A case of hyperglycaemia in a young woman using an insulin pump

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The immediate management and investigation of an acute endocrine presentation in general practice is discussed in this section. It is inspired by, but not based on, a real patient situation.

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Clare, aged 26 years, presents to your medical centre on Sunday morning at 9 am reporting high blood glucose levels (BGLs) since waking at 6 am. She has had type 1 diabetes since the age of 17 years.

Clare currently uses an insulin pump. She transitioned from multiple daily injections (MDI) of insulin six months ago when she started planning pregnancy. This was under the care of her usual endocrinologist at the local hospital's diabetes centre. Clare does not have any known complications of diabetes nor associated autoimmune disease.

Apart from mild lethargy and thirst, Clare does not appear distressed or unwell. She denies any chest pain, infection, or concurrent illness. On examination, she is afebrile and her blood pressure and pulse are in the normal range. Her cardiovascular, respiratory and abdominal examination results are normal.

Clare is concerned because her glucose levels have not been this high since she started using the pump. She has been unable to contact her usual diabetes care team after hours.

What immediate investigations would you perform?

Answer: Diabetic ketoacidosis (DKA) is a potentially life-threatening emergency and should be checked for in all people with type 1 diabetes who present with hyperglycaemia. Other situations where ketone checks are prudent include presentations with abdominal pain, decreased oral intake, nausea and vomiting, significant sepsis or during pregnancy. The key features of DKA are venous pH below 7.3 or bicarbonate level below 15 mmol/L, and positive ketones in the blood (usually in the presence of BGL higher than 11.1 mmol/L, although not exclusively). DKA can develop quickly, even with mildly elevated (or rarely, normal) glucose levels.

In the community setting, measurement of capillary blood ketone levels is best performed with a bedside glucometer with ketone-measurement function (using ketone testing strips). If this is not available, urine dipstick analysis for ketones is an alternative method of ketone estimation, although it is less accurate because urinary ketone detection is delayed by a few hours.

You perform a finger-prick BGL test and ketone measurement. Clare's current BGL is 21 mmol/L and her capillary blood ketone level is 0.9 mmol/L. A bedside pregnancy test is negative.

How should blood ketone levels be interpreted in this setting?

Answer: Increased blood ketone levels should be interpreted as shown in Table 1.

Clare's ketone production may be increasing but it is not yet at a level that would suggest DKA or require urgent referral to the emergency department. Prompt action to reduce ketone production is advisable.

What further history would you obtain?

Answer: After establishing that Clare is haemodynamically stable and not at immediate risk of DKA, a thorough history of recent events, BGL profiles and insulin use should

be taken. Potential triggers for hyperglycaemia should be identified and the self-management steps that Clare has already taken should be clarified.

Clare normally checks her BGL four times a day, before meals and before bed. Her levels have been well-controlled at between 4 and 10 mmol/L over the past few days, and she has not had any hypoglycaemic episodes. She has not experienced any intercurrent illness and there has been no change in her usual routine, including medications, diet and physical activity levels. She took a bolus of insulin with dinner last night, using the bolus wizard on her insulin pump to calculate the bolus amount. Clare's BGL was 7.5 mmol/L at midnight, when she went to bed.

At 6 am, her BGL upon waking was 19 mmol/L. Despite using the bolus wizard to deliver a correction dose of insulin with breakfast, her BGLs have remained elevated. She administered a further correction bolus at 8 am, but without effect. She has not performed a line change as she did this just before going to bed last night, and normally only changes the infusion set once every three days. She has been filling her pump with an existing supply of insulin that has been stored in the fridge. The pump battery appears to be functioning and no alarms have sounded.

How does an insulin pump work?

Answer: There are several types of insulin pumps on the market, but all deliver rapid-acting insulin (insulins aspart, lispro or glulisine) continuously through a subcutaneous catheter, 24 hours a day. The insulin is stored within a reservoir inside the pump and delivered to the person via an infusion set consisting of an insertion site and line connected to the reservoir. The pump and line can be disconnected for short periods of time (up to two hours) such as during bathing. As the pump delivers only rapid-acting insulin without the need for additional long-acting insulin, prolonged disconnection can rapidly lead to hyperglycaemia, ketone formation and DKA. The infusion set should be changed every three days; longer intervals increase the risk of insulin delivery failure.[1]

Table 1. Interpretation of capillary blood ketone measurements

Ketone level (mmol/L)	Significance
<0.6	Normal levels
0.6 to 1.5	Increased ketone production, retest 2 hours after insulin administration
1.5 to 3	High levels and risk of diabetic ketoacidosis
>3	Dangerous levels requiring immediate treatment

The rate at which insulin is delivered from hour to hour is known as the basal rate. It varies throughout the day and is tailored specifically to the person's individual requirements such that their BGL should remain stable in the absence of dietary carbohydrate intake.

