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PREGNANCY IN ADOLESCENTS WITH TYPE 1 DIABETES

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INTRODUCTION

Adolescence is a time of many changes. For an adolescent with type 1 diabetes mellitus (T1DM), change means becoming more self-reliant in dealing with chronic illness. Rebellion, acting out, and the desire to be "normal" may drive the adolescent with chronic disease to make poor choices.[1,2] Such choices may have detrimental effects on dietary intake, medication usage, and social behavior.[1,3] For diabetic adolescents, low self-esteem and depression may contribute to behavior resulting in an unplanned pregnancy. This is of high risk to both the woman and fetus and is associated with high rates of congenital malformations, spontaneous abortions, and stillbirths.[4,5] Additionally,

Highlights In This Issue

E-Abstracts (Abstracts On Line)

From The Editor's Desk

Volume 20, number 4, of *GGH* marks the first year of the journal under my direction. I am proud of what we accomplished and I thank the editorial board for their support. The scope of pediatric endocrinology keeps on diversifying and with it, the journal's contents. The lead articles of the 2004 volume reviewed important subjects, some beyond the immediate concerns of our colleagues. In this issue the topic of pregnancy in adolescents with type 1 diabetes mellitus by Brindley & Jovanovic addresses the risks and consequences of adolescent pregnancy; these may be costly to both the mother and the fetus, thus underlining the importance of dealing with contraception as part of the treatment of our patients. Also included are the abstracts and editorial comments of exciting papers selected by our editorial board, these deal with pertinent clinical concerns and basic discoveries in the etiopathology of patients encountered in pediatric endocrine practice. Please note the **new feature** introduced to the journal in this issue, namely the electronic abstracts which are only displayed on the website. This new feature allowed the publication of important abstracts with erudite comments; these could not be included in the printed version of the journal because of space limitations. These e-abstracts are concurrently listed in the table of highlights with those published in both the printed and the electronic version of the journal.

During the last year, we accomplished a tremendous growth in the number of subscribers that enjoy *GGH* through the Web and we welcome over 1700 new readers. The reach of the journal also increased, over 37% of our online readers are now from countries beyond the United States, almost a 45% increase in worldwide distribution, with an excess of 30,000 visitors to date. However, we were often challenged with wrong email addresses and returned notifications. The protective filters pose obstacles to the exchange of legitimate scientific information through the internet. We no longer include a Table of Contents in the email announcement as this may trigger filters (ie, intersex). Thus, I want to remind our subscribers to please inform us of email address changes and to notify their I.T. staff to allow www.GGHjournal.com through the institutional filter systems.

I am pleased to inform you that we **will not** discontinue the printed version of the journal as was planned. It will be published and distributed by surface mail within the United States. Finally, a word of thanks to our sponsor, Genentech Inc., for their continuous support through an unrestricted educational grant award for the publication of *GGH*.

Respectfully,
Fima Lifshitz, MD

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the pregnancy can complicate diabetes. Retinopathy and nephropathy may worsen,[6,7] and preeclampsia and hypertension of pregnancy occur more frequently.[8] However routine physician visits usually focus on the state of the disease without addressing the sexual habits and/or contraceptive options for adolescents. Planned pregnancies are not relevant for most teenagers, thus pregnancy is usually unintended.[9,10] Medical intervention usually begins after embryogenesis and organogenesis,[11] and the level of glycemic control, is often sub optimal at the time of conception and early development.[9,12] This review aims to bring to the attention of pediatric endocrinologists the importance of this issue.

MENARCHE AND MENSTRUAL DISTURBANCES

The hypothalamic-pituitary-ovarian axis is often incompletely mature in adolescents with T1DM[13] resulting in delay of menarche, irregular menses, and secondary hypogonadotropic amenorrhea, oligomenorrhea or polymenorrhea. Those with poorer control were those with oligomenorrhea/amenorrhea. Strotmeyer, et al[14] also reported a highly significant difference between age of menarche in patients with debut of diabetes before age 10 years compared to healthy controls and sisters (Table 1).

