

Diabetes in Pregnancy

The following section is entitled “**Diabetes in Pregnancy**”. This section deals with some of the basic concepts important in caring for type 1, type 2 and gestational diabetes in pregnancy. The section begins with a *learner handout* with space for the learner to make their own notes. The *learner handout* is followed by a *teaching script* for the educator. The section then concludes with several cases for discussion and a brief bibliography for this topic.

DIABETES IN PREGNANCY

DIABETES

TYPE I DIABETES: PRECONCEPTION COUNSELING

The most important aspect of the management of the Type I diabetic during pregnancy is preconception counseling that emphasizes the importance of euglycemia at the time of conception.

Hyperglycemia in the early first trimester greatly increases the risk of fetal cardiac and neurologic malformations.

If euglycemia is achieved throughout the first trimester, pregnant Type I diabetics will not have an increased risk of fetal malformation compared with the non-diabetic.

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TYPE I DIABETES: MANAGEMENT

Pregnant Type I diabetics usually require insulin three times a day to maintain adequate control.

Postprandial glucose is monitored.

Hyperglycemia can compromise the fetus even after organogenesis is completed and therefore tight control should be maintained throughout gestation.

TYPE I DIABETES: MANAGEMENT GOALS OF THERAPY

Fasting	<100 mg/dL	(<5.6 mmol/L)
1 hour postprandial	<149 mg/dL	(<7.7 mmol/L)
2 hours postprandial	<120 mg/dL	(<6.6 mmol/L)

TYPE I DIABETES: COMPLICATIONS

Type I diabetics are at increased risk of preeclampsia.

Type I diabetics with renal or coronary artery disease prior to pregnancy are at particularly high risk for poor maternal and fetal outcome.

Diabetic retinopathy and nephropathy can worsen during pregnancy.

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TYPE I LABOR

Type I diabetics should be managed with an insulin drip during labor.

TYPE II DIABETES

Type II diabetics often require insulin therapy during pregnancy as oral hypoglycemic agents do not generally provide the type of glucose control necessary for fetal health.

GESTATIONAL DIABETES

Gestational diabetes is usually an illness of the third trimester. It is related to the anti-insulin effects of many of the hormones associated with pregnancy. Its main risk is that it causes large babies with an increased risk for delivery by instrumentation or cesarean section.

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GESTATIONAL DIABETES

Risk factors for gestational diabetes include family history of Type II diabetes, obesity, age, ethnic background, and previous large babies.

It is controversial whether all, some, or no pregnant women should be tested for gestational diabetes.

If the gestational diabetes screen is positive, an oral glucose tolerance test is done. If the OGTT is also positive, the woman is placed on dietary or insulin therapy for the duration of her pregnancy.

GESTATIONAL DIABETES

The majority of gestational diabetics eventually develop Type II diabetes.

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Teaching Script

The Importance of Preconception Counseling in Type I Diabetes

The single most important aspect of managing the type I diabetic in pregnancy is preconception counseling. By talking to type I diabetics about pregnancy prior to conception, medical providers can have a dramatic impact on their patient's pregnancy outcome. Studies have repeatedly shown that hyperglycemia at the time of conception and in the early first trimester will greatly increase the risk of cardiac and neurologic malformations in the children of type I diabetics. However, studies have also shown that if euglycemia is achieved throughout the first trimester, pregnant type I diabetics do not have an increased risk of fetal malformation as compared to the non-diabetic population. Therefore, it is very important to tell female type I diabetic patients of reproductive age that their pregnancy should be planned and that attempts at conception should occur in a context of tight glucose control and a normal HBA1C.

Management Goals for Type I Diabetics in Pregnancy

Type I diabetics planning to conceive and those who are already pregnant will usually require insulin three times a day to maintain the tight euglycemic control that optimizes fetal outcome. This tight glucose control is advocated even after the teratogenic potential has passed after the first trimester. Euglycemia in the second and third trimester is also associated with an improved pregnancy outcome. In general, we monitor the postprandial glucose rather than the preprandial glucose in pregnant diabetics and aim to keep the blood glucose:

- less than 100 mg/dL (5.5 mmol/L) fasting**
- less than 140 mg/dL (7.7 mmol/L) at 1 hour postprandial**
- less than 120 mg/dL (6.6 mmol/L) at 2 hours postprandial**

Risks of Pregnancy for the Type I Diabetic

Type I diabetics are at an increased risk for preeclampsia. In fact, up to 50% of type I diabetics with nephropathy will develop preeclampsia during their pregnancy. The diagnosis of preeclampsia in this setting can be difficult as many individuals with decades of diabetes will have baseline proteinuria and hypertension.

