

DIABETES IN CHILDREN AND ADOLESCENTS

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Learning Objectives

1. Distinguish between various forms of diabetes mellitus (DM) that can affect children including type 1 DM, type 2 DM, hybrid diabetes, and maturity onset diabetes of the young.
2. Differentiate between traditional insulin and basal/bolus insulin regimens in children with DM.
3. Given a specific patient, design or evaluate the effectiveness of an insulin regimen to optimize glycemic control in a child with type 1 DM.
4. Assess and alter, if necessary, a therapeutic regimen to control hyperglycemia or comorbidities in a child with type 2 DM.
5. Given a specific patient case, design or evaluate the effectiveness of a continuous subcutaneous insulin pump to optimize glycemic control in a child with DM.
6. Develop a patient education strategy for children with DM and their caregivers that includes information on pharmacologic and nonpharmacologic therapy to optimize glycemic control and limit complications.

Introduction

The effect of diabetes mellitus (DM) regarding morbidity, mortality, and health care expenditures is well documented. Most evidence in DM care is in the treatment of adults with DM, specifically type 2 DM, because this group represents the largest segment of adults with DM. In children with DM, despite a growing prevalence of type 2 DM and hybrid diabetes, the largest number have type 1 DM. Thus, most evidence for DM management in children is for type 1 DM.

Although the disease pathophysiology and the insulins used in treating adult and pediatric patients with type 1 DM are the same, specific issues must be considered when treating DM in children. For example, there are dynamic internal (e.g., physical maturation) and external (e.g., schedule variability) considerations in childhood and adolescence that can render the treatment of DM more challenging compared with adults (in this chapter,

adolescence corresponds with the onset of puberty in a child). All aspects of care must be understood and followed, not just by the patient, but also by several potential caregivers. In addition, less clinical evidence is available for the treatment of children with DM than for the treatment of adults with DM. The growing number of children and adolescents with type 2 DM and hybrid diabetes makes the lack of available support for managing these conditions in children of particular concern. Management decisions must be made using limited evidence and guidelines that are primarily based on clinical experience.

Pathophysiology

A significant amount of evidence documents the pathophysiologic differences between type 1 and type 2 DM. In general terms, type 1 DM is a deficit of endogenous insulin production caused by autoimmune-induced damage to the pancreatic islet cells. Type 2 DM is primarily a problem of increased insulin resistance. There is a growing awareness of less-common types of DM, especially in the pediatric population. Genetic mutations have been identified that alter endogenous insulin release, leading to maturity onset diabetes of the young (MODY). In addition, patients are being seen with both type 1 and type 2 DM or hybrid diabetes. Table 1-1 characterizes the four types of DM that affect children and adolescents.

Screening

Routine screening for type 1 DM in asymptomatic children is not recommended. This is because of the low disease prevalence and the lack of consensus for the specific tests, reference values, and procedures that should be used to confirm the diagnosis. In children experiencing common signs or symptoms of hyperglycemia (e.g., sudden weight loss, polyphagia, polyuria, polydipsia), checking a random or fasting plasma glucose concentration is warranted. If the plasma glucose concentration is markedly elevated, a urinalysis should be obtained.

Given the increase in the prevalence of obesity and type 2 DM in adolescents, screening for DM in overweight, asymptomatic adolescents with concomitant risk factors should occur every 3 years beginning at age 10 or at the

Abbreviations in This Chapter

ADA	American Diabetes Association
BMI	Body mass index
DKA	Diabetic ketoacidosis
DM	Diabetes mellitus
I:CHO	Insulin-to-carbohydrate ratio
ISF	Insulin sensitivity factor
LDL-C	Low-density lipoprotein cholesterol
MODY	Maturity onset diabetes of the young
NPH	Neutral protamine Hagedorn

onset of puberty, whichever occurs first. A fasting plasma glucose test is the preferred and easiest screening tool.

The criteria for defining overweight and obese, as well as some of the risk factors for type 2 DM, differ between children and adults. In adolescence, overweight is defined as a body mass index (BMI) greater than the 85th percentile for age but less than the 95th percentile for age on the sex-specific Centers for Disease Control and Prevention BMI charts (www.cdc.gov/growthcharts). Obesity is defined as a BMI at the 95th percentile for age or higher. An overweight or obese adolescent with any two of the following risk factors should be screened for DM: (1) maternal history of DM or gestational diabetes; (2) high-risk race or ethnicity (e.g., Hispanic, African American); (3) a first- or second-degree relative with type 2 DM; or (4) any sign or condition associated with insulin resistance (e.g., polycystic ovarian syndrome, hypertension, dyslipidemia, acanthosis nigricans).

Diagnosis

Diagnostic boundaries for DM are the same for children and adolescents as for adults: a fasting plasma glucose concentration of 126 mg/dL or greater, a plasma glucose concentration of 200 mg/dL or greater measured 2 hours after an oral glucose tolerance test (ingesting 75 g of glucose),

or a random plasma glucose concentration of 200 mg/dL or greater in a patient experiencing classic symptoms of hyperglycemia. Abnormal values for either a fasting plasma glucose or post-oral glucose challenge should be repeated on a different day to confirm the diagnosis. Given the potential for a worsening prognosis with very high plasma glucose concentrations in this patient population, repeating the test on a subsequent day in symptomatic patients who have a random glucose concentration of 200 mg/dL or greater is not recommended.

Historically, the young patient presenting with hyperglycemia would most likely be classified as having type 1 DM; this is still the case for the young patient who is not overweight and who presents with classic symptoms of hyperglycemia. Similarly, the overweight adolescent from a high-risk ethnic group or who has a family history for type 2 DM and is experiencing hyperglycemia very likely has type 2 DM. However, differentiation between type 1 and type 2 DM at diagnosis is paramount because clinical presentation alone may not be sufficient. Furthermore, the increase in adolescent patients with type 1 DM who are overweight and the incidence of ketonuria or diabetic ketoacidosis (DKA) at diagnosis in young patients with type 2 DM add to the importance of making the correct diagnosis. In such cases, additional laboratory assessment is warranted (Table 1-1). C-peptide concentrations and the presence or absence of biomarkers for cellular-mediated immune destruction of beta cells (e.g., glutamic acid decarboxylase antibodies, insulin autoantibodies, islet cell antibodies) are the most common laboratory tests used to differentiate type 1 DM from type 2 DM.

Therapeutic Goals

The primary goal for any patient with DM is to prevent the onset of acute (e.g., hypoglycemia, DKA) and chronic (e.g., microvascular, macrovascular) complications. For those who present with chronic complications, the goal is to attenuate progression. For children with DM, maintaining normal growth and development is also a primary concern. For type 2 DM, controlling glucose to near-normal concentrations is a principal means of obtaining these goals. The American

Table 1-1. Types of DM in Children and Adolescents

Type	Definition	Presentation	Defining Laboratory Characteristics
Type 1 DM	Insufficient insulin production primarily related to autoimmune destruction	Weight loss, polydipsia, polyphagia, polyuria	Low C-peptide, measurable GAD antibodies, insulin autoantibodies, islet cell antibodies
Type 2 DM	Insulin resistance	Weight gain, polydipsia, polyphagia, polyuria	Normal or high C-peptide, elevated blood glucose with normal or high insulin concentrations
MODY (types 1–6)	Genetic mutations resulting in reduced insulin release and response	May present like either type 1 or type 2 DM	Modest or limited hyperglycemia, genetic MODY subtypes, absence of insulin autoantibodies
Hybrid	Insufficient insulin production coupled with insulin resistance; a combination of pathophysiologic features from type 1 and 2 DM	Presents like both type 1 and type 2 DM	Low C-peptide, GAD antibodies, insulin autoantibodies, islet cell antibodies, elevated blood glucose with high exogenous insulin administration

DM = diabetes mellitus; GAD = glutamic acid decarboxylase; MODY = maturity onset diabetes of the young.

Diabetes Association (ADA) recommends near-normal hemoglobin A1C levels (i.e., less than 7%) and fasting blood glucose concentrations below 126 mg/dL for adolescents with type 2 DM. Some practitioners may use the fasting glucose concentrations of 70–130 mg/dL recommended for adults. The ADA provides age-specific glycemic goals for children with type 1 DM. The need for different goals based on age stems from variable physiologic characteristics and developmental needs as children grow and mature, as well as the need to minimize excessive hypo- or hyperglycemia.

The ADA recommends that the hemoglobin A1C be maintained between 7.5% and 8.5% in children younger than 6 years. This goal is based on the potential for intellectual or neuropsychological impairment associated with hypoglycemia in the very young child, the inability to adequately communicate problems, an immature physiologic response to hypoglycemia, and his/her unpredictable activity and food intake. The ability to recognize and treat hypoglycemia improves for children age 6–12 years; however, these children are more likely to require insulin administration away from home, where there is potentially less supervision (e.g., during school, recreational activities). Therefore, the hemoglobin A1C goal for this age group is 8% or less.

In adolescence, the physiological and psychological effects of puberty play an important role in the patient's ability to adequately control blood glucose concentrations. The adolescent generally has increasing autonomy with decreasing parental supervision. Erratic eating habits and activity schedules can make glycemic control increasingly difficult. For patients aged 13–19 years with type 1 DM, the ADA recommends a hemoglobin A1C goal of 7.5% or less. Near-normal glucose concentrations should be the goal as the individual patient matures. Regardless of age group, decisions on target glucose concentrations should be individualized and discussed with the patient and all caregivers.

In the child or adolescent with DM, control of both blood pressure and cholesterol is important. Systolic and diastolic blood pressure measurements should be maintained at levels below the 90th percentile for age, sex, and height. The American Heart Association recommends a low-density lipoprotein cholesterol (LDL-C) concentration below 100 mg/dL in children with type 1 DM and below 130 mg/dL in those with type 2 DM. The American Academy of Pediatrics recommends considering pharmacologic therapy if the LDL-C is 130 mg/dL or greater.

Quality Patient Care

New Drugs and New Drug Roles

During the past 15 years, numerous new classes of orally administered hypoglycemic drugs, incretin mimetics, and insulins have been introduced. Data from evaluations of the use of newer insulin formulations in children and adolescents are increasingly available. Unfortunately, there are few data available evaluating the use of oral diabetes drugs in children.

Insulins

Insulin formulations are classified into three main categories: short acting, intermediate acting, and long acting. Short-acting insulins include regular human insulin, glulisine, aspart, and lispro. The latter three are often referred to as rapid-acting insulins because their onset of activity and time to peak concentration are more rapid than those of regular human insulin. The rapid-acting insulins also have a shorter duration of activity and a time to peak action that is independent of the insulin dose, whereas regular insulin shows an increased time to peak action with increasing doses.

Short-acting insulins are used primarily to control postprandial hyperglycemia. Because of their quick onset of activity, rapid-acting insulins are preferred for children and adolescents, who often have variable and inconsistent mealtimes and food consumption. Regular human insulin should be injected no more than 30 minutes before a meal, whereas rapid-acting insulins can be injected 15 minutes before a meal. Preprandial injections carry the risk of postprandial hypoglycemia without adequate carbohydrate consumption, which can be a problem in young, choosy eaters. Insulin aspart and insulin lispro provide similar glycemic control when administered immediately after a meal compared with preprandial administration. Thus, in some patients with variable food intake, injection of rapid-acting insulin immediately after food consumption allows insulin adjustment based on actual carbohydrate consumption rather than a prescribed amount. The short-acting insulins are also used to correct hyperglycemic excursions (also known as correctional dosing) and for use in insulin pumps. The pharmacokinetic and pharmacodynamic profiles of the rapid-acting insulins in children and adolescents are similar to those seen in adults. Insulin aspart and insulin lispro are both available in pen delivery devices, allowing delivery in 0.5-unit increments for dose-sensitive patients. Insulin glulisine is available only in pens that deliver 1-unit increments.