Moreover, poor metabolic control of T1DM is associated with worsening menstrual disturbances.[15] Diabetic adolescents with irregular menses, primary amenorrhea, secondary amenorrhea, or oligomenorrhea had a significantly higher glycosylated hemoglobin (A1C) level (11.4% vs 9.7%), than diabetic adolescents with regular menses.[15] As the A1C value increased above 10%, the prevalence of menstrual disturbances also increased; when the glycemic control improved, menstrual regulation ensued.[16] Diabetic adolescents with irregular cycles had a mean A1C of 12.8%, compared to a mean of 10.5% in those with regular cycles. Poor glycemic control is unfortunately a common problem in adolescents with T1DM.[3,17,18] The mean A1C in children was 8.6%[17] and in adolescents peaked at 9% to 9.5%. In the United Kingdom, the mean A1C was 9.1%, with less than 15% of pediatric and adolescent patients having an A1C level <8.0%.[18] Poor glycemic control among adolescent diabetic patients is also associated with other issues that compound the control of the disease.[1,3,19] The prevalence of eating disorders, anorexia nervosa and bulimia nervosa in adolescent females with T1DM is increased compared to age-matched controls. Those patients with an eating disorder (DSM-IV criteria) had a higher A1C level than those who did not (9.4 vs 8.6%).[1,19] Additionally, psychiatric disorders such as anxiety and depression are more common in female adolescents with chronic disease than in their healthy counterparts.[20] Although not specific to diabetes, the Adolescent Health Survey of Barcelona,[20] reported significantly elevated rates of low self esteem, personal problems, and feeling sad in chronically ill adolescents. A similar increase in psychological disorders occurred more often in adolescents with T1DM and was associated with poorer glycemic control.[21,22]

Table 1
Descriptive characteristics of women with and without T1DM[14]

	T1DM	Without Diabetes		*p*
		Sisters	Controls	
n	143	186	158	
Age at menarche (years)	13.5 ± 1.9	12.5 ± 1.4	12.6 ± 1.4	<0.001
Ever oral contraceptive use (%)	44.0	79.0	79.8	<0.001
Mean number of pregnancies*	2.3 ± 1.6	2.9 ±1.4	2.6 ± 1.4	<0.001
Miscarriages (%)*	31.2	32.1	27.9	0.76
Stillbirths (%)*	10.1	0.6	0.9	<0.001
Ever smoked (%)	41.8	48.4	50.0	0.33
College attendance (%)	64.6	65.6	75.9	0.06
Income >$40,000 (%)	40.8	59.1	52.7	0.006
Mean BMI (kg/m2)	24.6 ± 4.5	25.2 ± 5.3	27.4 ± 7.3	0.003

Data are mean ± SD.
* excluding women who had never been pregnant;

Adapted from Strotmeyer ES, Steenkiste AR, Foley TP Jr, Berga SL, Dorman JS. *Diabetes Care* 2003; 26:1016-1021.

The changing insulin needs of adolescents as they mature through puberty may also contribute to the tendency for poor glycemic control. The peak insulin requirement (up to 2 units/kg/day) occurs at Tanner Stage 3. As the diabetic young woman progresses through Tanner Stage 5, there is a gradual reduction in insulin requirements. Insulin misuse or insulin omission may also be used as a weight-control method.[1,3,19] As a result, glycosuria increases and the sense of being able to eat "anything" may be reinforced. On the other hand, when the daily insulin dose is high, there is a tendency for weight gain.

UNPLANNED PREGNANCY

Adolescents with T1DM are as likely as non-diabetic adolescents to engage in unprotected sexual activity. However, at their medical appointments, physician visits are more likely to focus on the state of T1DM, compliance with medical regimens, and laboratory data, and not deal with birth control and/or contraceptive usage. Chronically ill adolescents are less likely to receive contraceptive counseling and sexual education than healthy counterparts.[23,24] Young women with T1DM are less likely to receive the most effective hormonal contraceptive, a combined estrogen-progesterone pill, than those without the disease.[24-26] Other often less effective methods of contraception such as condoms, IUDs, and surgical sterilization are more often recommended for diabetic women than for non-diabetic women.

Furthermore, T1DM adolescents may, in an attempt at independence, act in ways that are counterproductive.[1] This may include changing medications or dosing schedules, eating forbidden foods, experimenting with drugs or alcohol or engaging in other behaviors that are risky to their health. For some adolescents with diabetes,

pregnancy may be the only way to prove that one is a "normal" adolescent female.

