of gestation is anticipated or planned, administration of betamethasone improves neonatal outcome. Administration of betamethasone to reduce neonatal complications associated with preterm birth should be done cautiously. Transient hyperglycemia induced by glucocorticoids can be severe in the women with diabetes; even when glucose levels are closely monitored and treated [81,82]. The hyperglycemic effect begins approximately 12 hours after the first steroid dose and lasts for about five days [83,84]. This was illustrated in a series in which 16 women with diabetes requiring insulin therapy were given betamethasone for fetal lung maturation [83]. Their daily insulin dose for the following five days increased by 6, 38, 36, 27, and 17 percent above baseline, respectively. Although administration of betamethasone also had potential benefits before preterm births between 34 and 37 weeks of gestation in a randomized trial (Antenatal Betamethasone for Women at Risk for Late Preterm Delivery [ALPS] [85]), women with diabetes were specifically excluded from this trial and, concordant with recommendations from specialty societies [86], we do not recommend late preterm steroid administration to improve neonatal outcome in diabetic pregnancies.

We monitor capillary blood glucose concentrations hourly, beginning 12 hours after the first dose of betamethasone and continuing for 24 hours after the second dose, and then reduce the frequency to several times per day thereafter if glucose levels are reasonably well controlled. For values >120 mg/dL (6.7 mmol/L), we treat with subcutaneous insulin but, in recognition of the risk of diabetic ketoacidosis in these patients, we begin continuous intravenous insulin infusion on the labor unit if values continue to rise in spite of such treatment, or if values are above 180 to 200 mg/dL (10 to 11.1 mmol/L). (See "Antenatal corticosteroid therapy for reduction of neonatal respiratory morbidity and mortality from preterm delivery".)

DELIVERY — A number of issues arise peripartum, such as assessment of fetal maturity, timing and route of delivery, and risk of birth trauma from macrosomia.

Fetal pulmonary maturity — Elective delivery before 39 weeks is increasingly discouraged, as the morbidities associated with early term ($37^{0/7ths}$ to $38^{6/7ths}$ weeks) and late preterm ($34^{0/7ths}$ to $36^{6/7ths}$ weeks) deliveries have become evident [87,88]. An amniocentesis demonstrating fetal lung maturity does not obviate all such morbidity [89].

When non-elective early delivery is being considered, it is important to remember that respiratory distress syndrome (RDS) is more likely to develop in infants of women with diabetes delivered early than in infants of women without diabetes delivered early; this risk does not become equivalent in the two groups until after 38.5 weeks of gestation [90]. The endocrine changes associated with maternal diabetes delay fetal lung maturation [91]. Specifically, high fetal insulin levels enhance cellular hypertrophy and hyperplasia at the expense of cellular maturation, thus leading to macrosomia and immature lung function. In the era prior to the availability of fetal pulmonary maturity tests, respiratory distress syndrome accounted for 52 percent of neonatal deaths among infants born to women with pregestational diabetes [92].

We evaluate timing of delivery based on clinical circumstances and maternal and fetal condition, mindful of the risk of pulmonary morbidity among preterm and early term newborns of women with diabetes, but do not use fetal pulmonary tests on amniotic fluid

to help make these decisions. Fetal lung maturity testing, in general, and in diabetic pregnancies, specifically, is no longer commonly performed.

We have not seen RDS in any infant of woman with diabetes delivered at or beyond 39 weeks of gestation; thus, we and others [93] do not assess fetal lung maturity at this gestational age. Although RDS occurs rarely at or after 39 weeks in patients with poor glycemic control, the risk of in-utero death in this setting probably far exceeds the risk of severe neonatal respiratory morbidity or mortality.

Timing of delivery — We and others [94] see little benefit in continuing pregnancy beyond 39 weeks in women with diabetes, particularly those with a favorable cervix. We suggest induction of labor for these pregnancies by 40 weeks of gestation [47]. Preterm delivery should be avoided, except when glycemic control is suboptimal or there are other maternal or fetal reasons for concern (eg, maternal vascular disease). In these cases, an acceptable approach is to induce labor at 37 weeks (or earlier) [95,96]. When such a plan is chosen, the risks of a failed induction due to an unfavorable cervix must be weighed against the risks associated with continuing the pregnancy.

