

# Preconception Care of Women With Diabetes

AMERICAN DIABETES ASSOCIATION

**DIABETES AND CONGENITAL MALFORMATIONS** — Major congenital malformations remain the leading cause of mortality and serious morbidity in infants of mothers with type 1 or type 2 diabetes. Several studies have established an association between elevated maternal glucose or glycohemoglobin levels during embryogenesis and high rates of spontaneous abortions and major malformations in newborns. Clinical trials of preconception care to achieve stringent blood glucose control in the preconception period and during the first trimester of pregnancy have demonstrated striking reductions in rates of malformations compared with infants of diabetic women who did not participate in preconception care. (For further discussion, see the American Diabetes Association technical review on this subject [1].) Unfortunately, unplanned pregnancies occur in about two-thirds of women with diabetes, precluding adequate preconception care and leading to a persistent excess of malformations in their infants. To minimize the occurrence of these devastating malformations, standard care for all women with diabetes who have child-bearing potential should include 1) counseling about the risk of malformations associated with unplanned pregnancies and poor metabolic control and 2) use of effective contraception at all times unless the patient is in good metabolic control and actively trying to conceive.

**DIABETES AND CONTRACEPTION** — There are no contraceptive methods that are specifically contraindicated in women with diabetes. Thus, the selection of a method for

an individual patient should be made by a provider who is familiar with contraceptive prescribing practices, using the same guidelines that apply to women without diabetes. Because unexpected failure of contraception can lead to such serious complications for the infant of a woman with diabetes, the focus should be on methods with proven high degrees of effectiveness.

**PRECONCEPTION CARE PROGRAM** — To prevent excess spontaneous abortions and congenital malformations in infants of diabetic mothers, diabetes care and education must begin before conception. This is best accomplished by a multidisciplinary team that includes a diabetologist, internist, or family practice physician skilled in diabetes management; an obstetrician familiar with the management of high-risk pregnancies; diabetes educators, including a nurse, dietitian, and social worker; and other specialists, as deemed necessary. Ultimately, the woman with diabetes must become the most active member of the team, calling upon the other members for specific guidance and expertise to help her achieve her goal of a healthy pregnancy and newborn.

The primary purpose of these guidelines is to define the elements of a preconception care program. This program should be sufficient to minimize congenital malformations and thereby substantially reduce health care costs. This document describes the recommended intensive outpatient treatment plan, based on risk assessment, health promotion, and intervention, and outlines effective team work strategies to implement

the plan before and during early pregnancy.

The model of diabetes preconception and early pregnancy health care described in this document is interactive. It includes four main elements: 1) patient education about the interaction of diabetes, pregnancy, and family planning; 2) education in diabetes self-management skills; 3) physician-directed medical care and laboratory testing; and 4) counseling by a mental health professional when indicated to reduce stress and improve adherence to the diabetes treatment plan. All four elements are important for patients to achieve the level of sustained glycemic control necessary to prevent excess congenital malformations and spontaneous abortions.

**SPECIFIC GOALS OF TREATMENT** — The desired outcome of the preconception phase of care is to lower A1C test values to a level associated with optimal development during organogenesis. Epidemiological studies indicate that A1C test values up to 1% above normal are associated with rates of congenital malformations and spontaneous abortions that are not greater than rates in nondiabetic pregnancies. However, rates of each complication continue to decrease with even lower A1C test levels. Thus, the general goal for glycemic management in the preconception period and during the first trimester should be to obtain the lowest A1C test level possible without undue risk of hypoglycemia in the mother. In particular, levels that are <1% above the normal range are desirable. Practical self-management skills essential for attaining this level of glycemic control in preparation for pregnancy are the same skills required for any insulin-based self-management program:

- Use of an appropriate meal plan
- Self-monitoring of blood glucose (SMBG)

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 The recommendations in this article are based on the evidence reviewed in the following publication: Preconception care of diabetes, congenital malformations, and spontaneous abortions (Technical Review). *Diabetes Care* 19:514–541, 1996.  
 Approved 1995. Most recent review/revision, 2000.  
**Abbreviations:** CAD, coronary artery disease; SMBG, self-monitoring of blood glucose.  
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- Self-administration of insulin and self-adjustment of insulin doses
- Treatment of hypoglycemia (patient and family members)
- Incorporation of physical activity
- Development of techniques to reduce stress and cope with denial

## INITIAL VISIT

### Medical and obstetrical history

A complete history is imperative before planning for pregnancy. This should include, but not be limited to, questioning for the following:

- Duration and type of diabetes (type 1 or type 2)
- Acute complications, including history of infections, ketoacidosis, and hypoglycemia
- Chronic complications, including retinopathy, nephropathy, hypertension, atherosclerotic vascular disease, and autonomic and peripheral neuropathy
- Diabetes management, including insulin regimen, prior or current use of oral glucose-lowering agents, SMBG regimens and results, medical nutrition therapy, and physical activity
- Concomitant medical conditions and medications, thyroid disease in particular for patients with type 1 diabetes
- Menstrual/pregnancy history; contraceptive use
- Support system, including family and work environment

An initial individual educational evaluation session with a diabetes educator, a registered dietitian, and, when needed, a psychosocial expert is valuable. Members of the patient's immediate family should participate in this session. In conjunction with the primary physician, these professionals will review the patient's current management plan and develop a comprehensive treatment plan.

