Investigating the child with hyperglycaemia

Each month we present authoritative advice on the investigation of a common clinical problem, specially written for family doctors by the Board of Continuing Medical Education of the Royal Australasian College of Physicians.

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Hyperglycaemia in a child is usually an indication of the development of insulin-dependent diabetes mellitus. In a small proportion of children, however, hyperglycaemia may occur in association with a stressful acute illness or as a side effect of certain medications.

Hyperglycaemia is defined as a fasting blood glucose level that is greater than 5.5 mmol/L or a random blood glucose that is greater than 8.5 mmol/L. Mildly elevated results obtained by blood glucose strips should be confirmed by a formal venous blood glucose measurement; however, in the presence of symptoms of diabetes and evidence of ketosis, a child who has an elevated blood glucose strip result should be referred immediately if there is likely to be a delay in obtaining a formal venous blood glucose measurement.

Causes of hyperglycaemia in childhood

Diabetes mellitus

Diabetes mellitus is a heterogenous disease. The types of diabetes mellitus that occur in childhood are listed in the box on page 67.

Some children have a catastrophic onset to their diabetes and present within a few days in diabetic ketoacidosis; others have a long slow onset over several months. Atypical presentations in which diabetes should be considered and investigations should be performed are listed in the Table. The onset of severe insulin deficiency is more rapid in very young patients, and therefore these patients often present in severe ketoacidosis if the diagnosis is not considered early (see Figure).

A child presenting with a classic history of increasing polyuria, polydipsia and weight loss over a period of two to six weeks does not usually

IN SUMMARY

- **Hyperglycaemia in childhood is usually an indication of the development of insulin-dependent diabetes mellitus. However, not all children with mild hyperglycaemia will progress to insulin-dependent diabetes mellitus.**
- **Urinary dipstick testing for glycosuria and ketonuria provides a simple and sensitive tool for excluding diabetes in a patient with a less typical presentation. A blood glucose measurement would confirm the hyperglycaemia and enable the practitioner to make the diagnosis.**
- **The majority of children who develop stress or drug-induced hyperglycaemia will have normal outcomes. However, the acute illness or medication may occasionally unmask a child who is in the 'prediabetes' phase of insulin-dependent diabetes mellitus.**
- **All children with hyperglycaemia should receive follow up, especially those who present with hyperglycaemia in the absence of a stressful illness.**

pose a diagnostic difficulty. However, an atypical presentation or failure to consider the possibility of diabetes may result in late diagnosis. Difficulties leading to misinterpretation of symptoms include:

- hyperventilation of ketoacidosis (may be misdiagnosed as pneumonia or asthma)
- abdominal pain associated with ketoacidosis (may be misdiagnosed as an acute abdomen)
- polyuria and enuresis (may be misdiagnosed as a urinary tract infection)
- polydipsia (may be thought to be psychogenic)
- vomiting (may be misdiagnosed as gastroenteritis).

Stress hyperglycaemia

Transient glucose intolerance during infection or trauma (stress hyperglycaemia) has been well recognised in children, with most early reports suggesting that it most commonly occurred during acute gastroenteritis, especially gastroenteritis with dehydration. However, recent studies have concluded that stress hyperglycaemia has no correlation with a specific diagnosis, but that there is a correlation with the patient's degree of temperature elevation, hydration status and need for admission to hospital.

Children with stress hyperglycaemia may develop insulin-dependent diabetes mellitus on follow up (2.3% of cases). However, the incidence of type 1 diabetes has been reported to be as high as 32% in children presenting with hyperglycaemia in the absence of a stressful illness.

Drug-induced hyperglycaemia

Drug-induced hyperglycaemia is most often seen in children receiving oral corticosteroids, but it has been reported with other medications. Drugs that induce hyperglycaemia include:

- glucocorticoids, which increase insulin resistance, stimulate gluconeogenesis and inhibit glycogen synthesis
- L-asparaginase, which decreases insulin synthesis
- β-adrenergic agonists, which stimulate hepatic glucose secretion
- β-blockers and diazoxide, which inhibit insulin secretion
- growth hormone, which increases insulin resistance.