Basal insulin formulations, such as the newer intermediate- or long-acting synthetic insulin analogs (e.g., insulin detemir, glargine), are effective basal insulin options for children with DM. Their primary use, particularly in type 1 DM, is to mimic the body's natural basal insulin secretion to limit gluconeogenesis and lipolysis, thereby reducing the potential for ketosis. Insulin detemir contains a 14-carbon fatty acid moiety that is acylated to lysine on the B chain of insulin. This fatty acid moiety allows insulin detemir to bind reversibly to albumin and other proteins, extending its duration of activity. The duration of action of insulin detemir appears to be dose-dependent and variable between subjects. With smaller daily doses (less than 0.4 units/kg/day), a shorter duration of action may be expected and will often require twice-daily dosing. Unlike neutral protamine Hagedorn (NPH) and insulin glargine, insulin detemir is soluble at a neutral pH. Insulin glargine is administered while soluble in its acidic formulation; when exposed to a higher pH by subcutaneous injection, it forms a precipitate, which permits an extended duration of activity and no pronounced peak concentration compared with NPH. Both insulin detemir and glargine have been studied in children as young as 6 years, and both insulins are available in either vial or injectable pen devices. The

incidence of hypoglycemia in children is less with either insulin detemir or glargine compared with NPH; these agents produce similar or improved glycemic control. Neither insulin detemir nor glargine should be mixed with other insulins.

Noninsulin Subcutaneous Drugs

The use of the synthetic amylin analog pramlintide has been evaluated in a small number of adolescents with type 1 DM as a single preprandial injection in patients receiving insulin therapy. Pramlintide may suppress glucagon secretion, delay gastric emptying, and reduce postprandial hyperglycemia in children with type 2 DM, but it also markedly increases the risk of hypoglycemia. Pramlintide’s efficacy and safety in children have not been established. The use of exenatide, a glucagon-like peptide-1 analog, is currently being assessed in children with type 2 DM.

Oral Diabetes Drugs

The only oral drug labeled for use in the treatment of type 2 DM in children is metformin. For children who are at least 10 years old, the recommended maximal daily metformin dose is 2000 mg, which is less than the recommended 2550-mg maximal daily dose for adults. Metformin appears to have a similar adverse event profile in both children and adults. The use of the sulfonylurea glimepiride has been studied in children; although it appears to reduce hemoglobin A1C values, it causes the same risk of weight gain and hypoglycemia as in adults. No clinical data are available to assess the efficacy and safety of monotherapy with thiazolidinediones, meglitinides, α -glucosidase inhibitors, or dipeptidyl peptidase-4 inhibitors in children.

Devices

The appropriate use of medical devices is a vital part of DM management. During the past decade, there have been many improvements to traditional diabetes-oriented medical devices, as well as the introduction of new devices. The goals of these advances are to facilitate management, improve adherence, and improve quality of life for patients with DM and their caregivers.

Subcutaneous Injection Port

A subcutaneous injection port is a device that allows a cannula to be inserted under the skin by the patient, similar to an insulin pump insertion site. Insulin injections

are administered into the port instead of the skin, thereby reducing repeated skin punctures and the need to rotate injection sites. The port site is changed every 2–3 days, and the port must be primed with a specific amount of insulin (e.g., 0.5 units) to fill the cannula after each change. For some patients, subcutaneous injection ports may reduce discomfort and improve adherence. In addition, a port can be used as the initial step toward insulin pump use. Cost may be an issue because the cost of these ports is currently not covered by most third-party payers.

Insulin Pumps

The use of a subcutaneous insulin pump may permit tighter, more tailored glycemic control and more flexibility in lifestyle; however, it also requires greater responsibility on the part of the patient to follow appropriate procedures and safeguards. Insulin infusion pumps have been available for several years, and newer models feature numerous improvements. These devices, which fit in the palm of a hand, contain a reservoir filled with insulin. The insulin is carried through tubing into a catheter that is inserted under the skin by the patient. The pumps deliver short-acting insulin at a programmed flow rate into the subcutaneous fat, mimicking basal insulin administration. Pumps can be manually operated to deliver additional bolus amounts for mealtime glucose excursions or correctional insulin doses. The infusion site is located in the same body locations where insulin injections would be given and must be changed every 2–5 days.

Insulin pumps offer the option of a basal/bolus approach with a single insulin and device, more closely matching a patient’s specific needs. Because these pumps are not limited to delivering doses in increments of 0.5 units or 1 unit, they allow more precise insulin dosing. In addition, the pump can provide better basal control because insulin release rates are not fixed, like a once-daily injection, but can be adjusted to different rates on an hourly basis throughout the day. Insulin pumps can record all insulin actions taken by a patient, an asset to practitioners in assessing patient adherence and understanding (extremely important in children and adolescents). Newer features provide other applications to improve adherence, assist in better glycemic control, and minimize potential problems (Table 1-2). The cost of the insulin pump is high, and the associated monthly supply costs are usually a little higher than intermittent injection

Table 1-2. Advanced Features Available on Insulin Infusion Pumps

Feature	Description
Carbohydrate/diet guide	Helps make food choices and calculate carbohydrate
Bolus dose calculator	Uses carbohydrates and/or blood glucose concentrations entered and calculates matching insulin doses
Programmable alarms	Sets reminder alarms for monitoring and/or bolus dosing
Insulin action	Figures the percentage of insulin that may still be working from the previous bolus when calculating new doses
Combination boluses	Allows change of the release curve of a bolus to better match food absorption
Small dosing increments	Allows administration of very small insulin amounts (usually between 0.025 units and 0.05 units)
Multiple basal programs	Allows different programs for different days when insulin requirements may differ from the usual requirements
Multiple basal rate segments	Allows several different rates of insulin release throughout the day

supplies. Most third-party payer plans cover at least part of the cost of the pump and the necessary supplies.

Insulin pumps are not appropriate for every patient; they demand greater adherence to ensure safety and efficacy. Older studies involving the use of insulin pumps, both in children and adults, showed a slight increase in the risk of developing DKA, primarily because of disruptions in insulin delivery caused by mechanical failure, tubing occlusion, or a problem at the administration site. Newer insulin pumps have many safeguards, internal diagnostics, and alarms to help prevent, detect, and alert patients to these problems. Recent literature points to the necessity of proper patient education and adherence to reduce the risk of complications from insulin pump use. Optimal benefit from an insulin pump requires intensive education for practitioners, patients, and caregivers.

Continuous Blood Glucose Monitors

Continuous glucose monitors give constant feedback on blood glucose status. Four monitors are currently available in the United States, with more in various stages of development. All have a sensor that is inserted under the skin, similar to an insulin pump site. Because the device samples interstitial plasma, the recorded glucose concentrations are not always representative of circulating blood glucose concentrations. This discrepancy is caused by the slower rate of glucose exchange between the vasculature and the interstitial space. Because of potential inaccuracies, these monitors do not eliminate the necessity of peripheral samples (fingersticks). The devices may be useful for tracking glucose trends, especially between normally scheduled fingersticks (e.g., overnight). However, they cannot be used to identify hypoglycemia, and they are not considered accurate during unstable periods such as after meals or insulin administration. Newer models have the ability to communicate directly with an insulin pump, but the patient will still require a separate insertion site for each device. The sensor site, which must be replaced every few days, can be more painful than an injection or insulin pump site. This additional discomfort is likely caused by the sensor's lack of flexibility and larger size relative to an insulin pump. As the technology continues to evolve, these disadvantages may be reduced, and continuous glucose monitors may gain an established role in DM management.

Management Plans

Treatment plans for patients with DM are designed to treat the pathophysiology of the specific type of DM, individualize short- and long-term goals, and compensate for any patient-specific limitations. Management incorporates analysis of both pharmacologic and nonpharmacologic issues. Given the broad scope of challenges in managing DM, a multidisciplinary team-based approach is recommended.

Individualized Goals

In general, the recommended goals for blood glucose concentrations and hemoglobin A1C values in published guidelines are designed to help reduce the chances of complications. When developing a patient-specific treatment plan, blood glucose monitoring and hemoglobin A1C values are only part of the overall plan. In children and adolescents, the overall therapeutic plan must also address

surviving the challenges of day-to-day disease management. The resumption of normal activities should be a prime consideration in creating a patient-specific treatment plan. Plans and goals that include activities such as school, sports, and family vacations will provide patients and their families a more well-rounded understanding of DM management than if goals are primarily number driven (i.e., glucose concentrations).

Prevention of acute complications should also be included in the treatment plan. This approach takes minimizing extremes one step further and entails helping the patient recognize that “when I get this high or that low, I am not myself and I may feel bad.” A patient-specific plan provides goals to prevent DKA and hypoglycemia, as well as instructions for how to treat them when they occur. Finally, self-management is perhaps the most important goal for this patient population. Setting age- and ability-appropriate self-management goals will allow patients to take ownership of their DM management and may influence their long-term adherence, glycemic control, and emotional outlook.

Management of Type 1 DM

ADA Guidelines

In 2005, the ADA believed there was sufficient evidence to publish a position statement targeted directly at the management of type 1 DM in children. Much of the evidence for these guidelines comes from The Diabetes Control and Complications Trial and its follow-up study, Epidemiology of Diabetes Interventions and Complications (specifically, data from the subpopulation of children and adolescents in these landmark studies). These data, coupled with data from smaller studies and expert opinions, led to the ADA's recommendation that this group's treatment be approached in a manner similar to adults, specifically with the application of intensive treatment. The guidelines provide insight into age-specific priorities and self-management expectations.

Basal/Bolus Insulin Regimens

Current management of type 1 DM focuses on the use of basal/bolus (basal/prandial) insulin regimens to more closely mimic natural insulin secretion. The basal insulin provides background insulin release to regulate homeostatic glucose concentrations and increased nocturnal glucose release from the liver (known as the dawn phenomenon). Bolus insulin doses are designed to match new carbohydrate intake and correct for postprandial hyperglycemic excursions. Several combination insulin regimens can be chosen. The choice of insulin regimen depends on the patient's lifestyle, ability to adhere to the regimen, and physiologic limitations.

Insulin regimens are based on the time-action curve of the particular insulin used. A traditional combination regimen consists of NPH plus a short-acting insulin. Although NPH is not a basal insulin by the strict interpretation of the definition, it is still widely used. The most common regimens use NPH with short-acting insulin in the morning and NPH administered again at dinner with the short-acting insulin or given separately at bedtime. The short-acting insulin is used to lower the postprandial glucose concentration to target concentrations by matching the carbohydrate intake at breakfast and dinner. The NPH administered in the morning is used to cover for carbohydrate intake at lunch and offer some basal coverage during the day. Evening or

bedtime administration offers basal coverage throughout the night. This NPH insulin plus short-acting insulin regimen requires a fairly strict adherence to prescribed mealtimes and carbohydrate intakes (especially at lunch) because NPH given at breakfast will not reach its peak effect for 4–6 hours.

The perceived advantages of NPH regimens are reduced injection frequency (only two or three injections daily if mixing insulins); relative cost savings compared with newer synthetic insulins; and less patient involvement in the decision-making process. A disadvantage is the necessity of having a precise carbohydrate intake at a specific time to match the time-action curve of NPH insulin. In addition, there are prolonged periods of elevated insulin concentrations, on either side of the peak concentration, that are typically greater than natural basal insulin requirements; these are a potential cause of prolonged hypoglycemia. Achieving tight glycemic control requires patients to count carbohydrates, so the need for extensive education is not eliminated. This particular insulin regimen does not have a mechanism for correcting high blood glucose concentrations at lunch. The inclusion of a short-acting insulin at lunch will resolve this problem but increase injection frequency to three or four injections daily, thereby eliminating one of its advantages.