In women with unfavorable cervices, excellent glycemic control, no vascular disease or preeclampsia, normal fetal growth, reassuring antepartum fetal surveillance, and no history of stillbirth, induction can be safely delayed until $40^{0/7ths}$ weeks [47,97,98]. If these criteria for continued pregnancy are not met or the patient is not compliant, induction is warranted before the cervix is favorable. Cervical ripening agents should be employed and are safe. (See "Induction of labor".)

A 2011 NIH workshop, “Timing of Indicated Late Preterm and Early Term Births,” echoed these recommendations [95]. For women with pregestational diabetes without vascular disease whose diabetes was well controlled, the workshop experts recommended delivery at ≥39 weeks. For those with pregestational diabetes and vascular disease, they suggested that delivery at 37 to 39 weeks was appropriate, and that delivery as early as 34 weeks could be considered on an individualized basis among patients with poor glycemic control. The American College of Obstetricians and Gynecologists (ACOG) has published similar recommendations [96].

Preterm delivery is also performed for the usual obstetrical indications (eg, preeclampsia, fetal growth restriction, abruption, premature labor with or without premature rupture of membranes, non-reassuring fetal testing) or for worsening maternal renal insufficiency or active proliferative retinopathy. (See "Pregnancy in women with diabetic kidney disease".)

Rationale — Decisions to undertake a preterm delivery because of maternal diabetes are balanced against morbidity associated with delivery at an early gestational age. In past eras, elective early delivery of women with pregestational diabetes had been advocated to prevent fetal death in late gestation [99-101]. This was a reasonable approach prior to 1950 since one-half of stillbirths in this population occurred after the 38th week of gestation [102]. However, fetal mortality has fallen precipitously among both diabetic women and the general obstetric population over the past few decades; thus, for most patients, the morbidity and mortality from prematurity and failed induction should be weighed carefully against contemporary estimates of potential benefit from early delivery [103]. Currently, it is unclear whether women with good glycemic control and reassuring antepartum surveillance are at any increased risk of an intrauterine demise at term. Although there are case reports of fetal deaths occurring within hours of reassuring fetal testing in gravidas with diabetes (and in nondiabetic women, as well), despite maternal euglycemia [104], there are insufficient data from large well-designed studies to convincingly demonstrate that the risk of fetal demise with modern, intensive perinatal care is increased compared to controls without diabetes.

The only randomized trial evaluating the timing of delivery of 200 women with uncomplicated insulin-requiring diabetes (13 pregestational, 187 gestational) and appropriately grown fetuses showed induction during the 38th week was advantageous compared to expectant management [105]. Women randomly assigned to active induction of labor within five days of reaching 38 weeks of gestation had a lower prevalence of macrosomia compared to those managed expectantly with biweekly nonstress tests and amniotic fluid volume assessment until 42 weeks (10 versus 23 percent) and fewer cases of shoulder dystocia (0 versus 3 percent). The rate of cesarean delivery was similar for the two groups. Moreover, 50 percent of women in the expectant management group ultimately required induction for obstetric indications.

Is early induction recommended when macrosomia is suspected? — Due to the difficulty in accurately diagnosing macrosomia, and the relatively small probability of permanent neurologic injury resulting from shoulder dystocia, induction of labor for women with suspected macrosomic infants has not decreased the risk of maternal or neonatal morbidity in women without diabetes or mixed populations of women with and without diabetes. (See "Shoulder dystocia: Risk factors and planning delivery of at risk pregnancies", section on 'Planning delivery in at risk pregnancies'.)

Route of delivery — Maternal diabetes alone is not an indication for cesarean birth in the absence of the usual obstetric indications. Macrosomia may be considered an indication for cesarean delivery due to the risk of morbidity from shoulder dystocia [106-109]. It has been suggested that neonates with shoulder dystocia have greater shoulder and chest-to-head disproportion than macrosomic infants without this complication [58,110]. In particular, macrosomic infants of mothers with diabetes are more likely to exhibit this disproportion than infants of nondiabetic mothers of comparable weight [108]. (See 'Accelerated fetal growth' above.)

