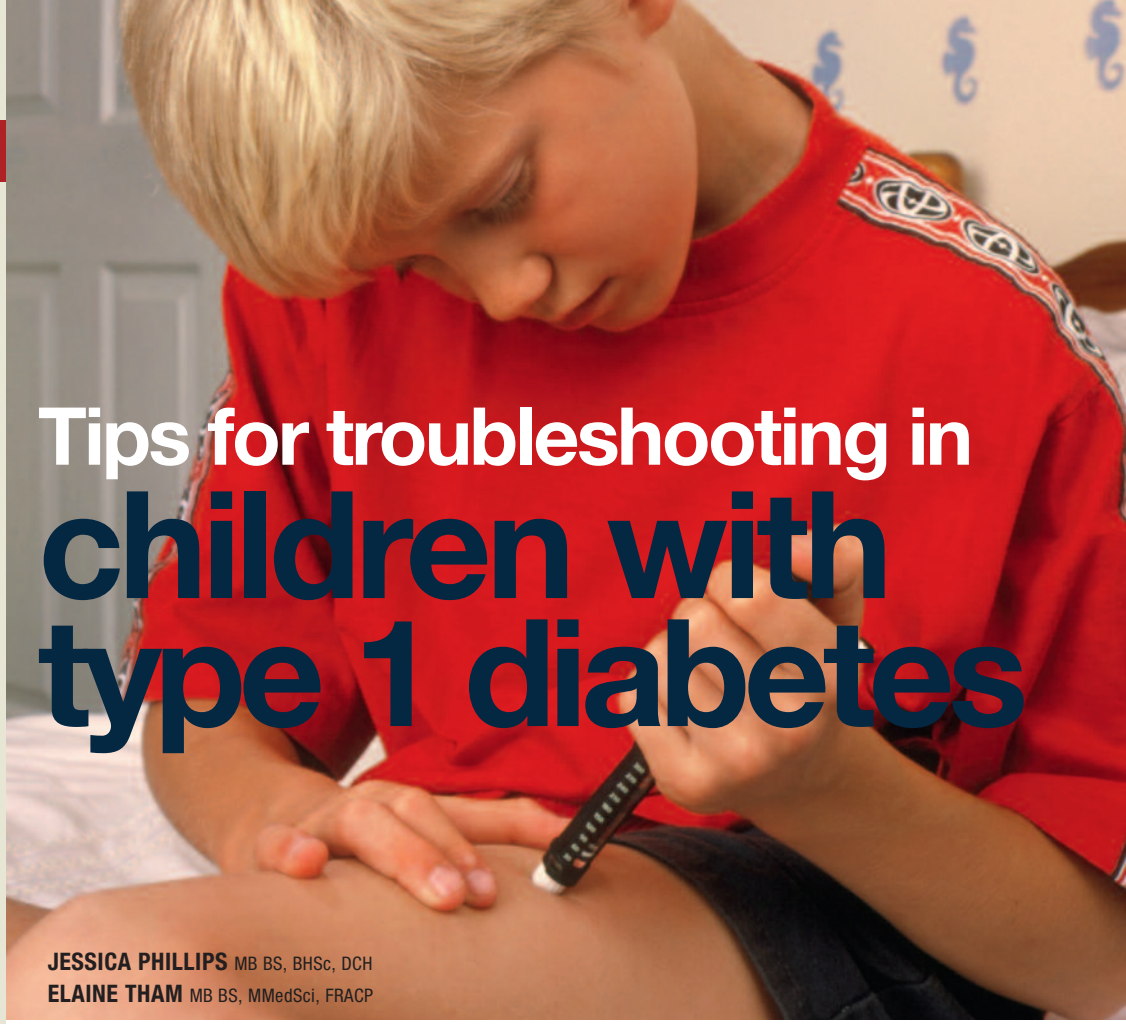
MedicineToday 2012; 13(10): 28-35

PEER REVIEWED FEATURE
POINTS: 2 CPD/2 PDP



Tips for troubleshooting in children with type 1 diabetes

JESSICA PHILLIPS MB BS, BHSc, DCH
ELAINE THAM MB BS, MMedSci, FRACP

Key points

- Early diagnosis of type 1 diabetes and prompt referral to a physician skilled in managing children with diabetes is important to avoid diabetic ketoacidosis.
- There is no need to wait for a fasting blood glucose level (BGL) in a child who has symptoms suggestive of diabetes. The fasting BGL may remain normal early on.
- Common insulin regimens for children with type 1 diabetes are multiple daily injections, twice-daily injections and insulin pumps. Knowledge of speed of onset and duration of action of the various insulins is useful for problem solving.
- Management of diabetes during illness requires frequent monitoring of blood glucose and ketone levels as adjustments to insulin doses are usually needed.
- The use of insulin pumps is increasing. The pump only delivers rapid-acting insulin so if delivery of insulin is interrupted, BGLs rise quickly. Immediate attention is required, and even small levels of ketones should not be ignored.

GPs are part of the multidisciplinary team caring for children and adolescents with type 1 diabetes and have an important role in managing intercurrent illnesses and general health needs.

Every day in Australia two children will be diagnosed with type 1 diabetes.[1] The peak incidence occurs in adolescence, as shown in Figure 1.[2] Globally, Australia has the sixth highest rate for new diagnoses of type 1 diabetes (Figure 2).[3]

A genetic predisposition together with an environmental trigger is thought to initiate the autoimmune destruction of beta cells that leads to type 1 diabetes. Autoimmune destruction of the pancreas occurs over months to years before the symptoms of diabetes become evident.[4] Currently there is no way to prevent diabetes, even in those identified as being at high risk.

Problem solving for patients with type 1 diabetes requires a basic knowledge of the different insulin regimens and the types of insulin available (Tables 1 and 2).[5]

The Australian guidelines for type 1 diabetes, the *National Evidence-Based Clinical Care Guidelines for Type 1 Diabetes in Children, Adolescents and Adults,* recommend that children with type 1 diabetes be cared for by a multidisciplinary team that includes a GP, a paediatric endocrinologist/paediatrician skilled in managing diabetes, a diabetes nurse educator, a dietitian and a psychologist.[6]

