

WINTER 2011

MDINSIGHTS



Features

Diabetes: The Past,
Present and Future

Diabetic Nephropathy

Adherence Challenges
for Adolescents with
Diabetes



LA RABIDA
CHILDREN'S HOSPITAL

Perspectives in Care for Children with Special Healthcare Needs

MDINSIGHTS
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About La Rabida

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Spotlight



Premier Kids

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Each Premier Kid receives routine check-ups, immunizations, and urgent care through a board certified pediatrician who also coordinates the care for the child's unique medical condition. The physician leads a team of nurse case managers, licensed clinical social workers, a master's level developmental therapist and a clinical dietician.



MD to MD

In this publication, we present articles about the management of pediatric diabetes written by three experts at La Rabida Children's Hospital. Dr. Anita Swamy is a Pediatric Endocrinologist and faculty member at Northwestern University, and the new medical director of the Chicago Children's Diabetes Center. Dr. Izhar Qamar is a Nephrologist and the interim Chief of the Chronic Disease Section in the University of Chicago's Pediatrics Department. Dr. Nancy Fritz belongs to the Chronic Disease Section at the University of Chicago as well, and is board certified in Adolescent Medicine.

Dr. Swamy gives us a comprehensive and practical overview of diabetes management in children. As we all know, diabetes management starts with insulin administration but cannot stop there. Dr. Swamy's article provides some very useful information regarding the calculation of basal-bolus regimen doses and carbohydrate counting. Along the way, Dr. Swamy provides us a glimpse of advanced and specialized methods used in specialty clinics. However, the most important management principle for pediatric chronic disease still holds: interventions need to be tailored and monitored according to the patient's and family's needs and circumstances.

Dr. Qamar informs us about one of the most common and severe consequences of diabetes, diabetic nephropathy. With its substantial impact on life span and quality of life, diabetic nephropathy is one of the reasons why we try so hard to achieve blood glucose control. Dr. Qamar's article emphasizes the importance of early screenings and multidisciplinary interventions that are tailored to the patient's needs and circumstances.

One of the needs that arises during diabetes management is making adjustments to the developmental level of the child. Dr. Fritz's article places the frustrating and dreaded "non-adherence" of a diabetic teen within the framework of adolescence and suggests looking at non-adherence as a normal stage of adolescent chronic disease. By doing so, Dr. Fritz provides a more hopeful and perhaps more productive alternative to the traditional methods. The examples she provides are fascinating in that most of them are feasible and quite economical. Dr. Fritz is leading La Rabida Children's Hospital in this area.

We invite you to help shape future issues of MDINSIGHTS. Email your editorial suggestions to info@larabida.org.

Dilek Bishku, MD
Vice President, Medical Affairs
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Editor-In-Chief

INSIDEINSIGHTS

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Dilek Bishku, MD, MPH, is an attending physician who cares for children with complex health care needs during their acute hospitalizations. She joined La Rabida Children's Hospital in 1998 as Director of the Failure to Thrive Program and since 2007, she has been Vice President of Medical Affairs. Dr. Bishku is an Assistant Professor of Pediatrics at the University of Chicago Pediatrics Department, Section of Chronic Disease.

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Diabetes: The Past, Present and Future

Presented by Anita N. Swamy, MD

Medical Director and Program Co-director,
Chicago Children's Diabetes Center at La Rabida Children's Hospital;
Attending Physician, Endocrinology, Children's Memorial Hospital;
Instructor in Pediatrics, Northwestern University Feinberg School of Medicine

Tuesday, February 22, 2011
12:00 – 1:30 p.m.

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Objectives:

At the completion of this learning activity, participants should be able to:

1. Explain how carbohydrate counting affects insulin dosing in the basal-bolus regimen.
2. Utilize the data provided by continuous glucose monitoring systems to modify insulin dosing regimens versus the use of metered blood glucose values alone.
3. Name at least two benefits and one drawback of insulin pump therapy versus multiple daily injections.



