



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

A The preponderance of data supporting this statement is derived from level 1 studies, which meet all of the evidence criteria for that study type

B The preponderance of data supporting this statement is derived from level 2 studies, which meet at least one of the evidence criteria for that study type

C The preponderance of data supporting this statement is derived from level 3 studies, which meet none of the evidence criteria for that study type or are derived from expert opinion, commentary or consensus

Study types and evidence criteria are defined at <http://pier.acponline.org/criteria.html>

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.

Table of Contents

1. Prevention: Recognize the role of measures to reduce the risk of gestational diabetes and prevent fetal malformations in diabetic pregnancies.	2
1.1 Counsel all diabetic women of childbearing potential on the need for pregnancy planning.	3
1.2 Counsel all obese women of childbearing age on the need for diet and exercise to decrease the risk of gestational diabetes.	3
1.3 Stop ACE inhibitor therapy, switch oral hypoglycemics to insulin, and review all other medications before conception.	4
2. Screening: Not applicable to this module.	5
3. Diagnosis: Use history, physical exam, and laboratory evaluation to confirm and classify diabetes, to assess control, and to identify comorbid conditions.	5
3.1 Evaluate women with pregestational diabetes for diabetic complications before conception and review issues of diabetic control, and review symptoms of hyperglycemia in all pregnant women.	5
3.2 Use laboratory testing to evaluate diabetic control and to screen for related medical conditions.	6
3.3 Not applicable to this module.	8
4. Consultation for Diagnosis: Consider consultation in all women with pregestational diabetes to assess the status of chronic complications of diabetes.	8
4.1 Consult appropriate subspecialists for help in defining the status of diabetic complications before conception.	8
4.2 Consider consultation with an endocrinologist for help in classifying gestational diabetes.	9
5. Hospitalization: Hospitalize patients with elevated glucose levels during pregnancy or in the pre-conception planning stages if necessary for glucose control.	9
5.1 Hospitalize pregnant women with elevated glucose levels and poor outpatient control.	10
5.2 Hospitalize pregnant women with evidence of ketoacidosis.	10
6. Non-drug Therapy: Recommend lifestyle changes and self-care to prevent complications in pregnant diabetic patients.	11



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

6.1 Stress diet and exercise in pregnant diabetic patients to control glucose levels.	11
6.2 Continue foot care in women with pregestational diabetes.	12
6.3 Recommend smoking cessation in all women with diabetic pregnancies.	12

7. Drug Therapy: Use drug therapy to treat hyperglycemia in the pre-conception period and throughout pregnancy, and recognize the toxicities of many drugs commonly used in diabetes. 12

7.1 Use insulin in patients with gestational diabetes to achieve optimal glycemic control.	13
7.2 Switch all women with pregestational diabetes on oral diabetic treatments to insulin before conception.	13
7.3 Stop ACE inhibitor therapy and review the patient's other medications before conception.	14

8. Patient Education: Emphasize the importance of pre-conception counseling in women with diabetes and of patient self-management during pregnancy. 14

8.1 Instruct all diabetic women of childbearing potential on the need for pre-conception planning.	14
8.2 Stress the importance of diet and exercise to control glucose levels in pregnant diabetic patients.	15
8.3 Continue preventive foot care in women with pregestational diabetes.	17
8.4 Recommend smoking cessation in all women with diabetic pregnancies.	17
8.5 Teach patients and family members to recognize hypoglycemia and to treat it appropriately.	17
8.6 Counsel patients on the need for an ophthalmology exam before conception or in early pregnancy.	18

9. Consultation for Management: Consult appropriate specialists in managing pregnant diabetic patients to ensure optimal care and best outcome. 18

9.1 Ensure specialized obstetric care for diabetic women who are pregnant or planning pregnancies.	18
9.2 Consider consultation with an endocrinologist and other professionals to ensure ideal glucose levels before and during pregnancy in diabetic women.	18
9.3 Obtain specialty consultation for help in managing complications of diabetes in pregnant women or before conception.	19

10. Follow-up: Monitor pregnant diabetic patients closely for adherence to glucose monitoring, issues of glucose control, and the development of diabetic complications. 20

10.1 Review blood glucose logs at every visit and adjust insulin accordingly.	20
10.2 Review diabetes drugs after delivery and make changes as necessary.	21
10.3 Screen women with pregestational diabetes for the development or worsening of diabetic complications during pregnancy.	21
10.4 Plan future pregnancies postpartum.	22
10.5 After delivery, classify patients found to be diabetic during pregnancy and arrange for long-term follow-up.	22

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP.

Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

1. Prevention: Recognize the role of measures to reduce the risk of gestational diabetes and prevent fetal malformations in diabetic pregnancies. A B

1.1 Counsel all diabetic women of childbearing potential on the need for pregnancy planning. A

Specific recommendation:

- Ensure effective birth control at all times, unless the patient is trying to conceive and is in good diabetic control.
- Counsel women with type 1 or 2 diabetes on the risks of fetal malformation associated with unplanned pregnancies and poor metabolic control.
- Achieve fasting whole-blood glucose levels of 70 to 100 mg/dL and 2-hour postprandial levels of <140 mg/dL in diabetic women planning pregnancies.

Rationale:

- There is an association between elevated maternal glucose or glycohemoglobin levels during embryogenesis and high rates of pregnancy loss and major congenital malformations.

Evidence:

- In a meta-analysis of 14 cohort studies, the pooled rates of major and minor fetal anomalies were lower in diabetic women who had received pre-conception care (2.1%) compared with those who had not (6.5%; RR 0.36 [CI, 0.22 to 0.59]) ([1](#)).
- Population-based cohort studies have found an association between adverse fetal outcomes and maternal hyperglycemia ([2](#); [3](#)).

Comments:

- Pre-conception counseling also should include advice on folic acid intake, vaccinations for rubella and varicella, weight control, and a review of current diseases and medications in addition to an assessment of diabetes management.

1.2 Counsel all obese women of childbearing age on the need for diet and exercise to decrease the risk of gestational diabetes. B

Specific recommendation:

- Provide nutritional counseling to obese women of childbearing age consistent with American Diabetes Association [recommendations](#).
- Consider recommending to obese women planning pregnancy or already pregnant:
 - A 30% to 33% calorie restriction if BMI >30
 - Limiting fat intake to <30% of calories
 - Increasing physical activity, as recommended outside pregnancy, or a program of moderate exercise if the woman is already pregnant

Rationale:

- Prepregnant obesity increases the risk of gestational diabetes.

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

- Maternal prepregnant obesity, hyperglycemia, or both are associated with fetal malformations and macrosomia.
- Dietary fat restriction during pregnancy is associated with a reduced risk of gestational diabetes.
- Increased physical activity is associated with a reduced risk of gestational diabetes.

Evidence:

- Higher maternal prepregnancy BMI and weight gain during pregnancy are associated with macrosomia and an increased risk of fetal malformations (4).
- A study on 1698 women enrolled in the Pregnancy, Infection, and Nutrition Study found that the predicted probability of gestational diabetes was reduced by one half with a 10% decrease in dietary fat and a 10% increase in carbohydrate (5).
- In a prospective study of 909 women in Washington, those who participated in any physical activity during the previous year experienced a 56% risk reduction in the incidence of gestational diabetes compared with inactive women (RR, 0.44 [CI, 0.17 to 0.70]). The greatest reduction in the risk for gestational diabetes was seen among women who exercised both before and during pregnancy (adjusted RR, 0.31 [CI, 0.12 to 0.79] (6).
- Among 21,765 women participating in the Nurses's Health Study II, total and vigorous activity scores before pregnancy were associated with a significantly lower risk of developing gestational diabetes during the next pregnancy (RR, 0.77 [CI, 0.69 to 0.94], $P < 0.02$ for trend) when comparing the highest vs. the lowest quintile of physical activity during the period before pregnancy. Women who spent 20 hours per week or more watching television but did not perform vigorous physical activity had a significantly higher risk of developing gestational diabetes than those who spent less than 2 hours per week watching television and were physically active (multivariate RR, 2.30 [CI, 1.06 to 4.97] (7).

Comments:

- None.

1.3 Stop ACE inhibitor therapy, switch oral hypoglycemics to insulin, and review all other medications before conception. **B**

Specific recommendation:

- Stop all ACE-inhibitors and angiotensin-receptor blockers.
- Switch oral hypoglycemic agents to insulin therapy.
- Stop cholesterol-lowering drugs.
- Stop aspirin therapy.
- Review other medications and stop any potential teratogens.

Rationale:

- ACE inhibitors and angiotensin-receptor blockers have been associated with fetal malformations.
- Although oral hypoglycemics are not thought to be teratogenic, they do not allow for subtle and immediate adjustments in maternal glucose

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

levels.

- No adverse maternal effects are likely to occur with a 9-month hiatus from cholesterol-lowering agents.
- Because HMG-CoA reductase inhibitors have been implicated as possible teratogens, the risks of their use outweigh the benefits to the mother.
- Daily aspirin therapy may lead to maternal and newborn hemorrhage, increased perinatal mortality, intrauterine growth retardation, and teratogenic effects.