The United States and the United Kingdom have the highest rates of teenage pregnancy in the world; in the U.S., 52 of 1000 adolescents between the age of 15 and 19 gave birth in the year 2000.[27] Within the first month of initial intercourse, 20% of adolescent young women become pregnant and nearly 50% have a second pregnancy while in their teenage years.[9] Young women with diabetes are more likely to become pregnant than their age-matched controls (ages 16–24), or age-matched young women with phenylketonuria, another chronic metabolic disorder with strict dietary control issues. They are more likely to have been pregnant before, but not more likely to have given birth.[10]

Adolescent pregnancy is associated with higher than expected rates of intrauterine growth retardation (IUGR) and premature births.[28,29] Low birth weight, preterm delivery, small for gestational age, and other malformations were associated with maternal age <18 years.[29] Poorly controlled diabetic women have higher rates of perinatal mortality and fetal malformations than nondiabetic women.[5,30] Although the data on pregnant women with diabetes is obtained from groups involving various age groups, the adolescent with T1DM may be at a greater risk.[31] Lack of dietary folate supplementation prior to conception, as well as lack of proper nutrition, inadequate weight gain, and poor metabolic control may contribute to poor pregnancy outcome in T1DM.[31,32] Inadequate weight gain during pregnancy also increases risks of neural tube defects.[33,34] Other negative factors include lack of pregnancy planning and delayed access to prenatal care or poorly attended prenatal classes; the majority of such pregnancies occur in unwed and poorly educated young women.[28,29]

EFFECT OF DIABETES ON PREGNANCY

Unplanned pregnancies are often complicated in healthy teenagers, but pregnant adolescents with chronic diseases are at greater risk. Pregnancy in T1DM is considered a high risk to both the woman and the fetus. In these pregnancies, the rates of pregnancy-induced hypertension, preeclampsia, premature delivery, and cesarean section were more than 4-fold the rates observed in the non-diabetic population. Also, the prevalence of infants born large for gestational age was much higher (20% vs 3.5%) and the gestational age was significantly less. Elevated maternal A1C level early in pregnancy was an independent risk factor for pregnancy-induced hypertension and preeclampsia.[8] Moreover, the presence of diabetic nephropathy (defined as persistent proteinuria or albuminuria >300 mg/day) in the first 20 weeks of pregnancy, was associated with an increased risk of IUGR, fetal distress, and preeclampsia. Preterm deliveries and/or cesarean section births were increased as well. The presence of microalbuminuria (30-300 mg/day) can also complicate the pregnancy of T1DM patients; they present increased rates of preeclampsia, preterm births, and infants with IUGR.[35] The pregnancy of a diabetic young woman may also be complicated by the use of multiple medications. Treatment of chronic hypertension or pregnancy-induced hypertension may be required.[36] Unfortunately compliance with medical regimens is low in T1DM adolescents,[1,3] making the treatment of hypertension challenging.

Maternal hyperglycemia has been shown to complicate pregnancy more than any other factor. A1C levels at the time of fertilization and embryogenesis have been linked to a higher rate of spontaneous abortions and congenital malformations.[5] Those with A1C levels >7.5% had a 4-fold increase in spontaneous abortions and a 9-fold increase in congenital malformations. The risks of diabetic ketoacidosis (DKA) during pregnancy include life threatening metabolic derangements for the woman and intrauterine demise for the fetus.[37] DKA in adolescents usually results from insulin omission and infection.[38] Furthermore, the tightly controlled blood sugars recommended in pregnancy[39,40] increase the risk for maternal hypoglycemia and fetal injury. Of interest is that pregnant T1DM women have a lower risk of miscarriage and of delivering infants with birth defects and congenital malformations than women with T2DM.[41]