A pump also delivers specific boluses of insulin on demand, to cover for carbohydrate ingestion (meal bolus) or to bring down high BGLs (correction bolus). Although the basal rate is maintained independent of the user, bolus doses require specific user input in order to be administered.

The bolus wizard

The bolus wizard is an inbuilt function of insulin pumps that allows insulin doses to be calculated according to the person's planned carbohydrate intake and/or prevailing glucose level. It calculates the insulin dose based on information that the user and their diabetes care team have programmed into the pump settings, namely the individual's insulin to carbohydrate ratio, insulin sensitivity factor, target BGL and active insulin time. As the insulin to carbohydrate ratio and insulin sensitivity factor may vary at different times of the day, different ratios and sensitivity factors can be programmed for different time blocks in the 24-hour period.

The insulin to carbohydrate ratio specifies the amount (in grams) of carbohydrate one unit of insulin is expected to cover. If the pump user enters their planned carbohydrate intake for a meal into the pump, a meal bolus is calculated.

The insulin sensitivity factor refers to the reduction in BGL that one unit of insulin is expected to produce. A target BGL is set in the pump by the user or diabetes care provider (e.g. 6.0 mmol/L during the day, 7 mmol/L before bed). If the user enters their current BGL and this level is higher than the target BGL then the pump will calculate the insulin dose required to bring the level back to target – the correction bolus.

If the BGL is above target before a meal, and is entered into the pump along with the planned carbohydrate intake, the wizard bolus calculates a dose that combines both the meal bolus and correction dose. At each bolus, the final dose is a combination of the dose as calculated by the insulin to carbohydrate ratio and the insulin sensitivity factor.

The pump is also able to adjust the recommended dose based on recent insulin boluses that are still expected to be active in the user.

The user has to confirm and action the dose suggested by the pump for it to be delivered. There is also the option to override the suggested dose and administer a manual bolus.

What are potential causes of hyperglycaemia in an insulin pump user and how will you help Clare?

Answer: Potential causes of hyperglycaemia in an insulin pump user are shown in Box 1.

You suspect Clare's insulin pump has a mechanical issue with insulin delivery that has not triggered an alarm. You advise Clare to perform a complete site, line and reservoir change. In the meantime, you suggest she administers insulin by subcutaneous injection to correct her BGLs, stop ketone production and prevent further deterioration.

What dose and type of insulin should Clare take?

Answer: All insulin pump users should have available insulin pens or syringes for

1. Potential causes of hyperglycaemia in insulin pump users

Mechanical

- Pump
  - pump malfunction (alarm should sound)
  - out of battery (alarm should sound)
  - pump in STOP mode
- Infusion set
  - tubing or infusion set occlusions (alarm should sound)
  - leaks in tubing or cartridge, kink in cannula or air bubbles in set
  - reservoir empty of insulin
  - dislodged cannula site
  - infusion set used for longer than 3 days

User-related

- Improperly primed tubing
- Poor absorption related to cannula site (e.g. lipohypertrophy due to prolonged use of site, inflammation around site)
- Extended time disconnected from pump
- Insulin expired or degraded by heat (insulin may look cloudy or clumped)
- Inadvertent change in pump settings
- Failure to confirm and action meal and correction bolus
- Underestimation of carbohydrate intake

Nonpump-related (applicable to any person with diabetes)

- Intercurrent illness – infections, surgery, trauma, myocardial infarction
- Medications triggering hyperglycaemia
- High glucose levels after overtreatment of hypoglycaemia

emergency use in the event of pump malfunction. In the first instance, rapid-acting insulin should be given by subcutaneous injection. The dose can be manually calculated using the insulin sensitivity factor, which is found by referring to the settings on the pump. Ideally, pump users should also keep paper records of their current basal rates, insulin to carbohydrate ratios and insulin sensitivity factors.