Evidence:

- A review revealed numerous case reports of multiple anomalies, including fetal hypocalvaria and renal defects, in babies exposed in utero to ACE inhibitors and angiotensin-receptor blockers (8).
- In a surveillance study of lovastatin exposures during pregnancy, the overall rate of normal outcomes was 85%, and the following rates of occurrence were found: congenital anomalies, 4%; spontaneous abortions, 8%; fetal deaths or stillbirths, 1%; and miscellaneous adverse outcomes, 2% (9).
- In one case-controlled study, 3 of 14 newborns exposed to aspirin within 1 week of delivery had minor hemorrhaging compared with 1 of 17 controls (10). In two retrospective studies, mothers of 1,291 malformed infants were found to have consumed aspirin during pregnancy more frequently than mothers of normal infants (11; 12).
- Use of insulin during pregnancy is recommended by consensus of an expert panel (13).

Comments:

- Many diabetic women take a variety of medications; therefore, pre-conception planning should include a review of all drugs and their potential for teratogenesis.

2. Screening: Not applicable to this module.

3. Diagnosis: Use history, physical exam, and laboratory evaluation to confirm and classify diabetes, to assess control, and to identify comorbid conditions.

A

3.1 Evaluate women with pregestational diabetes for diabetic complications before conception and review issues of diabetic control, and review symptoms of hyperglycemia in all pregnant women. B

Specific recommendation:

- Screen pregnant patients with no previous history of diabetes for hyperglycemic symptoms.
- Assess history of acute diabetic complications.
- Review history of retinopathy, nephropathy, hypertension, atherosclerotic

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

disease, and neuropathy.

- Review duration and type of diabetes and current diabetes management.
- Document other concomitant medical conditions and drugs.
- Review basic pregnancy issues, such as past pregnancy history, menstrual history, and support system for the patient.
- Obtain dilated retinal exam before pregnancy.
- Measure blood pressure and test for orthostatic changes.
- Perform cardiovascular exam to look for evidence of cardiac or peripheral vascular disease.
- See table [History and Physical Examination Elements for Diabetes in Pregnancy](#).

Rationale:

- Women may be diagnosed with diabetes during pregnancy, which may be a self-limited condition or may indicate chronic diabetes mellitus.
- Women with a history of acute diabetic complications may be more likely to have recurrences during pregnancy.
- Conditions such as retinopathy and nephropathy may worsen during pregnancy.
- Hypertension complicates many diabetic pregnancies.
- Maternal cardiovascular disease is associated with a high mortality rate during pregnancy.
- Diabetic pregnancies require management of the pregnancy, management of diabetes and its complications, and involvement of the patient's social support structure.

Evidence:

- The term "gestational diabetes" has traditionally included all diabetes diagnosed during pregnancy resulting in heterogeneity among patients with this diagnosis. Patients with elevated glucose levels before the second trimester of pregnancy; acute complications, such as diabetic ketoacidosis; and elevated postprandial glucose levels likely have type 1 or 2 diabetes newly diagnosed during pregnancy (14).
- Expert opinion suggests screening for history of acute diabetic complications and notes the need for social support in patients with pregestational diabetes (15).
- In a study of 31 continuous diabetic pregnancies, 71% developed nephrotic range proteinuria. In all of these patients, proteinuria reverted to previous levels after delivery (16).
- In a prospective study to determine the effects of pregnancy on diabetic retinopathy, pregnancy was associated with progression after adjustment for glycosolated hemoglobin measurements ($P < 0.005$; adjusted OR, 2.3) (17).
- One case series review found a high mortality rate in pregnant, diabetic women with known ischemic heart disease (18).

Comments:

- None.

3.2 Use laboratory testing to evaluate diabetic control and to screen

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

for related medical conditions. **B**

Specific recommendation:

- Obtain the following in women with pregestational diabetes before conception:
 - HbA_{1c} level
 - 24-hour urine test for protein and creatinine levels
 - ECG
- Obtain blood glucose level in all pregnant women:
 - In the first trimester or at the first prenatal visit
 - With symptoms of hyperglycemia, to monitor for the development of diabetes
- Check thyroid levels with the first set of antepartum labs in patients with type 1 diabetes.
- See table [Laboratory and Other Studies for Diabetes in Pregnancy](#).

Rationale:

- New onset diabetes mellitus may be discovered during pregnancy, and hyperglycemia may adversely affect the fetus.
- Euglycemia before conception reduces fetal cardiac and neurologic anomalies.
- Patients with urinary protein excretion >190 mg per 24 hours are at risk of hypertensive disorders during later pregnancy.
- There is a 5% to 10% coincidence of hyperthyroidism or hypothyroidism and type 1 diabetes; thyroid disease can affect the fetus.
- All diabetes discovered during pregnancy is termed “gestational diabetes.” Controversy exists surrounding universal screening for the condition in late pregnancy.
- Diabetic women with coronary artery disease have increased mortality rates during pregnancy.

Evidence:

- In a review of 14 cohort studies, the pooled rates of major and minor fetal anomalies were lower in diabetic women who had received pre-conception care (2.1%) compared with those who had not (6.5%; RR 0.36 [CI, 0.22 to 0.59]) (1). Population-based cohort studies have found an association between adverse fetal outcomes and maternal hyperglycemia (2; 3).
- In a case study of 311 diabetic pregnant women with proteinuria, 31% to 58% of the women developed pre-eclampsia. The increased risk persisted after controlling for parity, chronic hypertension, retinopathy, and glycemic control (20).
- In a study of 31 continuous diabetic pregnancies of diabetic women with nephropathy before the pregnancy, 71% of the women developed nephrotic range proteinuria during gestation. In all of these patients, proteinuria reverted to previous levels after delivery (16).
- A retrospective observational study demonstrated lower IQ scores in children of pregnant women with subclinical hypothyroidism (21). An increased prevalence of subclinical hypothyroidism has been reported in pregnant diabetic patients (22).

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

- A 50-year series of diabetic patients showed increased maternal mortality in women with ischemic heart disease (18). Consensus opinion recommends an ECG (13).

Comments:

- Nephropathy may worsen transiently during diabetic pregnancies, but permanent worsening occurs at rates no higher than the rates for nonpregnant diabetics.
- In one series of diabetic patients being evaluated for renal transplantation, the authors found virtually no significant coronary disease by angiography if the patient was younger than 45 years, the diabetes duration was <25 years, and there were no ST-T wave changes on ECG (23).
- The U.S. Preventive Services Task Force concluded that no randomized, controlled clinical trial provides evidence for the benefits of screening for gestational diabetes (24). Most obstetricians screen all women for gestational diabetes mellitus in late pregnancy, but this remains controversial.

3.3 Not applicable to this module.

4. Consultation for Diagnosis: Consider consultation in all women with pregestational diabetes to assess the status of chronic complications of diabetes. B

4.1 Consult appropriate subspecialists for help in defining the status of diabetic complications before conception. B C

Specific recommendation:

- Refer women with pregestational diabetes to an ophthalmologist for dilated retinal exam before conception, or at least early in pregnancy.
- Consider referral of women with pregestational diabetes and proteinuria to a nephrologist if proteinuria is noted before conception or early in pregnancy.
- Consider referring to a cardiologist for the diagnosis of coronary artery disease those women with pregestational diabetes who:
 - Are older than 45 years
 - Have had diabetes for >25 years
 - Show ST-T wave changes on ECG
 - Have symptoms of coronary artery disease
- Consider referral of women with pregestational diabetes and signs or symptoms of neuropathy to a neurologist before pregnancy.

Rationale:

- Retinopathy and nephropathy may worsen during pregnancy.
- Diabetic women with coronary artery disease have increased mortality rates during pregnancy.
- Neuropathy, particularly autonomic neuropathy, may complicate the management of diabetes in pregnancy and should be identified and treated before pregnancy.

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

Evidence:

- In a prospective study to determine the effects of pregnancy on diabetic retinopathy, pregnancy was associated with progression after adjustment for glycosolated hemoglobin measurements ($P < 0.005$; adjusted OR, 2.3) (17).
- In a study of 31 continuous diabetic pregnancies, 71% of the patients developed nephrotic range proteinuria. In all of these patients, proteinuria reverted to previous levels after delivery (16).
- In a case study of 311 diabetic pregnant women with proteinuria, 31% to 58% of the patients developed pre-eclampsia. The increased risk persisted after controlling for parity, chronic hypertension, retinopathy, and glycemic control (20).
- A 50-year series of diabetic patients showed increased maternal mortality in women with ischemic heart disease (18).
- In one series of diabetic patients being evaluated for renal transplantation, the authors found virtually no significant coronary disease if the patient was younger than 45 years, the diabetes duration was <25 years, and there were no ST-T wave changes on ECG (23).
- There is consensus opinion on subspecialist consultation in the American Diabetes Association guidelines on [pre-conception care of women with diabetes](#) (13).

Comments:

- None.

4.2 Consider consultation with an endocrinologist for help in classifying gestational diabetes. C

Specific recommendation:

- Consider consultation with an endocrinologist or high-risk obstetrician to further classify gestational diabetes as type 1, type 2, or transient diabetes of pregnancy.

Rationale:

- Patients with type 1 or 2 diabetes diagnosed during pregnancy may be at higher risk for acute and chronic diabetic complications than patients diagnosed with hyperglycemia late in pregnancy, because those diagnosed earlier in pregnancy probably had unrecognized underlying diabetes.