Types of diabetes mellitus in children and adolescents

Insulin-dependent diabetes mellitus (type 1)

Almost all children (98%) with diabetes have this type, which is induced by an autoimmune process that progressively destroys the pancreatic beta cells. Children with type 1 diabetes are prone to ketosis.

Noninsulin-dependent diabetes mellitus (type 2)

This type of diabetes is rare in childhood, although some countries are reporting an increasing number of cases in adolescence. It is usually associated with obesity.

Maturity onset diabetes of the young

This is a rare, dominantly-inherited form of noninsulin-dependent diabetes mellitus. It is mostly manifested during or after puberty.

Diabetes due to mitochondrial DNA defects

Mitochondrial DNA defects are the underlying cause of maternally inherited diabetes and deafness (MIDD), which is sometimes combined with renal abnormalities.

Nonautoimmune diabetes caused by pancreatic damage

Nonautoimmune diabetes occurs in patients with cystic fibrosis, for example, as a result of progressive pancreatic fibrosis or thalassaemia due to damage by iron deposition.

Diabetes mellitus associated with other diseases or syndromes

This type of diabetes can be either insulin-dependent or noninsulin-dependent. It occurs in association with genetic syndromes (such as Prader–Willi syndrome), chromosomal abnormalities (Turner or Down syndromes), congenital rubella and autoimmune diseases such as polyendocrine autoimmune deficiencies.

Like stress hyperglycaemia, drug-induced hyperglycaemia may be indicative of prediabetes, and patients therefore require careful follow up.

Diabetes related to cystic fibrosis

Diabetes related to cystic fibrosis is distinctly different from type 1 or type 2 diabetes, but it shares features with both types. The usual age at onset is 18 to 21 years, but it may present at any time after 10 years of age. Diabetes related to cystic fibrosis occurs in slender young adults, and appears to develop in more females than males. It may be more likely to affect individuals who are homozygous for the most common cystic fibrosis mutation (ΔF508).

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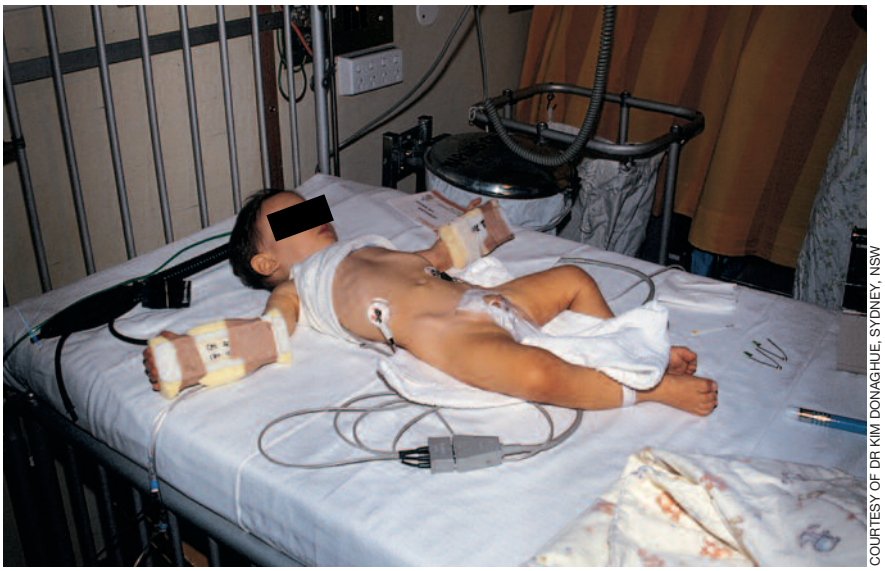
Table. Presentations of diabetes mellitus in children

Emergency presentations

- Severe dehydration
- Shock (rapid pulse rate, low blood pressure, poor peripheral circulation, mottling, peripheral cyanosis and hypothermia)
- Frequent vomiting
- Continuing polyuria despite dehydration
- Weight loss (due to fluid loss and loss of muscle and fat)
- Flushed cheeks (due to ketoacidosis)
- Detectable acetone on the breath
- Hyperventilation of diabetic ketoacidosis (Kussmaul's respiration), characterised by a high respiratory rate and obviously large tidal volume of each breath which gives a sighing quality
- Disordered sensorium (disoriented, semicomatose or comatose)

