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# Moving Up a Level

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EDITORS' NOTE

Diabetes is characterized by insulin deficiency. In type 1 diabetes, loss of insulin production may be rapid and profound with life-threatening consequences. In type 2 diabetes, loss of insulin production is slower, but progressive and relentless (1). In type 1 diabetes with almost total loss of insulin production, intensive management with basal-bolus insulin or insulin pump therapy is recommended by the Canadian Diabetes Association clinical practice guidelines (2). At the time of diagnosis of type 2 diabetes, about 50% of maximal insulin-producing ability has been lost, and this loss continues at a rate of approximately 5% per year. When insulin production declines to approximately 20% of maximum (±6 years from diagnosis), the individual with diabetes becomes metabolically unstable, glucose levels and glycated hemoglobin (A1C) start to rise into double digits, and insulin is required to restore control.

Unfortunately, in Canada we are reluctant to initiate insulin. In 2003, the Diabetes In Canada Evaluation (DICE) study (3) showed that the average length of time between diagnosis of diabetes and initiation of insulin therapy was over 10 years. In 2010, the SOLVE study showed that our behaviour had not improved in the ensuing 7 years, and it still takes an average of 10.2 years between onset of diabetes and insulin initiation (4). Unfortunately, our reluctance to initiate and titrate insulin therapy is one of the main reasons that only approximately 50% of persons with diabetes in Canada achieve a target of A1C <7% (3).

Dr. Alice Cheng discussed insulin initiation in the spring 2011 issue of *Canadian Diabetes* (5). She discussed how insulin initiation is safe and effective. The importance of starting insulin early when glucose control can no longer be achieved with oral agents and lifestyle was discussed. She also emphasized the need to keep adjusting the insulin dose as needed to achieve a fasting glucose target of 4 to 7 mmol/L.

This issue of *Canadian Diabetes* takes us past this point of insulin initiation to look at what we need to do when we have managed to achieve fasting glucose levels of 4 to 7 mmol/L, but A1C remains above 7%. Dr. Stuart Ross leads us through the intensification of insulin. He points out that physiologic insulin secretion is biphasic; that is, there is a fairly steady background secretion of basal insulin throughout the day, with other peaks of insulin secretion associated with meals, referred to as bolus insulin. Initially, we are able to achieve glycemic control with basal insulin alone, but as insulin deficiency becomes progressively more profound due to ongoing beta-cell failure, we need to add mealtime insulin. As Dr. Ross points out, there are many different ways to provide for both basal and bolus needs (such as using pre-mixed insulin). Ultimately, with ongoing progressive pancreatic failure, we reach a point where we need basal-bolus insulin replacement, similar to that which is needed for individuals with type 1 diabetes. It may, therefore, be easier to make a logical transition from basal insulin alone to "basal plus" (with short-acting insulin at the largest meal of the day), and then progress to insulin at each meal with or without high glucose corrections, as needed.

While some of our patients with diabetes may have special needs and could benefit from compromises such as pre-mixed insulins; for the majority, it is better to progress to basal-bolus insulin because it gives the flexibility to adjust to progressively increasing insulin deficiency. We start intensification by adding a mealtime dose of short-acting insulin analog, aspart (NovoRapid), glulisine (Apidra) or lispro (Humalog) at the largest meal of the day. We may start at an arbitrary dose of 3 to 5 units with the meal, and then titrate up this mealtime dose until generally 4 hours later (at the next meal or bedtime) glucose levels have returned to the normal level (4 to 7 mmol/L). If despite this basal plus approach we still have not achieved the glycemic target of A1C <7%, then we can add bolus insulin at the next meal and, ultimately, to the third meal. We can start the mealtime bolus dose from 3 to 5 units, then increase in 1 unit increments every few days

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until we achieve normal glucose values 4 hours after the meal (or before the next meal). If we have titrated up the bolus insulin dose at each meal and have still not reached an A1C target <7%, it may be necessary to add a high glucose correction for each meal to correct preprandial hyperglycemia. Alternatively we can use regular human insulin as the mealtime insulin; it has a cost advantage over the rapid acting analogues and, in type 2 diabetes where there is still some endogenous insulin production, it may provide adequate control. The problem with regular insulin is that it needs to be given about 30 minutes before a meal; it peaks about 2 to 4 hours after injection; so in an individual with severe insulin deficiency, it may not adequately cover the immediate postprandial period, and the peak effect may lead to hypoglycemia by 3 to 4 hours after injection.

While each person has different insulin sensitivity, a common glucose–correction algorithm is shown in Table 1.

