One of the many consequences of the worldwide increase in obesity rates is increased rates of diabetes in both adults and children. In 2010, approximately 215,000 people younger than age 20 years in the United States had type 1 diabetes mellitus (T1D) or type 2 diabetes.

In children and adolescents, T1D is the most frequently diagnosed type of diabetes. In the United States, the incidence of T1D in children younger than age 10 years was estimated to be 19.7 per 100,000 each year from 2002 to 2005, and this rate increases with age. Within the age group of 0 to 14 years, the highest incidence is found among children age 10 to 14 years, followed by those age 5 to 9 years, and then those age 0 to 4 years.

**METHODOLOGY**

A PubMed literature search was conducted to identify relevant peer-reviewed clinical and review articles published between January 2000 and May 2013 related to T1D in children. Search terms included “type 1 diabetes,” “children,” “pediatric,” “insulin,” “insulin analogues,” “rapid-acting,” “long-acting,” “basal insulin,” “bolus insulin,” “aspart,” “lispro,” “glulisine,” “glargine,” “detemir,” “multiple daily injections or MDI,” and “external pumps, continuous subcutaneous insulin infusion, or CSII.” Case studies and editorials were excluded. Clinical study design, methodology, and clinical relevance were assessed. Additionally, the bibliographies of articles of interest were reviewed. A total of 37 articles were selected and analyzed.

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**TREATMENT CHALLENGES**

T1D in pediatric patients presents unique treatment challenges. For example, management of T1D must account for differences among children of various ages and adults, and insulin doses based only on body size are likely to be incorrect. This “one size fits all” strategy does not work well for pediatric patients because of the gamut of sizes and ages in patients with diabetes. However, health care providers must have generalized ways of managing pediatric patients with T1D in order to have systemization. Puberty, which may dictate the need for a higher dose of insulin due to hormonal changes, can impact the risk for diabetic complications. The “dawn phenomenon” — a steep rise in glucose levels in the early morning — has been reported in children younger than age 6 years. Achieving tight glycemic control while reducing the risk for hypoglycemia is challenging because young patients depend on caregivers (eg, parents, daycare providers, school nurses) at home and school for diabetes care. Furthermore, young patients have variable patterns regarding mealtime and exercise, and the general fear of hypoglycemia and its sequelae increases the risk of hyperglycemia. Thus, diabetes management should be adjusted to the age and developmental stage of the patient, so involving and engaging parents and caregivers is crucial.

Current clinical evidence supports the use of intensive diabetes management to slow the progression of vascular and neurologic complications of diabetes in adults and adolescents. Benefits of tighter glycemic control also have been observed in pre-adolescent patients. Therefore, guidelines from the American Diabetes Association (ADA) recommend glycated hemoglobin (HbA1c) levels of < 8.5% for toddlers and preschool children, < 8% for school-aged children, and < 7.5% for adolescents and young adults. However, the drawbacks of intensive insulin therapy can include hypoglycemia and weight gain. The risk for adverse neurologic effects of hypoglycemia may be greatest in very young children. Appropriate use of insulin pumps may assist in avoiding these complications.

**INSULIN ANALOGUES**

Basal-bolus insulin dosing provides the greatest level of glucose control and flexibility. For children or adolescents with T1D, the American Association of Clinical Endocrinologists (AACE) recommends basal-bolus insulin regimens delivered through either multiple daily injections (MDI) or external pumps (continuous subcutaneous insulin infusion [CSII]). The potential benefits and drawbacks of each should be considered when choosing therapy for individual patients (Table 1).

The long-acting (basal) insulin analogues, glargine and detemir, are approved for use in children with T1D either alone or in combination with prandial (rapid-acting) insulin analogues. The long-acting analogues have onsets of effect from ≤ 1 to 4 hours, but the effects can last up to 24 hours. The rapid-acting analogues, lispro, aspart, and glulisine, are also approved for use in children with T1D and have an onset of action of 5 to 15 minutes, with a duration of effect of a few hours. The favorable pharmacologic attributes of rapid-acting analogues when administered in a basal-bolus regimen led to superior or equal efficacy compared with regular human insulin in patients with T1D. Moreover, long-acting insulin analogues are injected once daily, are associated with a lower incidence of hypoglycemia, and are available in a pen device (as are the rapid-acting analogues), all of which are advantageous for pediatric patients.