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Diabetes: The Past, Present and Future

Anita Swamy, MD

Introduction

The management of type 1 diabetes in children requires a specialized team of endocrinologists, nurse practitioners, nurse educators, dietitians, and psychologists. Yet the availability of comprehensive programs is limited. In fact, a recent study published in the *Journal of Pediatrics* revealed that there is a tremendous need for pediatric diabetes specialists. The ratio of endocrinologists to children with type 1 diabetes is 1 to 290. Furthermore, the rates of type 1 and type 2 diabetes continue to rise rapidly, more so than the number of endocrine fellowship graduates. Therefore, the primary pediatrician will play an increasingly important role in the management of this chronic disease.

This article highlights the history, diagnosis, current management and challenges of caring for children with type 1 diabetes.

History

The evolution of diabetes management is noteworthy. The term diabetes mellitus was first coined in the late 1400s. It originated from the Greek word *diabainein*, to siphon or drain fluid from the body, and the word for honey *miel*, referring to the sugary urine of diabetic persons. Over the next two centuries, various unconscionable therapies for the disease were attempted: opium, starvation, blood-letting. It was not until 1921 that surgeon Frederick Banting and medical student Charles Best worked together to isolate a pancreatic extract. In 1922, the first human, a 14 year old boy with diabetes, was successfully treated with the extract insulin, and he went on to live another 13 years.

Below is a time line of other major developments in diabetes treatment over the last century:

1940s advent of NPH insulin

1969 the first portable glucose meter is created

1979 Hemoglobin A1c assay is developed

1980s recombinant DNA technology is used to produce human insulin commercially

1983 the first insulin pump

1996 Lispro rapid-acting insulin available in the US

2001 the first "24-hour" basal insulin Glargine

Diagnosis

The diagnosis of type 1 diabetes requires one of the following:

- Fasting blood glucose of 126 or greater
- Random blood glucose of 200 or greater with symptoms consistent with diagnosis of diabetes
- Oral glucose tolerance test 2 hour glucose of 200 or greater, with or without symptoms

The use of Hemoglobin A1c as a diagnostic tool is applicable to type 2 diabetes only.

Previously, we were taught that type 1 diabetes occurs in childhood, in lean persons, and involves autoimmunity; whereas, type 2 diabetes is related to obesity, insulin resistance and lack of autoimmunity. The distinction between these entities is becoming more nebulous. With the pandemic of obesity, many type 1 diabetic children are obese, and may exhibit some insulin resistance. Though antibodies were previously only thought to be seen in classic type 1 diabetes, studies have shown that many children with type 2 diabetes may have some antibody positivity as well. This suggests that there is a spectrum of disease, and notable variability with the recent recognition of atypical forms of both type 1 and type 2 diabetes.

Management

As aforementioned, the management of diabetes in children extends far beyond insulin administration. It involves significant and ongoing education. We teach families about nutrition and carbohydrate counting, educate them about how to use basic mathematics skills to calculate doses, inform them of the changing dynamics of management as children age and become more independent, and we provide them with support to address the various economic, social, school, and psychological stressors which arise.

Data from the Diabetes Control and Complications Trial, which was published in 1993 and involved over 1400 type 1 diabetics, clearly demonstrated the benefits of intensive insulin therapy (more than 2 injections per day) in the prevention of long-term complications. Further, the use of intensive therapy at onset of disease has been shown to preserve beta cell function, leading to longer duration of the "honeymoon period."

(continued on page 6)

Intensive therapy today is labeled as the basal-bolus regimen. Insulin may be delivered via syringes or pens, which offer a more convenient, less stigmatizing alternative to syringes. With these methods, two types of insulin are administered:

- 1) Basal insulin which provides 24-hour coverage
- 2) Bolus insulin which is rapid-acting and taken with meals for elevated blood sugars and has a 3-4 hour duration.

The doses of basal insulin and bolus insulin are calculated as follows: Initially the total daily dose is calculated, which is usually between 0.5-1 unit per kilogram of body weight, and requirement generally increases with age.



“The use of intensive therapy at onset of disease has been shown to preserve beta cell function.”

About half of the total daily dose is given as basal insulin (Glargine or Detemir). The remaining half is administered as bolus insulin (Lispro, Aspart, Glulisine), divided and given with meals.