Achieving tight glycemic control in children with type 1 DM with an NPH regimen can be challenging. Children's diets and carbohydrate needs (and wants) often fluctuate, making it difficult to follow the strict dietary requirements of this regimen. Small children may need more than the standard three meals per day, making it hard to match NPH insulin's time-action curve. It may also be a challenge to have lunch at the appropriate time to match NPH insulin's peak effect. For example, schools often vary their lunch schedules or do block scheduling, which means that a child's lunchtime can vary by up to 2 hours on different days of the week. In addition, NPH will have its peak effect sometime between 10:00 PM and 3:00 AM depending on the evening or bedtime administration; this peak may not match the patient's evening basal requirements.

If a child experiences a hypoglycemic event because of too much NPH, treatment of hypoglycemia may have to be continued for several hours because of the insulin's extended duration of action. Both clinical evidence and practical experience have shown that in the course of lowering hemoglobin A1C to goal levels, there is an increased incidence of hypoglycemia. Additional measures must typically be taken to reduce the extreme ranges in blood glucose concentrations that occur with standard NPH regimens. Patients and caregivers must be willing and able to follow the strict timing and prescribed carbohydrate intakes for meals and snacks. Additional blood glucose readings pre- and post-NPH insulin's peaks are required before and after initiating or changing the NPH dose to monitor for both hypo- and hyperglycemia.

Newer regimens using insulin glargine or detemir for basal insulin coverage can provide a closer approximation to true physiologic secretion. Basal insulin is given once or divided twice daily, and all meals and corrections for hyperglycemia are covered with a short-acting insulin. The time-action profiles of a basal/bolus regimen make it easier to adapt to patient-specific needs. These regimens tend to be more injection intensive (often four or five injections

daily) because most meal and correction boluses are given separately from the basal injection. However, patients have much more flexibility in the timing of meals and the ability to decrease elevated glucose concentrations to target goals. There is less risk of hypoglycemia and cyclic hyper- and hypoglycemia because of the basal insulin's flatter time-action profile. In addition, carbohydrates in the meal can be varied with a corresponding change in the insulin bolus dose. This may make it easier to achieve tight glycemic control and reduce the hemoglobin A1C to goal; however, injection frequency and cost may be increased. Overall, a true basal/bolus regimen may be less challenging than an NPH insulin regimen.

Regardless of the insulin chosen, it must be dosed to best match the patient's insulin needs. In children and adolescents, insulin requirements can change quickly and dramatically; therefore, there is no perfect formula that will always match insulin needs. In patients newly diagnosed with type 1 DM, several methods can be used to estimate daily insulin requirements. If insulin is initiated in the hospital, it may be possible to estimate daily needs based on the total amount of insulin required in the previous 24 hours during a continuous infusion of regular insulin. However, the child may have a temporary restoration of partial insulin production (honeymoon period). At discharge, the combination of increased activity and the honeymoon period may reduce the daily insulin requirements relative to the amount needed in the hospital. Therefore, many practitioners initiate insulin conservatively by starting at 80% of the daily insulin requirement in the hospital.

Without adequate information from hospitalization, a weight-based approach (0.3–0.5 units/kg/day) is the best method for estimating total daily insulin requirements in children. Other valid approaches include assessing the in-hospital insulin requirement, if available, and the weight-based insulin dose and then taking the average of the two results (or using the more conservative value). Once the total daily insulin requirement is estimated, it is common to split the amount into 50% basal and 50% bolus insulin coverage for meals. The bolus insulin estimate is then split equally among meals. A similar approach can be taken when switching from a more traditional insulin regimen: calculate the patient's average total daily insulin from the previous insulin regimen and give 50% as basal insulin and 50% as bolus insulin doses.

Newer Insulin Dose Adjustment Techniques

Older insulin regimens that use sliding-scale insulin dosing or fixed mealtime insulin regimens are no longer recommended. A more effective way to reduce blood glucose fluctuations throughout the day is to dose the mealtime insulin proactively rather than retroactively and to avoid the use of fixed or sliding-scale insulin dosing. The insulin-to-carbohydrate ratio (I:CHO) and insulin sensitivity factor (ISF; insulin-to-blood glucose correction ratio) are relatively simple techniques that give practitioners the ability to better match insulin doses to blood glucose concentrations. The I:CHO and ISF may also be used to allow patients or their caregivers more flexibility in meal timing and food intake. Once the patient is taught these techniques, instead of a fixed amount of carbohydrates tied to a fixed dose of regular

or rapid-acting insulin, the patient can adjust (within reason) food intake and the corresponding insulin dose.

The I:CHO is a prediction of the amount of insulin required to match the rise in blood glucose expected with dietary carbohydrate intake. There are several ways to make this prediction for the individual patient. In a patient with DM newly diagnosed who is making the transition from the hospital setting to home, the estimated response can be based on insulin requirements during the hospitalization. However, it is likely that another predictive method will be necessary. The *500 rule* is a commonly used method based on clinical experience. To use this method, 500 is divided by the estimated total daily insulin requirement in units; the resulting number is the grams of carbohydrate that will be matched by 1 unit of insulin. An even simpler approach, which matches a traditional carbohydrate food exchange, is to start at 1 unit of insulin for every 15 g of carbohydrates (1:15). However, this ratio may result in hyperglycemia in some adolescents and produce hypoglycemia in small children.

If the patient is being changed to a new regimen, the effects of the previous insulin regimen can be used to predict an I:CHO. Insulin can only be administered in increments of 0.5 unit or 1 unit when given as an injection; this necessitates rounding, which can result in doses that do not precisely match the calculated needs. With this imprecision, it is acceptable to round ratios up or down into units of 5 or 10 for ease of calculation (e.g., 1:10, 1:15, 1:20, 1:30). Regardless of the method used to estimate the I:CHO, it is merely a starting point. The patient's blood glucose concentrations will determine what adjustments should be made to reduce postprandial glycemic excursions.

Because all these regimens require estimating blood glucose increases on the basis of carbohydrate intake, it is necessary for patients to determine their mealtime carbohydrate intake. This mainstay of DM management is commonly referred to as carbohydrate counting. Using this technique, a specific food or meal carbohydrate amount (in grams) is calculated. Patients and caregivers can also approximate how many 15-g carbohydrate exchanges are in a meal. Carbohydrate counting is an important tool that allows the patient to administer the appropriate amount of insulin to match the glucose that will be absorbed and released into the blood. Without this technique, it would be difficult and potentially dangerous to proactively dose insulin. Whether on a fixed or flexible meal plan, patients and their caregivers must be able to consistently match carbohydrate intake with the appropriate insulin dose.

The stable patient with optimal carbohydrate counting and effective use of the I:CHO should rarely need additional insulin administration to correct for hyperglycemia (i.e., correctional insulin dosing). However, with changes to internal stressors, metabolism, and hormone release, there will be times when the basal regimen does not match the hepatic glucose release or the bolus insulin dose does not precisely match the glucose released into the blood. Using the ISF is a way to more accurately bring the blood glucose concentration back to the target range. The ISF predicts how much 1 unit of insulin will lower the blood glucose concentration. This correlation is difficult to accurately predict, even with past records, because several factors can vary the response of the blood glucose concentration

to insulin. The *1800 rule* for synthetic insulins (or the *1500 rule* for regular human insulin) requires that 1800 (or 1500) be divided by the patient's total daily insulin; the resulting number is an estimate of how much the blood glucose will decrease in milligrams per deciliter for every additional 1 unit of the respective insulin given.

When developing an insulin regimen for the child with type 1 DM, the focus is on optimizing insulin type, dosing schedule, and dose to best match glucose release into the blood (Figure 1-1). After initiating an insulin regimen, adjustments should not be based on a single glucose measurement but on patterns documented for several days. Basal doses are adjusted on the basis of fasting glucose concentrations, whereas bolus doses are altered on the basis of postprandial glucose concentrations. In addition to the typical premeal and bedtime blood glucose monitoring, postprandial measurements (2–2.5 hours after meals) and several overnight glucose measurements are required. This increased frequency of testing should be performed when any change occurs in the regimen. Pattern areas of poor control must be identified, together with the probable cause (e.g., nonadherence, insulin dose). Management then becomes a cycle of evaluating how well the regimen is matched to the patient's blood glucose profile, making adjustments as necessary, and reevaluating. In children and adolescents, frequent and substantial changes in the insulin regimen may be necessary.

Insulin Pump Management

Another way to administer a basal/bolus insulin regimen is to use an insulin pump. Although insulin pumps use only short-acting insulins, basal and bolus issues are monitored and controlled separately, similar to the management of an injection-based regimen.

An insulin pump regimen is initiated by estimating the basal and bolus insulin requirements. Initial basal, I:CHO, and ISF estimates can be taken from a patient's current regimen or may be calculated and then programmed into the pump. Patients can manually calculate carbohydrate and correction boluses, or they can use advanced pump features to assist with calculating and administering the bolus. Setting up the basal program requires a few steps. After estimating total basal requirements, the total basal dose must be distributed throughout the day. The easiest approach is to program one consistent hourly basal insulin rate for the full 24-hour period until necessary adjustments are identified. The total daily basal insulin estimate divided by 24 provides an estimate for the hourly insulin infusion rate. Changes in insulin requirements during certain periods (e.g., increased activity) may necessitate the use of varying insulin infusion rates throughout the day. In many cases, there are enough data at initiation of insulin pump therapy to identify at least two distinct periods of differing basal insulin requirements. For example, if the total estimate for basal insulin were 24 units, a single rate would yield 1 unit/hour for the 24-hour period. However, at initiation, a patient might need increased basal insulin coverage overnight (8:00 PM to 8:00 AM) and less during the day. Thus, the practitioner might increase the overnight basal rate by 20% with a corresponding rate decrease of 20% during the day.