Glucose control varies depending on carbohydrate intake, insulin dose and activity levels but the additional challenge of managing diabetes during illness may leave some parents unsure of how to cope. Some tertiary paediatric centres have a 24-hour emergency number for parents seeking specialist advice but in many instances, and especially in rural areas, GPs are the first port of call. GPs have an important role in managing intercurrent illnesses and

Dr Phillips is a Senior Registrar and Dr Tham is a Paediatric Endocrinologist at the Women's and Children's Hospital, Adelaide, SA.

general health needs in children with diabetes, as well as providing psychological support.

This article will discuss several common problems encountered when caring for children with type 1 diabetes.

PROBLEM 1: DIAGNOSIS

The first problem often encountered by GPs in the care of children with type 1 diabetes is making the diagnosis. Symptoms of diabetes in children can be vague, especially in younger children. Abdominal pain and vomiting from ketoacidosis may be assumed to be gastroenteritis or appendicitis. Rapid breathing secondary to ketoacidosis may be diagnosed as pneumonia. Polyuria, polydipsia or secondary nocturnal enuresis may be misdiagnosed as a urinary tract infection.

When a urinalysis shows glucose and ketones instead of the anticipated white blood cells, the diagnosis of diabetes can be made. Whenever glucosuria is found, a blood glucose level (BGL) measurement should be performed immediately with a blood glucose meter. If the BGL is elevated (7.0 mmol/L or higher for fasting BGL, 11.1 mmol/L or higher for random or postprandial BGL) and symptoms of diabetes are present, further investigation is required.[7] If the measured BGL is not a fasting glucose level, it is not necessary to wait for the results of a fasting test before acting as this is often normal in early stages of type 1 diabetes and delays diagnosis. If the BGL suggests diabetes, testing for ketones in urine or blood is a fast and easy way of assessing the severity of acidosis (Table 3).[8] Urine ketone strips are easily available and blood ketones can be measured using a blood ketone meter if available.