EFFECT OF PREGNANCY ON DIABETES

While diabetes can complicate pregnancy, the pregnancy itself may complicate the woman's diabetes. The ever-changing insulin needs of a pregnant diabetic can be very difficult to meet, even for the most dedicated patient. The diabetic adolescent is challenged to strictly follow the dietary demands of pregnancy and the rigorous insulin regimens. There are also medical complications of diabetes that may develop and/or worsen during pregnancy. Young adults with a mean duration of diabetes of 12.7 years were shown to have retinopathy (70% background and 10% proliferative) at baseline.[42] Bouhanick et al reported a retinopathy rate of 50% 15 years after the onset of disease.[43] The Diabetes in Early Pregnancy Study[44] assessed the progression of retinopathy with fundus photography early after conception and followed through 1 month postpartum. There was progression to retinopathy in 10% of those who had none to start with, and in 50% of those who had baseline moderate-to-severe non-proliferative retinopathy. The Diabetes Control and Complications Trial (DCCT)[6] also reported an increased risk of progression of retinopathy in both the conventionally treated and in the intensively treated group of pregnant women. The proposed mechanism of the progression of this complication is either suboptimal control or a rapid change in the control of the illness that occurs early in pregnancy. Elevated A1C at baseline and degree of improvement of glucose control through week 14 were found to correlate with greater progression of retinopathy.[38] The progression slows or regresses after pregnancy; 6½-year follow-up studies indicated that

retinopathy in previously pregnant patients was similar to that observed in never pregnant controls.[6]

In contrast, pregestational diabetic nephropathy may not be adversely affected by pregnancy.[6,36] Although the albumin excretion rate in T1DM pregnant women increased in the intensive treatment group of the DCCT, it was not different from that in non-pregnant controls at 6.5 years of follow-up. Although microalbuminuria may worsen in pregnancy, it generally returns to baseline within a few months postpartum.[45] Maintaining glycemic levels and blood pressure close to normal are the best strategies to prevent progression of renal disease.[36] Patients with moderate to severe nephropathy early in pregnancy may progress and continue to do poorly postpartum. Purdy et al[7] reported that postpartum renal function in diabetic women with creatinine >1.4 mg/dL at the onset of pregnancy, declined permanently in 45%, transiently worsened in 28%, and remained stable in 27% of the women.

Table 2. Congenital malformations in infants of diabetic mothers

System	Malformation	Age of gestation*
Neurologic	anencephaly, holoprosencephaly, microcephaly	4
Skeletal	sacral agenesis, caudal agenesis	3
Cardiovascular	ventricular septal defect, transposition of the great vessels, patent ductus arteriosus, pulmonary stenosis	5-6
Renal	duplication of ureter, renal agenesis,	5
Other	hypospadias	4

*** weeks**

FETAL OUTCOMES

Congenital malformations are 4 to 10 times more likely in offspring of diabetic women than in non-diabetic women. These anomalies account for the majority of the increased perinatal mortality associated with pregnancies complicated with diabetes.[4,5,30] The major congenital malformations include cardiovascular, neural tube and skeletal abnormalities (Table 2).[46,47] Renal abnormalities and hypospadias also occur at increased rates.[30] Spontaneous abortions are more frequent,[5] but the degree of increase is somewhat controversial. Hanson et al[46] reported a highly significant increase when the mother's glycemic control was poor (A1C >10.1%). Danish women with diabetes self-reported rates of spontaneous abortions at 17.5% compared to 10% to 12% in nondiabetic controls.[48] In the review of Strotmeyer et al,[14] 10% of the pregnancies in T1DM ended in stillbirth, compared to 0.6% of the sisters and 0.9% of the controls ($p<0.001$, Table 1). Similarly, Casson et al[30] reported a 5-fold increase in stillbirths in such pregnancies. In an audit of stillbirths in T1DM, Lauenborg et al[49] identified causes for stillbirths as DKA, chorioamnionitis, placental abruption, placental infarctions, severe IUGR, and thrombosis of the umbilical cord. The women with stillbirths had sub optimal glycemic control (A1C >7.5%) early in pregnancy more often than the women without stillbirths, 64% vs 33% ($p<0.004$), and continued to have poor control during pregnancy. Maternal DKA was associated with a very high fetal mortality rate.[37,38] Other adverse outcomes of pregnancies complicated by diabetes include a higher rate of macrosomia, IUGR, neonatal respiratory distress syndrome, and shoulder dystocia.[30,39] Folate deficiency and inadequate weight gain are well established causes of neural tube defects, especially in poorly nourished adolescents.[31-34]

