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Insulin and type 2 diabetes

A simple guide to prevent 'stuff ups'

Starting insulin in type 2 diabetes should follow the KISS principle (Keep It Safe and Simple) but too often the 'stuff ups' sneak in. This article discusses the 10 common ways to stuff up insulin therapy and how to avoid them.

1. Insulin as a threat

The patient enters the consulting room. Dr thinks: 'Oh no, John's put on more weight. I bet he's not stuck to his diet and activity schedules'. Dr says: 'John you're 3 kg heavier since your last visit. If things don't change soon, the next step is insulin. Neither of us want that, do we?'

The threat may be implied or stated, but people may already have bad associations with insulin (*Table 1*). Fear of insulin is intensified if the doctor sees insulin as a bad thing as well. Don't use insulin as a threat that makes patients even more scared of starting it.

2. Delaying insulin

The common scenario is:

Month	A1c	Reason A1c not lower
February	8.2	Christmas, New Year, holidays
May	8.4	Stress of work after the break. Things better now
August	8.5	Winter – too cold and dark to get out for my regular walk but I'm joining a gym
December	8.5	It's been hectic with Christmas parties, buying presents and getting ready for the holidays...but my new year's resolution is to get the sugar down
February	8.7	...

Patients with type 2 diabetes have both physiological and psychological insulin resistance to insulin. Doctors dealing with type 2 diabetes may have professional and psychological resistance to insulin as well (*Table 2*).

Often we never learn how to start insulin as students, interns, or in our training. If we are taught, we may have been taught insulin schedules appropriate for type 1 diabetes. These are not appropriate for starting insulin in type 2 diabetes. We may share some patients' bad associations and we may

believe that insulin often increases weight and causes hypoglycaemia.

Most of the barriers we perceive are easily overcome (see below). It's true that starting insulin may be associated with weight gain but this is not inevitable. If you encourage the patient to 'eat less and walk more' weight can remain stable or even decrease¹. If weight gain becomes a problem, consider a bariatric medication (sibutramine, xenical) or bariatric surgery (laparoscopic gastric banding, gastric bypass).

As for hypoglycaemia, it's true insulin may decrease blood glucose to the point that the patient feels a bit trembly or hungry, but severe hypoglycaemia – where help is required from another person – is rare. This is a big problem for type 1 diabetes, but with equivalent glycaemia severe hypoglycaemia occurs at 1/20 the rate in type 2 diabetes.² Most hospital admissions for hypoglycaemia are associated with oral hypoglycaemics, specifically the long acting sulphonylureas with active metabolites (glibenclamide, glimepiride) not insulin.

3. Stopping oral hypoglycaemics

The following sequence occurs:

Day 0 FBG 9.5 mmol/L; metformin 850 mg tds, glibenclamide 10 mg bd, rosiglitazone 8 mg mane
Day 1 FBG 9.5; insulin starts; tablets stop
Day 2 FBG 10.1
Day 3 FBG 13.6
Day 4 Phone call: 'All my blood glucose values are in the high teens. This insulin isn't working'.

The insulin is working but stopping the tablets was a mistake. The oral hypoglycaemics were working. The insulin sensitisers (metformin and rosiglitazone) were reducing insulin resistance and the insulin secretagogue (glibenclamide) was increasing insulin secretion. They just weren't working enough to overcome the increasing insulin resistance and decreasing insulin secretion that occurs with time in type 2 diabetes (*Figure 1*).

Stopping the tablets won't cause an immediate dramatic increase in blood glucose. The effects of metformin decrease over the next day or so. Glibenclamide has a long half life (especially in those with renal impairment)

Table 1. Fears about insulin	
Special fears	Explanation or action
Insulin will cause complications	Explain that insulin will improve diabetes control and thus reduce the risk of complications
Insulin will cause coma or loss of control	Explain that blood glucose control in type 2 diabetes is more stable than in type 1 diabetes and big swings are uncommon
Injection will be very painful	Demonstrate that today's fine needles do not hurt. 'Human' insulin is manufactured and not derived from human tissue
Insulin treatment will lead to addiction	People with diabetes use syringes to inject insulin because it cannot be taken by mouth. Thousands of people use insulin but they are not addicted to it