**Clinical Studies of Rapid-Acting Analoguecs in Pediatric Patients**

A study of children with T1D younger than age 7 years compared CSII with...
aspart, MDI with aspart (with intermediate-acting neutral protamine Hagedorn [NPH]), and MDI with recombinant human insulin (with NPH). The mean age of participants was 5.2, 5.4, and 5.7 years in the three groups, respectively. Efficacy was equivalent among the three groups, although caregivers reported greater satisfaction with treatment with aspart CSII. Similarly, a large non-inferiority study (n = 572) of glulisine and lispro as part of a basal-bolus regimen in children and adolescents with T1D (mean age, 12.5 years) found comparable efficacy between the two rapid-acting analogues.

To reduce the number of daily injections, some practitioners may combine long- and rapid-acting insulin analogues into one injection, although this is not recommended by the manufacturers. A study of 11 adolescents (mean age, 15.1 years) with T1D demonstrated that co-administration of lispro with glargine reduced the early pharmacodynamic peak of lispro and caused a shift to the right in the glucose infusion rate curve. Similarly, a study of eight adolescents (mean age, 17.3 years) with T1D found that the co-administration of aspart with detemir as a single mixed injection diminished the early action of aspart and prolonged its time action profile. However, another study of adolescents (n = 14; mean age, 14.75 years) found equivalent effects of co-administration on blood glucose compared with separate administration.

Clinical Studies of Long-Acting Analogues in Pediatric Patients

One pharmacokinetic study of children and adolescents (mean age, 13 years) compared the profiles of detemir and glargine. In this study, detemir was associated with a more reproducible pharmacokinetic profile than glargine in children and adolescents.

A subanalysis of patients with T1D age 2 to 5 years from a randomized, open-label trial comparing detemir with NPH was conducted. In this limited age group (n = 82; mean age, 4.4 years), detemir provided similar glycemic control compared with NPH. Another study in children age 2 to 16 years demonstrated that detemir was non-inferior to NPH after 52 weeks and was associated with a significantly lower risk of hypoglycemia and significantly lower weight standard deviation score compared with NPH.

All of our patients whose initial treatment is insulin therapy are started on long-acting insulin, along with a rapid-acting insulin.

A study of 34 children and adolescents (mean age, 12.7 years) found that switching from NPH to glargine or detemir resulted in a significant reduction in HbA1c levels (P < .05 for both). Significant differences were not observed between the glargine and detemir groups, although the detemir group had a smaller increase in body mass index (BMI) compared with either the NPH or glargine groups (P < .05 for both). Because this study lasted for 6 months, the BMI results may have been influenced by growth during the study. Moreover, a large prospective study (n = 10,682) examined the use of glargine or detemir compared with NPH in children and adolescents with T1D (mean age, 15.0 and 13.5 years in the long-acting and NPH groups, respectively). In this study, the incidence of diabetic ketoacidosis was higher in patients using insulin glargine or detemir compared with those using NPH (6.6 ± 0.4 vs 3.6 ± 0.3; P < .001).

An ultra-long-acting insulin analogue, degludec, has been approved for the treatment of adults with T1D in Europe, Japan, and Mexico. In the United States, the Food and Drug Administration has requested more data to complete its review. No efficacy studies of degludec in children have been reported, although a study of degludec in children and adolescents with T1D is in progress. Another novel long-acting basal insulin in development consists of pegylated lispro, a large hydrodynamic molecule that slows absorption and reduces clearance, resulting in a prolonged duration of action. Likewise, no efficacy studies of pegylated lispro in children have been reported.

AUTHORS’ CLINICAL EXPERIENCE IN DIABETES MANAGEMENT

All of our patients whose initial treatment is insulin therapy are started on long-acting insulin, such as glargine or detemir, along with a rapid-acting insulin such as aspart, lispro, or glulisine. We begin treatment with insulin pens because they are easy to use for patients or caregivers. Ideally, we also have the patients take insulin before meals in order to achieve blood sugar control. Because glycemic control in the first year after diagnosis of diabetes is predictive of future glycemic control, we provide the most intensive patient education during this time.