For these reasons, the position of the American College of Obstetricians and Gynecologists is that, although the diagnosis of macrosomia is imprecise, prophylactic cesarean delivery is reasonable to prevent brachial plexus injury when the estimated fetal weight is greater than 4500 g in a woman with diabetes [111]. If the patient has had a previous child with shoulder dystocia, then estimated fetal weight, gestational age, and the severity of the prior neonatal injury, if any, should also be considered in making the decision about route of delivery [112]. (See "Shoulder dystocia: Risk factors and planning delivery of at risk pregnancies".)

Since assisted vaginal delivery is associated with an additional risk for shoulder dystocia, a lower weight threshold (eg, 4000 g) should be used when deciding on performing an operative vaginal delivery on a woman with diabetes [113].

Maternal diabetes is not a contraindication to a trial of labor after a previous cesarean delivery (TOLAC); however, the success rate may be lower than in women without diabetes (64 versus 74 percent [114]). (See "Choosing the route of delivery after cesarean birth".)

Labor and delivery — The woman with diabetes and her fetus are continuously monitored on the labor and delivery unit, as these pregnancies are at increased risk for nonreassuring fetal heart rate patterns [115,116]. Peripartum maintenance of maternal euglycemia is essential and generally requires hourly capillary glucose determinations, intravenous solutions containing glucose, and intravenous insulin infusion if hyperglycemia is present. Management of glucose and insulin during labor, induction, and cesarean delivery, is discussed separately. (See "Pregestational and gestational diabetes: Intrapartum and postpartum glycemic control".)

We try to schedule induction or cesarean delivery early in the morning, as this facilitates management of glucose and insulin in a fasting patient. There are no contraindications to natural childbirth, epidural anesthesia, or general anesthesia. However, maternal hypotension, more commonly associated with spinal than epidural anesthesia, may be associated with a lower pH and a greater base deficit in the infant of a diabetic mother [117]. (See "Umbilical cord blood acid-base analysis at delivery".)

POSTPARTUM — Breastfeeding should be encouraged [118]. (See "Infant benefits of breastfeeding".)

Insulin requirements drop sharply after delivery and should be recalculated at this time based on serial blood glucose determinations. Postpartum calorie requirements are approximately 25 kcal/kg per day, but somewhat higher (27 kcal/kg per day) in lactating women. (See "Pregestational and gestational diabetes: Intrapartum and postpartum glycemic control".)

Postpartum depression is more common among women with diabetes (pregestational or gestational) than in nondiabetic women [119], so screening is warranted. (See "Postpartum unipolar major depression: Epidemiology, clinical features, assessment, and diagnosis".)

The United States Medical Eligibility Criteria for Contraceptive Use consider all hormonal methods acceptable for women with diabetes and no vascular disease [120]; thus, selection should be based upon the same factors that apply to women without diabetes [121] (see "Contraceptive counseling and selection"). Although evidence from randomized trials is limited, both progestin-only methods and low-dose combined oral contraceptives appear to have only minor effects on glucose and fat metabolism [122]. Depot medroxyprogesterone acetate (DMPA) and combined estrogen-progestin contraceptives are generally avoided in women with vascular disease [120]. The progestin-releasing IUD, copper IUD, and etonogestrel implant have lower risk of thromboembolic events than estrogen-progestin contraceptives [123].

Ophthalmologic follow-up during the first year postpartum is advised since retinopathy can be aggravated anytime during pregnancy or postpartum [10].

DIABETIC KETOACIDOSIS — Physiological changes and pathological conditions related to pregnancy predispose women with diabetes to worsening glycemic control. Despite this, diabetic ketoacidosis (DKA) occurs in only about 0.5 to 3 percent of diabetic pregnant women [124]. (See "Pregestational diabetes: Preconception counseling, evaluation, and management" and "Pregestational diabetes mellitus: Glycemic control during pregnancy".)

