Juvenile Diabetes:
Type 1 vs. Type 2

Laurent Legault, MD, FRCP

Adapted from a presentation given at McGill University's Thursday Evening Learning Series, September 2007.

The pediatric diabetes picture has become more complex over time. Fifteen years ago, there was only one thing that would come to mind, Type 1 diabetes (T1DM). The emergence of Type 2 diabetes (T2DM) in recent years makes this diagnosis not so straightforward anymore.

Clinical features

All types of diabetes lead by definition to an increase in blood glucose and, when reaching the renal threshold, are accompanied by polyuria, which in turn, leads to polydipsia. In the case of T1DM, prolonged insulinopenia will lead to ketone body production in the blood and eventual acidosis (*i.e.*, diabetic ketoacidosis [DKA]), which presents with GI symptoms (abdominal pains and vomiting). This process only takes a few weeks.

Symptoms have become well known and quicker assessments have led to a dramatic decrease in the number of children presenting in DKA at diagnosis. In our setting, it has come down to < 20%, so many T1DM cases will come to the emergency room in good shape. One thing to keep in mind, of course, is the increase in incidence in T2DM. On the basis of clinical features, it might be difficult to make the distinction. DKA is found occasionally in these patients as well as polyuria and polydipsia. Over time, the polyuria leads to weight loss in both situations.

Having a glucometer and the possibility to do a urine analysis in the office clearly avoids undue diagnostic delays and could prevent DKA.

Meet Shannon...

Shannon is 15-years-old. She is a typical teenager.

She presents with a 15 lbs weight loss, frequent visits to the bathroom and an urge to drink all the time.

She has struggled with her weight so is not unhappy with this significant drop and thinks it is due to her recent efforts towards better lifestyle choices.

It is quite obvious to you she likely has new onset diabetes but what type of diabetes is it?

Approach and differential diagnosis

T1DM still represents the vast majority of cases in Canada. T2DM has nevertheless seen a rapid increase mostly due to the obesity epidemic seen everywhere in this country. Overall, T1DM represents > 80% of cases. T2DM around 7% to 10% and secondary diabetes or genetic cases the rest—we will cover those individually.

T1DM is well known and seen at all ages and typically has seasonal peaks in the spring and fall, prompting a lot of investigators to look for the still evasive triggering factor. With the experience gathered from numerous preventive studies, T1DM's natural history is quite predictable with a gradual decline of β-cell function over months to years leading to the typical symptomatology. Insulinopenia leads to ketone body production which can now be picked up by both a urine analysis or by capillary ketone levels with the help of a meter. Antibody detection is usually present in these situations but antibody

Table 1

Screening guidelines

Screening to be considered if child is obese and > 10 years and meets 2 of the following 3 criteria:

1. Family history of Type 2 diabetes
2. From a high-risk ethnic group (Aboriginal, African-American, Hispanic, Asian)
3. Features of insulin resistance:
   - Acanthosis nigricans (darkened skin in the folds, nape of the neck, umbilicus)
   - Dyslipidemia
   - Polycystic ovarian syndrome (combination of hirsutism, acne or oligomenorrhea and obesity)

levels are not easily available for most clinicians and more than likely should be reserved for questionable cases. Of note, 15% of Canadian children are overweight which makes it possible that an overweight child will develop T1DM.

T2DM, on the other hand, is almost exclusively seen in overweight children. Certain ethnic groups are at higher risk but no groups are spared. The extremely high risk seen in aboriginal communities is a well described phenomemon but relatively few clinicians see a significant number of these patients. Another key feature is that T2DM is rare before puberty. This has led both the Canadian and American diabetes associations to propose screening guidelines incorporating these features.

Screening guidelines

Screening guidelines are listed in Table 1. It is thus important to explore the points in more detail: What is her family history (including gestational diabetes, which confers a high risk to develop T2DM for both the mother and eventually for the daughter)? As well, is she from one of those high-risk ethnic groups? Does she present any of the aforementioned features typical of PCOS? How long has she been symptomatic? T2DM can take months to years to diagnose.