After initiation, adjustments are generally done as with injection regimens, although hourly control of the basal rate

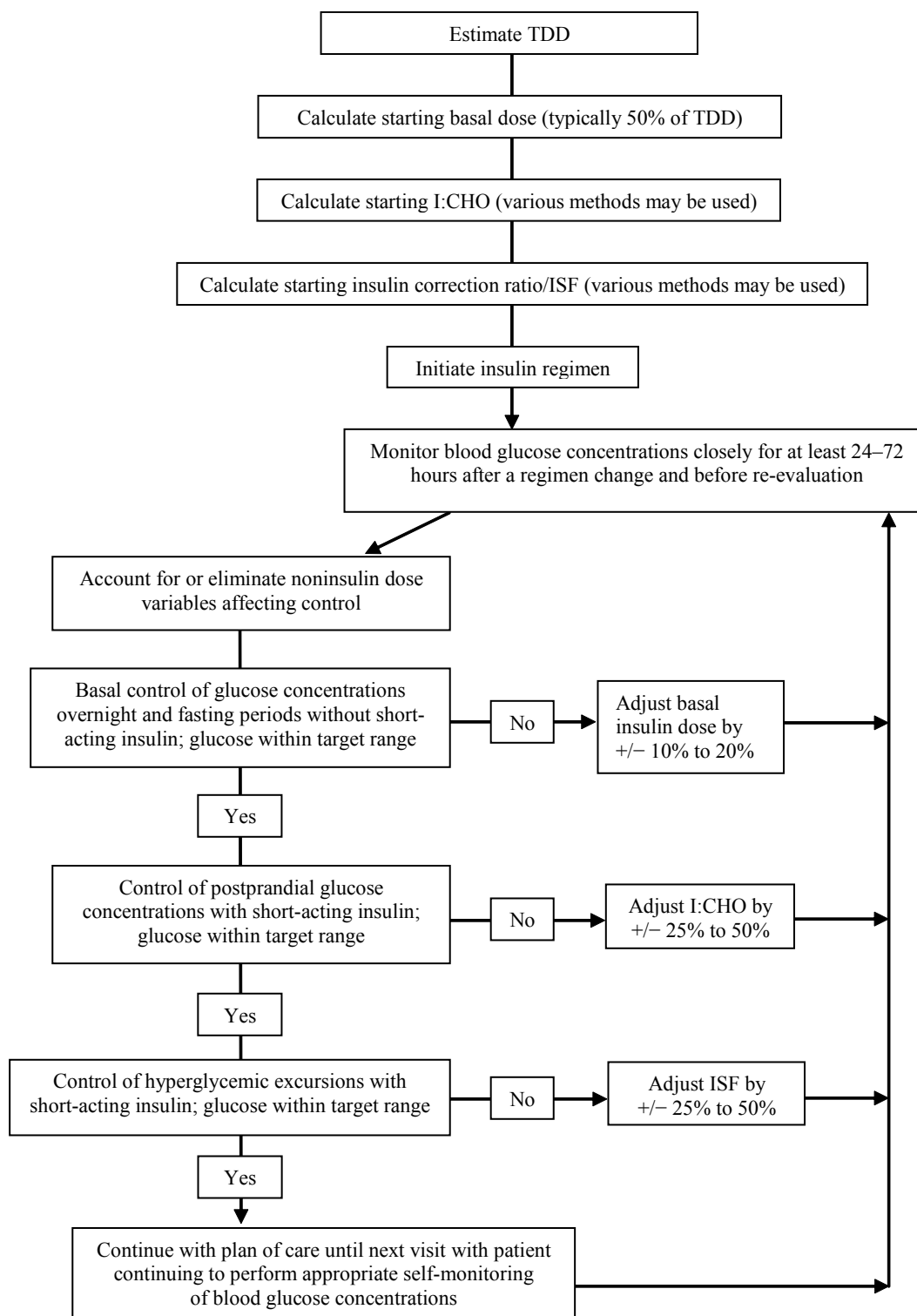


Figure 1-1. Algorithm for management of a basal/bolus insulin regimen in children and adolescents.

I:CHO = insulin-to-carbohydrate ratio; ISF = insulin sensitivity factor; TDD = total daily insulin dosage or requirement.

with pumps may provide more opportunities to specifically adjust and meet the patient's insulin requirements. Typically, dose adjustments are made every 48–72 hours until blood glucose concentrations are within the target range. It is generally easier and safer to adjust one category of insulin dosing at a time, focusing first on basal control, then on carbohydrate boluses, and finally on correction coverage. Early in treatment, frequent blood glucose monitoring (every 2–2.5 hours) is required.

Lifestyle Modification

Dietary needs in children with type 1 DM are focused on well-balanced intake. Depending on the insulin regimen, there may be additional specific carbohydrate and meal-timing requirements. A primary goal is the resumption of normal activities for the child, including physical activity and maintenance of general health. In patients with type 1 DM, it is important to monitor physical activity because of its effect on blood glucose concentrations.

Management of Type 2 DM

In an effort to limit the effect of insulin resistance on glycemic control and reduce the risk of cardiovascular damage from high blood pressure or dyslipidemia, all patients with type 2 DM should strive to limit carbohydrate and fat consumption and perform regular physical activity. Given the high incidence of DM and its risk factors in parents of adolescents with type 2 DM, improvement in diet and exercise is often a family issue, not just an issue for the child with DM. It is difficult for most adolescents to change their behavior if their parents or caregivers do not also change. Practitioners must consider these influences when counseling adolescents and their families.

The initial drugs chosen to improve glycemic control are primarily determined by the severity of hyperglycemia and whether acute complications are present (Figure 1-2). The patient with plasma glucose concentrations greater than 250 mg/dL, a hemoglobin A1C greater than 8.5%, or a recent diagnosis of an acute complication (e.g., DKA) should be placed on insulin therapy to improve metabolic control. When glucose concentrations are controlled and any initial symptoms have resolved, oral drugs may be added to the insulin regimen with a subsequent reduction in insulin dosage, and in some cases, discontinuation of insulin. For patients with only mild hyperglycemia who are relatively asymptomatic, lifestyle modifications (diet and exercise) in addition to oral diabetes drug therapy are warranted.

When choosing oral therapy, most practitioners and the ADA consider metformin the initial drug of choice for treating children and adolescents with type 2 DM. This is because of metformin's ability to limit gluconeogenesis, its limited hypoglycemic potential when used as monotherapy, and its modest but positive effect on both weight and triglyceride concentrations. In addition, metformin is available as a liquid formulation for patients who cannot swallow tablets. Based on limited studies in adolescents, the average hemoglobin A1C reduction from baseline with metformin is between 0.85% and 1%. In contrast, glimepiride monotherapy reduces hemoglobin A1C levels by 0.7% in adolescents with type 2 DM.

There are no well-conducted clinical trials to provide information on which class of oral diabetes drugs to add

to metformin in the adolescent population when glycemic control is no longer adequate. However, the combination of rosiglitazone and metformin is being studied. Adding agents that have not been at least studied as monotherapy for safety and efficacy in adolescents is risky. If metformin therapy does not adequately control blood glucose concentrations, the addition of an intermediate-acting insulin or sulfonylurea is the next step in therapy. Given the presence of polycystic ovarian syndrome in women with type 2 DM, all female adolescents receiving metformin should be warned about the increased risk of unplanned pregnancy with its use because of the drug's ability to help normalize abnormalities in ovulation.

Screening for dyslipidemia should occur at diagnosis and, if the initial screening is normal, be repeated every 2 years. If an elevated LDL-C concentration is identified, lifestyle modifications and optimization of glucose concentrations should occur. If the LDL-C concentration remains elevated after 6 months of dietary and lifestyle changes, statin therapy is justified for patients at least 8 years of age. Bile acid sequestrants could be considered because of their limited systemic absorption; however, they do not lower LDL-C concentrations to the same degree as statin therapy. If triglyceride concentrations are greater than 1000 mg/dL, fibric acid derivatives should be used.

As many as one-third of children diagnosed with type 2 DM will have concomitant hypertension; thus, regular assessment of blood pressure is required. Optimal evidence-based treatment options in this patient population are lacking, but the use of drugs similar to those used to treat hypertension in the adult population is warranted to limit potential complications. Adolescent girls should be counseled on the fetal risks associated with the use of statins or agents that interfere with the renin-angiotensin-aldosterone system.

MODY and Hybrid Diabetes

The focus of managing less common forms of DM also is control of blood glucose concentrations, and treatment is not significantly different from that for either type 1 or type 2 DM. Maturity onset diabetes of the young is usually only suspected when goal glucose concentrations are achievable with low-dose insulin regimens. There is limited evidence in adults that diet and physical activity are sufficient for patients with the mutation that produces one category of MODY, MODY2; sulfonylureas may be sufficient for the treatment of adults with MODY1, MODY3, and MODY4. Children and adolescents with the MODY1, MODY3, or MODY4 mutations may require low-dose insulin; there are limited safety and efficacy data with long-term use of sulfonylureas in this population. Because insulin therapy is the primary method of managing MODY, dosing regimens and monitoring of these patients are similar to those for patients with type 1 DM.

Monitoring

Blood glucose measurements are the best way to monitor the effectiveness of any regimen. Testing and recording results numerous times daily allows patterns of control or noncontrol to be identified. These records should be reviewed during visits, together with hemoglobin A1C results, urinalysis and other screening tests, and findings

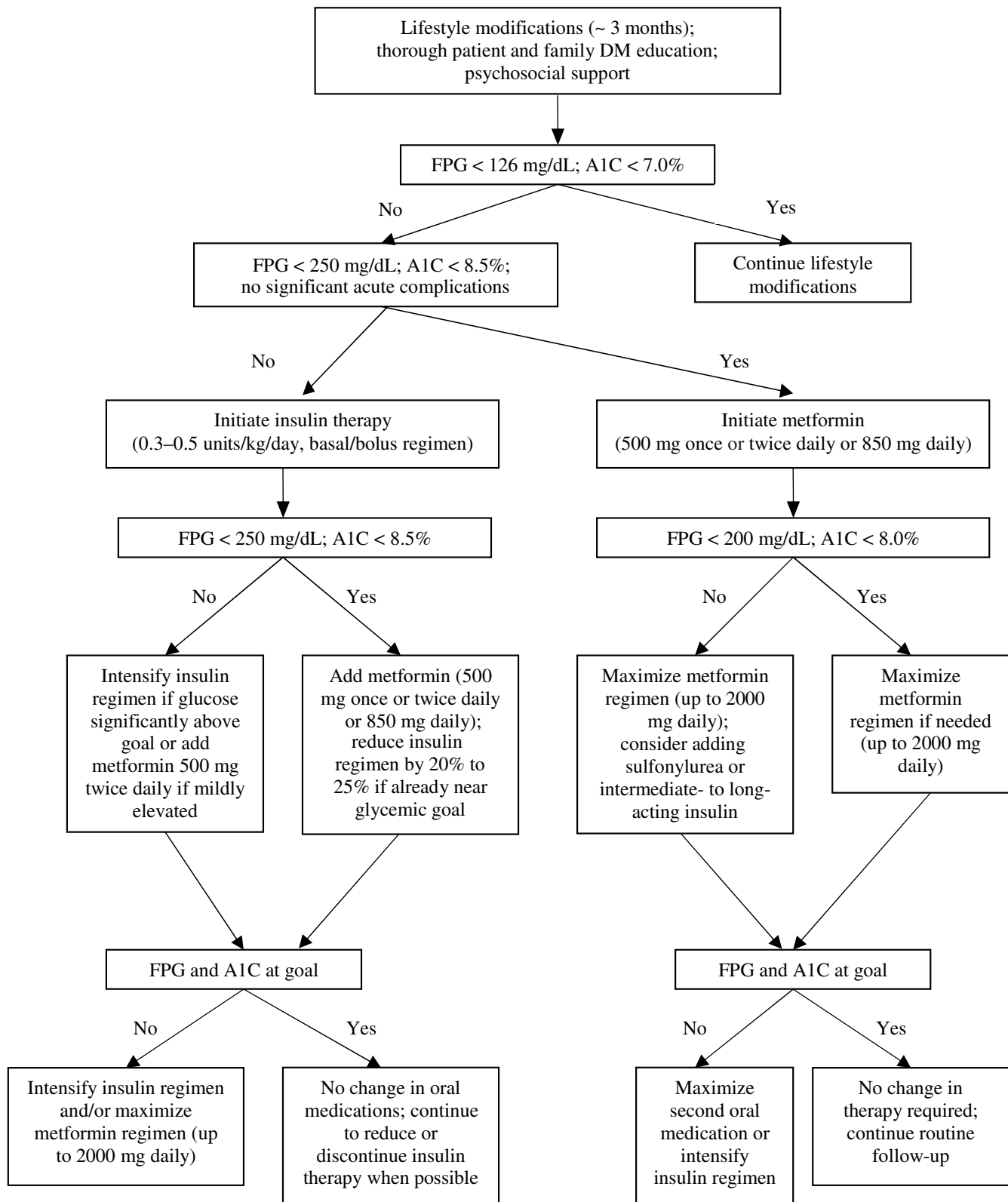


Figure 1-2. Treatment algorithm for type 2 diabetes mellitus in adolescents.
A1C = hemoglobin A1C; DM = diabetes mellitus; FPG = fasting plasma glucose.

on physical examination. The patient's own perspective is a vital part of optimizing DM management. On a daily basis, the patient should be cognizant of symptoms that might indicate the micro- or macrovascular complications associated with DM (e.g., vision disturbances, unexplained peripheral pain, numbness). Regular clinic visits allow practitioners frequent opportunities to monitor for these complications. Hemoglobin A1C is the primary tool for assessing long-term complication risk.