Diabetic ketoacidosis results from absolute or relative insulin deficiency combined with counterregulatory hormone excesses (ie, glucagon, glucocorticoids, catecholamines, and growth hormone). Pregnancy is a state of relative insulin resistance, which can be exacerbated by systemic infection and insulin pump technical failure. Counterregulatory hormone excesses can result from betamimetic tocolytic therapy and high dose glucocorticoid therapy administered to accelerate fetal lung maturity. (See "Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Clinical features, evaluation, and diagnosis", section on 'Precipitating factors'.)

The presentation of DKA is similar in pregnant women to that in nonpregnant persons, with symptoms of nausea, vomiting, thirst, polyuria, polydipsia, abdominal pain, and, when severe, a change in mental status. Laboratory findings include hyperglycemia (usually >250 mg/dL [13.9 mmol/L]), acidemia (arterial pH <7.30), an elevated anion gap (>12 mEq/L), ketonemia, low serum bicarbonate (<15 mEq/L), elevated base deficit (>4 mEq/L), and renal dysfunction [125]. (See "Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Clinical features, evaluation, and diagnosis", section on 'Clinical presentation' and "Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Clinical features, evaluation, and diagnosis", section on 'Laboratory findings'.)

Hyperglycemia is usually severe in non-pregnant persons, however, DKA is well documented to occur at much lower blood glucose levels during pregnancy. In one series, 4 of 11 pregnant women with DKA had blood glucose levels less than 200 mg/dL (11.1 mmol/L) [126]. Severe hyperglycemia can cause an osmotic diuresis resulting in maternal volume depletion. This, in turn, can result in reduced uterine perfusion and, in association with the metabolic abnormalities of DKA, produce life-threatening fetal hypoxemia and acidosis. Maternal mortality is less than 1 percent, but fetal mortality rates of 9 to 36 percent have been reported, as well as increased risks of preterm birth [124]. Thus, DKA is a true obstetrical emergency.

During acute DKA, the fetal heart rate often has minimal or absent variability and absent accelerations, as well as repetitive decelerations [124]. These abnormalities usually resolve with resolution of DKA, but it may take several hours before the tracing is normal [127].

Other than close attention to fetal heart rate monitoring, DKA is managed similarly in pregnant and nonpregnant patients [124]. This includes the use of intravenous insulin, appropriate volume replacement, correction of electrolyte abnormalities (including potassium, phosphate, and magnesium), monitoring acidosis, and a search for precipitating causes, such as infection or insulin noncompliance. Glucocorticoids and beta-mimetics should be avoided during DKA, as they will worsen hyperglycemia. (See "Diabetic ketoacidosis and hyperosmolar hyperglycemic state in adults: Treatment".)

DKA alone is generally not an indication for delivery. Emergent delivery before maternal stabilization should be avoided because it increases the risk of maternal morbidity and mortality, and may result in delivery of a hypoxic, acidotic preterm infant for whom in utero resuscitation may have resulted in a better outcome. The timing of delivery needs to be individualized based on multiple factors including gestational age, maternal condition (whether the mother is responding to aggressive therapy or deteriorating), and fetal condition (whether the fetal heart rate pattern is improving or deteriorating). Fetal heart rate abnormalities resulting from maternal acidosis will often improve as DKA is treated and maternal condition improves [124].

SOCIETY GUIDELINE LINKS — Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Diabetes mellitus in pregnancy".)

INFORMATION FOR PATIENTS — UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Beyond the Basics topics (see "Patient education: Care during pregnancy for women with type 1 or 2 diabetes mellitus (Beyond the Basics)" and "Patient education: Gestational diabetes mellitus (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- Ideally, women with pregestational diabetes will have received preconceptional counseling to assess their baseline medical status and educate them about the management and potential complications of diabetes in pregnancy. (See 'First prenatal visit' above.)
- In addition to routine prenatal testing, assessment of the diabetic gravida should include: glycated hemoglobin concentration, baseline renal function, thyrotropin and free thyroxine, electrocardiogram, dilated and comprehensive eye examination by an ophthalmologist, and first trimester ultrasound examination if pregnancy dating is uncertain. (See 'Testing' above.)