Evidence:

- There is consensus opinion in the American Diabetes Association guidelines on [pre-conception care of women with diabetes](#) (13).

Comments:

- None.

5. Hospitalization: Hospitalize patients with elevated glucose levels during pregnancy or in the pre-conception planning stages if necessary for glucose control. B

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

5.1 Hospitalize pregnant women with elevated glucose levels and poor outpatient control. **B**

Specific recommendation:

- Hospitalize pregnant patients when:
 - Fasting whole-blood glucose levels consistently exceed 70 to 100 mg/dL
 - 2-hour postprandial levels exceed 140 mg/dL

Rationale:

- There is an association between elevated maternal glucose or elevated glyco-hemoglobin levels during embryogenesis and high rates of pregnancy loss and major congenital malformations.
- Organogenesis of the fetus may take place before pregnancy is diagnosed.
- High glucose levels in late pregnancy increase the risk of fetal macrosomia.

Evidence:

- In a systematic review of cohort studies, major fetal malformations were associated with elevated glycohemoglobin levels in early pregnancy on a dose-response curve. The total proportion of infants with malformation from the pooled data were 2.2% in mothers with moderately elevated glycohemoglobin levels, 8.6% in mothers with high glycohemoglobin levels, and 26.6% in mothers with the highest glycohemoglobin levels. Pre-conception care of diabetic women with efforts to control glucose have shown a decrease in major congenital anomalies (2.5% of women with pre-conception care compared with 7.8% of women with no pre-conception care [pooled data]) ([13](#)).
- In a systematic review of the literature, 17% to 29% of infants born to women with untreated gestational diabetes weighed >4,000 g at birth compared with 10% of infants born to women in the general population ([24](#)).

Comments:

- None.

5.2 Hospitalize pregnant women with evidence of ketoacidosis. **C**

Specific recommendation:

- Immediately hospitalize pregnant women with evidence of ketoacidosis.
- Search for secondary causes of ketoacidosis, including infection.

Rationale:

- Ketoacidosis is a dangerous medical condition commonly associated with type 1 diabetes, and it may occur with increased frequency during pregnancy.

Evidence:

- Consensus.

Comments:

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP.

Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

- Treatment for ketoacidosis does not change during diabetic pregnancy.

6. Non-drug Therapy: Recommend lifestyle changes and self-care to prevent complications in pregnant diabetic patients. B C

6.1 Stress diet and exercise in pregnant diabetic patients to control glucose levels. A

Specific recommendation:

- Consider recommending to pregnant diabetic patients:
 - A calorie restriction of 30% to 33% in pregnant women with diabetes and a body mass index >30
 - Limiting carbohydrate intake to 35% to 40% of calories
 - A program of moderate exercise

Rationale:

- Calorie restriction may reduce hyperglycemia in obese diabetic pregnant patients.
- Carbohydrate restriction may decrease maternal glucose levels and improve maternal and fetal outcomes in diabetic pregnancies.
- Moderate exercise may reduce glucose levels in diabetic pregnancies.
- Maternal hyperglycemia is associated with fetal malformations and macrosomia.

Evidence:

- A small randomized, controlled trial of obese women with gestational diabetes showed a reduction in 24-hour mean glucose levels from 121 mg/dL to 97.3 mg/dL in women assigned to a diet of 1,200 calories per day compared with women on 2,400 calories per day; however, maternal ketonuria of unknown clinical significance was also seen ([25](#); [26](#)).
- In a controlled trial, calorie restriction of 33% and 50% in obese women with gestational diabetes decreased maternal glucose levels by 10% to 20% and reduced triglyceride levels when compared with insulin therapy ([27](#)).
- In a 12-week controlled trial of obese pregnant women, half of whom had previous gestational diabetes, all of the women had higher triglycerides while on a 55% carbohydrate diet than while on a 40% carbohydrate diet and comparable weight loss ([28](#)).
- A small randomized, controlled trial showed increased cardiac fitness in women with gestational diabetes who exercised 30 minutes 3 to 4 days per week and achieved 70% of estimated maximal heart rate. No complications were seen ([29](#)).
- A small randomized, controlled trial showed reduced glucose levels in women with gestational diabetes who performed upper-extremity aerobic exercise ([30](#)).
- A small randomized study showed a decreased need for insulin in overweight women with gestational diabetes assigned to resistance exercise ([31](#)).

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

Comments:

- Little data exist concerning women with pregestational diabetes and diet or exercise. Consensus in patients with diabetes mellitus stresses the importance of diet and exercise for weight and glycemic control.

6.2 Continue foot care in women with pregestational diabetes. **C**

Specific recommendation:

- Stress the importance of continuing daily foot inspection, proper foot coverings, and toenail care in women with pregestational diabetes.

Rationale:

- Foot care may reduce the complications of diabetic foot ulcers in patients with diabetes.

Evidence:

- A randomized controlled trial has shown that patient education and increased surveillance results in decreased serious foot lesions ([32](#)).
- Cohort data suggest a similar relationship between surveillance, education, and a lower risk of foot lesions ([33](#)).
- There is consensus opinion in the American Diabetes Association guidelines on [preventive foot care](#) ([34](#)).

Comments:

- These data are derived from studies of non-pregnant patients.

6.3 Recommend smoking cessation in all women with diabetic pregnancies. **C**

Specific recommendation:

- Stress smoking cessation at each visit in diabetic women who are pregnant, or planning pregnancies.
- See module [Smoking Cessation](#).

Rationale:

- Cigarette smoking increases the risk of diabetic complications and may result in intrauterine growth retardation.

Evidence:

- Epidemiologic evidence suggests that smoking and type 2 diabetes synergistically increase risk of macrovascular disease ([35](#); [36](#)).
- There is consensus opinion in the American Diabetes Association guidelines on [standards of medical care for patients with diabetes mellitus](#) ([37](#)).

Comments:

- These data are derived from studies of non-pregnant patients.

7. Drug Therapy: Use drug therapy to treat hyperglycemia in the pre-conception period and throughout pregnancy, and recognize the toxicities of many drugs commonly used in diabetes. **B**

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

7.1 Use insulin in patients with gestational diabetes to achieve optimal glycemic control. **B**

Specific recommendation:

- Adjust insulin doses to achieve fasting whole-blood glucose levels of 70 to 100 mg/dL and 2-hour postprandial levels of <140 mg/dL.
- See table [Drug Treatment for Diabetes in Pregnancy](#).

Rationale:

- There is an association between elevated maternal glucose or glycohemoglobin levels and high rates of pregnancy loss, major congenital malformations, and fetal macrosomia.
- Reducing glycosolated hemoglobin levels may decrease complications.

Evidence:

- In a systematic review of cohort studies, major fetal malformations were associated with elevated glycohemoglobin levels in early pregnancy on a dose-response curve. The total proportion of infants with malformation from the pooled data were 2.2% in mothers with moderately elevated glycohemoglobin levels, 8.6% in mothers with high glycohemoglobin levels, and 26.6% in mothers with the highest glycohemoglobin levels. [\(13\)](#).
- In a systematic review of the literature, 17% to 29% of infants born to women with untreated gestational diabetes weighed >4,000 g at birth compared with 10% of infants born to women in the general population [\(24\)](#).
- In a systematic review, the risks of major congenital malformations and fetal macrosomia were inversely related to glycemic control [\(38\)](#).

Comments:

- None.

7.2 Switch all women with pregestational diabetes on oral diabetic treatments to insulin before conception. **C**

Specific recommendation:

- Stop all oral diabetic medication 3 months before conception.
- Use insulin in all pregnancies requiring medication for glucose control.
- See table [Drug Treatment for Diabetes in Pregnancy](#).

Rationale:

- Although oral hypoglycemics are not thought to be teratogenic, they do not allow for subtle and immediate adjustments in maternal glucose levels.

Evidence:

- There is consensus opinion in the American Diabetes Association guidelines on [standards of care for patients with diabetes mellitus](#) [\(37\)](#).

Comments:

- None.

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

7.3 Stop ACE inhibitor therapy and review the patient's other medications before conception. **B**

Specific recommendation:

- Do the following before conception:
 - Stop all ACE inhibitors and angiotensin-receptor blockers
 - Stop cholesterol-lowering drugs
 - Stop aspirin therapy
 - Review other medications and stop potential teratogens
- See table [Drugs To Avoid in Pregnancy](#).

Rationale:

- ACE inhibitors and angiotensin-receptor blockers have been associated with fetal malformations.
- No adverse maternal effects are likely to occur with a 9-month hiatus from cholesterol-lowering agents, and because HMG-CoA reductase inhibitors have been implicated as possible teratogens, the risks of their use outweigh the benefits to the mother.
- Daily aspirin therapy may lead to maternal and newborn hemorrhage, increased perinatal mortality, intrauterine growth retardation, and teratogenic effects.

Evidence:

- A review revealed numerous case reports of babies exposed to ACE inhibitors and angiotensin-receptor blockers in utero who had multiple anomalies, including fetal hypocalvaria and renal defects (8).
- In a surveillance study of lovastatin exposures during pregnancy, the overall rate of normal outcomes was 85%, and the following rates of occurrence were found: congenital anomalies, 4%; spontaneous abortions, 8%; and fetal deaths or stillbirths, 1% (9).
- In one case-controlled study, 3 of 14 newborns exposed to aspirin within 1 week of delivery had minor hemorrhaging compared with 1 of 17 controls (10). In two retrospective studies, mothers of 1,291 malformed infants were found to have consumed aspirin during pregnancy more frequently than mothers of normal infants (11; 12).