Clare has a target BGL of 6.0 mmol/L and an insulin sensitivity factor of 3 mmol/L per unit of insulin. As her current BGL is 21 mmol/L, she needs to lower her BGL by 15 mmol/L. Her calculated correction bolus is 5 units of rapid-acting insulin, which she administers using an insulin pen.

What plan will you give Clare for the next few hours?

Answer: After injecting the correction dose, Clare should change her complete pump set to correct any potential site or line problems. This involves refilling the reservoir, changing the tubing, priming the line and resiting the cannula. The pump can then be restarted at the usual basal rate. She should check her blood glucose and ketone levels after two hours, and, if satisfied that the site or line problem has been resolved, continue to monitor these at frequent intervals for the remainder of the day to ensure there are no other factors contributing to hyperglycaemia. Further correction boluses should be administered via the bolus wizard as necessary, but not more frequently than two-hourly as rapid-acting insulin has a duration of action of approximately three hours.

If the blood glucose and ketone levels respond after subcutaneous injection of the correction dose but rise again once the pump is reconnected and do not respond to further correction boluses delivered via the pump, it is likely that the system is still not delivering insulin appropriately. Clare should remove the pump and use both short-acting and longer-acting (intermediate- or long-acting) insulin subcutaneous injections in a standard basal–bolus regimen until the problem is corrected. In the event of obvious pump failure, pump companies have a 24-hour phone line that may be called to arrange a replacement, usually within a day.

Even brief interruptions in insulin delivery can evolve into diabetic ketoacidosis. People with type 1 diabetes are advised to have blood glucose meters that also measure ketone levels, and to keep up-to-date ketone testing strips at home. If ketone levels continue to rise despite attempted correction of a pump problem, the person should promptly seek medical advice. Some diabetes care providers provide rapid access to specialist medical advice during working hours. Alternatively, assessment and management in an emergency department is often required.

In general, if a pump user has persistent nausea or vomiting, has vomited more than once in four hours, is unable to bring down their blood glucose or ketone levels after the use of two insulin correction doses despite performing a pump set and line change, or is unable to maintain BGL over 4 mmol/L then specialist advice should be sought. In these situations, presentation to the nearest emergency department is recommended.

After the subcutaneous bolus dose of insulin and reconnection of the pump, you advise Clare to recheck her blood glucose and ketone levels in two hours. You ensure she has a supply of ketone strips and knows how to use them. She should continue to monitor levels closely for the rest of the day and present to the emergency department if the levels fail to drop in two hours, or fail to normalise over the course of the day.

That afternoon, Clare advises that her BGL is now 10 mmol/L and her blood ketones have cleared. Although she has appreciated the convenience of the pump, she is frightened by this experience and wants to know if it is the best option heading into a pregnancy.

What are the major considerations that will guide your advice to Clare?

Answer: The five major considerations guiding the advice you will give Clare are discussed below.

Risk of diabetic ketoacidosis

Issues with pump, line or infusion site malfunction occur from time to time in insulin pump users, and diabetic ketoacidosis may occur more quickly because only rapid-acting insulin is used. To minimise the risk, it is advisable to monitor BGLs at least four times a day, and to check them one to two hours after each line change. Line changes should be avoided within four hours of bedtime so that any problems are identified before the onset of sleep. In-date rapid-acting and basal insulins (as pen devices or vials) and insulin needles/insulin syringes should be kept at home and used in case of pump failure. A pump

identification card and a written record of all pump settings should be carried, along with spare pump batteries and pump consumables.

Users of insulin pumps should understand the causes of diabetic ketoacidosis and recognise its warning signs (Box 2). They are advised to present to hospital or contact their diabetes care providers if these occur.

All pump users and their primary care physicians should have a written plan for sick day management and how to respond to hyperglycaemia and ketosis. Users can contact the pump manufacturer in the case of pump failure to discuss any mechanical issues.

When used appropriately, with adequate education and support, pump therapy is a safe alternative to multiple daily injections.

Theoretical advantages of insulin pump therapy over multiple daily injections

Potential advantages of insulin pump therapy over MDI are listed in Table 2.