Non-emergency presentations

- Recent onset of enuresis in a previously toilet-trained child (may be misdiagnosed as a urinary tract infection or a result of excessive fluid ingestion)
- Vaginal candidiasis (especially in prepubertal girls)
- Vomiting
- Chronic weight loss or failure to gain weight in a growing child
- Irritability, lethargy and decreasing school performance
- Recurrent superficial skin infections
- Blurred vision



COURTESY OF DR KIM DONAGHUE, SYDNEY, NSW

Figure. A 10-month-old baby boy who presented in diabetic ketoacidosis. He was unconscious and in shock. Two weeks earlier he had been a healthy baby.

Ketoacidosis is rare but does occur, especially at the initial presentation of diabetes if there has been a long period of symptomatic hyperglycaemia before diagnosis. As in type 2 diabetes, most patients with diabetes related to cystic fibrosis may make enough insulin to suppress ketogenesis. Microvascular complications of diabetes are recognised in cystic fibrosis, but macrovascular complications have not been described. Patients do not have the immunological serum markers typical of type 1 diabetes. However, most patients with diabetes related to cystic fibrosis do require insulin therapy.

As advances in the treatment of pulmonary and gastrointestinal complications have led to increased longevity in patients with cystic fibrosis, diabetes mellitus and glucose intolerance have become common complications. There is evidence that diabetes and even glucose intolerance might adversely affect morbidity and mortality rates in these patients.

Investigations

Urinary dipstick testing for glycosuria and ketonuria provides a simple and sensitive tool for excluding diabetes in a patient with a less typical presentation. Then, a blood glucose measurement would confirm the hyperglycaemia and enable the practitioner to make the diagnosis. An approach to investigating the child with hyperglycaemia is outlined in the flowchart on page 70.

An oral glucose tolerance test is rarely indicated in making the diagnosis of diabetes in children and adolescents. If doubt exists, it is easier to perform a fasting blood glucose test or to monitor the child or adolescent regularly with urine testing for glycosuria. If concern persists, a random blood glucose test should be performed.

In difficult cases, the presence of autoimmune markers may be of assistance, such as antibodies directed against islet cell antigens, insulin and glutamic acid decarboxylase. These tests are usually best performed and interpreted by tertiary centres.

Follow up and outcomes

All children presenting with hyperglycaemia should receive follow up, especially those who present with hyperglycaemia in the absence of a stressful illness. If untreated, a child with diabetic ketoacidosis will die. Therapy is urgent and referral to specialised services is essential.