### Physical examination

Diabetic retinopathy, nephropathy, autonomic neuropathy (especially gastroparesis), and coronary artery disease (CAD) can be affected by or can affect the outcome of pregnancy. Thus, physical examination should give particular attention to the following:

- Blood pressure measurement, including testing for orthostatic changes

- Dilated retinal exam by an ophthalmologist or other eye specialist knowledgeable about diabetic eye disease
- Cardiovascular exam for evidence of cardiac or peripheral vascular disease. If found, patients should have screening tests for CAD before attempting pregnancy to assure they can tolerate the increased cardiac demands.
- Neurological exam, including examination for signs of autonomic neuropathy

### Laboratory evaluation

The evaluation should focus on assessment of metabolic control and detection of diabetic complications that may affect or be affected by pregnancy:

- A1C test
- Serum creatinine and urinary excretion of total protein and/or albumin (albumin-to-creatinine ratio or 24-h excretion rate). Patients with protein excretion  $>190$  mg/24 h have been shown to be at increased risk for hypertensive disorders during pregnancy. Patients with protein excretion  $>400$  mg/24 h also are at risk for intrauterine growth retardation during later pregnancy. No specific treatments are indicated, but patients should be counseled about these risks. Since patients should not take angiotensin-converting enzyme (ACE) inhibitors during pregnancy, these assessments should be carried out after cessation of these drugs.
- Measurement of serum thyroid stimulating hormone and/or free thyroxine level in women with type 1 diabetes because of the 5–10% coincidence of hyper- or hypothyroidism
- Other tests as indicated by physical exam or history

### Management plan

The initial management plan should include the following components:

- Counseling about the risk and prevention of congenital anomalies; fetal and neonatal complications of maternal diabetes; effects of pregnancy on maternal diabetic complications; risks of obstetrical complications that occur with increased frequency in diabetic pregnancies (especially hypertensive disorders); the need for effective contraception until glycemia is well-controlled; and the cost-benefit

relationship between preconception care and prevention of malformations.

- Selection of antihyperglycemic therapy. Insulin should be prescribed for type 1 and type 2 diabetic patients, because the safety of currently available oral antidiabetic agents is not assured during early pregnancy.
- Establishment of plan to achieve low-risk glycemia. The main tool for assessing the risk of malformations in the infant is the maternal A1C test result. Two steps are recommended for achieving a low-risk concentration ( $<1\%$  above the normal range, lower if possible).

1. Set goals for self-monitored glucose. Successful preconception care programs have used the following pre- and postprandial goals:

Before meals:

capillary plasma glucose  
80–110 mg/dl (4.4–6.1 mmol/l)

2 h after meals:

capillary plasma glucose  
 $<155$  mg/dl ( $<8.6$  mmol/l) at 2 h.

There are no data to suggest that postmeal glucose monitoring has a specific role in preconception diabetes care beyond what is needed to achieve the target for A1C. Thus, a focus on preprandial monitoring is recommended initially to assist patients in self-selection of insulin doses.

2. Implement the treatment plan and monitor A1C levels at 1- to 2-month intervals until stable. Then, counsel patient about the risk associated with her level. If she does not achieve a low-risk level of  $<1\%$  above the upper limit of normal, consider modification of the treatment regimen, including addition of postprandial glucose monitoring. It is important to note that glycemic goals may need to be modified according to the patient's recognition of hypoglycemia and risk of severe neuroglycopenia. Outpatient management is the appropriate forum for achieving preconception glycemic goals.

**CONTINUING CARE**— After the initial visit, patients should be seen at 1- to 2-month intervals depending on their mastery of the management program and

the presence or absence of coexisting medical conditions. Frequent phone contact for adjustment of insulin doses and other aspects of the treatment regimen is advised as well. Once the patient has achieved stable glycemic control (assessed by the A1C test) that is as good as she can achieve, then she can be counseled about the risk of malformations and spontaneous abortions. If the risk as well as the status of maternal diabetic complications and any coexisting medical conditions are acceptable, then contraception can be discontinued. If conception does not occur within 1 year, the patient's fertility should be assessed.