Comments:

- Many diabetic women are on a variety of medications; therefore, pre-conception planning should include a review of all drugs and their potential for teratogenesis.

8. Patient Education: Emphasize the importance of pre-conception counseling in women with diabetes and of patient self-management during pregnancy. B

8.1 Instruct all diabetic women of childbearing potential on the need for pre-conception planning. **B**

Specific recommendation:

- Ensure effective birth control at all times unless the patient is trying to

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

conceive and is in good diabetic control.

- Counsel women with type 1 or 2 diabetes on the risks of fetal malformation associated with unplanned pregnancies and poor metabolic control.
- Plan the pregnancies of diabetic women to achieve fasting whole-blood glucose levels of 70 to 100 mg/dL and 2-hour postprandial levels of <140 mg/dL at least 8 to 12 weeks before conception.
- Arrange for a certified diabetic educator instruction on diabetes self-management.

Rationale:

- There is an association between elevated maternal glucose or glycohemoglobin levels during embryogenesis and high rates of pregnancy loss and major congenital malformations.

Evidence:

- In a meta-analysis of 14 cohort studies, the pooled rates of major and minor fetal anomalies were lower in diabetic women who had received pre-conception care (2.1%) compared with those who had not (6.5%; RR, 0.36 [CI, 0.22 to 0.59]) (1).
- Population-based cohort studies have found an association between adverse fetal outcomes and maternal hyperglycemia (2; 3).

Comments:

- Pre-conception counseling should include advice on folic acid intake, vaccinations for rubella and varicella, weight control, and a review of current diseases and medications in addition to an assessment of diabetes management.

8.2 Stress the importance of diet and exercise to control glucose levels in pregnant diabetic patients. **A**

Specific recommendation:

- Provide nutritional counseling consistent with the American Diabetes Association recommendations.
- Consider recommending to pregnant diabetic patients:
 - A 30% to 33% calorie restriction in pregnant women with diabetes and a body mass index >30
 - Limiting carbohydrate intake to 35% to 40% of calories
 - A program of moderate exercise

Rationale:

- Calorie restriction may reduce hyperglycemia in obese diabetic pregnant patients.
- Carbohydrate restriction may decrease maternal glucose levels and improve maternal and fetal outcomes in diabetic pregnant patients.
- Moderate exercise may reduce glucose levels in diabetic pregnant patients.
- Maternal hyperglycemia is associated with fetal malformations and macrosomia.

Evidence:

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP.

Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

- A small randomized, controlled trial of obese women with gestational diabetes showed a reduction in 24-hour mean glucoses from 121 mg/dL to 97.3 mg/dL in women assigned to a 1,200 calories per day diet as compared with women on a 2,400 calories per day diet; however, maternal ketonuria of unknown clinical significance was also seen ([25](#); [26](#)).
- In a controlled trial, calorie restriction of 33% and 50% in obese women with gestational diabetes decreased maternal glucose levels by 10% to 20% and reduced triglyceride levels when compared with insulin therapy ([27](#)).
- In a 12-week controlled trial of obese pregnant women, half of whom had previous gestational diabetes, all of the women had higher triglycerides while on a 55% carbohydrate diet than while on a 40% carbohydrate diet and comparable weight loss ([28](#)).
- A small randomized, controlled trial demonstrated increased cardiac fitness in women with gestational diabetes who exercised 30 minutes, 3 to 4 days per week, and achieved 70% of estimated maximal heart rate. No complications were seen ([29](#)).
- A small randomized, controlled trial showed reduced glucose levels in women with gestational diabetes who performed upper-extremity aerobic exercise ([30](#)).
- A small randomized study showed a decreased need for insulin in overweight women with gestational diabetes assigned to resistance exercise ([31](#)).
- Two cohort studies have prospectively examined the role of exposure to diabetes *in utero* on childhood growth, later obesity, and risk for type 2 diabetes in the offspring: the Pima Indian Study ([43](#)) and the Diabetes in Pregnancy Study at Northwestern University in Chicago ([44](#)).
- The excess growth experienced by offspring of diabetic mothers is not due to genetic factors alone but is also the direct consequence of exposure to maternal altered intrauterine environment as shown in a study of 58 siblings ([45](#)). In another study of 150 HNF-1- α mutation carriers *in utero*, maternal diabetes resulted in diagnoses of diabetes in the carriers at a younger age ([46](#)).
- *In utero* exposure to diabetes confers risks for the development of cardiovascular disease later in life that are independent of adiposity and may be in addition to genetic predisposition to diabetes as shown in a study comparing 61 children born to diabetic mothers as compared to 57 control children of nondiabetic mothers ([47](#)), and in a study of 42 Pima Indian children born to diabetic mothers in whom most had higher levels of HbA1c and systolic blood pressure and lower levels of HDL independent of age, gender, or percent body fat ([48](#)).

Comments:

- Little data exist concerning women with pregestational diabetes and diet or exercise. Consensus opinion on patients with diabetes mellitus stresses the importance of diet and exercise for weight and glycemic control.

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

8.3 Continue preventive foot care in women with pregestational diabetes. **C**

Specific recommendation:

- Stress the importance of continuing daily foot inspection, proper foot coverings, and toenail care in women with pregestational diabetes.

Rationale:

- Foot care may reduce the complications of diabetic foot ulcer in patients with diabetes.

Evidence:

- There is consensus opinion in the American Diabetes Association guidelines on [preventive foot care \(34\)](#).

Comments:

- None.

8.4 Recommend smoking cessation in all women with diabetic pregnancies. **C**

Specific recommendation:

- Urge smoking cessation at each visit in diabetic women who are pregnant or planning pregnancy.
- See module [Smoking Cessation](#).

Rationale:

- Cigarette smoking increases the risk of diabetic complications and may result in intrauterine growth retardation.

Evidence:

- There is consensus opinion in the American Diabetes Association guidelines on [standards of medical care for patients with diabetes mellitus \(37\)](#).

Comments:

- None.

8.5 Teach patients and family members to recognize hypoglycemia and to treat it appropriately. **C**

Specific recommendation:

- Teach patients and family members to recognize the signs and symptoms of hypoglycemia and about its treatment.

Rationale:

- Intensive diabetic control during pregnancy and the pre-conception period increases the risk of maternal hypoglycemia.

Evidence:

- There is consensus opinion in the American Diabetes Association guidelines on [medical care of the patient with diabetes mellitus \(37\)](#).

Comments:

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP.

Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

- None.

8.6 Counsel patients on the need for an ophthalmology exam before conception or in early pregnancy. **B C**

Specific recommendation:

- Obtain a dilated retinal exam before pregnancy.

Rationale:

- Retinopathy may worsen during pregnancy.

Evidence:

- In a prospective study to determine the effects of pregnancy on diabetic retinopathy, pregnancy was associated with progression after adjustment for glycosolated hemoglobin measurements ($P < 0.005$; adjusted OR, 2.3) ([17](#)).

Comments:

- None.

9. Management Consultation: Consult appropriate specialists in managing pregnant diabetic patients to ensure optimal care and best outcome. **C**

9.1 Ensure specialized obstetric care for diabetic women who are pregnant or planning pregnancies. **C**

Specific recommendation:

- Refer all women with pregestational diabetes to an obstetrician, or a high-risk obstetrician if available, as soon as pregnancy is diagnosed.
- Consider referral to a high-risk obstetrician for:
 - Fetal and maternal risk determination as part of pregnancy planning
 - Ongoing management if pre-conception fasting whole-blood glucose levels of 70 to 100 mg/dL and 2-hour postprandial levels of <140 mg/dL cannot be achieved before conception

Rationale:

- Obstetricians will be the primary caregivers for pregnant women who are diabetic, and general internists, family physicians, and/or other specialists may be consulted to assist with management.

Evidence:

- Consensus.

Comments:

- None.

9.2 Consider consultation with an endocrinologist and other professionals to ensure ideal glucose levels before and during pregnancy in diabetic women. **C**

Specific recommendation:

- Consider referral to an endocrinologist if the diabetic woman cannot

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

achieve ideal glucose levels during pregnancy or before conception.

- Refer all women with diabetes during pregnancy, or women with diabetes considering pregnancy, to a:
 - Nutritionist for instruction on the American Diabetes Association diet
 - Certified diabetic educator for instruction in self-management of diabetes

Rationale:

- Euglycemia during pregnancy reduces fetal cardiac and neurologic anomalies and fetal macrosomia.

Evidence:

- In a meta-analysis of 14 cohort studies, the pooled rates of major and minor fetal anomalies were lower in diabetic women who had received pre-conception care (2.1%) compared with those who had not (6.5%; RR, 0.36 [CI, 0.22 to 0.59]) ([1](#)).
- Population-based cohort studies have found an association between adverse fetal outcomes and maternal hyperglycemia ([2](#); [3](#)).

Comments:

- None.