Case 1

Shiree is 2 years old. Her mother brings her to see you as she has been going to the toilet frequently and is now complaining of a sore tummy. Her mother is concerned Shiree might have a urinary tract infection and asks for a course of antibiotics. Urinalysis results are: specific gravity, 1.01; pH 5.0; leukocytes, negative; nitrites, negative; ketones, 1+; and glucose, 3+.

You send the urine for microscopy and culture and start Shiree on a course of trimethoprim.

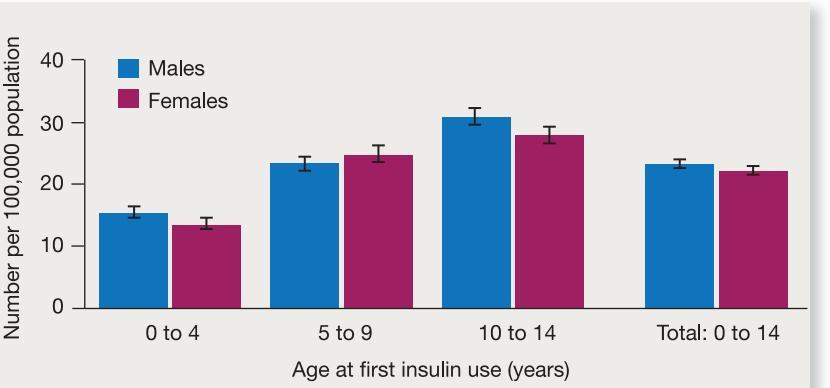


Figure 1. Average annual incidence rate of type 1 diabetes in children aged 0 to 14 years, by age of first insulin use, 2000 to 2009.[2]

Source: National Diabetes Register (data extracted June 2011). Reproduced from: *Incidence of Insulin-treated Diabetes in Australia 2000–2009.* Canberra: AIHW; 2012.[2] © Australian Institute of Health and Welfare.

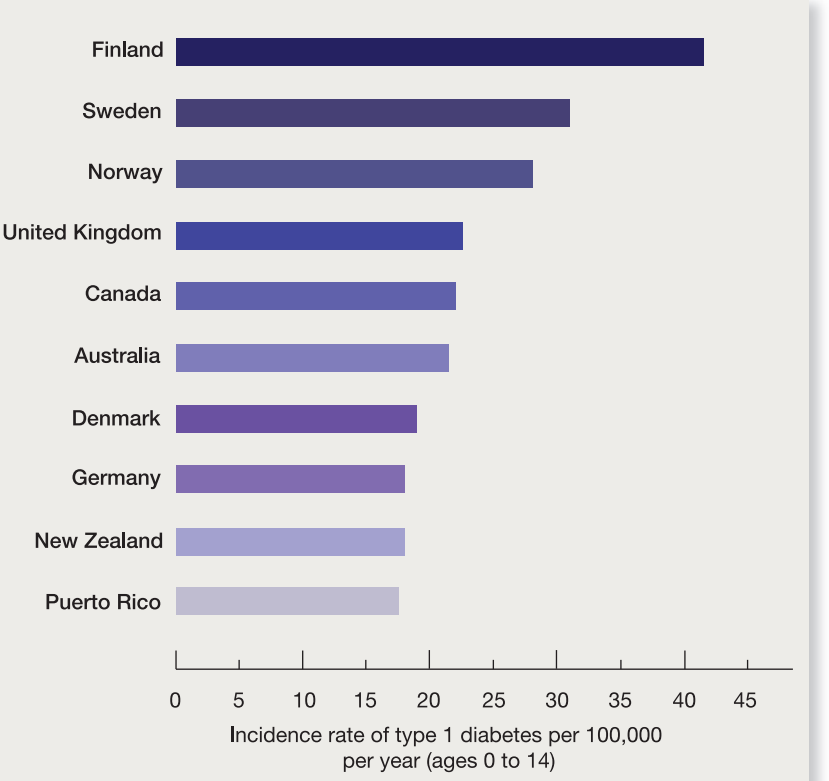


Figure 2. Incidence rate for type 1 diabetes in children (ages 0 to 14 years) by country – the top 10 countries.[3]

Source: *Diabetes Atlas,* 3rd ed.[3] © International Diabetes Foundation, 2006. Reproduced with permission of the International Diabetes Federation.