  Laboratory monitoring across the remainder of pregnancy is described in the table (table 6).
- The care of women with diabetes during pregnancy generally requires a team approach to provide the necessary expertise. Information on diet, insulin therapy, exercise and glucose monitoring should be provided by clinicians with experience in management of diabetes during pregnancy. (See 'Counseling and management' above.)
- A markedly elevated glycohemoglobin value in the first trimester is associated with increased risks of both first trimester miscarriage and congenital malformations. We typically advise patients of these risks and evaluate fetal development via second trimester sonographic examination and maternal serum multiple marker screening. (See 'Risk of congenital anomalies' above.)
- Screening for Down syndrome and neural tube defects (NTDs) are offered, according to routine obstetrical practice. Diabetes does not increase the risk of fetal aneuploidy, but does affect interpretation of the analyte panels. The risk of NTDs is increased for fetuses of diabetic gravidae. (See 'Screening for aneuploidy' above and 'Screening for neural tube defects' above.)
- We suggest ultrasound examination and fetal echocardiogram at approximately 18 weeks of gestation to evaluate for congenital anomalies, particularly congenital heart disease. (See 'Screening for other congenital anomalies' above.)
- We begin antepartum surveillance with weekly nonstress tests at 32 weeks of gestation, increasing the frequency of testing to two times per week from 36 weeks until delivery. (See 'Assessment of fetal well-being' above.)
- We obtain an ultrasound examination at approximately 38 weeks of gestation to estimate fetal weight and assist with delivery plans. (See 'Assessment of fetal growth' above.)

- We suggest nifedipine or indomethacin for tocolysis of preterm labor instead of a beta-adrenergic receptor agonist (**Grade 2C**). (See 'Preterm labor' above.)
- If antenatal betamethasone is administered to accelerate fetal lung maturation between 23 and 34 weeks of gestation, we monitor capillary blood glucose concentrations hourly beginning 12 hours after the initial dose and continuing for at least 24 hours after the second dose, and then several times per day thereafter. We administer insulin intravenously as needed to maintain euglycemia. (See 'Antenatal glucocorticoids' above.)
- If the expected fetal weight is over 4500 grams, we suggest cesarean delivery to avoid possible trauma from shoulder dystocia (**Grade 2B**). (See 'Route of delivery' above.)
- We suggest induction of labor at 39 to 40 weeks of gestation in women with favorable cervices and fetuses less than 4500 g (**Grade 2B**). The presence of high risk factors, such as poor glucose control, worsening nephropathy or retinopathy, preeclampsia, or restricted fetal growth warrant consideration of earlier delivery. Awaiting the spontaneous onset of labor is reasonable if there is good glycemic control and no pregnancy or additional maternal complications. However, extending pregnancy beyond 40 weeks of gestation is generally not advised unless the patient has gestational diabetes with excellent glucose control with dietary modification alone. If induction of an unfavorable cervix is planned, use of cervical ripening agents is safe and effective. (See 'Timing of delivery' above.)
- We suggest avoiding induction because of suspected fetal macrosomia (**Grade 2C**). This intervention has not been proven to improve maternal or fetal outcomes, and may increase the cesarean delivery rate. (See 'Is early induction recommended when macrosomia is suspected?' above.)

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Topic 4806 Version 42.0

GRAPHICS

Modified White's classification of diabetes in pregnancy

Class	Description
A	Abnormal GTT before pregnancy at any age or of any duration treated only by diet therapy
B	Onset at age 20 years or older and duration of less than 10 years
C	Onset at age 10 to 19 years or duration of 10 to 19 years
D	Onset before 10 years of age, duration over 20 years, benign retinopathy, or hypertension (not preeclampsia)
R	Proliferative retinopathy or vitreous hemorrhage
F	Nephropathy with over 500 mg/day proteinuria
RF	Criteria for both classes R and F
G	Many pregnancy failures
H	Evidence of arteriosclerotic heart disease
T	Prior renal transplantation
Gestational diabetes	
A1	Diet-controlled gestational diabetes
A2	Insulin-treated gestational diabetes

Classes B through T require insulin treatment.