**Table 1. High/low glucose correction**

| Preprandial glucose (mmol/L) | Action |
|---|---|
| <4.0 | Subtract 2 units from the mealtime bolus |
| 4.0–5.0 | Subtract 1 unit from the mealtime bolus |
| **5.1–7.0** | **Use planned mealtime bolus dose** |
| 7.1–8.0 | Add 1 unit to the mealtime bolus |
| 8.1–9.0 | Add 2 units to the mealtime bolus |
| 9.1–10.0 | Add 3 units to the mealtime bolus |
| 10.1–11.0 | Add 4 units to the mealtime bolus |
| >11.0 | Add 5 units to the mealtime bolus |

When we reach this point, we are providing full basal-bolus insulin support, which is similar to what we do in type 1 diabetes. The reason for the intensification is that insulin production has continued to decline. In the absence of endogenous insulin production, basal-bolus insulin is required to mimic normal physiology. The insulin pump is one way of providing this basal-bolus support. In Canada, 20% to 30% of patients with type 1 diabetes use an insulin pump. Several Canadian provinces, including Ontario, Newfoundland, Quebec and British Columbia support the cost of insulin pump therapy, at least for pediatric patients, as this form of intensive therapy has been shown to achieve better glycemic control and results in a decreased toll to complications.

While the pump is only a device for the injection of insulin and does not function automatically to control glucose levels, it does offer some advantages compared to basal-bolus therapy with an insulin pen or syringe. The first advantage is the ability to have different basal rates throughout the day. Basal insulin needs are often lowest during the early hours of sleep (10 PM to 4 AM), then dramatically increase during the early morning hours (4 to 8 AM) as growth hormone secretion peaks and the dawn phenomenon occurs. It is only with an insulin pump that we can provide for these different basal needs throughout the day. With most insulin pumps, a paired glucose meter may report wirelessly to the pump. One can then use mathematical formulae built into the pump to determine bolus or high glucose correction insulin needs. While the pump may do the calculations, there is still the need for the human interface to approve and start the insulin dosing.

Dr. Robyn Houlden has pointed out that pump use—particularly in type 1 diabetes—is increasing, so as physicians in the emergency room (ER) or in patient settings, we are inevitably going to deal with more patients with insulin pumps. Most people on insulin pump therapy become very capable of using these devices to precisely control glucose levels and are usually better than many healthcare professionals at running their pumps. In most circumstances, people with an insulin pump in an outpatient or inpatient setting can be permitted to do their own glucose monitoring and insulin adjustments, but it needs to be done in cooperation with hospital staff and a full interchange of information so that hospital staff know what the glucose results are and what action is being taken.

As these devices become more common, we need to have capable hospital staff familiar with insulin pumps, and have the proper procedures and policies in place to allow cooperative pump management. Usually, whatever the circumstances in hospital, the patient's normal basal rate can be continued and, if normal meals are being taken, then we can follow the patient's previously determined bolus and adjustment doses. If the patient is nil per os or on intravenous (IV) fluids (with no carbohydrate content), then only basal insulin is needed, though frequent monitoring still needs to be done, and high or low glucose corrections applied. If hypoglycemia occurs in an individual who cannot eat, we can suspend or give a temporary basal rate reduction until glucose levels return to normal.

With people on an insulin pump presenting to the ER with hypo- or hyperglycemic emergency, we need to have experienced staff who are trained in pump use on duty or rapidly available and adequate hospital policies to provide a framework for responsibilities of treatment. At the very least, emergency staff need to know how to react to pump patients—how to work back from their total daily dose (TDD—basal doses and usual meal boluses and corrections factors) to substitute basal bolus insulin for them if the

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patient is not well enough for self-care. For hypoglycemic emergencies, the pump is usually placed in a suspend mode while usual glucose-raising measures are taken of oral ingestion of carbohydrate where possible, or use of glucagon or IV glucose. We need to remember that the insulin pump delivers only rapid-acting insulin, so if the pump is not functioning or is suspended, then hyperglycemia and ketoacidosis can start very rapidly. As soon as the hypoglycemic emergency has been adequately treated, basal insulin delivery needs to be resumed through the pump or by injection.

In hyperglycemic emergencies, the first thing to do is to establish normal glucose levels by administering short-acting insulin analogues using a pen or syringe or use of IV regular insulin and fluids if very ill. Frequently, the cause of hyperglycemia is the failure of the pump to deliver insulin due to pump failure, blockage or disconnection, but because of the short space of time before ketoacidosis occurs, we should not waste time trying to troubleshoot the pump, but rather give the needed insulin. When glucose levels have returned to normal we can troubleshoot the problem with the assistance of the patient, who is often the most proficient in pump use.

Insulin pumps are a useful alternative for insulin administration in people with type 1 diabetes or advanced type 2 diabetes who have severely compromised insulin production. In most cases, people who have insulin pumps are well trained and can solve problems; however, there are circumstances where assistance is needed from trained hospital personnel. It is essential for us to have trained staff and policies in place to allow us to capably assist these people with diabetes in our modern healthcare institutions.

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