TABLE 1. COMMONLY USED INSULIN REGIMENS

Insulin regimen	Insulin type and time administered
Twice-daily injections	Breakfast and dinner: intermediate-acting insulin and rapid-acting insulin*
Twice-daily injections	Breakfast: intermediate-acting insulin and rapid-acting insulin* Dinner: long-acting insulin and rapid-acting insulin*
Multiple daily injections	Long-acting insulin once or twice a day, rapid-acting insulin with meals*
Insulin pump	Subcutaneous insulin infusion (rapid-acting insulin) with boluses to cover carbohydrate intakes

* Short-acting insulin results in greater postprandial hyperglycaemia than rapid-acting insulin and is therefore used less commonly.

TABLE 2. INSULINS CATEGORISED BY DURATION OF ACTION[5]

Insulin	Alternative names	Generic name	Peak/duration of activity
Bolus insulin			
Very short-acting (rapid)	Rapid-acting; Very rapid onset, short duration; Rapid-acting analogue; Ultra short-acting; Very quick-acting	Aspart, glulisine, lispro	Peak at 1 hour; duration, 3.5 to 4.5 hours
Short-acting	Rapid-acting human or neutral; Rapid onset, short duration; Quick-acting	Neutral	Peak at 2 to 5 hours; duration, 6 to 8 hours
Basal insulin			
Intermediate-acting	Basal-acting neutral insulin protamine Hagedorn (NPH) zinc	Isophane	Peak at 5 to 8 hours; duration, 12 to 24 hours
Long-acting	Basal analogue	Detemir, glargine	No peak; duration, 24 hours

TABLE 3. INTERPRETING KETONES IN NEWLY DIAGNOSED PATIENTS WITH TYPE 1 DIABETES[8]

Urine ketones	Blood ketones (mmol/L)	Assessment of ketoacidosis
Negative (-)	<0.5	Nil
Trace (-/+)	0.6 to 0.9	Nil
Small (1+)	1.0 to 1.4	Mild
Moderate (2+)	1.5 to 2.4	Moderate
Large (3+)	≥2.5	Severe

Because of the glucosuria, you perform a random BGL, the result of which is 16 mmol/L. You notice that Shiree is holding a bottle of fruit juice and on questioning her mother you determine that Shiree had been drinking the juice in the waiting room. You ask them to return in the morning for Shiree to have a fasting glucose test.

Overnight Shiree starts vomiting and the abdominal pain worsens. Her mother takes her to the emergency department. Shiree's BGL on arrival is 18 mmol/L, with blood ketones of 3.7 mmol/L. A blood gas analysis shows metabolic acidosis with a pH of 7.15 and bicarbonate of 10 mmol/L. Shiree is admitted to the paediatric intensive care unit and an insulin infusion started.

Diagnose promptly

As demonstrated in the case scenario above, children with diabetes can deteriorate quickly and it is not uncommon for them to present in severe diabetic ketoacidosis while waiting to have their fasting BGL measured. When considering the diagnosis of diabetes in a child, it is advisable to discuss the case with a paediatric endocrinologist or a paediatrician experienced in managing children with diabetes because children require insulin promptly at diagnosis. Alternatively, the child could be sent immediately to the emergency department. Children with newly diagnosed diabetes will either be admitted to hospital or attend an ambulatory program for stabilisation and diabetes education. As mentioned previously, fasting blood glucose tests are not necessary for diagnosing type 1 diabetes and in very early disease may remain normal. Postprandial BGLs are the first to rise.

With the increasing rates of overweight and obesity in children, type 2 diabetes is becoming more common in the paediatric population. In all overweight children presenting with symptoms of diabetes, and especially in adolescents, type 2 diabetes should be considered. Examining for signs of insulin resistance

(i.e. looking for acanthosis nigricans) may be helpful in these children, but often it is difficult to differentiate between type 1 and type 2 diabetes. Children with clear symptoms of diabetes should be referred promptly; performing an oral glucose tolerance test (OGTT) is not necessary as this may delay the diagnosis.