In contrast to the days of giving patients preset doses of insulin, the focus today is on tailoring the dose to a child’s needs, which vary with intake and activity. Generally, only the basal insulin dose is fixed, and must be given at approximately the same time every day, given its duration of action. The bolus doses vary, and depend upon two factors:

- 1) The pre-meal blood glucose
 - a. If the pre-meal glucose is elevated over target the formula below will enable families to determine a correction dose:

$$\frac{(\text{Child's blood sugar}) - (\text{target blood sugar})}{\text{correction factor}}$$

We provide the families with target blood sugars and correction factors, and these are frequently adjusted as the child grows and level of activity varies. Targets are generally between 120 and 180, and become more restrictive as the child ages and the concern of hypoglycemia diminishes. Correction or “sensitivity” factors are calculated by dividing 1800 by total daily dose of insulin.

2) The carbohydrate intake, such that the child is instructed to take 1 unit of insulin for every X number of carbohydrates consumed. This value is also frequently adjusted but is calculated initially by dividing 500 by the total daily dose.

The aforementioned 1800 and 500 rules were developed as guidelines, and different centers may utilize different formulas. The key concept is that these values are useful in determining initial doses. Correction factors, targets, and insulin to carbohydrate ratios need to be modified frequently, depending upon the child’s response.

For example, a 10 year-old, 40 kilogram child may require about 40 units per day of insulin; approximately 20 units may be given as basal insulin to start, and the other 20 units would be divided among meals as follows:

- 1) To calculate a correction dose, first determine the correction factor. To do this, divide 1800 by total daily dose of 40, which gives us a correction factor of 45.

Then we must determine the target blood glucose for a child this age. The target may be 140 (variable).

Using these values, this child’s correction formula would be

$$[(\text{measured blood sugar}) - \text{target of } 140] / 45$$

- 2) To calculate an insulin to carbohydrate ratio, divide 500 by 20 → 25; therefore, this child would receive one unit for every 25 grams of carbohydrates consumed.

- 3) If his pre-meal blood glucose is 230 and he wants to eat 75 grams of carbohydrates, he would require a correction of $(230 - \text{target } 140) / 45 = 2$ units, and for his carbohydrates $75 / 25 = 3$ units, for a total of 5 units of bolus insulin to be taken prior to the meal.

Clearly, these are complex concepts, and may not be feasible for all families. We provide more simplified regimens for these families, yet reinforce these concepts at each visit.

With this regimen, a child requires one injection of basal insulin, which cannot be mixed in the same syringe as bolus insulin, plus an additional injection of bolus insulin with each meal, for a total of 4-6 injections per day. This is quite cumbersome; however if children are instructed about this regimen at diagnosis, they adapt surprisingly well and quickly. If, on the other hand, they commence with a simplified regimen of 2 injections per day, it is much more challenging to convert to the basal-bolus regimen afterward.

The insulin pump offers an easy, effective and safe alternative to multiple daily injections. The pump contains rapid-acting insulin only, which is programmed to function as both the basal and bolus insulin. The basal insulin rates, targets, correction factors and insulin to carbohydrate ratios are just a few of the programmable features.

The classic pump consists of a device the size of a pager, which contains a reservoir for insulin, as well as a “computer” which contains the settings and stores all data entered. It also computes the dose of bolus insulin required, based on the blood glucose and total carbohydrate content of the meal that the patient enters. This device is then connected to the patient via a catheter, which is inserted subcutaneously in the same locations as injections. The insertion is simple, performed at home, and with a force slightly greater than that required for a typical injection. The site of insertion is changed every 2-3 days; therefore the child requires one “injection” every few days rather than numerous times per day. There are also catheter-free pumps wherein the device is placed directly onto the area of insertion.

As the pump stores the blood glucose and carbohydrate intake a patient inputs, patients can simply upload this data using a computer. The data is then available for the diabetes team to view, allowing for frequent regimen changes between quarterly visits, which inevitably results in better diabetes control.

Another major advancement in diabetes management is the continuous glucose monitor (CGM). CGMs may be utilized in conjunction with the pump or independently, and consist of disc-like devices with subcutaneous catheters which measure interstitial fluid glucose, and provide a glucose reading every 5 minutes. Patients still have to check blood glucose several times daily to calibrate. However, this significantly reduces the number of routine finger sticks. It allows for detection of glucose trends, which aids in management. CGMs also provide parents with a sense of security when their child has a change in intake, activity level, or is sleeping overnight, as CGMS alert when the glucose is dropping or rising rapidly. Studies are currently underway to develop an “artificial pancreas” involving a CGM, which communicates with an insulin pump, to deliver insulin based upon the glucose value or trend detected.