Adherence

Adherence to diet, glucose monitoring, drugs, and other aspects of care is essential to successful long-term control of DM and its complications. For patients and their caregivers, adherence is often the biggest hurdle to successful treatment. Diabetes management requires significant effort, and the patient's age is an important factor. It is extremely difficult for a child, even with significant supervision and support, to meet all of the management expectations every day. Proper insulin administration is only one part of adherence. Other aspects of care include following the time schedule of the regimen, using appropriate monitoring and administration techniques, being cognizant of symptoms, and performing proper carbohydrate and insulin dose calculations. Adherence must be addressed, together with the drug regimen, when glycemic control is not achieved. Children and adolescents often view DM management as a chore; therefore, they may fear that they will be disciplined if they do not meet expectations. They may sometimes falsify blood glucose readings or may use their disease state as a means to exert independence from parental control.

Comorbidities

Children and adolescents with DM often present with comorbidities (e.g., depression, hypo- or hyperthyroidism, attention-deficient/hyperactivity disorder, enuresis, constipation) that cannot be treated successfully if viewed independently from their DM. These comorbidities and their respective treatments can affect both the blood glucose concentration and the patient's ability to adhere to a management regimen. All comorbidities must be treated in conjunction with the patient's DM to optimize outcomes.

Clinical Practice

Differences in the clinical treatment between adults and children with DM stem from the alterations required to meet a child's specific needs. The timing of visits is one example of an age-specific issue. In children with type 1 DM, physiologic changes occur rapidly, so spacing clinic visits to coincide with assessing a hemoglobin A1C concentration (usually drawn every 2–4 months) may be too long between visits. It is generally beneficial to see children with type 1 DM at least every 6 weeks, and sometimes more often. This visit frequency may not be feasible for all patients or practices. Children with type 2 DM may be evaluated less often because, although they also change quickly, the effects of the changes relative to their management plan are usually less dramatic. For most patients, visits every 2–3 months are appropriate and cost-effective.

Family members and other caregivers must also be involved in the development of the therapeutic care plan. The practitioner often has to discuss more factors that can affect

the plan's success (Figure 1-3), and it is often more difficult to extract accurate information from a child. Evidence-based treatment options are often limited in the pediatric population; thus, optimizing care is more challenging.

It is important to remember that children may have varied and atypical responses to typical treatment strategies. For example, insulin glargine offers a theoretical advantage of peakless, once-daily basal delivery; however, both experimental data and clinical experience suggest that insulin glargine does not always provide 24 hours of basal coverage in children. This decreased duration of action of insulin glargine primarily occurs in very young patients who are receiving very small insulin doses (usually 1–4 units). In some patients, glycemic control may decline 12–20 hours after a dose; this necessitates splitting the total basal dose into two injections daily. In addition, some patients' blood glucose concentrations may decrease significantly about 4–6 hours after an insulin glargine dose, which, although it may not qualify as a peak, can increase the risk of hypoglycemia. If this increased effect occurs, the insulin glargine dose can be administered at dinnertime instead of bedtime so that any potential hypoglycemia may be noted earlier rather than in the middle of the night.

In a small subset of children with DM, the use of very small doses of a dual insulin regimen may be too aggressive, resulting in hypoglycemia. These patients may need basal insulin coverage only for a specific period. Using one of the basal insulins with a flatter time-response curve tends to be more successful than NPH insulin in achieving target blood glucose concentrations without hypoglycemia. This phenomenon may be seen with detemir, but it is not unexpected because of its dose-dependent duration of activity.

For adolescent girls, there is the additional issue of increases in blood glucose concentrations often seen 2–4 days before and during the first 2–4 days after the start of the menstrual cycle. These glucose excursions can make achieving tight glycemic control during adolescence more difficult. With proper monitoring, glycemic control can be optimized by developing a specific insulin regimen for this particular time, which is especially easy to do with a separate program in an insulin pump.

Patient Education

Because adherence, drug administration, and self-monitoring of blood glucose concentrations play key roles in long-term success, the patient must have a strong foundation in self-care. Children can often do more than caregivers and practitioners believe or allow. The earlier the child gets involved in his or her own care, the better the chances this care will become a consistent part of the child's daily life. Children should be allowed and encouraged to do as much of their care as possible under direct supervision. Participation in self-care can allow children to believe that they have some control of their own lives. Involvement can be as simple as assisting with injection site selection, pressing down the syringe's plunger, or putting a strip in the meter. This semblance of control and independence can often reduce the struggle during insulin injections or finger sticks. Older children should be included in management decisions so that they can see the cause and effect of changes in their control. Overall, by increasing their involvement, children with DM

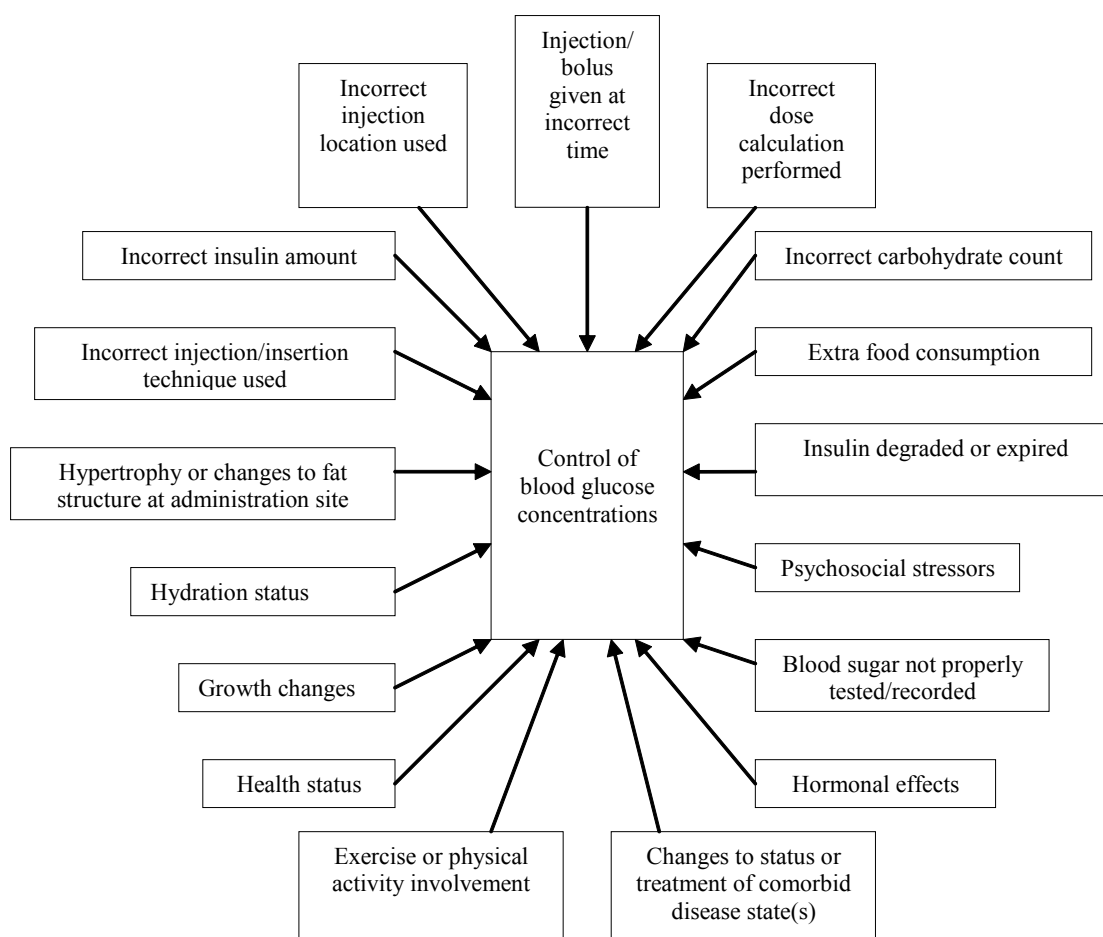


Figure 1-3. Variables affecting control of blood glucose concentrations.

will be better prepared to make management decisions as adults.

There are a few nuances to care in children with DM that are especially important for patient education. Insulin education should include information on stability and cost-effectiveness. Children often are exposed to temperatures hotter than room temperature for extended periods, either inside or outside during physical education, organized sports, or other recreational activities. High temperatures can degrade insulin and result in decreased performance; therefore, children who carry pens or vials must be educated to protect their drugs from high temperatures. Insulin in a pump for as little as 3 days can decline in effectiveness after exposure to high temperatures. During hot weather, insulin in the pump should be changed every 2 days. Waste can be prevented by filling the pump's reservoir with only enough insulin to last until the next change.

When insulin is used for longer than 28 days after the vial is opened (10–14 days for some premixed insulin pens or 42 days for insulin detemir), lack of efficacy can be seen. This stability information is especially important for patients receiving small doses. One potential solution for preventing waste is the use of an insulin pen or pen cartridge either to directly administer the insulin or to withdraw the insulin for

administration. Smaller volume cartridges (3 mL) expire 28 days after opening, but the smaller volume allows less waste and possible cost savings.

Patients and caregivers need a thorough education on appropriate techniques for insulin administration and monitoring. For example, children should leave the injection needle under the skin an additional 5–10 seconds to ensure release of the full dose into the subcutaneous tissue. This is vital because even a few drops of insulin could represent a large percentage of the desired dose. Another area for patient education is alternative-site glucose testing (e.g., forearm, palm, thigh). Alternative-site testing may be an option for patients with type 2 DM; however, it may not be accurate enough for patients with type 1 DM. Alternative-site testing measures glucose concentrations in the interstitial plasma; the concentrations by this testing do not always correlate with circulating glucose concentrations. Thus, the use of alternative-site testing to derive insulin doses or to evaluate hypoglycemic excursions can be dangerous. Another area that may require more diligence in children is the injection or infusion site. Appropriate site rotation is paramount, yet it can be challenging because some children do not have as much surface area to use for injections or may not have sufficient fat in the acceptable areas. Children may

overuse one area, resulting in decreased or erratic insulin performance.

Educational efforts should also include the child's lifestyle and its possible effects on DM management. Besides diet and schedule, the need for several smaller meals each day should be considered. Patients, caregivers, and practitioners must be aware of how physical activity affects the child's glucose concentrations and realize that these effects depend on both the type and timing of the activity. The patient may have adrenaline-associated increases in blood glucose concentrations, decreases in glucose concentrations from improved glucose use, or a combination of the two. Exercise can affect blood glucose concentrations for as long as 18 hours after the activity. Awareness of this effect is important, allowing patients and caregivers to monitor and potentially prevent hyper- and hypoglycemic excursions. Documenting the pattern of glucose fluctuations associated with exercise is useful, both for assessing the need for insulin dose adjustment and explaining glucose concentrations that are out of range.