PROBLEM 2: SICK DAY MANAGEMENT

Managing sick days in people with diabetes is a balancing act, especially in children. Insulin requirements change for several reasons: insulin resistance occurs because of an increase in stress hormones such as cortisol and adrenaline, but both consumption and absorption of carbohydrates may be decreased,

TABLE 4. GUIDELINES FOR SICK DAY MANAGEMENT IN TYPE 1 DIABETES[6]

Blood glucose level (mmol/L)	Ketones – blood* (mmol/L) or urine†	Supplemental insulin dose (can be given up to two-hourly)‡	Monitoring	Fluids
<4	<1.0 Negative	Insulin dose reduction may be required. Consider mini dose glucagon to prevent hypoglycaemia if vomiting, diarrhoea or reduced carbohydrate intake	Check every 20 to 30 minutes until BGL >4 mmol/L. Supervised medical care required if ketones remain positive and BGL remains low	Take sweetened fluids or quick-acting carbohydrate (or both); hospital admission for IV fluids may be needed if BGL cannot be maintained
	≥1.0 Positive	Priority is to increase BGL with fluid and carbohydrate		
4 to 8	<1.0 Negative/Trace	No change to insulin	Two-hourly	Give sweetened fluids or extra carbohydrate to maintain or increase BGL
	1.0 to 1.4 Small	No change to insulin. Ketones indicate carbohydrate and insulin deficiency	Two-hourly	
	≥1.5 Moderate/Large	5% supplemental insulin may be required	Two-hourly	
8 to 15	<1.0 Negative/Trace	May fall without extra insulin. If persistently elevated, consider 5% supplemental insulin	Two-hourly	Sweetened fluids recommended
	1.0 to 1.4 Small	If persistently elevated ketones, consider 5 to 10% supplemental insulin	Two-hourly	
	≥1.5 Moderate/Large	10% supplemental insulin dose	Hourly	
>15	<1.0 Negative/Trace	5 to 10% supplemental insulin dose	Hourly	Unsweetened fluids recommended
	1.0 to 1.4 Small	10 to 15% supplemental insulin dose	Hourly	
	≥1.5 Moderate/Large	15 to 20% supplemental insulin dose	Hourly	

ABBREVIATIONS: BGL = blood glucose level; IV = intravenous.

* Blood ketones measured as 3β-hydroxybutyrate.
† Urine ketones: Negative = -; Trace = -/+; Positive = 1+/2+/3+; Small = 1+; Moderate = 2+; Large = 3+.
‡ Refers to percentage of total daily insulin dosage (TDD) given as rapid or fast-acting supplemental insulin dose. Exercise caution with supplemental insulin doses in the presence of BGL <8 mmol/L – advise increasing sweetened fluid intake first.

Reproduced from: *National Evidence-Based Clinical Care Guidelines for Type 1 Diabetes In Children, Adolescents and Adults*; used by permission of the Australian Government.[6]

particularly in the presence of vomiting or diarrhoea.

Management requires frequent BGL and ketone level checks. Many patients with diabetes (and/or their parents) forget to check for ketones when they are unwell. Ketosis is an indication of insufficient carbohydrate intake, insufficient insulin or both. The degree of ketosis in the presence of hypoglycaemia or hyperglycaemia can guide decisions on whether extra insulin is required (Table 4).

Case 2

Jemma, a 4-year-old girl with type 1 diabetes, is unwell with a runny nose and fever. Her BGL is 8.2 mmol/L. Jemma's mother has not given Jemma her morning insulin because she refuses to eat her breakfast. Jemma is normally on a multiple daily injection insulin regimen, with rapid-acting insulin at meal times and long-acting insulin in the morning.

