

'Double diabetes'

in young people and

how to treat it

✉ Francine Kaufman

In most countries around the world, there has been an increase in the number of children and young people with diabetes. While in general it is relatively easy to distinguish whether a child or teenager has type 1 diabetes or type 2 diabetes, in some cases, young people have elements of both kinds of the condition. This new phenomenon has been labelled 'double diabetes' or 'hybrid diabetes'. Francine Kaufman reports on the existence of double diabetes and the implications of this condition for the initial categorization and treatment of young people who are diagnosed with diabetes.

young people with type 2 diabetes. But by 1994, in urban areas of the USA, children with type 2 diabetes represented up to 16% of the new cases of diabetes in children, and by 1999, that figure was as high as 45% in some areas.^{2,3} Similarly, there has been an approximate four-fold rise in the incidence of type 2 diabetes in six- to 15-year-olds in Japan.⁴

**Around the world,
type 1 diabetes
is increasing –
particularly in
very young children.**

The incidence of both type 1 diabetes and type 2 diabetes are on the rise in children and teenagers. Indeed, type 1 diabetes is increasing particularly in the very young. Recent multi-country data from the EURODIAB study indicate that the overall prevalence of type 1 diabetes among young people under 15 years is growing by over 3% each

year, and by more than 6% a year in children aged up to four years.¹ Over the last decade and a half, there has been an increase in the incidence of obesity-driven type 2 diabetes in young people in countries around the world.

Before the 1990s, it was rare for US paediatric diabetes centres to see

While, for the most part, it is easy to determine what type of diabetes a child or teenager has, in some instances it is not quite so clear. In my own practice at Childrens Hospital Los Angeles in the USA, I recently saw two cases that illustrated the potential difficulties in determining the type of diabetes.



Type 2 diabetes?

The first was a 13-year-old girl with obesity, who had had symptoms of diabetes for about three months. Her blood glucose level was 17.8 mmol/L (322 mg/dL). Fortunately, she did not have **ketones** in her urine or blood, but her blood cholesterol levels were very high, and there was darkening of the skin around her neck (called acanthosis nigricans). The clinical picture was apparently typical of a person with type 2 diabetes.

However, she showed the distinctive feature of type 1 diabetes: very high levels of antibodies against the

insulin-producing pancreatic beta cells. Therefore, she was treated with insulin injections rather than oral blood glucose-lowering medicines.

Type 1 diabetes?

The other case was that of a 13-year-old girl who had been diagnosed with type 1 diabetes when she was four years old. When she went through puberty – having been on insulin for nine years – she gained excessive weight and her body developed insensitivity to insulin. She needed to take more than 150 units of insulin each day; she developed elevated levels of blood cholesterol

In some cases, young people have elements of both type 1 diabetes and type 2 diabetes.

and acanthosis nigricans. The oral medication, metformin, was added to her regimen, which improved her diabetes control on a significantly reduced dosage of insulin.

Double diabetes

As mentioned earlier, the hallmark of type 1 diabetes is the presence of antibodies which attack the insulin-

producing pancreatic beta cells – an indication that type 1 diabetes is an autoimmune disorder. The autoimmunity leads to the destruction of the beta-cell mass that results in profound insulin deficiency.

The hallmark of type 2 diabetes is the combination of insensitivity to insulin and the continuing ability to make the hormone – although not enough to overcome the body’s insensitivity to the action of insulin.

Double diabetes suggests that elements of both type 1 diabetes and type 2 diabetes co-exist in the same person: people with type 1 diabetes have the insensitivity to insulin that is most often associated with obesity; people with type 2 diabetes have antibodies against the pancreatic beta cells. Blurring the issue further is the fact that people with type 1 diabetes have family members with type 2 diabetes and vice

versa. This means that a considerable number of people may be at genetic risk for both kinds of diabetes.