The decision to switch to CSII may be made after this time if the patient and family are well educated regarding diabetes care and are interested in switching. CSII can be initiated at any age, and it may particularly benefit younger children, as very small doses and dose changes can be implemented. Additionally, CSII eliminates multiple injections per day, as the insertion site only has to be changed every 2 to 3 days. However, use of CSII may be limited by the maturity and experience of the child and his or her caregivers. Also, because CSII does not provide a reserve of insulin, as does a basal insulin, risk for diabetic ketoacidosis is increased if insulin delivery is disrupted. However, some patients...
elect to use a long-acting basal insulin in select cases, while using their insulin pumps for food and blood sugar boluses. Although advances in CSII have led to greater convenience and flexibility, these advances are associated with increased treatment complexity. Therefore, care and good clinical judgment must be taken in choosing between MDI and CSII. 

Once the patient has switched to CSII, we provide the patient and family with support through good rapport between staff and patient, preparatory classes, and follow-up between appointments to monitor blood glucose and determine whether changes in the insulin regimen are necessary. We teach our patients how to download their results from their devices and print out reports for review, and then reward them with small tokens such as gift cards to Target® and other stores. In this way, it incentivizes patients to download their device and gives them, as well their health care providers, useful data. This can then demonstrate to patients the importance of these data in their care and may prompt them to continue to download. In addition, we recommend the use of a continuous glucose monitoring system. This device connects to the patient like an insulin pump, where a small, subcutaneous catheter is placed and provides continuous blood sugar measurements from the interstitial fluid. This valuable information helps both the patients and health care providers identify blood sugar trends and can also aid in adjustments to their insulin regimen.

### ENGAGING CAREGIVERS

The chronic care model must be applied to both the patients with T1D and their caregivers. Engaging the caregivers is most important in the youngest patients, whereas management of older children and adolescents can include increased focus on the patient. However, caregivers are intermediaries between the pediatric endocrinology team and the patients, and they must achieve confidence in implementing recommended treatment strategies (Table 2).

Treatment strategies consistent with the needs of the patient and the parents should be developed. A team approach should be implemented soon after diagnosis. This includes early psychosocial assessment of the family and involvement of a social worker or psychologist who can identify the needs of the family and transmit those needs to the team. In our practice, we have found that a small proportion of patients often make up a large percentage of diabetes readmissions. Implementing the team approach is important in addressing the patients’ needs and psychosocial issues, and in breaking the cycle of inadequate treatment.

Treatment of T1D in infants is focused on providing parents with immediate access to the diabetes team. Because toddlers cannot yet understand the need for glucose monitoring and insulin injections, they require consistent care and can benefit from a positive approach from parents. As children mature, the responsibility for care shifts from the caregivers to the patient (the “emerging adulthood” stage). This stage requires patients, their families, and healthcare providers to find a balance between respecting the patient’s independence and providing oversight and support.

Additionally, our clinic is nurse-centered to ensure provider continuity and achieve better diabetes care. We empower nurses by allowing them to “adopt” these patients and see them on their own under the health care provider’s supervision during certified diabetes educator visits. We also have extended this model to include an endocrinology hospitalist, such that the same attending physician covers all inpatient diabetes patients and helps to implement the best care possible. New patients are sent to a diabetes education center to begin their diabetes education, learn about insulin pumps, or just to review daily diabetic management. Support groups and other activities provided for our patients allow children to meet other children with diabetes and parents to meet other parents of children with diabetes.

A transition clinic is available for the older adolescent patients with diabetes to transition them to adult endocrinologists. Also, an adult endocrinologist sees transitioning patients with us to develop a rapport with the patient and address issues that may occur in adult patients with diabetes.

To engage the members of our team, we share the responsibilities of total patient care with nurses, nutritionists, and social workers. Therefore, the members of the team have a sense of responsibility for the well-being of their patients. We also allow, encourage, and support the members of the team to further explore diabetes care through conferences and other educational forums.