Her mother brings Jemma to see you at 8.30 a.m. You diagnose her with a viral illness. Her mother asks you what to do with Jemma's insulin doses. You advise her to reduce the basal insulin dose by 20% and to not give the rapid-acting insulin if Jemma is not eating. You warn Jemma's mother that Jemma may require some extra rapid-acting insulin during the day if her blood glucose and ketone levels rise.

Fear of hypoglycaemia

If their child is not eating, parents may be hesitant to give insulin because of a fear of causing hypoglycaemia, as in the case scenario above. In this situation, it needs to be reinforced that without any insulin, hyperglycaemia and ketoacidosis will result. Insulin doses can be reduced to avoid hypoglycaemia, but they should never be stopped. Intermediate-acting or long-acting insulin can be reduced by 20 to 50%. The rapid-acting insulin may not be required, depending on the BGL and ketones. Additional doses of rapid-acting insulin can be given every two to four hours; the dose is a percentage of the total daily dose (TDD) of insulin, i.e. the total number of units of all types of insulin given in 24 hours (Table 4).

Case 3

John, 14 years old, has been unwell since yesterday morning. Initially he had mild nausea but as the day progressed he started vomiting. He comes to see you this morning with his father, who is concerned John has gastroenteritis. John has type 1 diabetes and normally has multiple daily injections. He has 25 units of long-acting insulin at night and eight units of rapid-acting insulin with meals. His last insulin dose was last night, and he had his usual dose of long-acting insulin.

You measure John's BGL as 13 mmol/L. On examination, John is mildly dehydrated and his abdomen is generally tender but soft. A check of his ketone levels shows his urine ketone level to be 2+ and his blood ketone level to be 1.8 mmol/L.

You advise John to drink more sweetened fluids and to have five units of rapid-acting insulin now and recheck his BGL and ketones in two hours. He phones you two hours later and tells you his BGL is 5.0 mmol/L and the ketones have cleared. You tell him to continue two-hourly BGL and ketone monitoring and to eat or drink some carbohydrates. He is feeling much better and is no longer vomiting.

Differentiating ketoacidosis and gastroenteritis

The scenario in Case 3 illustrates the importance of checking ketones when a person with type 1 diabetes is vomiting to differentiate between ketoacidosis and gastroenteritis. If ketones and BGL are both high then ketoacidosis is likely, and extra insulin (either subcutaneously or via infusion) will be required. If the ketones are low, gastroenteritis can be assumed. Drinking regular carbohydrate-containing fluids such as a sport drink or juice can help avoid hypoglycaemia.

High ketones with normal or low BGL in the setting of gastroenteritis indicate dehydration with insufficient carbohydrate intake. If oral rehydration is not possible, admission to hospital for intravenous or nasogastric rehydration will be required. The younger the child, the harder this can be to manage.

PROBLEM 3: WRONG DOSES

Mix ups and mistakes happen. The wrong amount of insulin may be given, an injection may be forgotten or a parent may be unsure whether they have given a dose or not. Managing these scenarios requires knowledge of the pharmacokinetics of the insulin the patient uses (see Table 2).

Case 4

Jack, 7 years old, was diagnosed with type 1 diabetes a week ago. He is on twice-daily injections. His mother rings in a panic because she gave Jack his morning insulin five minutes ago and now realises she gave the wrong dose. He usually has six units of intermediate-acting insulin and three units of rapid-acting insulin but she has given him three units of intermediate-acting insulin and six units of rapid-acting insulin. His pre-breakfast BGL was 7 mmol/L.

Adjusting carbohydrate intake

In this scenario Jack has had too much rapid-acting insulin and not enough intermediate-acting insulin. He will be at risk of hypoglycaemia after breakfast and of hyperglycaemia later in the morning.

Jack has had twice his usual rapid-acting insulin, so eating double his usual breakfast carbohydrate intake would help prevent hypoglycaemia. He is at risk of hyperglycaemia later in the day because he has not had enough intermediate-acting insulin. Eating less carbohydrate at lunch would help lessen hyperglycaemia, or he could be given extra rapid-acting insulin at lunchtime (5% of his total daily dose). Frequent monitoring of his BGL will be needed to guide ongoing management.