9.3 Obtain specialty consultation for help in managing complications of diabetes in pregnant women or before conception.



Specific recommendation:

- Obtain consultation with a:
 - Nephrologist if proteinuria is detected in a pregnant patient
 - Ophthalmologist for management of diabetic retinopathy
 - Cardiologist in pregnant patients with coronary artery disease
 - Neurologist in women with neuropathy or autonomic dysfunction

Rationale:

- Conditions such as retinopathy and neuropathy may progress during pregnancy.
- Diabetic women with coronary artery disease have increased mortality rates during pregnancy.
- Neuropathy, particularly autonomic neuropathy, may complicate the management of diabetes in pregnancy and thus should be identified and treated before the onset of pregnancy.

Evidence:

- In a prospective study to determine the effects of pregnancy on diabetic retinopathy, pregnancy was associated with progression after adjustment for glycosylated hemoglobin measurements ($P < 0.005$; adjusted OR, 2.3) ([17](#)).
- In a study of 31 continuous diabetic pregnancies, 71% developed nephrotic range proteinuria. In all of these patients, proteinuria reverted to previous levels after delivery ([16](#)).
- In a case study of 311 diabetic pregnant women with proteinuria, 31% to 58% developed pre-eclampsia. The increased risk persisted after

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

controlling for parity, chronic hypertension, retinopathy and glycemic control (20).

- A 50-year series of diabetic patients showed increased maternal mortality in those women with ischemic heart disease (18).
- In one series of diabetic patients being evaluated for renal transplantation, the authors found virtually no significant coronary disease by angiography if the patient was younger than 45 years, the diabetes duration was <25 years, and there were no ST-T wave changes on ECG (23).

Comments:

- None.

10. Follow-up Issues: Monitor pregnant diabetic patients closely for adherence to glucose monitoring, issues of glucose control, and the development of diabetic complications. ©

10.1 Review blood glucose logs at every visit and adjust insulin accordingly. ©

Specific recommendation:

- Encourage pregnant diabetic women to check glucose levels fasting and 2 hours after every meal, and to record the levels with time of day, food intake, activity, and insulin doses given.
- Adjust insulin to achieve fasting whole blood glucose levels of 70 to 100 mg/dL and 2-hour postprandial levels of <140 mg/dL.
- Inform women about the signs and symptoms of hypoglycemia and develop an action plan to treat it acutely.
- Monitor hemoglobin A_{1c} levels every 2 to 3 months and aim for normal levels.
- Continue frequent, daily blood glucose testing after delivery.
- See table [Elements of Follow-up for Pregestational and Gestational Diabetes Mellitus](#).

Rationale:

- Hyperglycemia during pregnancy is associated with fetal malformations and fetal macrosomia.
- Hypoglycemia is a frequent complication of tight glucose control.
- In the postpartum period, altered schedules, lactation, and changing physiology may change a woman's insulin requirements.

Evidence:

- Population-based cohort studies have found an association between adverse fetal outcomes and maternal hyperglycemia (2; 3).
- Case series have reported decreased insulin requirement after delivery in women with pregestational diabetes (19).

Comments:

- None.

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP.

Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

10.2 Review diabetes drugs after delivery and make changes as necessary. ©

Specific recommendation:

- Adjust insulin in patients with type 1 pregestational diabetes postdelivery according to multiple, daily blood glucose testing to maintain hemoglobin A_{1c} at <7%.
- Stop insulin in women with gestational diabetes after delivery and monitor glucose levels.
- Consider the reinstatement of oral diabetes medication in women with type 2 pregestational diabetes postdelivery.
- See table [Elements of Follow-up for Pregestational and Gestational Diabetes Mellitus](#).

Rationale:

- In the postpartum period, altered schedules, lactation, and changing physiology may change a woman's insulin requirements.
- Gestational diabetes is generally a transient state, and insulin resistance decreases immediately postpartum.
- Women on oral agents before pregnancy can usually restart them after delivery.

Evidence:

- Case series have reported decreased insulin requirement after delivery in women with pregestational diabetes (19).
- There is limited evidence available outlining the risks and benefits to the breast-feeding infant when the mother is taking oral hypoglycemic agents (49).

Comments:

- The effect of oral diabetes drugs on breast-feeding infants is largely unknown. The issue should be addressed in conjunction with the infant's primary care provider.
- The term "gestational diabetes" covers a wide array of physiologic syndromes, including types 1 and 2 diabetes first detected during pregnancy and pregnancy-related insulin resistance. Therefore, postpartum diabetes care should be individualized.

10.3 Screen women with pregestational diabetes for the development or worsening of diabetic complications during pregnancy. ©

Specific recommendation:

- Refer patients with pregestational diabetes for a dilated retinal exam early in pregnancy and postpartum.
- Measure blood pressure and screen for proteinuria at each prenatal and postpartum visit.
- Ask about symptoms of neuropathy at each prenatal and postpartum visit.
- Screen women with type 1 diabetes for thyroid disease postpartum.

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP.

Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

- See table [Elements of Follow-up for Pregestational and Gestational Diabetes Mellitus](#).

Rationale:

- Retinopathy and severe nephropathy may worsen during pregnancy.
- Hypertensive disorders frequently complicate diabetic pregnancies.
- Patients with neuropathy need increased counseling on the importance of foot care.
- There is a 5% to 10% coincidence of hyperthyroidism or hypothyroidism and type 1 diabetes.

Evidence:

- In a prospective study to determine the effects of pregnancy on diabetic retinopathy, pregnancy was associated with progression after adjustment for glycosylated hemoglobin measurements ($P < 0.005$; adjusted OR, 2.3) ([17](#)).
- In a study of 31 continuous diabetic pregnancies of women with pregestational diabetes, 71% developed nephrotic range proteinuria. In all of these patients, proteinuria reverted to previous levels after delivery ([16](#)).
- In a case study of 311 diabetic pregnant women with proteinuria, 31% to 58% developed pre-eclampsia. The increased risk persisted after controlling for parity, chronic hypertension, retinopathy, and glycemic control ([20](#)).
- In a small, prospective study of women with type 1 diabetes, the incidence of postpartum thyroid disease was 25%, which is three times higher than a similar nondiabetic population ([50](#)).

Comments:

- None.

10.4 Plan future pregnancies postpartum. ©

Specific recommendation:

- Recommend birth control immediately postpartum.
- Stress the importance of pre-conception counseling.
- See table [Elements of Follow-up for Pregestational and Gestational Diabetes Mellitus](#).

Rationale:

- Pregnancies in women with diabetes have more favorable outcomes if they are planned.

Evidence:

- In a meta-analysis of 14 cohort studies, the pooled rates of major and minor fetal anomalies were lower in diabetic women who had received pre-conception care (2.1%) compared to those who had not (6.5%; RR, 0.36 [CI, 0.22 to 0.59]) ([1](#)).

Comments:

- None.

10.5 After delivery, classify patients found to be diabetic during

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes

2008-10-29

pregnancy and arrange for long-term follow-up. ©

Specific recommendation:

- Continue home glucose monitoring in women found to be diabetic during pregnancy at least 6 weeks postpartum to determine if they have underlying type 1 or 2 diabetes or if their hyperglycemia resolves.
- Counsel patients with transient gestational diabetes on the long-term need for diabetes screening.
- Recommend [nutrition](#) and [exercise](#) consistent with American Diabetes Association guidelines to patients with transient hyperglycemia of pregnancy after delivery.
- See table [Elements of Follow-up for Pregestational and Gestational Diabetes Mellitus](#).

Rationale:

- Women may be diagnosed with diabetes during pregnancy, which may be a self-limited condition or may indicate chronic diabetes mellitus.
- A history of gestational diabetes increases the likelihood of developing type 2 diabetes mellitus.

Evidence:

- In a systematic review of the literature, the cumulative incidence of diabetes ranged from 2.6% to >70% in studies that examined women 6 weeks postpartum to 28 years postpartum ([51](#)).

Comments:

- None.

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP.

Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

- 1 Studies that meet all of the evidence criteria for that study type
- 2 Studies that meet at least one of the criteria for that study type
- 3 Studies that meet none of the evidence criteria for that study type or are derived from expert opinion, commentary, or consensus

Study types and evidence criteria are defined at <http://pier.acponline.org/criteria.html>

The number in parentheses at the end of the reference citations identify PubMed abstracts, which can be found on the National Library of Medicine's web site <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi>

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.