## SPECIAL CONSIDERATIONS

### Hypoglycemia

It is clear from the Diabetes Control and Complications Trial that attempts to achieve normal glycemic control in patients with type 1 diabetes increase the risk of severe hypoglycemia. The occurrence of severe, frequent, or unexplained episodes of hypoglycemia may be due to a number of factors, such as defective counterregulation, hypoglycemia unawareness, insulin dose errors, and excess alcohol intake. There is no solid evidence that such hypoglycemia is an independent risk to the developing human embryo. There is, however, clear risk to the mother. Thus, it is imperative that this risk be explained to the woman with diabetes contemplating pregnancy and that means of prevention or ultimate treatment be provided to her and her family. Inclusion of family members and close associates of the patient in both education and management is imperative. Frequent contact with the patient for readjustment of the treatment program is integral to the prevention of severe hypoglycemia.

### Retinopathy

Diabetic retinopathy may accelerate during pregnancy. The risk can be reduced by gradual attainment of good metabolic control before conception and by preconceptual laser photocoagulation in women with standard indications for that therapy. Thus, a baseline dilated comprehensive eye examination is necessary before conception, and women with pre-existing diabetes should be counseled on the risk

of development and/or progression of diabetic retinopathy. In settings in which a retina specialist is unavailable, other experienced examiners may be acceptable. Follow-up ophthalmological examination should be anticipated during pregnancy for all women with diabetes.

### Hypertension

Hypertension is a frequent concomitant or complicating disorder of diabetes. Patients with type 1 diabetes frequently develop hypertension in association with diabetic nephropathy, as manifested by the presence of gross proteinuria. Patients with type 2 diabetes more commonly have hypertension as a concomitant disease. In addition, pregnancy-induced hypertension is a potential problem for the woman with diabetes, particularly when proteinuria in excess of 190 mg/day is present before conception or in early pregnancy. Aggressive monitoring and control of hypertension in the preconception period is advised, if—for no other reason—to reduce the risk of worsening diabetic nephropathy or the development of retinopathy or clinical atherosclerosis. ACE inhibitors,  $\beta$ -blockers, and diuretics should be avoided in women contemplating pregnancy.

### Nephropathy

Baseline assessment of renal function by serum creatinine and some measure of urinary protein excretion (urine albumin-to-creatinine ratio or 24-h albumin excretion) should be undertaken before conception and followed at regular intervals because of the potential impact of pregnancy on proteinuria and the impact of renal insufficiency on fetal growth and development. Women with incipient renal failure (serum creatinine  $>3$  mg/dl or creatinine clearance  $<50$  ml/min) should be counseled that pregnancy may induce a permanent worsening of renal function in  $>40\%$  of patients. In subjects with less severe nephropathy, renal function may worsen transiently during pregnancy, but permanent worsening occurs at a rate no different from the background. Therefore, it should not serve as a contraindication to conception and pregnancy. As mentioned above, the presence of proteinuria in excess of 190 mg/24 h before or during early pregnancy is associated

with a tripling of the risk of hypertensive disorders in the second half of pregnancy. ACE inhibitors for treatment of microalbuminuria should be discontinued in women who are attempting to become pregnant.

### Neuropathy

The presence of autonomic neuropathy, particularly manifested by gastroparesis, urinary retention, hypoglycemic unawareness, or orthostatic hypotension, may complicate the management of diabetes in pregnancy. These complications should be identified, appropriately evaluated, and treated before conception. Peripheral neuropathy, especially compartment syndromes such as carpal tunnel syndrome, may be exacerbated by pregnancy.

### Cardiovascular disease

Untreated CAD is associated with a high mortality rate during pregnancy. Evidence of CAD should be sought according to the American Diabetes Association consensus statement on the diagnosis of coronary heart disease (2). Successful pregnancies have been undertaken after coronary revascularization in women with diabetes. Exercise tolerance should be normal to maximize the probability that the patient will tolerate the increased cardiovascular demands of gestation.

### Early pregnancy management

At the earliest possible time after conception, pregnancy should be confirmed by laboratory assessment (urinary or serum B-hCG). The woman should be reevaluated by the health care team to reinforce goals and methods of management, which should remain essentially stable throughout the first trimester.

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## References

1. Kitzmiller JL, Buchanan TA, Kjos S, Combs CA, Ratner R: Preconception care of diabetes, congenital malformations, and spontaneous abortions (Technical Review). *Diabetes Care* 19:514–541, 1996
2. American Diabetes Association: Consensus development conference on the diagnosis of coronary heart disease in people with diabetes (Consensus Statement). *Diabetes Care* 21:1551–1559, 1998