Figure 3. Insulin pumps provide more freedom around meal times than other insulin injection regimens.

TABLE 5. INSULIN DOSES FOR KETOSIS

Blood ketones	Urine ketones	Dose of rapid-acting insulin
0.5 to 1.5 mmol/L	1+	10% total daily dose
More than 1.5 mmol/L	2+/3+	20% total daily dose

PROBLEM 4: HYPERGLYCAEMIA AND HYPOGLYCAEMIA

The International Society for Pediatric and Adolescent Diabetes (ISPAD) Clinical Practice Consensus Guidelines recommend a target BGL before meals of 5.0 to 8.0 mmol/L and after meals of 5 to 10 mmol/L.[9] Causes for changing requirements include illness, stress, changing eating pattern, exercise and puberty. Exercise generally lowers the BGL because of increased glucose usage and increased sensitivity to insulin. Illness, stress and puberty are times of insulin resistance resulting in hyperglycaemia. Hypoglycaemia usually suggests too much insulin, too little carbohydrate, increased activity or a combination.

The first step in restoring normoglycaemia is to look for a pattern and decide whether a dose adjustment to the basal or bolus insulin is required. A quick guide to managing hyperglycaemia and hypoglycaemia is:

- look for a pattern: is the hyper/hypo at a consistent time of the day?
- can the hyper/hypo be explained by too much/too little exercise or too much/too little food?
- would a change in the dose of the basal or bolus insulin solve the problem? A safe starting point is to adjust doses by 5 to 10% at a time.

If the three points above do not help solve the problem, other causes for failed delivery should be considered, such as lipohypertrophy at injection sites altering insulin absorption, insulin stored at the wrong temperature or forgetting an insulin dose.

Case 5

Joel is 9 years old and has had type 1 diabetes for three years. His father has brought Joel to see you today because Joel has had several high BGL readings over the past few weeks and his parents are concerned he may need a dose adjustment. On review of Joel's recent BGL readings he generally has good control but over the past three weeks has had four high levels before dinner and two low levels (hypoglycaemic) after dinner. Joel is on multiple daily injections (long-acting and rapid-acting insulins).

Effects of exercise

The guide to managing hyper- and hypoglycaemia described above can be used in this case scenario:

- Look for a pattern: is the hyper/hypo at a consistent time of the day?
  Joel's BGLs are high on Wednesdays and Fridays before dinner. The hypos after dinner both occurred on a Friday.
- Can the hyper/hypo be explained by too much exercise or too little food?
  Joel has just joined a soccer team and has practice on Wednesdays after school and a game on Fridays after school. He has extra carbohydrate before exercising and sips on a sports drink throughout the game. A combination of excitement, adrenaline and too much sports drink has resulted in the high BGLs before dinner. You advise that Joel reduces the amount of sports drink he consumes during the game.
- Would a change in the dose of the long-acting or rapid-acting insulin fix the problem?
  Joel needs less rapid-acting insulin with dinner on days when he is exercising after school. The exercise has made him more sensitive to insulin and increased the utilisation of glucose. Hypoglycaemia can occur up to six hours after exercise. You advise that Joel's pre-dinner dose of rapid-acting insulin be reduced by 10% on the days he plays sport.

PROBLEM 5: PUMP PROBLEMS

An insulin pump is a programmable device that delivers insulin via tubing and a subcutaneous plastic cannula (infusion set) that the patient changes every three days (Figure 3). The pump delivers a continuous and variable dose of rapid-acting insulin to cover basal insulin requirements and delivers boluses to cover meals. Insulin pumps have advantages, particularly providing freedom around meal times, but when a problem occurs the adverse effects can happen quickly.

Case 6

Stuart is 15 years old and has had type 1 diabetes for five years. For the past two years he has been using an insulin pump (continuous subcutaneous insulin infusion, or CSII).

One morning Stuart wakes up feeling sick and vomiting. The night before he was well and his pre-bed BGL was 7.0 mmol/L. His blood glucose meter records his BGL as 'HI'. Urine ketones are 3+ (equivalent blood ketones, greater than 2.5 mmol/L). Stuart gives himself a dose of subcutaneous rapid-acting insulin by injection. He changes the site of his subcutaneous cannula and notices there was a kink in the cannula. By lunchtime he is feeling well and his ketones have cleared.