Patients with known renal or coronary artery disease are at a particularly high risk for a poor maternal and fetal outcome. It is also important to remember that type I diabetics with over 10-20 years of diabetes may have previously unrecognized renal disease or coronary artery disease that can be unmasked by the physiologic changes of pregnancy.

Diabetic nephropathy - particularly diabetic proteinuria - often worsens in pregnancy but *generally* reverts back to baseline after delivery. All pregnant diabetics should have a baseline 24 hour urine for protein and creatinine clearance done at the beginning of gestation. If an abnormality is present, it should be followed with serial 24-hour urines for protein and creatinine clearance every 1 to 3 months during gestation. ACE inhibitors should *not* be used in pregnancy despite their known benefits of decreasing the progression of diabetic nephropathy. Diabetics on ACE inhibitors who are trying to conceive should do monthly pregnancy tests and promptly discontinue their ACE inhibitor once they conceive.

Diabetic retinopathy may worsen in pregnancy and all pregnant diabetics should have a complete ophthalmologic evaluation early in gestation. The frequency of subsequent evaluations during pregnancy will be determined on the basis of the severity of retinal disease noted on the initial evaluation and the pace of its deterioration during the pregnancy. Retinal laser surgery can and should be performed when indicated during pregnancy.

Management of the Type I Diabetic in Labor

Management of the type I diabetic in labor is best accomplished through the use of an insulin drip with regular glucose monitoring being done to keep blood glucose between 60 and 120 mg/dL (3.5 to 6.5 mmol/L).

Type II Diabetes

Type II diabetics also need tight blood sugar control in the first trimester to decrease the risk of teratogenesis. In women with type II diabetes who want to conceive but are not euglycemic on their oral hypoglycemic therapy, it is advisable to stop oral hypoglycemia therapy and to use insulin to achieve euglycemia prior to trying to conceive. Insulin should then be continued throughout the subsequent gestation with similar goals for control as have already been described for type I diabetics. Oral hypoglycemics are not known to be teratogens but are not recommended for use in pregnancy because they do not usually provide the tight glucose control necessary to the diabetic gravida.

Gestational Diabetes

Gestational diabetes is defined as carbohydrate intolerance that is first diagnosed during pregnancy. The majority of glucose intolerance presenting for the first time in pregnancy presents in the third trimester and resolves rapidly post partum. This pregnancy associated glucose intolerance occurs because of the anti-insulin effects of many of the hormones associated with pregnancy. In particular, human placental lactogen (HPL) is a strong insulin antagonist. This hormonal milieu can lead to hyperglycemia in a genetically predisposed patient.

Since the vast majority of gestational diabetes occurs only in the second half of Pregnancy, there is no association between gestational diabetes and teratogenesis. However,

elevated blood glucoses from gestational diabetes can cause fetal macrosomia (large babies) and therefore are associated with an increased risk that the fetus will require delivery by instrumentation or cesarean section.

Risk factors for gestational diabetes include a family history of type II diabetes, age, obesity, ethnic background and previous history of a large baby. It is controversial whether all, some, or no pregnant woman should be tested for gestational diabetes. Screening for gestational diabetes occurs by a 12 hour 50 gram glucose tolerance test. If this screening test is positive (generally, this is accepted to mean greater than 130 mg/dL or 7.2 mmol/L one hour after the oral intake of the glucose load), the more formal 3 hour 100 g oral glucose tolerance test is performed. If this test is positive, the woman is placed on dietary control. When dietary control is not successful, insulin therapy is initiated. This is necessary in over 30% of gestational diabetics.

An important point for medical providers to know about gestational diabetes is that the majority of gestational diabetics will eventually develop type II diabetes. Therefore, all women who have a history of gestational diabetes should probably have a yearly fasting glucose measured to help identify early new onset of type II diabetes.

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Case Discussion

Case #1

SD is a 35-year-old G3P2 woman who was admitted to hospital for control of blood sugars. Four days ago she found out that she was 6 weeks pregnant, and institution of home glucose monitoring by her obstetrician revealed hyperglycemia that on two occasions in the past 2 days was over 300 mg/dL. The patient has had 2 previous pregnancies complicated by gestational diabetes but she tells you that her blood glucose levels between pregnancies have always been normal.