GTT: glucose tolerance test.

Adapted from: Hare JW, White JP. Diabetes Care 1980; 3:394.

Graphic 79735 Version 7.0

Initial prenatal laboratory examination

Blood type and antibody screen
Rhesus type
Hematocrit or hemoglobin
PAP smear
Rubella status (immune or nonimmune)
Syphilis screen
Urinary infection screen
Hepatitis B surface antigen
HIV counseling and testing
Chlamydia

Graphic 63296 Version 1.0

Indications for ultrasound examination during pregnancy

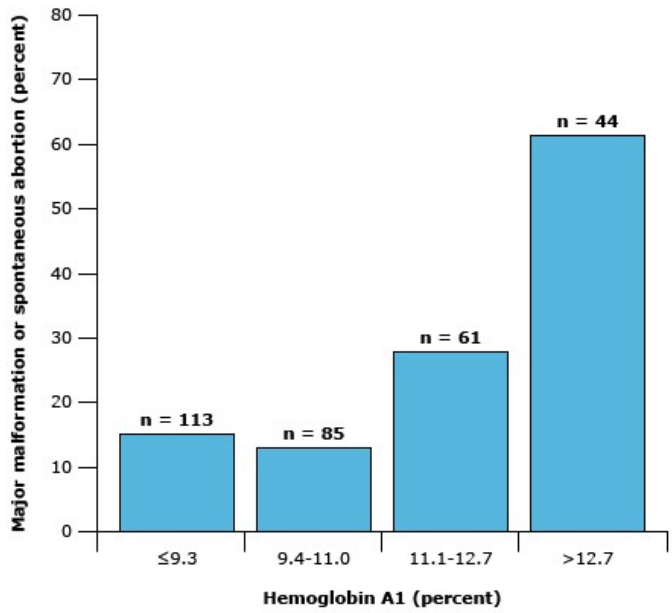
First-trimester ultrasonography
Indications for first-trimester ultrasonography include, but are not limited to the following:
To confirm the presence of an intrauterine pregnancy
To evaluate a suspected ectopic pregnancy
To evaluate vaginal bleeding
To evaluate pelvic pain
To estimate gestational age
To diagnose or evaluate multiple gestations
To confirm cardiac activity
As adjunct to chorionic villus sampling, embryo transfer, or localization and removal of an intrauterine device
To assess for certain fetal anomalies, such as anencephaly, in patients at high risk
To evaluate maternal pelvic or adnexal masses or uterine abnormalities
To screen for fetal aneuploidy
To evaluate suspected hydatidiform mole
Second- and third-trimester ultrasonography
Indications for second- and third-trimester ultrasonography include, but are not limited to the following:
Screening for fetal anomalies
Evaluation of fetal anatomy
Estimation of gestational age
Evaluation of fetal growth
Evaluation of vaginal bleeding
Evaluation of abdominal or pelvic pain
Evaluation of cervical insufficiency
Determination of fetal presentation
Evaluation of suspected multiple gestation
Adjunct to amniocentesis or other procedure
Evaluation of a significant discrepancy between uterine size and clinical dates
Evaluation of a pelvic mass
Evaluation of a suspected hydatidiform mole
Adjunct to cervical cerclage placement
Suspected ectopic pregnancy
Suspected fetal death
Suspected uterine abnormalities
Evaluation of fetal well-being
Suspected amniotic fluid abnormalities
Suspected placental abruption
Adjunct to external cephalic version
Evaluation of prelabor rupture of membranes or premature labor
Evaluation of abnormal biochemical markers
Follow-up evaluation of a fetal anomaly
Follow-up evaluation of placental location for suspected placenta previa
History of previous congenital anomaly
Evaluation of the fetal condition in late registrants for prenatal care
Assessment for findings that may increase the risk of aneuploidy

A sonographic study should only be performed for a valid medical indication. Nonmedical use of obstetric ultrasonography has been discouraged by major societies, including the American College of Obstetricians and Gynecologists (ACOG), the American Institute of Ultrasound in Medicine (AIUM), and the International Society of Ultrasound in Obstetrics and Gynecology.