Ketosis

Because the pump delivers only rapid-acting insulin, if the pump fails, insulin levels in the body rapidly drop and ketones rise. Without immediate attention, diabetic ketoacidosis occurs.

Troubleshooting with pumps requires knowledge and practice in managing pumps, and patients should be advised to contact their diabetes team if they have a problem. If BGL exceeds 15 mmol/L and blood ketones exceed 0.5 mmol/L (urine ketones are less accurate when diagnosing pump delivery problems), assume the pump is not delivering insulin; further boluses should not be given via the pump until the cannula has been resited. Many diabetes centres would advise a dose of rapid-acting insulin be given by injection, followed by resiting of the cannula; suggested doses are given in Table 5. This will help to clear ketones and allow time to assess what has caused the failure in insulin delivery. Other centres may recommend immediately resiting the pump and giving a temporarily increased basal rate together with correction boluses to normalise BGLs.

The bottom line is that whenever hyperglycaemia with ketones develops in a patient using a pump it should be assumed the pump is not delivering insulin. The pump problem needs to be rectified before insulin can be confidently given through the pump.

SUMMARY

The management of type 1 diabetes in children is rapidly changing. With the newer insulin regimens and advances in delivery devices, keeping up with changes in management is difficult outside of a specialist paediatric diabetes unit.

Recognising the symptoms of type 1 diabetes early, with prompt referral to hospital, helps prevent children with new onset type 1 diabetes from developing diabetic ketoacidosis. An understanding of the insulin regimens and the onset and duration of action of the different types of insulin provides the basis for managing and modifying insulin in the face of changing requirements.

GPs are well placed to provide support to young patients and their families. This relationship will be particularly important at times of change, providing continuity through transition periods in life. MT

ACKNOWLEDGEMENTS

The authors would like to acknowledge the helpful comments and suggestions of Associate Professor Jenny Couper and Dr Jan Fairchild at the Women's and Children's Hospital, Adelaide, SA.

REFERENCES

1. Australian Institute of Health and Welfare (AIHW). Prevalence of type 1 diabetes in Australian children, 2008. Diabetes series no. 15. Cat. no. CVD 54. Canberra: AIHW; 2011.
2. Australian Institute of Health and Welfare (AIHW). Incidence of insulin-treated diabetes in Australia 2000–2009. Canberra: AIHW; 2012. Available online at: http://www.aihw.gov.au/diabetes/incidence (accessed September 2012).
3. International Diabetes Foundation. IDF diabetes atlas, 3rd ed. Brussels: IDF; 2009.
4. Craig ME, Hattersley A, Donaghue KC. Definition, epidemiology and classification of diabetes in children and adolescents. Pediatr Diabetes 2009; 10 Suppl 12: 3-12.
5. Endocrinology Expert Group. Therapeutic Guidelines: Endocrinology. Version 4. Melbourne: Therapeutic Guidelines; 2009.
6. Craig ME, Twigg SM, Donaghue KC, et al; for the Australian Type 1 Diabetes Guidelines Expert Advisory Group. National evidence-based clinical care guidelines for type 1 diabetes in children, adolescents and adults. Canberra: Australian Government Department of Health and Ageing; 2011.
7. American Diabetes Association. Diagnosis and classification of diabetes [position statement]. Diab Care 2012; 35 Suppl 1: S64-S71.
8. Metzger DL. Diabetic ketoacidosis in children and adolescents: an update and revised treatment protocol. B C Med J 2010; 52: 24-31.
9. Rewers M, Pihoker C, Donaghue K, Hanas R, Swift P, Klingensmith G. Assessment and monitoring of glycemic control in children and adolescents with diabetes. In: ISPAD clinical practice consensus guidelines 2009 compendium. Ch 7. Pediatr Diabetes 2009; 10(Suppl. 12): 71-81.

COMPETING INTERESTS: None.