In summary, it has been less than a century since the advent of insulin. We have made incredible strides in the understanding and management of diabetes, and with the rapid rate of progress in this field, I am confident that a cure will be developed within the

next few decades. Until that time, it is our obligation as diabetes experts to educate and collaborate with primary pediatricians, parents, and school staff to enable children with diabetes to live happy, healthy, and active lives.



Anita Swamy, MD, is a Pediatric Endocrinologist, and medical director of the Chicago Children's Diabetes Center at La Rabida Children's Hospital.

Additional Readings

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- Rollnick S, Miller WR, Butler C. Motivational interviewing in health care: Helping patients change behavior. New York: Guilford Press: 2008.
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Diabetic Nephropathy

Izhar Qamar, MD

Diabetes mellitus (DM) is one of the most common chronic illnesses in the world. DM is the leading cause of end stage renal disease (ESRD) requiring dialysis and transplantation in adults. The two common types of DM are Type 1 DM (T1DM) secondary to an autoimmune process leading to insulin deficiency, and Type 2 DM (T2DM) due to a combination of insulin resistance and inadequate insulin secretion. Although T1DM is more frequently observed in pediatric ages, with the rising epidemic of obesity in the world, the incidence of T2DM has been increasing, becoming a major public health concern.

In this article, we describe diabetic nephropathy (DN) in pediatric ages with T1DM and T2DM. Other complications of DM include:

- Hypo/hyperglycemia
- Microvascular complications (nephropathy, retinopathy)
- Macrovascular complications (coronary artery disease, cerebrovascular accidents)
- Neuropathic complications
- Increased risk of infection

DN occurs in 15-20% of patients with T1DM and in a higher percentage of patients with T2DM. Although DN, if and when it develops in either type, has similar histological findings and ultimately results in ESRD in adults, there are clinical differences in the onset and progression between the two types (see table).

Table: Diabetic Nephropathy in Children and Adolescents

	T1DM	T2DM
Onset of DM	Usually clear	Usually insidious
Microalbuminuria (MA)	2-5 yrs of onset or later	Can be present at diagnosis
Rate of MA	6%	28%
MA & overt DN 5-10 yrs of disease	5-27%	18-72%
DN Hereditary factors	Familial susceptibility	Familial susceptibility
DN Overall incidence	Declining	Remains the same
DN progression	Slow	Rapid
Screening for MA	If 2 yrs of DM, then screen at 11 yrs If 5 yrs of DM, then screen at 9 yrs Pubertal onset screen 2 yrs after diagnosis then every year	In view of insidious onset of DM, screening at time of diagnosis and every year
Patients with risk factors Screening for MA	More frequently every 3-6 months	More frequently every 3-6 months

Five stages of renal changes in DM:

- I. Onset of DM: Increased renal size (25-50%) and GFR with hyperfiltration (20-40%). Not associated with histologic changes. May be reversible.
- II. 2-5 years of DM: Glomerular basement membrane thickening and mesangial expansion with intermittent microalbuminuria (urinary albumin excretion UAE 30-300 mg/24hr, albumin excretion rate AER 20-200 mcg/min in timed urine collection, or albumin creatinine ratio on spot urine ACR 30-300 mg/g) only during poor glycemic control.
- III. 7-10 years: Persistent microalbuminuria associated with 4-5 fold increase in the risk of progression of DN.
- IV. 15-25 years: Overt or clinical proteinuria (urinary albumin excretion UAE >0.5g/24hr)
- V. 5-10 years after onset of overt proteinuria: ESRD
Early preventive interventions such as intensive glycemic control with HbA1C of 7-7.5% or less, control of hypertension, smoking cessation, management of dyslipidemia, promoting healthy diet and exercise have been shown to improve or even reverse the changes of early DN prior to development of persistent microalbuminuria or overt proteinuria (Stage IV). Patients with overt proteinuria usually progress with steady rise in BP and steady decline in GFR (10ml/min/yr). This process can be slowed, but not necessarily arrested, by secondary measures such as use of ACE inhibitors (ACEI) or angiotensin receptor blocking agents (ARBs).