The majority of children who present with hyperglycaemia during stress will

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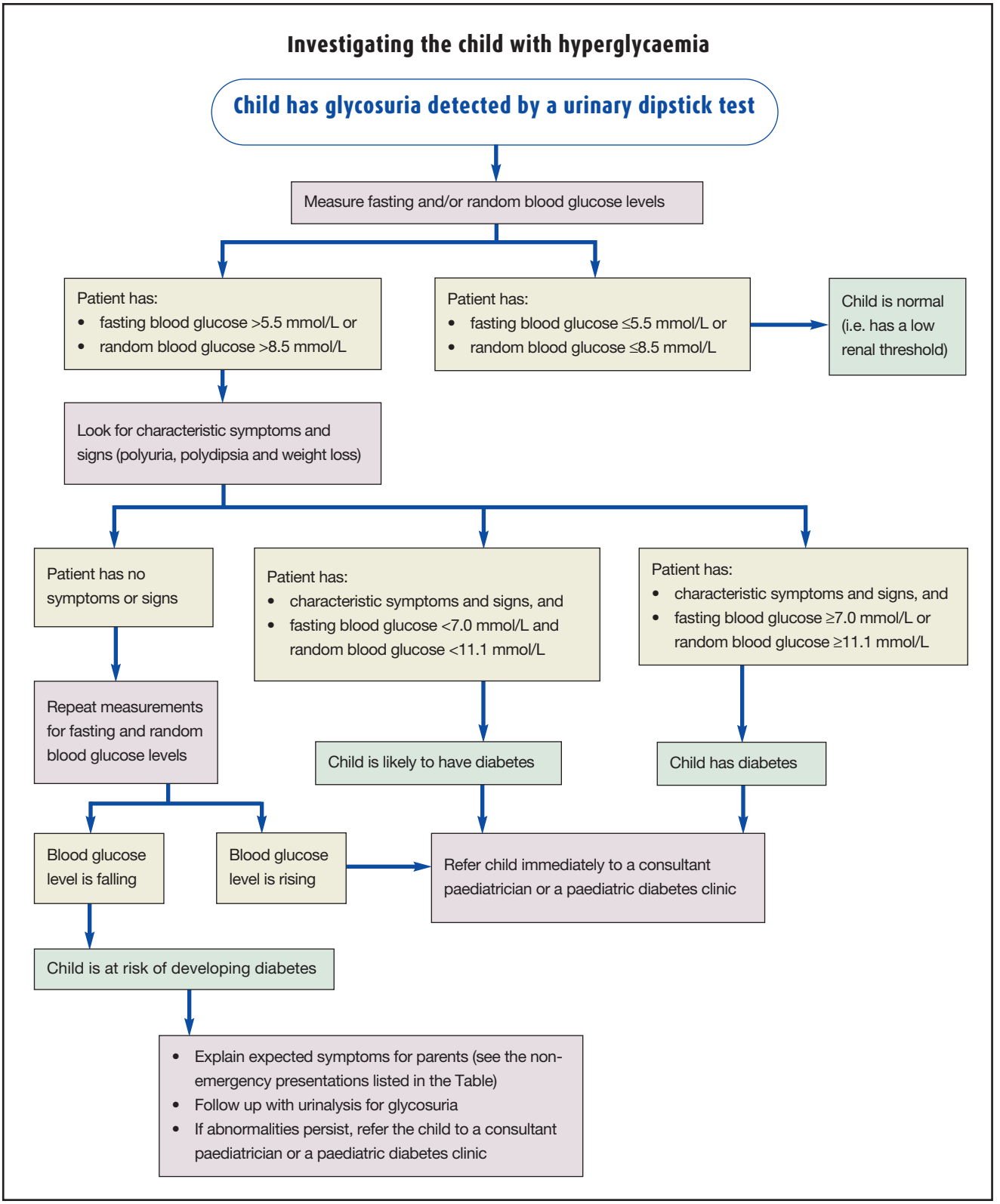

have normal outcomes, as will a substantial proportion of children who present with drug-induced hyperglycaemia. However, the acute illness or medication will occasionally unmask a child who is in the prediabetes phase of insulin-dependent diabetes mellitus – therefore, careful follow up of these patients is required.

Children and adolescents with a positive family history of type 2 diabetes or obesity who develop transient hyperglycaemia following stress or drug therapy should be encouraged to modify their lifestyle with weight reduction and increased physical activity in the hope of preventing type 2 diabetes in the future.

Concluding comments

General practitioners need to be alert to the various presentations of diabetes in children in order to prevent a delay in diagnosis. Urinary dipstick testing for glycosuria and ketonuria provides a simple and sensitive tool for excluding diabetes in a patient with a less typical presentation. Any child who presents with hyperglycaemia should receive follow up, especially a patient who presents with hyperglycaemia in the absence of a stressful illness. MT

Suggested reading

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2. Herskowitz-Dumont R, Wolfsdorf JI, Jackson RA, Eisenbarth GS. Distinction between transient hyperglycemia and early insulin-dependent diabetes mellitus in childhood: a prospective study of incidence and prognostic factors. J Pediatr 1993; 123: 347-354.
3. Moran A, Doherty L, Wang X, Thomas W. Abnormal glucose metabolism in cystic fibrosis. J Pediatr 1998; 133: 10-17.
4. Silink M, ed. APEG Handbook on childhood and adolescent diabetes. Sydney: Australasian Paediatric Endocrine Group, 1996. (Distributed by the Child Health Promotion Unit, The Children's Hospital at Westmead, NSW.)