Perhaps the most difficult period of management in children with DM is puberty, a time when physical, cognitive, social, and behavioral changes make self-care and adherence more difficult. In addition, a relative insulin resistance can be seen in adolescents during pubertal development. Preadolescents, adolescents, and their caregivers benefit from education focusing on these expected changes and their potential implications for management. Other areas that should be reviewed are the social stigma of having DM, work, high-performance sports, alcohol and drug use, and the challenges surrounding special events (e.g., prom, homecoming).

Conclusion

Childhood and adolescence are periods of constant and rapid change, both internally and externally; this makes the treatment of DM potentially much more challenging than in adults. Although the basic guidelines and tools used in the treatment of DM in children are the same as for adults, adaptations must be made to accommodate the specific challenges presented by this population. A multidisciplinary, team-based approach allows more detailed investigation, improved patient and caregiver involvement, and creativity, elements required for success in reaching management goals in children and adolescents.

Annotated Bibliography

1. Gottshalk M, Danne T, Vlainic A, Cara J. Glimepiride versus metformin as monotherapy in pediatric patients with type 2 diabetes. *Diabetes Care* 2007;30:790–4.

Few studies directly assess the efficacy of oral diabetes drugs in children. This single-blind, randomized, comparative, international study included 285 adolescents (mean age 13.8 years) with type 2 DM who had inadequate glycemic control despite lifestyle modifications during at least 3 months of monotherapy with oral diabetes drugs. After

a 2-week stabilization period, subjects were randomized to receive either glimepiride initiated at 1 mg/day and gradually increased to 8 mg/day or metformin initiated at 500 mg twice daily and gradually increased to 2000 mg daily for 24 weeks. At the end of the study, subjects taking glimepiride had a 0.7% reduction in hemoglobin A1C, and those receiving metformin had a 0.85% reduction in hemoglobin A1C ($p=0.542$). The proportion of subjects who experienced one or more adverse events was similar in both groups. The frequency of clinically relevant hypoglycemia was also similar between metformin and glimepiride (8.5% vs. 10.6%, respectively; $p=0.554$). Subjects taking metformin had a significant change from baseline in BMI (-0.33 kg/m^2) compared with those taking glimepiride (0.26 kg/m^2) ($p=0.003$). Results of this study are applicable to the treatment of adolescents with oral drugs because this population formed the largest number of subjects and was assessed for the longest duration while receiving either metformin or a sulfonylurea. It is also the only comparative trial in this population.

2. American Diabetes Association. Type 2 diabetes in children and adolescents. *Diabetes Care* 2000;23:381–9.

Although it was published more than 8 years ago, this consensus statement from the ADA is still the most comprehensive recommendation by a large professional organization on the subject of type 2 DM in children and adolescents. This statement, which was developed by an eight-member panel of experts, continues to be supported by the American Academy of Pediatrics. It serves as the cited reference in the yearly updated ADA guidelines in the subsection related to the care of adolescents with type 2 DM. This consensus statement provides details on the pathophysiology and epidemiology of DM in children and adolescents. It clarifies the issues of how and why to appropriately distinguish between type 1 and type 2 DM in children and provides suitable screening criteria. This statement was the first to recommend initial pharmacotherapy with metformin in the absence of important acute complications such as significant hyperglycemia (in which insulin should be the initial treatment). This recommendation was lacking in the ADA's guidelines on the treatment of type 2 DM in adults until 2006. This statement concludes with general recommendations for the prevention or delay of onset of type 2 DM in overweight and obese children. It cites the lack of information on these subjects but recommends lifestyle modifications used successfully in adults with type 2 DM.

3. Silverstein J, Klingensmith G, Copeland K, Plotnick L, Kaufman F, Laffel L, et al. Care of children and adolescents with type 1 DM. A statement of the American Diabetes Association. *Diabetes Care* 2005;28:186–212.

Until this particular publication, the ADA provided little and rather general information in its yearly guidelines for treating type 1 DM in the pediatric population. This position statement provides a fairly complete, though not exhaustive, resource specifically addressing type 1 DM in children. It provides detailed information on the diagnosis, initial care, education, and nutrition requirements of this population. An overview of the age-specific blood glucose and hemoglobin A1C goals of therapy is presented, and the document explains many of the nuances and pitfalls of treating children with DM. Initiation and management of insulin therapy is discussed, and the statement strongly encourages basal/bolus insulin regimens either with numerous daily insulin injections or an insulin pump. Specific recommendations for the screening and treatment of both acute and chronic complications of

DM in children are also reviewed. Although there are many reviews on the topic of treating type 1 DM in the pediatric population, no other is as encompassing as this statement or is backed by a major professional organization dedicated to DM management.

4. American Diabetes Association. Clinical Practice Recommendations 2009. *Diabetes Care* 2009;32(suppl 1):S1–S98.

Although many professional organizations have published consensus recommendations on the treatment of DM, the most-recognized ones come from the ADA. These evidence-based guidelines are published yearly in the January supplement of *Diabetes Care*. Although not focused specifically on the treatment of children, the guidelines do provide specific recommendations for screening, diagnosis, and glycemic goals of treatment in this population. In addition, the Standards of Medical Care in Diabetes section provides an overview of general approaches to both type 1 and type 2 DM, medical nutrition therapy, physical activity, and evidence-based treatments and goals for diabetes-related complications. It also includes position statements on DM care in school and day care settings, as well as delineation of standards in DM self-care education. These guidelines refer to the more specific position statements from the ADA for more detail on the treatment of type 1 and 2 DM.

5. Chase H, Arslanian S, White N, Tamborlane W. Insulin glargine versus intermediate-acting insulin as the basal component of numerous daily injection regimens for adolescents with type 1 diabetes mellitus. *J Pediatr* 2008;153:547–53.

Although numerous studies have been published on the use of newer insulin products in the adult population, data are sparse regarding their use in children. This multisite, open-label study specifically addressed the concept of basal/bolus insulin therapy in adolescents (mean age 13 years) with type 1 DM. Use of the insulin analog glargine was compared with the more traditional insulins NPH and lente. Subjects (n=175) were randomized to receive either once-daily insulin glargine or twice-daily NPH or lente for 24 weeks. All subjects received prandial doses of insulin lispro. Basal insulin doses were titrated weekly to achieve target fasting plasma glucose concentrations between 70 mg/dL and 100 mg/dL. At the end of the study, the total daily insulin dose did not differ between the two groups (no p value given); however, the daily basal insulin dose was lower in the glargine group compared with the NPH/lente group (0.75 units/kg vs. 0.86 units/kg; $p=0.0143$). The mean change in hemoglobin A1C from baseline did not differ between the two groups ($p=0.1725$). The rate of hypoglycemic events (i.e., glucose concentration less than 70 mg/dL) per patient-year was higher in the insulin glargine group than in the NPH/lente group (116 vs. 94; $p=0.0298$). However, the event rate for severe hypoglycemia (an event requiring assistance from another individual and associated with either prompt recovery with glucagon, glucose, or oral carbohydrate or a blood glucose concentration less than 36 mg/dL) did not differ between the two groups. This study is the largest to assess the efficacy and safety of insulin glargine compared with NPH/lente in pediatric subjects. As in studies in adult patients, the glycemic control is similar to the use of the newer insulin analog. In this study, the rate of hypoglycemic events was higher in subjects receiving insulin glargine; however, smaller studies have shown reduced hypoglycemia, particularly nocturnal hypoglycemia, with the use of insulin glargine compared with NPH/lente.

6. Robertson K, Schoenle E, Gucev Z, Mordhorst L, Gall M, Ludvigsson J. Insulin detemir compared with NPH insulin in children and adolescents with type 1 diabetes. *Diabetic Medicine* 2007;24:27–34.

This study, the largest and longest clinical trial of its kind, evaluated basal/bolus insulin strategies. The use of the newer basal insulin analog detemir was compared with the use of NPH in both children and adolescents with type 1 DM. This multicenter, international study randomized children (n=347; age 6–17 years) to receive either insulin detemir or NPH (once or twice daily depending on the patient's basal regimen before randomization). Basal insulin doses were titrated to obtain a fasting glucose concentration between 81 mg/dL and 140 mg/dL. Subjects in both groups received premeal insulin aspart boluses, with a desired range of postprandial glucose concentrations between 121 mg/dL and 182 mg/dL. After 26 weeks of therapy, hemoglobin A1C levels in patients in both basal insulin groups were decreased by the same degree (0.8%), there were equal frequencies of once-daily basal insulin administration (about 30%), and neither the basal nor bolus daily insulin requirements differed between the two groups. Mean fasting plasma glucose concentrations were significantly lower in the subjects receiving insulin detemir compared with NPH (152 mg/dL vs. 173 mg/dL; $p=0.022$). Although the risks of severe or diurnal hypoglycemia were similar between the groups, the risk of nocturnal hypoglycemia was 26% lower in the insulin detemir group. This study is the first to evaluate the safety and efficacy of insulin detemir compared with traditional NPH therapy and showed that insulin detemir can be used safely in children and adolescents, providing similar hemoglobin A1C control with lower fasting glucose concentrations and decreased risk of nocturnal hypoglycemia.

7. Slingerland AS. Monogenic diabetes in children and young adults: challenges for researcher, clinician and patient. *Rev Endocr Metab Disord* 2006;7:171–85.

Forms of DM caused by genetic mutations are less common than type 1 and type 2 DM, and the availability of information for practitioners and the layperson regarding their management is limited. This article is one of the more comprehensive reviews of the subject and offers detailed information on all six genetic subtypes of MODY. The article covers the specific pathophysiology of the various mutations and resultant pancreatic beta-cell functional changes. Perhaps more beneficial to the practitioner is the discussion on the clinical manifestations seen with these variants. Beyond an atypically low insulin dose or even no insulin requirement to control the patient's blood glucose concentrations, this review points to several additional features that may indicate this type of DM. Key potential signs of MODY discussed include the extended honeymoon phase (longer than 3 years), absence of islet cell antibodies, presence of endogenous insulin, low ethnic risk of type 2 DM, and a normal or below-normal weight. The review offers a basic overview of management options including insulin, sulfonylureas, diet, and exercise; it does not address the lack of both short- and long-term evidence of safety and efficacy of sulfonylurea use in children. This review may be too advanced for a caregiver or child but is a good resource for practitioners.

8. Burdick J, Chase HP, Slover RH, Knievel K, Scrimgeour L, Maniatis AK, et al. Missed insulin meal boluses and elevated hemoglobin A1C levels in children receiving insulin pump therapy. *Pediatrics* 2004;113:e221–4.

These authors performed a cross-sectional study involving 48 youths who were receiving insulin pump therapy for type 1 DM. To identify causes of suboptimal glycemic control, the researchers evaluated missed mealtime boluses, pump disconnection, insulin use for exercise, and number of daily blood glucose measurements. Information sources included patient, caregiver, and practitioner questionnaires; insulin pump downloads; and glucose meter readings. Missed mealtime boluses correlated with increased hemoglobin A1C levels. Patients averaging less than one missed meal bolus per week had a mean hemoglobin A1C level of 8.0% compared with a mean hemoglobin A1C of 8.8% in those with an average of more than one missed meal bolus per week (mean, 2.1 missed boluses/week; $p=0.0001$). Although this study assessed how the youths managed insulin dosing for exercise, it did not include any information on the amount, type, or patterns of exercise that can affect blood glucose concentrations. It is also possible that there were other factors, not accounted for, that could have altered glucose concentrations (e.g., illness, other stressors). Overall, the study is informative regarding the effects of adherence on glycemic control. The correlation between missed meal boluses and increased hemoglobin A1C levels is important, but perhaps more clinically significant is the degree of increase. This study also included information gathered from patient and physician surveys, as well as objective data from the pump downloads regarding missed boluses. Data showed the patients underreported missed boluses by almost 50%. The authors discuss the reasons cited by patients for missed boluses and discuss a sample patient profile from a nonadherent adolescent. This article is quite informative regarding nonadherence in the treatment of DM in children, specifically regarding insulin pump use.