References

- 1 1 Ray JG, O'Brien TE, Chan WS. Preconception care and the risk of congenital anomalies in the offspring of women with diabetes mellitus: a meta-analysis. *QJM*. 2001;94:435-44. (PMID: [11493721](#))
- 2 2 Temple R, Aldridge V, Greenwood R, Heyburn P, Sampson M, Stanley K. Association between outcome of pregnancy and glycaemic control in early pregnancy in type 1 diabetes: population based study. *BMJ*. 2002;325:1275-6. (PMID: [12458245](#))
- 3 2 Sheffield JS, Butler-Koster EL, Casey BM, McIntire DD, Leveno KJ. Maternal diabetes mellitus and infant malformations. *Obstet Gynecol*. 2002;100(5 Pt 1):925-30. (PMID: [12423854](#))
- 4 2 Ehrenberg HM, Mercer BM, Catalano PM. The influence of obesity and diabetes on the prevalence of macrosomia. *Am J Obstet Gynecol*. 2004;191:964-8. (PMID: [15467573](#))
- 5 2 Saldana TM, Siega-Riz AM, Adair LS. Effect of macronutrient intake on the development of glucose intolerance during pregnancy. *Am J Clin Nutr*. 2004;79:479-86. (PMID: [14985225](#))
- 6 2 Dempsey JC, Sorensen TK, Williams MA, Lee IM, Miller RS, Dashow EE, et al. Prospective study of gestational diabetes mellitus risk in relation to maternal recreational physical activity before and during pregnancy. *Am J Epidemiol*. 2004;159:663-70. (PMID: [15033644](#))
- 7 2 Zhang C, Solomon CG, Manson JE, Hu FB. A prospective study of pregravid physical activity and sedentary behaviors in relation to the risk for gestational diabetes mellitus. *Arch Intern Med*. 2006;166:543-8. (PMID: [16534041](#))
- 8 1 Shotan A, Widerhorn J, Hurst A, Elkayam U. Risks of angiotensin-converting enzyme inhibition during pregnancy: experimental and clinical evidence, potential mechanisms, and recommendations for use. *Am J Med*. 1994;96:451-6. (PMID: [8192177](#))
- 9 2 Manson JM, Freyssinges C, Ducrocq MB, Stephenson WP. Postmarketing surveillance of lovastatin and simvastatin exposure during pregnancy. *Reprod Toxicol*. 1996;10:439-46. (PMID: [8946557](#))
- 10 2 Bleyer WA, Breckenridge RT. Studies on the detection of adverse drug reactions in the newborn. II. The effects of prenatal aspirin on newborn hemostasis. *JAMA*. 1970;213:2049-53. (PMID: [5272707](#))
- 11 2 Richards ID. Congenital malformations and environmental influences in pregnancy. *Br J Prev Soc Med*. 1969;23:218-25. (PMID: [5355276](#))
- 12 2 Nelson MM, Forfar JO. Associations between drugs administered during pregnancy and congenital abnormalities of the fetus. *Br Med J*. 1971;1:523-7. (PMID: [4396080](#))
- 13 3 American Diabetes Association. Preconception care of women with diabetes. *Diabetes Care*. 2003;26 Suppl 1:S91-3. (PMID: [12502628](#))
- 14 3 Lucas MJ. Diabetes complicating pregnancy. *Obstet Gynecol Clin North Am*. 2001;28:513-36. (PMID: [11512498](#))
- 15 1 Kitzmiller JL, Buchanan TA, Kjos S, Combs CA, Ratner RE. Pre-conception care of diabetes, congenital malformations, and spontaneous abortions. *Diabetes Care*. 1996;19:514-41. (PMID: [8732721](#))
- 16 2 Reece EA, Coustan DR, Hayslett JP, Holford T, Coulehan J, O'Connor TZ, et al. Diabetic nephropathy: pregnancy performance and fetomaternal outcome. *Am J Obstet Gynecol*. 1988;159:56-66. (PMID: [3394754](#))
- 17 2 Klein BE, Moss SE, Klein R. Effect of pregnancy on progression of diabetic retinopathy. *Diabetes Care*. 1990;13:34-40. (PMID: [2404715](#))



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

- 18 ② Hare JW, White P. Pregnancy in diabetes complicated by vascular disease. *Diabetes*. 1977;26:953-5. (PMID: [908464](#))
- 19 ③ Jovanovic L. Medical emergencies in the patient with diabetes during pregnancy. *Endocrinol Metab Clin North Am*. 2000;29:771-87. (PMID: [11149161](#))
- 20 ② Combs CA, Rosenn B, Kitzmiller JL, Khoury JC, Wheeler BC, Miodovnik M. Early-pregnancy proteinuria in diabetes related to preeclampsia. *Obstet Gynecol*. 1993;82:802-7. (PMID: [8414328](#))
- 21 ② Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, et al. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. *N Engl J Med*. 1999;341:549-55. (PMID: [10451459](#))
- 22 ② Jovanovic-Peterson L, Peterson CM. De novo clinical hypothyroidism in pregnancies complicated by type I diabetes, subclinical hypothyroidism, and proteinuria: a new syndrome. *Am J Obstet Gynecol*. 1988;159:442-6. (PMID: [3044113](#))
- 23 ② Manske CL, Thomas W, Wang Y, Wilson RF. Screening diabetic transplant candidates for coronary artery disease: identification of a low risk subgroup. *Kidney Int*. 1993;44:617-21. (PMID: [8231036](#))
- 24 ① Brody SC, Harris R, Lohr K. Screening for gestational diabetes: a summary of the evidence for the U.S. Preventive Services Task Force. *Obstet Gynecol*. 2003;101:380-92. (PMID: [12576264](#))
- 25 ① Knopp RH, Magee MS, Raisys V, Benedetti T, Bonet B. Hypocaloric diets and ketogenesis in the management of obese gestational diabetic women. *J Am Coll Nutr*. 1991;10:649-67. (PMID: [1770194](#))
- 26 ① Magee MS, Knopp RH, Benedetti TJ. Metabolic effects of 1200-kcal diet in obese pregnant women with gestational diabetes. *Diabetes*. 1990;39:234-40. (PMID: [2227131](#))
- 27 ① Knopp RH, Magee MS, Raisys V, Benedetti T. Metabolic effects of hypocaloric diets in management of gestational diabetes. *Diabetes*. 1991;40 Suppl 2:165-71. (PMID: [1748251](#))
- 28 ① Peterson CM, Jovanovic-Peterson L. Randomized crossover study of 40% vs. 55% carbohydrate weight loss strategies in women with previous gestational diabetes mellitus and non-diabetic women of 130-200% ideal body weight. *J Am Coll Nutr*. 1995;14:369-75. (PMID: [8568114](#))
- 29 ① Avery MD, Leon AS, Kopher RA. Effects of a partially home-based exercise program for women with gestational diabetes. *Obstet Gynecol*. 1997;89:10-5. (PMID: [8990428](#))
- 30 ② Jovanovic-Peterson L, Peterson CM. Is exercise safe or useful for gestational diabetic women? *Diabetes*. 1991;40 Suppl 2:179-81. (PMID: [1748254](#))
- 31 ① Brankston GN, Mitchell BF, Ryan EA, Okun NB. Resistance exercise decreases the need for insulin in overweight women with gestational diabetes mellitus. *Am J Obstet Gynecol*. 2004;190:188-93. (PMID: [14749658](#))
- 32 ① Litzelman DK, Slemenda CW, Langefeld CD, Hays LM, Welch MA, Bild DE, et al. Reduction of lower extremity clinical abnormalities in patients with non-insulin-dependent diabetes mellitus. A randomized, controlled trial. *Ann Intern Med*. 1993;119:36-41. (PMID: [8498761](#))
- 33 ② Rith-Najarian SJ, Stolusky T, Gohdes DM. Identifying diabetic patients at high risk for lower-extremity amputation in a primary health care setting. A prospective evaluation of simple screening criteria. *Diabetes Care*. 1992;15:1386-9. (PMID: [1425105](#))
- 34 ③ Mayfield JA, Reiber GE, Sanders LJ, Janisse D, Pogach LM; American Diabetes Association. Preventive foot care in people with diabetes. *Diabetes Care*. 2003;26 Suppl 1:S78-9. (PMID: [12502623](#))