Medications taken prior to conception, especially during fertilization and organogenesis, may have detrimental effects on the fetus. For example, angiotensin-converting enzyme (ACE) inhibitors may cause fetal oliguria, severe fetal hypotension, and osseous cranial anomalies.[36] Likewise, the use of the acne medication isotretinoin during pregnancy has been associated with very severe fetal abnormalities of the central nervous system, cardiovascular system, craniofacial formation, as well as parathyroid hormone deficiency.[50] Moreover, cigarette smoking, drugs, and alcohol use may cause untoward effects on the fetus. Severe hypoglycemia may lead to maternal seizures and loss of consciousness which may cause automobile accidents and may result in neuropsychological problems, with electrophysiological impairment in the child.[2,39,40] Rebound hyperglycemia after hypoglycemic events is thought to be a cause of fetal macrosomia.[40]

PRECONCEPTION CARE AND MANAGEMENT DURING PREGNANCY

A diabetic woman who wishes to become pregnant needs preconception advice and counseling. Before pregnancy, glycemic control should be maximized and the underlying disease should be assessed thoroughly. Preconception counseling in T1DM decreases the risk of congenital malformations, spontaneous abortions, and stillbirths (Table 3).[11,12,47,51,52] Although the data reported were in adult pregnant women, the information is applicable to adolescents. Malformation rates and mortality rates dropped from 14% to 2.2% and 7% to 2%, respectively during a 15-year period.[51] The rates began to rise when the program was discontinued. The T1DM women who received preconception counseling for a mean duration of 17 weeks prior to becoming pregnant had a reduced rate of congenital malformations compared with controls (1.2% vs 10.9%), though the level of glycemia in both groups was similar.[11] Thus, preconception intervention is most beneficial in positively impacting the critical periods of embryogenesis and organogenesis. Preconception care in diabetic adolescents, coupled with ongoing prenatal intervention, reduces the high rate of spontaneous abortions and improves infant outcome.[12,52] Glycohemoglobin levels at first diagnosis of pregnancy are lower in women who attend such programs and correlate with better glycemic control during conception and embryogenesis.[11,12,52]

The majority of teenage pregnancies are not intended and out-of-wedlock adolescent pregnancies are not well received in the United States.[27,29] Thus, preconception counseling is usually not applicable. The necessary intense care of a pregnant adolescent with T1DM is cumbersome and difficult, though when applied through the entire pregnancy it leads to better outcomes. A team approach to care for T1DM is most effective and should be instituted as soon as possible.[11,12,47,51,52] Prenatal care should include nutritional counseling and weight gain guidance based on the preconception body weight and adequacy of the nutritional intake to avoid hypoglycemia and ketosis.[53] Dietary habits and preferences need to be considered to facilitate compliance and to meet nutrient requirements. Although controversial, most agree in striving for euglycemia, while ensuring appropriate weight gain of the woman and fetus. Jovanovic allows for an intake of 40% calories as carbohydrate, 20% as protein, and 40% as fat, with the caveat that breakfast is small (less than 10% of total calories). These percentages should be adjusted for glycemic control, insulin usage, and level of activity. Others favor a more liberal intake of carbohydrates (45%-55%) as long as the premeal insulin dose is adjusted appropriately.[53] Much of the available data on dietary intake are from gestational diabetes studies without the specific concerns of T1DM adolescent patients who more easily experience hypoglycemia or ketosis and are not very compliant.

Prenatal vitamins including folate and calcium should be initiated as soon as pregnancy is diagnosed. Folate doses are often increased up to 5 milligrams in order to prevent the neural tube abnormalities frequently found in infants of T1DM mothers.[54] If there is any indication of drug, alcohol, or cigarette use, these should be discouraged and discontinued. Any prepregnancy medications such as diuretics, ACE inhibitors, or acne treatments should be stopped immediately. Antihypertensive medications that are safe in pregnancy should be started and adjusted to maintain tight blood pressure control (ie, calcium channel blockers).[55] Alpha-methyldopa and hydralazine are two antihypertensive medications that have been used more extensively in pregnant women.