Table 2. Professional and psychological insulin resistance	
Professional	Concern about weight gain, hypoglycaemia Lack of access to patient education Lack of knowledge of insulin doses and devices
Psychological	Perception that starting is difficult Perception of failure to control blood glucose Bad associations similar to that of patients

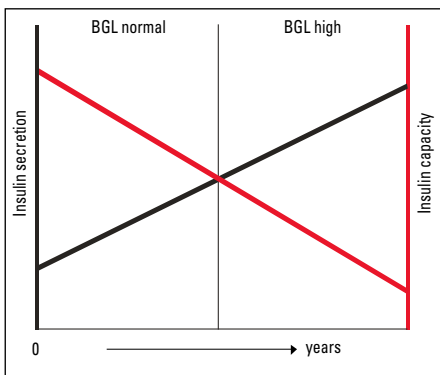


Figure 1. The natural history of type 2 diabetes
With time insulin resistance increases and insulin capacity decreases. Once resistance exceeds capacity, blood glucose progressively rises

and the glitazone effects come on and wear off over weeks. However, it is predictable that their effects will wear off and blood glucose will increase.

Theoretically you could prescribe enough insulin to make up for the loss of the oral hypoglycaemic effects. However, if you do this you'll prescribe too much insulin on days 1 and 2 when the remaining oral hypoglycaemic effects continue.

It all sounds a bit hard, and it is if you stop the tablets when you start the insulin. Don't stop the oral hypoglycaemics now. Get the blood glucose under control and consider stopping them later. You may decide to stop the sulphonylurea which was probably losing its effect anyway as the pancreas' capacity to secrete insulin has decreased since starting it.

You may also decide to stop the glitazone, more particularly if weight gain or oedema are issues. Both insulin and the glitazone can cause these problems. However, you will probably keep the metformin given its effect on insulin resistance, which is maintained or increased throughout the duration of type 2 diabetes (Figure 1). In future years you may decrease metformin dose or stop it because of declining renal function, pulmonary or heart failure, but for the foreseeable future metformin will continue to be useful.

4. Starting with a premix

The following sequence occurs:

- Twice daily premixed insulin is started – so far so good

- Morning dose increased to get lunch and dinner blood glucose under control – hypoglycaemia occurs mid morning
- Evening dose increased to get breakfast blood glucose under control – hypoglycaemia occurs late evening
- Weight gain for the patient – disappointment and frustration for both doctor and patient.

Worldwide, premixed insulins are most commonly prescribed and are promoted as if 'one size fits all'. In clothing, XL will fit all but not very comfortably or elegantly. For type 2 diabetes insulin premixes rarely fit anyone and cause several avoidable problems. Remember that in type 2 diabetes insulin secretion continues, but there is not enough. Starting insulin aims to boost the effect of the oral hypoglycaemic agents. What is needed is a long acting 'basal' insulin not a quick acting 'bolus' insulin which will increase the risk of hypoglycaemia and weight gain. The premixes have both basal and bolus insulin. Titrating the dose to provide enough basal insulin to control blood glucose overnight or throughout the day will also titrate the dose of quick acting insulin. This causes the problems. Very occasionally the proportion of basal and bolus are right for a particular individual but this is unusual. It will also usually only be temporary as circumstances and requirements change. Premixes have two built in problems as starters in type 2 diabetes:

- the quick acting insulin is usually not needed and can cause hypoglycaemia and weight gain
- the fixed proportions make titration difficult because the basal and bolus components serve different purposes but are necessarily titrated together.

5. Starting with a twice per day dose

The 'rule of thumb' for insulin is two-thirds in the morning and one-third in the evening. This may be one way to start insulin for type 1 diabetes but not for type 2 diabetes.³

The usual problem is a high fasting blood glucose (FBG) associated with hepatic glucose output during the night (Figure 2a). The usual dose of basal insulin at bedtime will control overnight glycaemia and FBG. Less often, the

problem is during the day when the muscles are not using enough glucose (Figure 2b). Here a morning basal dose will do the job.