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

- 35 ② Kannel WB, McGee DL. Diabetes and cardiovascular disease. The Framingham study. *JAMA*. 1979;241:2035-8. (PMID: [430798](#))
- 36 ② Suarez L, Barrett-Connor E. Interaction between cigarette smoking and diabetes mellitus in the prediction of death attributed to cardiovascular disease. *Am J Epidemiol*. 1984;120:670-5. (PMID: [6496447](#))
- 37 ③ American Diabetes Association. Standards of medical care for patients with diabetes mellitus. *Diabetes Care*. 2003;26 Suppl 1:S33-50. (PMID: [12502618](#))
- 38 ③ Ryan EA. Pregnancy in diabetes. *Med Clin North Am*. 1998;82:823-45. (PMID: [9706123](#))
- 39 ② Bhattacharyya A, Brown S, Hughes S, Vice PA. Insulin lispro and regular insulin in pregnancy. *QJM*. 2001;94:255-60. (PMID: [11353099](#))
- 40 ③ Simmons D. The utility and efficacy of the new insulins in the management of diabetes and pregnancy. *Curr Diab Rep*. 2002;2:331-6. (PMID: [12643193](#))
- 41 ② Glueck CJ, Wang P, Kobayashi S, Phillips H, Sieve-Smith L. Metformin therapy throughout pregnancy reduces the development of gestational diabetes in women with polycystic ovary syndrome. *Fertil Steril*. 2002;77:520-5. (PMID: [11872206](#))
- 42 ① Langer O, Conway DL, Berkus MD, Xenakis EM, Gonzales O. A comparison of glyburide and insulin in women with gestational diabetes mellitus. *N Engl J Med*. 2000;343:1134-8. (PMID: [11036118](#))
- 43 ② Pettitt DJ, Baird HR, Aleck KA, Bennett PH, Knowler WC. Excessive obesity in offspring of Pima Indian women with diabetes during pregnancy. *N Engl J Med*. 1983;308:242-5. (PMID: [6848933](#))
- 44 ② Silverman BL, Rizzo T, Green OC, Cho NH, Winter RJ, Ogata ES, et al. Long-term prospective evaluation of offspring of diabetic mothers. *Diabetes*. 1991;40 Suppl 2:121-5. (PMID: [1748240](#))
- 45 ② Dabelea D, Hanson RL, Lindsay RS, Pettitt DJ, Imperatore G, Gabir MM, et al. Intrauterine exposure to diabetes conveys risks for type 2 diabetes and obesity: a study of discordant sibships. *Diabetes*. 2000;49:2208-11. (PMID: [11118027](#))
- 46 ② Stride A, Shepherd M, Frayling TM, Bulman MP, Ellard S, Hattersley AT. Intrauterine hyperglycemia is associated with an earlier diagnosis of diabetes in HNF-1alpha gene mutation carriers. *Diabetes Care*. 2002;25:2287-91. (PMID: [12453975](#))
- 47 ② Manderson JG, Mullan B, Patterson CC, Hadden DR, Traub AI, McCance DR. Cardiovascular and metabolic abnormalities in the offspring of diabetic pregnancy. *Diabetologia*. 2002;45:991-6. (PMID: [12136397](#))
- 48 ② Bunt JC, Tataranni PA, Salbe AD. Intrauterine exposure to diabetes is a determinant of hemoglobin A(1)c and systolic blood pressure in pima Indian children. *J Clin Endocrinol Metab*. 2005;90:3225-9. (PMID: [15797952](#))
- 49 ① Merlob P, Levitt O, Stahl B. Oral antihyperglycemic agents during pregnancy and lactation: a review. *Paediatr Drugs*. 2002;4:755-60. (PMID: [12390047](#))
- 50 ② Alvarez-Marfany M, Roman SH, Drexler AJ, Robertson C, Stagnaro-Green A. Long-term prospective study of postpartum thyroid dysfunction in women with insulin dependent diabetes mellitus. *J Clin Endocrinol Metab*. 1994;79:10-6. (PMID: [8027213](#))
- 51 ① Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. *Diabetes Care*. 2002;25:1862-8. (PMID: [12351492](#))
- 52 ③ Breastfeeding and the use of human milk. American Academy of Pediatrics. Work Group on Breastfeeding. *Pediatrics*. 1997;100:1035-9. (PMID: [9411381](#))

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP. Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

New References of Interest

- 53 Correa A, Gilboa SM, Besser LM, Botto LD, Moore CA, Hobbs CA, et al. Diabetes mellitus and birth defects. Am J Obstet Gynecol. 2008;199:237.e1-9. (PMID: [18674752](#))
- 54 Murphy HR, Rayman G, Lewis K, Kelly S, Johal B, Duffield K, et al. Effectiveness of continuous glucose monitoring in pregnant women with diabetes: randomised clinical trial. BMJ. 2008;337:a1680. (PMID: [18818254](#))

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP.

Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



Diabetes in Pregnancy

Author(s):

Elisha L. Brownfield, MD

Status:

Editorial changes
2008-10-29

Glossary

ACE
HMG-CoA
TSH

angiotensin-converting enzyme
3-hydroxy-3-methylglutaryl coenzyme A
thyroid-stimulating hormone

The information included herein should never be used as a substitute for clinical judgment and does not represent an official position of ACP.

Because all PIER modules are updated regularly, printed web pages or PDFs may rapidly become obsolete. Therefore, PIER users should compare the date of the last update on the website with any printout to ensure that the information being referred to is the most current available.



History and Physical Examination Elements for Diabetes in Pregnancy

Category	Element	Notes
History	Duration and type of diabetes	May help to predict complications of diabetes (15)
History	Symptoms of hyperglycemia, including polyuria, polydipsia, blurred vision, and fatigue	Patients with no previous history of diabetes may be diagnosed during pregnancy, which is considered “gestational diabetes” and includes women with diabetes limited to pregnancy, as well as those with type 1 and 2 diabetes (14)
History	Acute complications of diabetes	Ask about infections, ketoacidosis, hypoglycemia (15)
History	Chronic complications of diabetes	Ask about history of retinopathy, visual changes, and dilated retinal exam in the past year; nephropathy or presence of urinary albumin or microalbumin; hypertension; symptoms of atherosclerotic vascular disease and autonomic and peripheral neuropathy. Ischemic heart disease has been associated with high maternal mortality in diabetic women (15)
History	Diabetes management	Ask about medications, nutrition, self-monitoring, physical activity (15)
History	Concomitant medical conditions and drugs	Ask about thyroid disease, particularly in patients with type 1 diabetes (19)
History	Menstrual and pregnancy history	Important for timing of pregnancy (15)
History	Support system	Family and work environment; needed support to maintain tight diabetic control (15)
Physical exam	Vital signs for blood pressure and orthostatic changes	Hypertension frequently complicates diabetic pregnancies. Blood pressure goal is 130/80 mm Hg. Autonomic neuropathy may be present (15)
Physical exam	Dilated retinal exam	Performed by an ophthalmologist. Retinopathy may progress during pregnancy (15)
Physical exam	Cardiovascular exam for evidence of cardiac or peripheral vascular disease	Age >45 years, diabetes duration for >25 years, or signs of cardiovascular disease should prompt consideration for coronary artery disease testing before conception (15)
Physical exam	Neurologic exam	Focus on autonomic and peripheral neuropathies (15)



Laboratory and Other Studies for Diabetes in Pregnancy

Test	Sensitivity (%)	Specificity (%)	Notes
Serum glucose			<p>Levels should be checked with the first antepartum labs or in a patient with symptoms of hyperglycemia. However, the U.S. Preventive Services Task Force concluded that no randomized, controlled clinical trial provides evidence for the benefits of screening for gestational diabetes (24).</p> <p>Patients with pregestational diabetes ideally should be doing frequent fingerstick glucose levels before and during pregnancy</p>
Hemoglobin A _{1c} in pregestational diabetic pregnancies			<p>Ideally <1% above normal before conception for pregestational diabetic pregnancies.</p> <p>In a meta-analysis of 14 cohort studies, the pooled rates of major and minor fetal anomalies were lower in diabetic women who had received pre-conception care (2.1%) compared with those who had not (6.5%; RR, 0.36 [CI, 0.22-0.59]) (1).</p> <p>Population-based cohort studies have found an association between adverse fetal outcomes and maternal hyperglycemia (2; 3)</p>

Table Continued...



Laboratory and Other Studies for Diabetes in Pregnancy

Test	Sensitivity (%)	Specificity (%)	Notes
24-hour urinary excretion of total protein in pregestational diabetic pregnancies			<p>Patients with protein excretion of >190 mg per 24 hours are at risk for hypertensive disorders during pregnancy.</p> <p>In a case study of 311 diabetic, pregnant women, 31%-58% developed pre-eclampsia.</p> <p>The increased risk persisted after controlling for parity, chronic hypertension, retinopathy, and glycemic control (20).</p> <p>In a study of 31 continuous pregnancies of diabetic women with nephropathy pre-conception, 71% developed nephrotic range proteinuria during gestation.</p> <p>In all of these patients, proteinuria reverted to previous levels after delivery (16)</p>
Serum TSH in pregnancies of type 1 diabetics			An increased prevalence of subclinical hypothyroidism has been reported in pregnant diabetic patients (22)
Glucose tolerance testing	71-83	78-87	<p>Controversial use in all pregnancies, but widely practiced to diagnose gestational diabetes.</p> <p>See table Diagnosis of Gestational Diabetes Mellitus with a 100-Gram Oral Glucose Load</p>
Electrocardiogram before conception			A 50-year series of diabetic patients showed increased maternal mortality in those women with ischemic heart disease in the perinatal period (18)

TSH = thyroid-stimulating hormone.



Drug Treatment for Diabetes in Pregnancy

Agent	Mechanism of Action	Dosage	Benefits	Side Effects	Notes
Insulin lispro	Protein hormone that regulates glucose metabolism	As needed	Reduced postprandial hyperglycemia; short onset of action, rapid acting, reduces postprandial hyperglycemia	Hypoglycemia, hypokalemia, injection-site reactions, lipodystrophy	Patient satisfaction in one study favored insulin lispro with long-acting insulin over regular insulin (39)
Insulin regular	Protein hormone that regulates glucose metabolism	As needed	Short-acting	Hypoglycemia, hypokalemia, injection-site reactions, lipodystrophy	Must use multiple injections per day for tight control
Insulin lente	Protein hormone that regulates glucose metabolism	As needed	Long-acting	Hypoglycemia, hypokalemia, injection-site reactions, lipodystrophy	May use with or without the shorter-acting insulins
Insulin ultralente	Protein hormone that regulates glucose metabolism	As needed	Long-acting	Hypoglycemia, hypokalemia, injection-site reactions, lipodystrophy	May use with or without the shorter-acting insulins
Insulin neutral protamine Hagedorn	Protein hormone that regulates glucose metabolism	As needed	Intermediate-acting	Hypoglycemia, hypokalemia, injection-site reactions, lipodystrophy	May use with or without the shorter-acting insulins
Insulin glargine	Protein hormone that regulates glucose metabolism	As needed	Long-acting	Hypoglycemia, hypokalemia, injection-site reactions, lipodystrophy	Little data exist on safety and efficacy of use in pregnancy (40)
Insulin aspart	Protein hormone that regulates glucose metabolism	As needed	Short onset of action rapid-acting, reduces postprandial hyperglycemia	Hypoglycemia, hypokalemia, injection-site reactions, lipodystrophy	Little data exist on safety and efficacy of use in pregnancy (40)
Folic acid	Vitamin supplementation	400 µg/d to 1.0 mg/d	Reduces fetal neural tube defects	Nausea, abdominal pain, rash, anorexia	Ideally begun before conception
Rubella vaccine	Live attenuated virus vaccine	0.5 mL sc x 1 dose	A vaccinated mother cannot transmit rubella virus to the fetus	Do not give to a pregnant patient due to a theoretical risk of congenital rubella syndrome	Give to all women planning conception with no evidence of immunity. Manufacturer recommends avoiding pregnancy for 3 months postvaccination

Table Continued...