Reprinted with permission from: Ultrasound in pregnancy. Practice Bulletin No. 175. American College of Obstetricians and Gynecologists. Obstet Gynecol 2016; 128:e241-56.

Graphic 58590 Version 2.0

Deleterious effect of poor glycemic control on fetal outcome



Combined incidence of major malformation and spontaneous abortion according to the hemoglobin A1 (HbA1) value during the first trimester of pregnancy in 303 women with type 1 diabetes. The risk rose markedly at HbA1 values above 11 percent (approximately equivalent to an AIC value of 8.5 percent). Other studies have found an increase in risk at A1C values above 9.5 percent.

Data from: Greene MF, Hare JW, Cloherty JP, et al, Teratology 1989; 39:225.

Graphic 67498 Version 4.0

Recommendations for total and rate of weight gain during pregnancy by prepregnancy BMI

	Total weight gain		Rates of weight gain* second and third trimester	
Prepregnancy BMI	**Range in kg**	**Range in lb**	**Mean (range) in kg/week**	**Mean (range) in lb/week**
Underweight (<18.5 kg/m^2)	12.5 to 18	28 to 40	0.51 (0.44 to 0.58)	1 (1 to 1.3)
Normal weight (18.5 to 24.9 kg/m^2)	11.5 to 16	25 to 35	0.42 (0.35 to 0.50)	1 (0.8 to 1)
Overweight (25.0 to 29.9 kg/m^2)	7 to 11.5	15 to 25	0.28 (0.23 to 0.33)	0.6 (0.5 to 0.7)
Obese (≥30.0 kg/m^2)	5 to 9	11 to 20	0.22 (0.17 to 0.27)	0.5 (0.4 to 0.6)

BMI: body mass index.
* Calculations assume a 0.5 to 2 kg (1.1 to 4.4 lb) weight gain in the first trimester.

Weight Gain During Pregnancy: Reexamining the Guidelines. Institute of Medicine (US) and National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines, Rasmussen KM, Yaktine AL (Eds), National Academies Press (US), The National Academies Collection: Reports funded by National Institutes of Health, Washington (DC) 2009. Available at: http://www.nap.edu/catalog/12584.html.

Graphic 75820 Version 15.0

Incidence of shoulder dystocia by birth weight in pregnancies with and without maternal diabetes

Birth weight (g)	Shoulder dystocia in nondiabetic pregnancies (percent)	Shoulder dystocia in diabetic pregnancies (percent)
Less than 4000	0.1 to 1.1	0.6 to 3.7
4000 to 4499	1.1 to 10.0	4.9 to 23.1
4500 or more	2.7 to 22.6	20.0 to 50.0

Data from:

1. *Acker DB, Sachs BP, Friedman EA. Risk factors for shoulder dystocia. Obstet Gynecol 1985; 66:762.*
2. *Nesbitt TS, Gilbert WM, Herrchen B. Shoulder dystocia and associated risk factors with macrosomic infants born in California. Am J Obstet Gynecol 1998; 179:476.*
3. *Sandmire HF, O'Halloin TJ. Shoulder dystocia: its incidence and associated risk factors. Int J Gynaecol Obstet 1988; 26:65.*

Graphic 75719 Version 6.0

Frequency of testing during pregnancy in women with pregestatonal diabetes

Test	Frequency
Hemoglobin A1C	Every 4 to 6 weeks
Blood glucose	Home measurements 4 to 8 times daily
Urine ketones	During period of illness; when any blood glucose value is >200 mg/dL (11.1 mmol/L)
Urine protein	Diptstick at office visits, quantitate 24 hour excretion each trimester in women with nephropathy
Serum creatinine	Each trimester in women with nephropathy
Thyroid function tests	Baseline TSH measurement
Eye examination	Baseline and then as necessary per retinal specialist

TSH: Thyroid stimulating hormone; A1C: Glycated hemoglobin

Graphic 51463 Version 4.0

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