Early photography of the fundi will serve as a baseline to assess the degree of retinopathy and may infer the degree of microangiopathy present. Close follow-up with an ophthalmologist is necessary at least every trimester, if baseline photographs are normal, and more frequently if baseline photographs show any degree of abnormality. A detailed antenatal evaluation for diabetic women with nephropathy, including evaluation of serum creatinine, uric acid, urea nitrogen, creatinine clearance, and urine culture is important. Creatinine clearance and protein excretion should be assessed at least every trimester, and more frequently if abnormal. Monitoring for anemia (due to renal loss of erythropoietin or iron deficits) and of thyroid function (due to the high rate of coexistent autoimmune thyroid disease in patients with T1DM[56]), are recommended and appropriate treatment instituted at once to avoid possible poor outcome for the infant.[57]

Many authors have reviewed the targets for optimum glycemic control; however, a consensus has not been reached. Jovanovic recommends 1-hour postprandial whole blood glucose <120 mg/dL (6.7 mmol/L), and fasting blood glucose <90 mg/dL (5.0 mmol/L). The American Diabetes Association recommends <140 mg/dL (7.8 mmol/L), and <100 mg/dL (5.6 mmol/L), respectively.[58] The A1C levels should be checked regularly to ensure compliance with the program and to guide insulin doses and dietary advice. The rapid-acting insulin analogs have been shown to be safe in gestational diabetes, and preliminary data indicate that they are safe in T1DM pregnancies. However, there are no data on long-acting insulin analogs use in pregnancy. Furthermore, obstetrical care and diabetes care should be jointly agreed upon to maximize patient participation and outcome of the pregnancy. Regular follow-up visits, ongoing dietary counseling, and emotional and psychosocial support are needed. Plans for the newborn, including child rearing, adoption, or alternative care (eg, grandparents) should be initiated as early as possible. A plan for the adolescent to complete her education is another major issue best approached early. Counseling for the mother-to-be, the father of the baby (if available), and the future grandparents is recommended.

PREGNANCY PLANNING AND PREVENTION

Due to the high risk nature of pregnancy in adolescents with T1DM, pregnancy planning and/or prevention should play a major role in their care. The focus should be on prevention of pregnancy and improving the sexual education of the adolescent population.[10,28] The American Diabetes Association recommends that all women with diabetes of child-bearing potential use appropriate contraception and receive counseling about the risk of malformations associated with unplanned pregnancies and poor glycemic control.[55] Unfortunately, contraception for teenagers has been politicized, thus without parental involvement and/or consent it may be difficult to obtain in the United States

Table 3. Outcome of Pregnancies Complicated by Diabetes

Authors	Congenital Malformations		Spontaneous Abortions		*p* value
	Preconception care	Routine care	Preconception care	Routine care	
Dicker, et al [52]			5/59 (8.5%)	10/35 (28.6%)	<0.001
Steel, et al [47]	2/143 (1.4%)	10/96 (10.4%)			<0.005
Kitzmiller, et al [11]	1/84 (1.2%)	12/110 (10.9%)			<0.01
Rosenn, et al [46]	0/28	1/71 (1.4%)	2/28 (7%)	17/71 (24%)	NS, <0.04

and the United Kingdom—the countries with the highest teen pregnancy rates.[27] Contraception in diabetic young women can be accomplished with cooperation between the patient, primary care physicians, gynecologists, and endocrinologists or diabetologists.[23] The factors associated with consistent birth control use in diabetic women and women with phenylketonuria were social support and positive attitudes toward birth control.[10] Low dose combination hormonal contraceptive pills are recommended; these can be safely used in adolescent T1DM patients in whom vascular disease is a low risk.[25] Barrier methods and spermicidal agents may be less acceptable to teenagers, resulting in poor compliance.

Emergency contraception, the so-called morning after pill, is another consideration. Use of such preparations has been limited due to prescription requirements, fear of hormones, possible adverse effects, and misinformation on availability and use.[59] The proposal to switch levonorgestrel emergency contraception (approved for prescription use in 1999, sold under the brand name Plan B®, Barr Pharmaceuticals, Pamona, NY) to over-the-counter status was not approved in May 2004 by the US Food and Drug Administration. Plan B consists of 2 (0.75 mg) pills of levonorgestrel to be taken as soon as possible within 72 hours after unprotected sexual intercourse. The rate of pregnancy is 0.4% if treatment is initiated within 24 hours and 2.7% if given within 72 hours. There are extensive data on the safety of this medication, though specific data on adolescents with diabetes are not available. The most frequent side effects are nausea and menstrual disruption. During a 29 month period, between 2001 and 2003, 40% of 7774 callers to a telephone prescription service in North Carolina (designed to increase access to emergency contraceptive pills) were teenagers.[57] Adolescents with diabetes frequently depend on pediatric endocrinologists for their care, thus a prescription for Plan B emergency contraception should be considered in advance of the crisis which may follow unprotected sexual intercourse. Additionally, the option for termination of pregnancy should be presented in a factual manner to the young woman, regardless of her religious background, so it may be performed as early as possible.