Drug Treatment for Diabetes in Pregnancy

Agent	Mechanism of Action	Dosage	Benefits	Side Effects	Notes
Varicella vaccine	Viral vaccine	0.5 mL sc x 2 doses at 0 and 4-8 wks	A vaccinated mother decreases the risk of transmission to the fetus	Not known whether the vaccine can cause fetal harm or affect reproductive capacity	Give to all women planning conception with no evidence of immunity. Manufacturer recommends avoiding pregnancy for 3 months postvaccination
Influenza vaccine	Viral vaccine	0.5 mL im x 1 dose annually	Reduces the incidence of influenza in pregnant patients	Fever, malaise, injection-site reaction, myalgia	Diabetic pregnant women should receive during flu season regardless of pregnancy trimester
Metformin	Increases insulin sensitivity	500-2,000 mg/d	May decrease the incidence of gestational diabetes among women with polycystic ovarian syndrome	Inadequately controlled blood glucose levels, lactic acidosis, diarrhea, nausea, and vomiting	In a small observational study, women with polycystic ovarian disease taking metformin before conception and throughout pregnancy had a 10-fold reduction in the development of gestational diabetes (41)
Sulfonylureas Glyburide	Stimulate pancreatic insulin release	Variable 1.25-20 mg/d	Reduces hyperglycemia	Inadequately controlled blood glucose levels, hypoglycemia, nausea, weight gain, rash	In a randomized study of 404 women with gestational diabetes, there was no difference in glucose levels, fetal macrosomia, or congenital anomalies in women taking glyburide compared with those using insulin (42)



Elements of Follow-up for Pregestational and Gestational Diabetes Mellitus

Category	Issue	How?	How Often?	Notes
History	Hyperglycemia	Inquire at each visit whether patient is experiencing polyuria, polydipsia, or blurred vision	Each prenatal visit and postpartum	Use this information in conjunction with home glucose logs to adjust insulin dose
History	Hypoglycemia	Inquire at each visit whether patient is experiencing episodes of sweating, nervousness, disorientation, or other symptoms associated with hypoglycemia	Each prenatal visit, postdelivery and postpartum	The tight glucose control required during pregnancy and changing insulin requirements predispose patients to hypoglycemia
History	Neuropathy	Inquire at each visit whether patient is experiencing numbness, tingling, or pain of the extremities	Each prenatal visit	Neuropathy may develop during pregnancy and may make necessary increased vigilance in foot care
History	Hypertension	Inquire at each visit whether the patient is experiencing edema, headaches, or visual changes	Each prenatal visit	Hypertensive disorders frequently complicate diabetic pregnancies
History	Hyperthyroidism and hypothyroidism	Inquire at each visit whether patient is experiencing weight changes, constipation or diarrhea, change in energy, skin changes	Each prenatal visit, at delivery, and at postpartum check-ups	Women with type 1 diabetes are at increased risk for the development of thyroid disease
Physical exam	Obesity	Determination of body mass index	At postpartum check and every visit thereafter	Achieving and maintaining ideal body mass index may prevent the development of type 2 diabetes in a woman with gestational diabetes
Physical exam	Diabetic retinopathy	Dilated retinal exam	Early in pregnancy and at postpartum visit	Pregnancy may accelerate diabetic retinopathy
Physical exam	Blood pressure	Blood pressure determination	Each prenatal visit	Hypertensive disorders frequently complicate diabetic pregnancies
Laboratory	Glucose levels	Obtain daily fingerstick glucose levels fasting and 2 hours postprandially throughout the pregnancies of women with pregestational diabetes and after the diagnosis of gestational diabetes	Review home glucose log at each prenatal visit and continue at least 6 weeks postpartum	Insulin requirements change throughout pregnancy, after delivery, and while breastfeeding; women with gestational diabetes need reclassification at least 6 weeks following delivery

Table Continued...



Elements of Follow-up for Pregestational and Gestational Diabetes Mellitus

Category	Issue	How?	How Often?	Notes
Laboratory	Diabetic nephropathy	Serum creatinine and urinary excretion of total protein in pregestational diabetic pregnancies	Urine dipstick for protein at each prenatal visit; 24-hr urine for protein and creatinine clearance after delivery in women with pregestational diabetes	Pregnancy may accelerate diabetic nephropathy
Laboratory	Glucose control	Hemoglobin A _{1c}	Check every 2-3 months during pregnancy to confirm home glucose monitoring results	
Laboratory	Thyroid disease	Serum thyrotropin	After delivery and with the development of symptoms	Women with type 1 diabetes are at increased risk for the development of thyroid disease
Non-drug therapy	Diet and exercise therapy	Provide nutritional and exercise counseling consistent with the American Diabetes Association guidelines	Throughout pregnancy and at each postpartum visit	Diet and exercise may decrease glucose levels in women with diabetes during pregnancy; achieving and maintaining ideal body mass index may prevent the postpartum development of type 2 diabetes in a woman with gestational diabetes
Drug therapy	Insulin	Adjust insulin levels throughout pregnancy based on home glucose readings	Each prenatal visit and at 6 weeks postpartum visit	Instruct patient to contact the office between appointments if glucose levels are too high or too low
Drug therapy	Oral diabetic agents	Restart oral diabetic agents in women with pregestational type 2 diabetes following delivery	Postdelivery	Risks of these agents to the breast-feeding infant are largely unknown and should be reviewed with pediatrician
Patient education	Blood glucose monitoring	Stress the importance of frequent glucose monitoring	Each prenatal visit should include a review of the patient home glucose log	
Patient education	Nutrition and exercise	Counsel patient on the American Diabetes Association recommendations for diet and exercise	Review diet and exercise at each prenatal visit and at 6-week postpartum visit	
Patient education	Planning for subsequent pregnancies	Discuss the need for pre-conception planning in all women who have had a diabetic pregnancy. Ensure adequate birth control between pregnancies	6-week postpartum visit	

Table Continued...



Elements of Follow-up for Pregestational and Gestational Diabetes Mellitus

Category	Issue	How?	How Often?	Notes
Patient education	Breast feeding	Review the benefits of breast-feeding with the patient and provide lactation support	Third trimester prenatal visits and postdelivery	The American Academy of Pediatrics recommends that all infants be exclusively breast-fed for the first 6 months of life and continue with solids until at least 1 year of age; review maternal medications and their compatibility with breast-feeding (52)



Diagnosis of Gestational Diabetes Mellitus with a 100-Gram Oral Glucose Load

Test	Plasma Concentration (mg/dL)	Plasma Concentration ($\mu\text{mol/L}$)
Fasting	95	5.3
1 hour	180	10.0
2 hour	155	8.6
3 hour	140	7.8

Two or more of the venous plasma concentrations must be met or exceeded for a positive diagnosis. The test should be done in the morning after an overnight fast of between 8 and 14 hours after at least 3 days of unrestricted diet (>150 g carbohydrate per day) and unlimited physical activity. The patient should remain seated and should not smoke throughout the test.



Drugs To Avoid in Pregnancy

Agent	Mechanism of Action	Dosage	Benefits	Side Effects	Notes
ACE inhibitor	Blocks the conversion of angiotensin I to angiotensin II	Variable 5-40 mg/d	Do not use in pregnancy	Fetal teratogen	Screen for ACE inhibitor use in pregestational diabetic patients and stop before conception
Angiotensin-receptor blocker	Blocks angiotensin II receptor sites	Variable 25-100 mg/d	Do not use in pregnancy	Fetal teratogen	Screen for angiotensin-receptor blocker use in pregestational diabetic patients and stop before conception
Aspirin	Cyclo-oxygenase inhibitor	81-325 mg/d	Do not use in pregnancy	Maternal and newborn hemorrhage, increased perinatal mortality, intrauterine growth retardation, and teratogenic effects	In one case-controlled study, 3 of 14 newborns exposed to aspirin within 1 week of delivery had minor hemorrhaging compared with 1 of 17 controls (10). In two retrospective studies, mothers of 1,291 malformed infants were found to have consumed aspirin during pregnancy more frequently than mothers of normal infants (11; 12)
HMG-CoA reductase inhibitors	Decreases synthesis of cholesterol in the liver	Variable	Do not use in pregnancy	Possible teratogen	In a surveillance study of lovastatin exposures during pregnancy, normal outcomes were 85%, congenital anomalies 4.0%, spontaneous abortions 8.0%, and fetal deaths/stillbirths 1.0% (9)

ACE = angiotensin-converting enzyme; HMG-CoA = 3-hydroxy-3-methylglutaryl coenzyme A.