9. Jakisch BI, Wagner VM, Heidtmann B, Lepler R, Holterhus PM, Kapellen TM, et al. Comparison of continuous subcutaneous insulin infusion (CSII) and numerous daily injections (MDI) in paediatric type 1 diabetes: a multicentre matched-pair cohort analysis over 3 years. *Diabet Med* 2008;25:80–5.

This study is one of the larger and longer comparisons of insulin pump use with numerous daily injections in children. The authors performed a matched-pair analysis of 434 youths (mean age at inclusion 10.9 years) who managed type 1 DM during a 3-year period after converting from a conventional regimen to numerous daily insulin injections or converting from either injection regimen to an insulin pump. The study's matching criteria were detailed and extensive and included many variables that can affect DM management. Key findings were a decrease in hemoglobin A1C levels in the first year ($p=0.0058$), lower total daily insulin doses during all 3 years ($p=0.0009$), and a decrease in hypoglycemia rates ($p=0.0001$) for those using an insulin pump. The incidence of DKA was also lower in the insulin pump group but was lower at baseline and stayed consistent throughout the study period. To keep the matched pairs equivalent, patients in both groups were new to their respective regimens. The study design could have had an effect on the hypoglycemia and DKA rates, at least initially, because the learning curve to transition from a two or less daily injection regimen could be different when transitioning from numerous daily injections to an insulin pump. In addition, both groups had mean baseline hemoglobin A1C levels of 7.5% and a low degree of hypoglycemia representing good glycemic control and adherence. It is not clear whether these reported benefits would be similar in a population with poorer baseline glycemic control or adherence. Overall, this study demonstrates that insulin pump therapy in children is as safe and efficacious for

blood glucose control as a numerous daily insulin injection regimen. Some patients may achieve even tighter glycemic control safely with the use of an insulin pump.

10. Walsh J, Roberts R. *Pumping Insulin: Everything You Need for Success on a Smart Insulin Pump*, 4th ed. San Diego, CA: Torrey Pines Press, 2006.

This book is the latest edition of one of the more comprehensive references on the use of insulin pumps. The authors use both medical opinion and insulin pump users' experiences to detail pump management, discussing considerations for using an insulin pump as well as how to initiate a regimen. The book's sections include specialized issues of care and self-care. This updated edition will be useful to practitioners who are new to insulin pump therapy, as well as those already experienced with this therapy. This book is also a great resource for general insulin management because many chapters cover material pertinent to numerous daily injection regimens (e.g., carbohydrate counting, I:CHO and ISF, basal dosing, sick-day management). Not everything in the book can be directly applied to the pediatric population, and the sections devoted to pediatric issues are not as detailed as those for adults. However, the authors do discuss some nuances of care in adolescents, including the use of separate basal programs to compensate for menstruation-related glucose increases and the use of various pump features to assist in control during sports and exercise. This book is detailed enough for practitioners but would also be a good resource for older children and their caregivers.

SELF-ASSESSMENT QUESTIONS

1. A physician in your multidisciplinary endocrinology clinic asks you to develop an initial insulin treatment plan to provide 0.05 units/kg/day. The patient is a 15-year-old girl (weight 40 kg, 35th percentile for age) with type 1 diabetes mellitus (DM) diagnosed today secondary to a markedly elevated blood glucose concentration (525 mg/dL), low C-peptide concentration, and recent weight loss. The patient's urine is negative for ketones, and she complains of polyuria. Which one of the following is the best insulin regimen to initiate in this patient?

- A. Insulin glargine 13 units subcutaneously once daily in the morning and regular insulin 3 units 30 minutes before each meal.
- B. Neutral protamine Hagedorn (NPH) insulin 8 units and insulin lispro 5 units subcutaneously 30 minutes before the morning meal and NPH 4.5 units and insulin lispro 2.5 units subcutaneously 30 minutes before the evening meal.
- C. Insulin detemir 10 units subcutaneously once daily in the morning and insulin aspart 3 units 15 minutes before each meal.
- D. Insulin glargine 10 units subcutaneously once daily in the morning and insulin glulisine 3 units 15 minutes before each meal.

2. N.F., a 4-year-old girl (weight 14 kg, 25th percentile for age; height 100 cm, 50th percentile for age) with type 1 DM, is seen in the clinic today for a 6-week follow-up visit. Her mother says they are getting used to their schedule and that N.F. is doing well, although she does not always want to finish all the food on her plate. N.F. is starting to take an active role in her management and is not fighting the shots or tests as much. She points to the spot where she wants the injection, and she presses the button on the lancing device for the glucose measurements. Her mother's only concern is that N.F. has higher blood glucose concentrations in the evening. Her hemoglobin A1C at this visit is 7.9%.

N.F. is taking the following regimen: insulin aspart subcutaneously three times/day at meals and as directed per carbohydrate and correction ratios; insulin glargine 2 units subcutaneously at dinnertime; insulin-to-carbohydrate ratio (I:CHO) 1:30 (1 unit of insulin for every 30 g of carbohydrates); insulin sensitivity factor (ISF) 400 (1 unit of insulin for every 400 mg/dL over target); and glucose target 150 mg/dL. Blood glucose records from the past 5 days are as follows:

Time	Carbohydrate Intake (g)	Blood Glucose (mg/dL)				
		Day 1	Day 2	Day 3	Day 4	Day 5
7:30 AM	Breakfast (30)	95	144	138	162	118
10:00 AM	Snack (15)	165	175	215	193	158
Noon	Lunch (30)	90	140	166	132	76
3:30 PM	Snack (15)	110	154	182	135	157
6:30 PM	Dinner (30)	255	285	289	265	302
9:30 PM	Snack (15)	150	140	156	132	155
12:30 AM		110	101	114	95	120

Based on N.F.'s blood glucose record, which one of the following is the best intervention to make in her therapy at this time?

- A. Discontinue N.F.'s snack at 3:30 PM.
- B. Split the insulin glargine dose into 1 unit twice daily.
- C. Increase the lunchtime insulin aspart dose to 1.5 units.
- D. Increase the dinnertime insulin glargine dose to 2.5 units.

3. S.L. is a 15-year-old boy (weight 64 kg, 75th percentile for age; height 170 cm, 50th percentile for age) with type 1 DM in the clinic for a scheduled visit. He says he is doing well and has no concerns. S.L.'s parents agree that he is doing a good job following his regimen, but they are concerned about the erratic blood glucose concentrations he has at lunch, with some of them being low. S.L. says he is doing well in school and participates in sports. He has an athletics period from 9:00 AM to 10:00 AM, and he practices after school. He is active with friends in the evenings after dinner. He is sleeping well and believes he gets enough food at meals. He states he is rotating his injection sites and administering his insulin, but about once every 1–2 weeks, he forgets to test his blood glucose. His hemoglobin A1C level this visit is 7.1%. S.L. is on the following regimen: insulin aspart subcutaneously three times/day at meals and as directed per carbohydrate and correction ratios; I:CHO of 1:10; ISF 30; glucose target 130 mg/dL; and insulin glargine 22 units subcutaneously at dinnertime. Blood glucose records from the past 5 days are as follows:

Time	Carbohydrate Intake (g)	Blood Glucose (mg/dL)				
		Day 1	Day 2	Day 3	Day 4	Day 5
7:00 AM	Breakfast (75)	118	95	132	111	89
11:00 AM	Lunch (75)	324	59	210	65	122
3:30 PM	Snack (15)	91	154	105	135	101
6:30 PM	Dinner (75)	155	202	155	165	169
9:30 PM	Snack (15)	122	140	106	118	100
12:30 AM		125	182	123	145	166

Given S.L.'s blood glucose record, which one of the following is the best therapeutic recommendation for him at this time?

- A. Add a snack at 9:00 AM before the athletic activities.
 - B. Reduce S.L.'s breakfast insulin aspart bolus by 1 unit.
 - C. Test S.L.'s blood glucose before and after athletic activity.
 - D. Tell S.L. that he cannot participate in athletic activity.
4. R.S. is a 17-year-old adolescent (height 165 cm; weight 82 kg; body mass index [BMI] 30 kg/m², greater than the 95th percentile for age) who received a diagnosis

of type 2 DM 6 months ago, after which his primary care physician recommended lifestyle modifications and initiated him on metformin 500 mg twice daily. At diagnosis, R.S.'s hemoglobin A1C level was 8.1%. Last week, his hemoglobin A1C level was 7.6%. R.S. forgot his glucometer and his blood glucose log at home, but he states that his fasting glucose concentrations during the past 1–2 weeks ranged from 135 mg/dL to 160 mg/dL. His blood pressure and lipid concentrations are well controlled. He states he is tolerating the metformin well. Which one of the following is the best treatment option for R.S. at this time?

- Add exenatide 5 mcg subcutaneously twice daily.
 - Increase R.C.'s metformin dosage to 1000 mg twice daily.
 - Discontinue metformin and start pioglitazone 15 mg/day.
 - Add insulin lispro 5 units subcutaneously 15 minutes before meals.
5. A physician with whom you collaborate in a family medicine clinic approaches you requesting guidance on a new patient. The 16-year-old African American patient (weight 73.6 kg; BMI 32 kg/m², greater than the 95th percentile for age) was discharged 2 days ago from a local hospital after recovering from diabetic ketoacidosis (DKA). Before her hospital admission, she had no history of DM. Her only family member with DM is her grandmother. The patient's laboratory values at hospital discharge were hemoglobin A1C 9.9%; fasting C-peptide 3.2 ng/mL (normal, 0.5–2.0 ng/mL); and insulin autoantibodies, negative. Her fasting plasma glucose concentration is 213 mg/dL, and her urine is negative for ketones. Given the information provided, which one of the following is the most likely diagnosis for this patient?
- Type 1 DM.
 - Type 2 DM.
 - Hybrid DM.
 - Maturity onset diabetes of the young (MODY).
6. H.T. is a 15-year-old adolescent boy (BMI 36 kg/m², greater than the 95th percentile for age, which is similar to his BMI at diagnosis) who was given a diagnosis of type 2 DM 2 years ago. His hemoglobin A1C level at diagnosis was 12.8%; 9 months ago, it was 6.9%, and today, it is 8.4%. H.T.'s blood pressure today and his fasting lipid panel 3 months ago are at target goals. He currently takes metformin 1000 mg twice daily, has been on this regimen for 12 months, and states he is adherent. According to his glucose log for the past 2 weeks, his fasting glucose concentrations in the morning have ranged from 190 mg/dL to 240 mg/dL. H.T. rarely checks his glucose at other times of the day unless he feels symptoms of hypoglycemia, which has not occurred in more than 1 month. In addition to continued reinforcement of adherence to lifestyle modifications, which one of the following is the best treatment option for H.T. at this time?