In adults, latent autoimmune diabetes in adults (LADA) may be a form of double diabetes. Young adults with LADA have antibodies against the insulin-producing beta cells. At first, these young people can be treated with an oral diabetes medication; they then require insulin treatment earlier than most people with type 2 diabetes.

Many people may be at genetic risk for both kinds of diabetes.

The SEARCH (Search for Diabetes in Youth) study in the USA identified a number of children with double diabetes.⁵ This study – designed to determine the incidence and prevalence of childhood diabetes in

the USA – has demonstrated that a relatively large proportion of the young people diagnosed with diabetes both continue to produce insulin and have antibodies against the beta cells.

The accelerator hypothesis

The accelerator hypothesis of diabetes development suggests that excessive weight gain – a significant and growing problem worldwide – results in insensitivity to insulin. This insensitivity to insulin puts the beta cells under stress by forcing them to manufacture more insulin.⁶ The stressed beta cells are more susceptible to autoimmune injury, which can lead to their destruction.

The accelerator hypothesis predicts that heavier children will develop type 1 diabetes.⁶ This is similar to type 2 diabetes: heavier children are also the ones who develop type 2 diabetes. The overall increase in insensitivity to insulin due to obesity is blurring

Table: Differential diagnosis – type 1 diabetes vs type 2 diabetes in children and adolescents

	Type 1 diabetes	Type 2 diabetes
Typical clinical course	Usually rapid onset	Slow onset
Weight	Primarily lean	80%-90% obese
Diabetes ketoacidosis	35%-40%	5%-25%
Family history	5% have a relative with type 1 diabetes Up to 20% may have a relative with type 2 diabetes	74%-100% have relative with type 2 diabetes
Co-morbid conditions	Thyroid and/or adrenal disorders Vitiligo Celiac disease	Polycystic ovary syndrome Acanthosis nigricans
C-peptide	Usually reduced levels but can be preserved at diagnosis	Always present
Presence of islet auto-antibodies	85%	15%

the lines that differentiate between type 1 diabetes and type 2 diabetes.

Diagnostic evaluation and treatment

At the time of a diagnosis of diabetes in children and teenagers, the healthcare provider should of course attempt to determine which type of diabetes is present.

The table on page 21 shows the clinical features that can help to differentiate the type of diabetes. In lean, young children, it is probably correct to assume that the young person has type 1 diabetes. However, in overweight teenagers, it may be difficult to differentiate type 1 diabetes from type 2 diabetes.⁷ Measuring antibodies that act against the pancreatic beta cells can be helpful; an assessment of insulin production by measuring **C-peptide** levels can also be used.

Ketones are chemicals that the body produces when there is not enough insulin in the blood and it must break down stored fat instead of glucose for its energy.

Ketoacidosis occurs when excessive amounts of ketones build up in the blood. Ketoacidosis can lead to coma or even death.

C-peptide is a by-product of insulin made in the pancreas. A measurement of the levels of C-peptide – made up of amino acids – in the blood can indicate whether or not a person is producing insulin and roughly how much.

Everyone with type 1 diabetes requires insulin therapy. If it is determined that a person has type 2 diabetes, lifestyle interventions or oral blood glucose-lowering medication can be started – if blood glucose levels are not excessively elevated and there is no significant dehydration or acidosis. If the type of diabetes cannot be determined, the young person should be started on insulin therapy while waiting for test results that hopefully will clarify the situation.

For people with double diabetes, it is likely that they need both insulin and oral diabetes medicines to improve sensitivity to insulin. However, studies are required to evaluate the benefits of a dual approach to increasing sensitivity to insulin.

Our focus should be on how to prevent childhood obesity.

Conclusions

It is important to determine who has double diabetes since that will help to dictate which diagnostic and therapeutic approaches should be taken. However, we need to learn more about this relatively newly recognized condition. Since the emergence of double diabetes seems to be linked to the epidemic of obesity in young people, our focus should be on how to prevent childhood obesity as a primary means of reducing the emergence of this potentially devastating condition.

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