This natural history of DN emphasizes early screening and interventions as effective measures for prevention of DN. Microalbuminuria is a sign of early nephropathy and can be used as a screen for DN. Microalbuminuria denotes excretion of albumin in the urine, which is not detectable on regular urine dipstick, but can be measured in the laboratory.

Risk factors for DN:

- Poor glycemic control - high HbA1C
- Earlier age of onset
- Longer duration of DM
- Onset of puberty with associated changes in growth hormone (GH) insulin like growth factor (IGF 1) and sex steroids secretion
- Hypertension
- Cigarette smoking
- Hyperlipidemia - high LDL, low HDL, high triglyceride levels
- Hereditary factors - familial and hereditary susceptibility

(continued on page 9)

Practice Insights

Dilek Bishku, MD

The new developments in our understanding and management of diabetes have not provided a simple, isolated cure to this disease. On the contrary, the more we learn about diabetes, the more we see the importance of a multidisciplinary approach.

Today, diabetes is not as easily separated into subtypes with sharp, clear lines. We now understand diabetes as a spectrum with varying overlaps – which is all the more reason to tailor our management to the patient.

Insulin is still the cornerstone of diabetes management but glycemic control is multi-factorial. Therefore diabetes should be managed by a team that includes physicians, nurses, nurse educators, nutritionists, social workers, psychologists and care coordinators.

Instead of giving pre-set doses of insulin, we are now using the basal-bolus insulin regimen tailoring the dose to the child's metabolism, intake and activity. (For main principles, see Dr. Swamy's article.)

Although basal-bolus regimen provides better control, we must recognize that it involves closer monitoring and ongoing education. Families (and eventually the child) must learn about basic nutrition concepts, carbohydrate counting and development.

“Insulin is still the cornerstone of diabetes management but glycemic control is multi-factorial.”

Insulin pumps are being used more widely now, and sometimes in junction with continuous glucose monitors. Your subspecialty consultants should be able to evaluate your patients for these modalities and guide you in management.

“Non-adherence” during adolescence can be frustrating, but we must see it as a normal stage of development within the framework of adolescent chronic disease. As the child approaches adolescence, it's best to expect management problems manifested by higher HgA1c levels and other lab changes. Prevention and anticipatory guidance focused on illness management issues can go a long way.

The dynamics of growth and development are important in understanding the changes in the diabetic teen's glycemic control. As primary care physicians we must support the development of transition programs and case management for teens.

Diabetic nephropathy can be prevented or slowed down by early screenings for microalbuminuria. In order to prevent future complications, primary care pediatricians should do urine screens during visits, emphasize the control of hypertension and dyslipidemia, promote healthy life style changes and make early referrals to nephrology and ophthalmology clinics.

(Diabetic Nephropathy continued)

Thus in T2DM, DN appears to develop earlier, is more likely to progress, and is less responsive to therapeutic interventions once overt proteinuria has developed. This further emphasizes the role of preventive measures.

In summary, development of DN in children and adolescents is multifactorial and consequently its prevention or delay requires a multidisciplinary approach to ensure optimal glycemic, hypertension and dyslipidemia control, life style modifications with special attention given to dietary changes, increased physical exercise, and cessation of smoking. Diabetic nephropathy cannot be prevented in patients with hereditary susceptibility, but for the majority of patients these measures can go a long way in preventing or delaying renal complications. The

pediatrician has a key role in this approach. Besides providing primary care, the pediatrician can also monitor the risk factors such as hypertension, poor glycemic control and non-adherence. The pediatrician can also coordinate care of these children by ensuring follow up with the endocrinologist, nephrologist and nutritionist.



Izhar Qamar, MD, is a nephrologist at La Rabida Children's Hospital and the interim Chief of the Chronic Disease Section in the University of Chicago's Department of Pediatrics.

Adherence Challenges for Adolescents with Diabetes

Nancy Fritz, MD

I would that there were no age between 10 and three and twenty, or that youth would sleep out the rest, for there is nothing in the between but getting wenches with child, wronging the ancients, stealing, and fighting...."