It is important to remember that both ketone bodies and antibodies can be found in T2DM individuals.

There are a few other types of diabetes seen in pediatrics and depending on the setting, could be considered. First is secondary diabetes seen in children regularly exposed to high doses of steroids for chronic diseases (rheumatology, hematology) and some chemotherapy agents. Second would be cystic fibrosis related diabetes starting to be seen after > 10-years-of-age, the proportion increasing gradually to one-third at 18-years-old.

Last but not least is the fascinating story of genetic diabetes which may potentially change the treatment. Keys to diagnosis are either dominant inheritance in the case of maturity onset of diabetes in the young (MODY) or very early onset (before the age of six months) for neonatal diabetes.

Management

Management closely depends on the diabetes type. While T1DM treatment is quite straightforward, insulinotherapy has evolved to accomodate the patient's lifestyle. Since the results of the Diabetes Control and Complications Trial (DCCT) study were published in 1993 clearly showing that better control reduces complication rates by 75%, there has been more emphasis put on trying to obtain the best possible hemoglobin A1C result.

With the advent of new short-acting analogs (insulin lispro injection and insulin aspart injection), the classical Humulin R® and Novolin® Toronto have gradually been almost phased out

as these new options provide for a more flexible lifestyle and a lesser risk for inter-meal hypoglycemia. With the more recent long-acting analogs now making their way into the arsenal, Novolin NPH® and Humulin N® might be following the same course. Both Glargine and Detemir have shown a better performance in preventing hypoglycemia, specifically overnight, which is always a concern in pediatrics. They also are more predictable which is a longstanding and frustrating problem with Novolin NPH® and Humulin N®. A typical starting daily dose would be 0.6 units/kg to 0.8 units/kg in three or four injections per day.

This new emphasis on better control has led the pediatric community to embrace more intensive regimens incorporating basal bolus adjustments as well as the increasingly popular insulin pump. A1C targets now also reflect this relatively new approach in recent Canadian diabetes association guidelines.

T2DM may be treated with a more varied approach. The key to making a decision may lie in two important pieces of information. What is the initial A1C and were there ketones at diagnosis?

Ketone production reflects either absolute or relative insulinopenia. So even with a strong clinical suspicion of T2DM, insulin therapy is warranted, usually at a dosage of 0.5 units/kg q.d. Oral agents have not been widely tested in pediatrics so are seldom used. The only medication for which any long-term experience has been gathered is Metformin. The usual starting dose is 500 mg b.i.d. This is well tolerated as long as the patient is started on half that dose for the first week. The usual contraindications of renal or liver impairment are seldom seen in pediatrics.

Dr. Legault is a Pediatric Endocrinologist; and Head of the Diabetes Clinic, Montreal Children's Hospital, McGill University, Montreal, Quebec.

Take-home message

1. Type 2 diabetes is on the rise in pediatrics but still represents < 15% of cases in most settings
2. Type 1 can be seen in overweight individuals
3. Ketone bodies or antibody presence do not rule out Type 2 diabetes
4. Careful history and evolution may help in discriminating between Type 1 and Type 2 diabetes
5. Having a glucometer and the possibility to do a urine analysis in the office clearly avoids undue diagnostic delays and could prevent diabetic ketoacidosis

While there is some controversy about the role of lifestyle changes, several children's initial A1Cs are within the normal range and it makes sense to try implementing those changes first.

To summarize, in the presence of ketones at diagnosis, insulin therapy should likely be the first option considered. In the absence of ketones, the initial A1C may dictate the best approach, a slightly elevated one might be kept under control with the help of an oral agent (Metformin) while a quite elevated one should, at least initially, be addressed by insulinotherapy.

As eluded to, genetic diabetes can lead to a change of treatment options. The exact diagnosis necessitates DNA being sent to a specialized lab but should be considered if present early (*i.e.*, before the age of six months) or if more than two generations are affected. Secondary diabetes is treated with insulin if glucose spilling (blood glucose > 10 mmol/L leading to glucosuria) is present. The only studied treatment option for cystic fibrosis related diabetes is insulin.