Randomised trial evidence in type 1 diabetes

Despite strong theoretical advantages, trial evidence for the greater efficacy and safety of insulin pumps compared with MDI is weak. Several randomised controlled trials have demonstrated greater HbA_{1c}-lowering with insulin pump therapy compared with MDI, but the effect is small (<1%). A meta-analysis of 12 such trials in adults with type 1 diabetes indicated a statistically significant difference in favour of insulin pump therapy of 0.29%.[2] Some studies have not shown benefit for hypoglycaemia, though two recent reviews found a reduction in severe hypoglycaemia.[2,3] Most studies have shown that pump use improves health-related quality of life in adults and children with type 1 diabetes.[4]

When to consider pump therapy

Insulin pumps are used when clinically significant reduction of HbA_{1c}, reduction in hypoglycaemia or improvement in quality of life are being considered. Strong motivation, realistic expectations, accurate carbohydrate-counting skills, technical mastery of the pump and ability to self-manage diabetes all contribute to pump success. Many people obtain an insulin pump 'free' through their private health fund; for those without private insurance, the cost of the pump may be prohibitive.

2. Warning signs of diabetic ketoacidosis

- Abdominal pain, persistent nausea and vomiting (more than once in four hours)
- 'Fruity-smelling' acetone breath, rapid breathing, shortness of breath
- Inability to bring down BGL or ketones despite two supplemental correction doses of insulin

Pump use in pregnancy

Insulin pump therapy is considered safe and effective in pregnancy, although few

Table 2. Potential advantages of insulin pump therapy over multiple daily injections of insulin

Insulin pump	Multiple daily injections
• Smaller depots, less variable absorption • Lower total daily dose of insulin	• More variable insulin absorption from larger subcutaneous depot
• Basal rates are set hour to hour depending on individual requirements • Basal rates can be programmed to remain low overnight and rise in the early hours of the morning, potentially reducing nocturnal hypoglycaemia	• Single or twice daily injection of basal insulin • Increasing dose of basal insulin to lower morning BGL may increase risk of overnight hypoglycaemia
• Bolus wizard specifically designed for flexible insulin therapy • Pump adjusts for previous bolus insulin still in action • Can deliver boluses over longer time periods, e.g. square wave or dual wave	• Possibility of flexible insulin therapy: bolus doses adjusted according to expected carbohydrate intake and pre-meal BGL • Doses calculated by user or by a 'smart meter'
• Cannula insertion site changed every 3 days	• Up to 4 to 5 injections per day

Abbreviation: BGL = blood glucose level.

randomised trials exist on their use in pregnancy. A Cochrane review suggested no difference in maternal or neonatal complications compared with MDI.[5] Theoretical benefits include reduced frequency of hypoglycaemia, reduced glycaemic variability and improved quality of life. Pumps can be worn throughout pregnancy and even during labour in hospital centres with specialised pump experience.

Outcome: Clare recalls receiving education about managing pump problems and hyperglycaemia six months ago when she started using an insulin pump. She had significantly reduced her contact with her diabetes educator in the past three months as her diabetes management seemed to be going well. She is keen to have a refresher session with the educator now. She has an existing appointment with her endocrinologist in a fortnight's time. You remind Clare to discuss her plans for pregnancy with this specialist.

You organise an HbA_{1c} measurement and check that Clare is taking prepregnancy vitamin supplements, including 5 mg folate daily, and ensure her complication screening is up to date. You reassure Clare that she is now better equipped to troubleshoot pump problems in the future. Continuing to use the pump may still be a good option during pregnancy, and you advise her to discuss this in more detail with her diabetes care team. ET

References

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Practice points

- Managing hyperglycaemia in the context of insulin pump therapy requires familiarity with this technology.
- Insulin pumps deliver small amounts of rapid-acting insulin continuously at set basal rates. Additional bolus doses are administered according to the user's insulin to carbohydrate ratio and insulin sensitivity factor, accounting for carbohydrates consumed and prevailing BGL.
- Causes of hyperglycaemia on a pump include:
  - mechanical problems with the pump, insulin reservoir, infusion line or insertion site
  - user-related causes, such as inadequate priming of the line, incorrect bolus administration, disconnection from the pump
  - nonpump-related causes, common to anyone with diabetes.
- Diabetic ketoacidosis can develop quickly in people with type 1 diabetes using an insulin pump if there is any interruption to insulin delivery.
- Blood ketone levels are useful in stratifying the urgency and severity of a person's hyperglycaemia. They rise earlier than urinary ketone levels.
- Pump users should always have a supply of insulin pens or insulin vials and pen needles or insulin syringes in case of pump failure.
- Insulin pumps may reduce hypoglycaemia and improve glycaemic control in motivated individuals, and improve quality of life. More randomised trials in pregnancy are needed; current evidence does not suggest harm.

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