She weighs 180 lbs. and is 5'2". Her examination is normal with a BP of 114/70 to 153/84. Her blood glucoses and insulin doses since admission to hospital are as follows:

<u>DAY 1</u>	<u>mg/dL</u>	<u>mmol/L</u>	
Fasting glucose	141	7.8	<i>patient given 20u N/ 10u R</i>
2 hours after breakfast	365	20.3	
2 hours after lunch	311	17.3	<i>given 10u R</i>
2 hours after dinner	271	15.	<i>given 10u R</i>

<u>DAY 2</u>	<u>mg/dL</u>	<u>mmol/L</u>	
Fasting glucose	261	14.3	<i>patient given 30u N/20u R</i>
2 hours after breakfast	314	17.3	<i>patient given 10u R</i>
2 hours after lunch	226	12.5	
2 hours after dinner	169	9.4	

You are asked to assist in managing her blood glucose.

What type of diabetes does this patient have?

What are the goals for her glucose control?

What are the dangers of her present glucose levels?

Why are her blood glucoses being checked following meals rather than before them?

How would you approach controlling this patient's blood glucose?

Why not try oral hypoglycemic agents for this patient?

What special tests (if any) does this women need to rule out any medical complications of diabetes?

You rule out diabetic ketoacidosis with by checking her anion gap, which is normal. You place the patient on an insulin drip of 2 units / hour and check her sugars hourly, titrating the dose of intravenous insulin to bring her glucose down to 120 mg/dL (6.7 mmol/L). Her hourly insulin requirements appear to be around 5u/hour including intravenous boluses given for meals.

How will you switch her over to subcutaneous insulin?

How do you plan to manage this patient's glucose as an outpatient?

How can pregnancy affect diabetic nephropathy? Retinopathy? Vasculopathy? Neuropathy?

Are there any special laboratory tests that might be advisable at this point in the pregnancy?

BONUS: In what ways does pregnancy affect glucose levels? How does pregnancy effect the interpretation of AFP testing and tests for fetal lung maturity?

DIABETES IN PREGNANCY

Case Discussion

Case #2

CH is a 27-year-old G₁P₀ diabetic (Priscilla White Class F/R) who is sent to you for preconception counseling. She developed diabetes mellitus at age 15 months. She self monitors blood glucose QID and takes Humulin NPH and regular in the a.m. regular with lunch and dinner, and NPH at bedtime. Her glucoses are frequently >240 mg/dl (13.3 mmol/L) in the fasting state. Her last hemoglobin A1C was 12.0% (normal: 4-8).

Her renal function is as follows: Serum Creatinine 0.8-1.0 mg/dl (70-88 μ mol/L), 1.36 gram of protein/24 hr, creatinine clearance 100 cc/min (1.66 cc/second). She is known to have a diabetic proliferative retinopathy requiring laser surgery on several occasions and complicated by a retinal detachment (repaired) 2 years ago. There is no evidence of autonomic dysfunction or peripheral neuropathy. She has no known large vessel vasculopathy. She has had chronic hypertension for over 8 years that is managed with Enalapril & Clonidine. She has regular menses and uses condoms for contraception.

What are the risks to her fetus if she chooses to get pregnant?

What goal should be set for her hemoglobin A1C and daily glucose during pregnancy and when should this level of glucose control be initiated?

How will pregnancy affect her kidneys? Her eyes? Her cardiac status? Her neuropathy?

What should be done with her antihypertensive medications?

After carefully considering the information you provide her with she decides to proceed with planning for a pregnancy but decides to wait until after she gets her glucose under better control. She is followed closely until she achieves great glucose control for a month and then her husband stops using condoms. She conceives on the second ovulation after stopping contraception. She is seen for her first prenatal visit at six weeks gestation. Medications now include Clonidine and Labetalol. Her BP is 140/86.

When can she “back off” of this tight glucose control?

What is the usual insulin regimen and monitoring schedule for a diabetic pregnant woman?

What will your counseling include this time?

Should she continue these medications?

What baseline data should be obtained?

What are her risks of spontaneous abortion? Of fetal anomalies?

The pregnancy progresses as follows:

At 16 weeks her BP is 130/78 with no signs or symptoms of preeclampsia. Her alpha feta protein and targeted (level 2) ultrasound are normal. Her ophthalmologist tells her she has had no progression in her retinal disease. Laboratory evaluation reveals a serum creatinine of 0.7 mg/dL (62 Φ mol/L), CrCl of 120 cc/min.(2mL/s), 24 hour proteinuria 3.7 gm/24 hours, and a MCBG of 125 mg/dl (6.9mmol/L).

If her eyes worsen can she have laser surgery on them while pregnant?

At 23 weeks, obstetrical evaluation of the fetus continues to look good. Ophthalmologic exam is unchanged. Her BP is measured at 130/81. Her serum creatinine is 0.8 mg/dL (70.72 Φ mol/L) with a CrCl 100 cc/min. (1.66 cc/s),and 4.2 g of protein in her urine /24 hour. MCBG is 118 mg/dl (6.5 mol./L).