### UNDERSTANDING POOR DIABETES MANAGEMENT

Many endocrinology healthcare providers contemplate why their patients

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### Table 2: Methods to Engage Caregivers of Children with Type 1 Diabetes

<table>
<thead>
<tr>
<th>Step</th>
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<tbody>
<tr>
<td>Emphasize a team approach (including a social worker or psychologist to identify needs of the family).</td>
</tr>
<tr>
<td>Provide parents with good access to the diabetes team.</td>
</tr>
<tr>
<td>Consider nurse-centered care to ensure provider continuity.</td>
</tr>
<tr>
<td>Use an endocrinology hospitalist (so the same attending physician covers all inpatient diabetes patients).</td>
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<tr>
<td>Encourage new patients/families to go to a diabetes education center.</td>
</tr>
<tr>
<td>Inform parents/patients about support groups for parents and children.</td>
</tr>
<tr>
<td>Share the responsibilities of total patient care with your team and encourage them to further their own knowledge of the condition.</td>
</tr>
</tbody>
</table>

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- Share the responsibilities of total patient care with the team and encourage them to further their own knowledge of the condition.

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are nonadherent with their diabetes regimen. What makes them not take their insulin, check their blood sugars, or not do the other aspects of their diabetes care? In a meta-analysis of pediatric observational studies, it was found that only approximately 38% of patients on pump therapy achieved the ADA HbA1c goal when a sensor-augmented pump was used. The SEARCH for Diabetestes in Youth Study demonstrated that in 2999 youths, only 44% met the ADA glycemic goals for their age. Elevated HbA1c levels and hyperglycemia are symptoms, and it is important to determine the root of these symptoms. Is it because we are not providing patients with adequate education to manage their diabetes? Could it be that they are not motivated to care? Is it lack of home supervision by parents or, more seriously, is it a mental health issue that we are not addressing? By finding out the root of the problem and addressing it, we can help patients to achieve better control of their diabetes. However, because this root can be multifaceted, it takes a team of nurses, doctors, social workers, and others to address these issues, and that is why a multidisciplinary approach to diabetes is key.

Screening

Screening is key to the proper care of patients with diabetes. Early detection of diabetes is important to avoid the co-morbidities of diabetes. In addition, proper diagnosis of diabetes is equally as important as early detection. For example, many studies have shown that maturity-onset diabetes of the young (MODY), or monogenic diabetes, has been erroneously diagnosed as T1D. The fundamental issue is that MODY, unlike T1D, is treated with oral medication and these patients tend to respond better to oral medications than to insulin. Whether this is from better adherence or better response, the end result is that these patients have improvement in their HbA1c level. In one study conducted by our group and a collaborating center, we found that we were able to diagnose MODY in patients whose original diagnosis was T1D, and then successfully switched these patients to oral medication. This patient group had near normalization of their HbA1c levels. This again illustrates the importance of screening in diabetes management and care.

In addition, we perform an annual screening on all of our patients with diabetes to monitor the development of co-morbidities. This screening includes evaluation for other autoimmune diseases such as celiac disease, autoimmune thyroiditis, and Addison’s disease, as well as screening for lipid levels and urine microalbumin. We also monitor blood pressure, and for those who are found to have elevated blood pressure on multiple visits, we have them perform ambulatory blood pressure monitoring.

CONCLUSION

Many challenges surround implementation of effective care in children with T1D that are not encountered with adult patients. Moreover, changes in the population, such as increasing rates of obesity, further complicate the diagnosis and treatment of T1D in children. However, evolving diagnostic and treatment options provide opportunities for improving and individualizing care. The favorable pharmacological attributes of insulin aspart, glulisine, and lispro, as well as several advantages of long-acting insulin analogues, including once-daily injection of insulin glargine, lower incidence of hypoglycemia, and availability in a pen device, are attractive options for pediatric patients. In addition to advances in pharmacological therapy, diabetes education, CSII, CGMS technology, and caregiver involvement in the treatment of the youngest patient group are important aspects of disease management. Finally, additional studies are needed to determine the efficacy and long-term effects of newer insulin analogues in young children with T1D.

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