- Continue metformin and add sitagliptin 100 mg once daily.
 - Discontinue metformin and initiate a weight-based basal/bolus insulin regimen.
 - Discontinue metformin and initiate glyburide 10 mg twice daily.
 - Continue metformin and add glimepiride 4 mg once daily.
7. E.S. is a 14-year-old girl (weight 49 kg, 50th percentile for age) who has had type 1 DM since age 12. She uses a combination of NPH and regular insulin, and her hemoglobin A1C level is 8.7%. Today, she complains of an increased frequency of low blood glucose concentrations in the early morning hours. Because these events used to be fairly rare but now occur four or five times per week, she is concerned. E.S.'s current basal insulin regimen is NPH 32 units subcutaneously in the morning and NPH 18 units in the evening. She counts carbohydrates at each meal and uses an I:CHO of 1:10. E.S. has been checking her glucose concentrations before each meal and before bedtime. Her most recent blood glucose concentrations (mg/dL) are as follows:

Time	Blood Glucose (mg/dL)			
	Day 1	Day 2	Day 3	Day 4
Morning fasting	168	177	165	189
Pre-lunch	106	99	122	77
Pre-dinner	113	121	134	102
Bedtime	155	128	142	131

Which one of the following is the best change to optimize E.S.'s glycemic control while minimizing her risk of early morning hypoglycemia?

- Increase the NPH to 35 units in the morning and continue 18 units in the evening.
- Change the NPH to insulin detemir using the current morning and evening NPH doses.
- Change the NPH to insulin glargine using the current morning and evening NPH doses.
- Continue NPH 32 units in the morning and increase to NPH 22 units in the evening.

Questions 8–10 pertain to the following case.

D.D. is a 6-year-old boy (weight 18 kg, 10th percentile for age) who has just been given a diagnosis of type 1 DM after presenting with DKA. He is now stable and ready to be transitioned from intravenous to subcutaneous insulin. D.D. has been receiving an average daily insulin dosage of 8.5 units, and his blood glucose concentrations have ranged from 90 mg/dL to 230 mg/dL.

8. Which one of the following basal insulin regimens is best to initiate in D.D.?
- Insulin detemir 2 units subcutaneously in the morning and 2 units in the evening.
 - Insulin glargine 8.5 units subcutaneously at bedtime.
 - Insulin detemir 4 units subcutaneously at bedtime.
 - Insulin glargine 3 units in the morning and 2 units in the evening.

9. Which one of the following bolus insulin regimens is best to initiate for D.D.'s meal coverage?
- 1:15 using insulin aspart.
 - 1:15 using regular insulin.
 - 1:30 using insulin lispro.
 - 1:60 using insulin lispro.
10. Which one of the following is best to initiate for D.D.'s ISF for correctional insulin dosing?
- 50 (1 unit insulin for each 50-g/dL increase above target goal).
 - 60 (1 unit insulin for each 60-g/dL increase above target goal).
 - 150 (1 unit insulin for each 150-g/dL increase above target goal).
 - 200 (1 unit insulin for each 200-g/dL increase above target goal).

Questions 11–13 pertain to the following case.

S.J. is an active 16-year-old boy (weight 61 kg, 50th percentile weight for age). He just received a diagnosis of type 1 DM in the outpatient clinic based on symptoms, elevated blood glucose concentrations, a low C-peptide concentration, and the presence of insulin autoantibodies. S.J. is currently not receiving insulin, but he is in the clinic today to be initiated on an insulin regimen. His diet usually provides 75–90 g of carbohydrates per meal.

11. Which one of the following basal insulin regimens is best to initiate in S.J.?
- Insulin detemir 15 units subcutaneously in the morning and 15 units in the evening.
 - Insulin glargine 15 units subcutaneously at bedtime.
 - Insulin detemir 30.5 units subcutaneously at bedtime.
 - Insulin glargine 8 units subcutaneously in the morning and 8 units in the evening.
12. Which one of the following is the best bolus insulin regimen and I:CHO to initiate for meal coverage for S.J.?
- 1:8 using insulin aspart.
 - 1:15 using insulin aspart.
 - 1:30 using insulin lispro.
 - 1:60 using insulin lispro.
13. Which one of the following is the best ISF for correctional dosing for S.J.?
- 15 (1 unit of insulin for each 15-g/dL increase above target goal).
 - 30 (1 unit of insulin for each 30-g/dL increase above target goal).
 - 60 (1 unit of insulin for each 60-g/dL increase above target goal).
 - 100 (1 unit of insulin for each 100-g/dL increase above target goal).

Questions 14 and 15 refer to the following case.

B.B. is a 12-year-old girl (weight 43 kg, 50th percentile for age) in the clinic this morning to initiate insulin pump therapy. She recently has adhered more often to her therapeutic regimen and is excited about getting the pump. B.B. has reviewed the educational material several times. About 6 weeks ago, her hemoglobin A1C level was 9.2%. B.B. is currently on the following regimen: insulin aspart injected subcutaneously three times/day at meals dosed per carbohydrate and correction ratios; I:CHO 1:15; ISF 50; glucose target 130 mg/dL; and insulin glargine 14 units subcutaneously at dinner (held last night in preparation for insulin pump start). Her blood glucose records from the past 5 days are as follows:

Time	Carbohydrate Intake (g)	Blood Glucose (mg/dL)				
		Day 1	Day 2	Day 3	Day 4	Day 5
3:30 AM		142	172	140	180	158
7:00 AM	Breakfast (75)	145	165	132	185	163
9:00 AM		192	199	185	230	183
11:00 AM	Lunch (75)	118	120	106	99	122
3:30 PM	Snack (15)	91	86	105	135	101
6:30 PM	Dinner (75)	115	118	130	116	110
9:30 PM	Snack (15)	100	109	145	126	100
12:30 AM		136	145	135	146	160

14. Which one of the following is the best insulin basal regimen at which to start B.B.'s insulin pump (which can be adjusted in increments of 0.025 units/hour)?
- 0.45 units/hour from 7:00 AM to 7:00 AM (i.e., 24 hours/day).
 - 0.6 units/hour from 7:00 AM to 7:00 AM (i.e., 24 hours/day).
 - 0.3 units/hour from 7:00 AM to midnight and 0.25 units/hour from midnight to 7:00 AM.
 - 0.525 units/hour from 7:00 AM to midnight and 0.625 units/hour from midnight to 7:00 AM.
15. Which one of the following is the best insulin aspart bolus regimen (I:CHO) to initiate for B.B.'s meal coverage?
- 1:10.
 - 1:15.
 - 1:23.
 - 1:30.
16. L.B., a 5-year-old boy (weight 16 kg, 25th percentile for age) with type 1 DM, is in the clinic today for a 6-week follow-up. L.B.'s hemoglobin A1C level today is 8.7%; 3 months ago, it was 7.8%. L.B. is very active and is cared for during the day by his mother. Adherence to his therapeutic regimen appears to be correct, and his mother voices no concerns. Recently, his mother noticed that his blood glucose concentrations are a little higher and more erratic than in the past. He is receiving insulin by means of a pump. He boluses insulin for all meals and snacks and adds correction amounts to these as necessary using the advanced pump features to calculate recommended doses based on blood glucose concentrations, carbohydrate intake, and insulin action. L.B.'s regimen is as follows: insulin lispro subcutaneously by insulin pump at a basal rate

of 0.05 units/hour from 7:00 AM to 9:00 PM and 0.075 units/hour from 9:00 PM to 7:00 AM; I:CHO of 1:20 for breakfast from 7:00 AM to 11:00 AM, I:CHO of 1:25 for lunch from 11:00 AM to 5:00 PM, I:CHO of 1:30 for dinner from 5:00 PM to 7:00 AM; ISF 350; and glucose target 150 mg/dL. Blood glucose records from the past 5 days are as follows:

Time	Carbohydrate Intake (g)	Blood Glucose (mg/dL)				
		Day 1	Day 2	Day 3	Day 4	Day 5
3:30 AM		165	150	155	165	145
7:00 AM	Breakfast (45)	225	199	185	250	206
9:00 AM	Snack (15)	160	170	200	155	158
11:00 AM	Lunch (45)	99	140	135	118	96
2:00 PM	Snack (15)	100	100	182	106	122
5:30 PM	Dinner (45)	87	99	112	120	93
9:30 PM	Snack (15)	150	106	108	132	101
12:30 AM		116	135	144	130	120

Which one of the following is the best intervention to make in L.B.'s insulin therapy at this time?

- Increase the basal insulin rate to 0.15 units/hour for 24 hours/day.
 - Create an additional basal insulin rate of 0.1 units/hour from 3:00 AM to 7:00 AM.
 - Change the breakfast I:CHO to 1:15.
 - Change the breakfast I:CHO to 1:25.
17. During the visit of a 4-year-old child with type 1 DM, the mother complains of difficulties during some injection times. She states her son will sometimes push her away or kick at her when she tries to give him his injection. In addition, he sometimes tries to take the syringe or insulin away from her. She tells him he is too young to touch the supplies, which makes him mad. She asks if you have any suggestions to help minimize these outbursts. Which one of the following is the best information to give this mother?
- Encourage her to give injections in the upper buttocks so the child cannot see her doing it.
 - Encourage her to continue to warn the child not to touch the supplies until he is at least 6 years old.
 - Encourage her to let her son pick the injection site until he can be more involved.
 - Encourage her to kneel on her son's legs while injecting until he learns to deal with the injections.
18. A 17-year-old girl (weight 50 kg, 25th percentile for age) with type 1 DM is currently being treated with a combination of insulin glargine and insulin aspart. She is receiving insulin glargine 1 unit subcutaneously at dinner and insulin aspart 1:60 with an ISF of 400 before meals. She does not complain of hypoglycemic episodes and believes her blood glucose concentrations are usually in the target range. She has been on this regimen for 4 years (since her diagnosis), and her hemoglobin A1C levels have ranged from 6.1% to 7% during that period. Her mother is concerned about her daughter's treatment because she knows other children her daughter's age who are receiving much higher insulin doses. She knows that her daughter's blood glucose concentrations are high if she misses her insulin dose but still wonders if something has been missed or

if she even has DM. Which one of the following is the best explanation for this patient's presentation?

- She is probably still in her honeymoon period, which can last a very long time.
 - She probably does not have DM; more tests should be ordered.
 - She probably has type 2 DM, so her needs are different from those of children with type 1 DM.
 - She probably has a type of DM known as MODY.
19. You have been asked by a colleague to assist with a new patient, a 15-year-old girl (weight 52 kg, 50th percentile for age) who recently moved from another state. From a review of her previous health records, you know she has type 1 DM and is currently using an insulin pump. Her most recent hemoglobin A1C level was 8.2%. According to her medical records, she uses two distinctly different daily basal insulin programs: one that uses about 20% more insulin daily for 5-day to 6-day periods each month and another that is used the rest of the time. Your colleague asks your opinion on the reason for the 5-day to 6-day (short) program. Which one of the following is the most likely reason for this program?
- She uses it for exercise.
 - She uses it during her menstrual cycle.
 - She uses it to compensate for nonadherence.
 - She uses it to compensate for insulin resistance.
20. C.P. is a 13-year-old boy (weight 52 kg, 75th percentile for age; height 168 cm, 75th percentile for age) with type 1 DM. His weight and height have been tracking the 75th percentile growth curves for the past 2 years. C.P. is in the clinic for his 6-week follow-up. He believes things are going well, and his blood glucose concentrations are usually within the target range. He has not had a hypoglycemic excursion for more than 1 year. His father is concerned, however, because C.P.'s insulin dose requirements have increased dramatically during the past year. C.P.'s hemoglobin A1C levels, from the oldest to most recent, were 8.0%, 8.5%, 7.9%, and 7.6%. His corresponding total daily insulin dosages were 0.5 units/kg, 0.6 units/kg, 0.65 units/kg, and 0.75 units/kg, respectively. Which one of the following is the best explanation for the increase in C.P.'s insulin requirements?
- He is going through puberty and requires a greater amount of insulin.
 - He is developing type 2 DM and requires a greater amount of insulin.
 - He is not adhering to his regimen; thus, it only appears that a greater amount of insulin is required.
 - He is increasing in weight; thus, he requires a greater amount of insulin.