Why has her proteinuria worsened?

At 28-33 weeks the baby continues to be active. She has normal reactive non-stress tests twice weekly. The Biophysical profile is 8-10/10 (with a slightly decreased amniotic fluid volume). Her BP remains stable. Hemoglobin A1C is 7.2%. Creatinine is 0.9 mg/dL (70.72 Φ mol/L). CrCl is 100 cc/min. (1.66 cc/s) with 4.4 gm of protein in /24 hours.

At 34 weeks the patient complains of increasing edema, headache and a 6 pound weight gain over 7 days. BP is found to be increased to 160-170 /90-96 mmHg. CBC shows a Hgb 15, WBC 4.2 Platelets 105. AST is 40 U/L (0.67 Φ kat/L), ALT is 62 U/L (1.03 Φ kat/L), and uric acid is 7.5 mg/dL (446 Φ mol/L).

She is admitted to hospital and a 24 hour urine is done which shows CrCl of 70 cc/min (1.16 cc/s)with proteinuria of 6.5 gm/24 hours.

Induction is begun that day for worsening PIH. She delivers a viable 1850 gm male infant with Apgars of 6 and 7.

How should her diabetes be handled peripartum?

What neonatal complications might be expected?

Should this patient breast feed?

What method of contraception should she use?

Given her early onset of pre-eclampsia in this pregnancy, should she be discouraged from attempting another pregnancy in the future?

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Case Discussion

Case #3

Adapted from ACP workshop syllabus

A 33-year-old obese multigravida is now at 27 weeks gestation. Her two prior pregnancies resulted in term deliveries of 9 lb. 2 oz and 9 lb. 13 oz. neonates. There is a strong family history of Type II diabetes mellitus. A gestational diabetes screen at 26 weeks (50 gm glucose load) was 180mgm% (10.0 nmol/L) at 1 hour (greater than 140mgm % is considered abnormal). A subsequent 100 gm three hour glucose tolerance test was also abnormal according to the criteria of O'Sullivan and Mahan.

What are the maternal and fetal risks associated with gestational diabetes?

How would you manage this woman during her pregnancy? After her pregnancy?

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Case Discussion

Case #4

Adapted from ACP workshop syllabus

A 44-year-old obese hypertensive type II diabetic comes into the office complaining of three months of secondary amenorrhea. Her diabetes has been poorly controlled on diet and glyburide (DiaBeta®). Her blood pressure is 150/100 on atenolol 50 mg daily and Hydrochlorothiazide 50 mg daily. Beta HCG reveals she is pregnant and a subsequent obstetrical ultrasound shows her to be at 11 weeks gestation.

What are the risks to the fetus in this scenario? How do they differ from those in a type 1 diabetic?

What are the risks to the mother in this scenario? How do they differ from those in a type 1 diabetic?

What changes in her diabetic management would you institute (if any) and why?

Should similar dietetic guidelines be used for the obese pregnant women as for women with normal weight for height?

DIABETES IN PREGNANCY

Case Discussion

Case #5

A 38-year-old type II diabetic with blood glucose moderately well controlled on glyburide (diabeta®) 7.5 mg. po daily comes in for her “every 3 month” evaluation. Her blood glucose has been running between 80 and 200. Although you have told her in the past that a diabetic of her age needs better glucose control, she has always refused to consider what she calls “the needle.” While examining her you notice an engagement ring on her hand. When you remark upon it, she explains to you that she and her boyfriend are planning to get married. She also tells you that they are already trying to start a family.

Key Points to Review

- 1. Hyperglycemia is a teratogen. Diabetic women have an increased incidence of children with congenital malformations and the incidence of these congenital malformations can be correlated directly with the woman’s hemoglobin A1C from her first trimester of pregnancy. Therefore, euglycemia is the goal of every diabetic pregnancy.***
- 2. Although many oral hyperglycemics have good pregnancy data, they are not generally used in pregnancy because they do not provide the necessary glycemic control.***
- 3. Diabetic women considering pregnancy should be encouraged to switch to an intensive insulin regimen that includes measuring 2 hour postprandial sugars and aiming for complete euglycemia. Ideally, this regimen should be established prior to conception.***
- 4. Although, in general, most type 1 diabetics can expect good pregnancy outcomes, there is an increased incidence of pregnancy complications in women who have retinopathy, nephropathy or vasculopathy. These complications include progression of retinal disease, progression of underlying renal disease (especially worsening of proteinuria), and an increased risk of preeclampsia. They are also at increased risk for intrauterine growth restriction (IUGR) and intrauterine fetal demise (IUFD) and therefore require increased fetal monitoring during pregnancy.***

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