There are other considerations that need to be addressed in the course of the treatment of the adolescent with T1DM, particularly the encouragement of daily use of folic acid supplementation, even in those who are not sexually active or when pregnancy is not a consideration.

CONCLUSION AND SPECULATION

The adolescent diabetic woman struggles with daily reminders of her disease—multiple fingerstick glucose checks, insulin injections, and an uncertain future of possible complications. Although preconception care is preferable, most adolescents do not intend to become pregnant. Unplanned pregnancy can be avoided with education, support, and contraceptives, offered to the adolescent by diabetic educators, parents, and physicians. If pregnancy does occur, timely institution of excellent diabetes and obstetrical care promises at least a brighter future for the young woman and the infant.

Future challenges for the physician caring for pregnant young women with T1DM may include use of the rapid-acting insulins, long-acting insulins, and insulin pumps. Furthermore, if islet cell transplantation continues to show promise, consideration for unplanned pregnancies in young women on long-term immunosuppressant medications will need to be addressed. Interesting new data on gestational diabetes using fetal growth ultrasound to manage a patient, rather than strict dietary control and stringent glycemic guidelines[60] may offer a useful approach in pregnant T1DM adolescents. Outcomes including caesarean rate, small and large neonates, hypoglycemia, and neonatal intensive care admissions, were equivalent. Perhaps the lighter the burden we place on the teenager to conform to medical guidelines, the better chance we have of dealing with rebellion. However, adolescents will always be adolescents, for generations to come.

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ABSTRACTS FROM THE LITERATURE

Celiac Autoimmunity, Celiac Disease and Growth

The objective of this study was to evaluate growth and clinical features of children who tested positive for antibodies associated with celiac disease (CD). A cohort of HLA-DRB1*03-characterized newborns from 1234 families in Denver, Colorado were prospectively followed since birth for the development of IgA autoimmune transglutaminase antibodies (TG). Clinical evaluation, growth, anthropometry and biochemical assessments, as well as small bowel biopsies were performed. There were 33 children who tested positive to TG; 18 of them completed the studies, underwent repeated testing and were compared with 100 pair-matched controls. The TG-positive children had antibodies detected at a mean age of 4.4 ($\pm$ 1.2) years and the mean age at clinical evaluation was 5.3 ($\pm$ 1.5) years. They had significantly lower z-scores for height, weight and BMI (–0.3 $\pm$ 0.7), but not for weight- or height-for-age. They also had decreased mid-arm circumference and mid-arm muscle mass area. TG-positive children experienced more symptoms which increased over time, including abdominal pain, constipation and irritability/lethargy and these were independently associated with decreased weight gain. Thirteen (72%) of the 18 TG children had small intestinal mucosa evidence of CD (Marsh 2-3), 2 showed increased intraepithelial lymphocytes (Marsh 1), and 3 had normal biopsies. No relationship was found between copies of HLA-DRB1*03 and biopsy scores. The authors concluded that screening for CD identified TG-positive children who demonstrated mild alterations in weight and body composition and reported more symptoms than control subjects. They also had intestinal mucosa evidence of CD.

Hofferberg EJ, Emery LM, Barriga KJ, et al. Clinical features of children with screening-identified evidence of celiac disease. *Pediatrics* 2004;113:1254-1259.

Editor's Comment: *This prospective study provided important data of the natural history of CD autoimmunity in a genetically susceptible population. It also discerned the clinical findings of TG-positive children and the small intestinal mucosa alterations. However, the response to a gluten-free diet was not reported; expert consensus panels require the assessment of the response to dietary therapy as important evidential data for the diagnosis of CD. Additionally, the nutrient intake or fecal-fat excretion was not reported. It is possible that children decreased food ingestion to minimize the discomfort of malabsorption, thus*