The shepherd in "A Winter's Tale." Shakespeare.

Clearly adolescents have gotten a bad rap for a long time. Even today, over 400 years after Shakespeare, many physicians would rather wrestle with 10 flailing toddlers over ear exams than struggle with one non-compliant diabetic teenager.

And adolescence is even tougher for the teenager. Healthy teens must maneuver through a series of milestones: finishing puberty, developing social skills and a network of friends, creating independence and coming to some understanding of who they are, how they will love, and what job will suit them. In the process, teenagers are supposed to "hang out," eat junk food, take risks, challenge authority, fall in and out of love and have moody moments. With luck and consistent parenting, the majority of them make it to adulthood minimally scathed.

But what of kids with diabetes – the kids for whom these normal developmental processes carry additional risks? Adolescents, with their spontaneity and sense of immortality, seem to come hard-wired to act precisely counter to the care of a chronic disease. In addition to the tasks mentioned above, a diabetic teen must mourn the loss of an idealized healthy self, must find time and motivation to control his/her diabetes, and must negotiate the new circumstances of relationships and goals. Non-adherence might rightly be seen as a normal stage of adolescent chronic disease; and multiple studies have shown deterioration in metabolic control during teen years. Additionally, teens with diabetes are as sexually active as their peers; and they have increased rates of depression and disordered eating, both associated with impaired glycemic control.

There is, however, promising work in adherence research:

One big adherence risk is missed appointments. In a program studying appointment compliance, visit frequency increased 50% by hiring a non-medically trained "Care Ambassador" to help set up appointments, re-schedule missed ones, and address billing

questions. Another program reduced HbA1C and DKA hospitalizations by providing appointment assistance and after-hours phone support for teens. These affordable measures seem to have improved outcomes in part by decreasing the hassle-factor of diabetes care.

Support systems are also important. Teens whose families are involved in diabetic management have better outcomes; and in certain cases family therapy improves glycemic control. Friend support also appears to predict better psychological adaptation, especially for girls, and has a positive influence on treatment. However, teens also have been noted to disregard self-care to avoid appearing "different." Studies suggest that context is important; and solutions will need to be individualized based on the teens' perceptions of family and peer supports.

Originally developed by Miller and Rollnick in the 1980s, Motivational Interviewing (MI) is another promising technique. MI is a patient-centered counseling approach that encourages commitment to change by helping patients reduce ambivalence and increase motivation. In a study, diabetic teens receiving MI have maintained lower HbA1C levels compared to controls and reported higher levels of well-being and improved quality of life, lower levels of anxiety, and the perception that diabetes impacted their lives less. As promising as it sounds, most clinicians have neither training nor time to conduct formal MI sessions. However, another study, using MI-trained non-professional "diabetes personal trainers" also showed improvements in HbA1C, particularly in older teens. These studies suggest that MI can help even with non-professional support staff, especially for certain age groups.

Recently, transition to adult care has been receiving attention. Like MI, transition programs aim to promote autonomy and personal responsibility. Most such programs begin early in adolescence and are structured to fit the developmental stages of the teen. Using MI techniques in the context of transition visits could potentially enhance the value of each.

Finally, screening for behavioral risks is important. Many diabetic teens are sexually active. STD infections (along with pregnancy) potentially impair metabolic stability. Also teens are known to skip

insulin doses to control their weight; and they have higher than average rates of depression. Therefore, repeated discussions about sexual decision-making, contraception, and STD screening are all indicated, as is screening for depression and eating disorders. Standard eating disorder screens may be unreliable for diabetic teens who appropriately scrutinize food intake; so a diabetes-specific screening tool has been developed.

In summary, non-adherence--while fitting into normative developmental trajectories of adolescence--nevertheless creates significant risks in teenaged diabetics. Strategies to address these are numerous and include: reducing the hassle factor, involving supportive others, screening for risk factors, and involving counseling services when appropriate. Motivational interviewing and transition programs are particularly promising modalities.

Ultimately, care needs to be individualized to the teenager and to his/her particular circumstances.



Nancy Fritz, MD, is a pediatrician at La Rabida Children's Hospital and is board certified in Adolescent Medicine. She is a faculty member at the University of Chicago.

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