The KISS principle

- Get the FBG under control with night time basal insulin if necessary
- Get the evening blood glucose under control with morning basal insulin if necessary
- Check overall blood glucose control with an A1C
- If the A1C is not on target, find the hidden ‘hypers’. Fix them by changing meal size or composition or by adding meal time quick acting insulin.

6. Starting low, but going too slow

Usually a bedtime dose is needed. Adapting Henry Ford’s comment (Ford is quoted as offering a range of colours for the Model T Ford: ‘Pick any colour, as long as it’s black’); ‘Pick any dose of insulin, as long as it is 10 units’ (Humulin NFH, Lantus, Protaphane). This is safe and gives a good introduction to insulin. Then increase the dose to bring the FBG under control. Simple so far.

The ‘stuff up’ occurs when doses are increased by small increments and infrequently. Changing by two units every 2 weeks is likely to take months (or even years) to get to target. Some people require 50 units or more. Increasing by two units every 2 weeks will get you to 50 units in 40 weeks! By that time both you and the patient will be understandably frustrated and will think the insulin is never going to work. Worse still, you may have given in to well meaning but inappropriate advice and fallen for the ‘premix stuff up’.

Start low, but don’t go too slow. Use an insulin adjustment algorithm every 2–3 days (Table 3). Your practice nurse or, better still, the patient, can adjust the dose until the FBG is on the specified target (eg. ~6 mmol/L) then, if necessary, repeat the process to control the evening blood glucose.

Most of the time fixing the FBG will fix the other values. You and the patient can then decide if one or more of the hypoglycaemic agents should stop. Stopping may increase blood glucose, which may require a second insulin shot. The patient can then decide whether to restart the oral hypoglycaemic or have two shots per day.

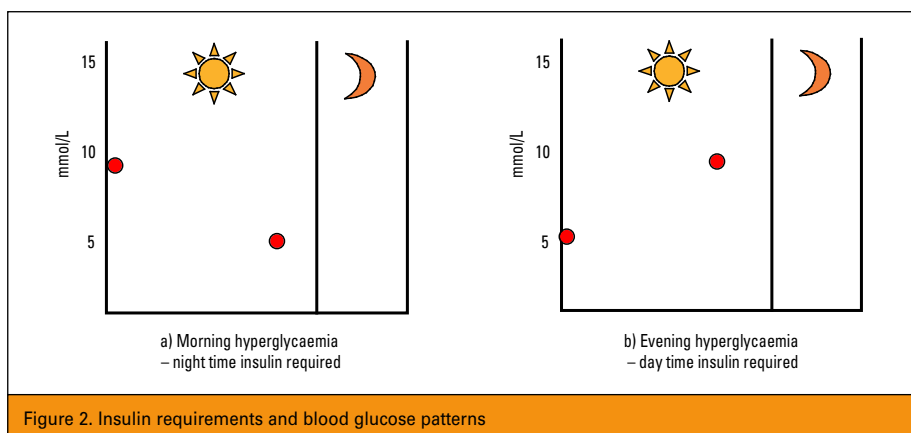


Figure 2. Insulin requirements and blood glucose patterns

7. Adjusting basal insulin to control blood glucose better controlled by bolus insulin

‘My blood glucose in the evening is always in double figures. You told me to increase my morning insulin but I keep going low in the afternoon. It is like a yoyo – up and down, up and down. Should I try increasing the evening insulin?’ No. If you do that, the FBG will be low and things will be worse.

Here the patient is telling you evening postprandial rather than preprandial values. Increasing the morning basal insulin won’t control the evening postprandial glucose but will, and did, cause hypoglycaemia in the afternoon.

The basal insulins, currently usually isophane, and the new analogues (insulin detemir, Levemir; insulin glargine, Lantus), control overall night and day glycaemia. The analogue bolus insulins (insulin Lispro, Humalog; insulin aspart, NovoRapid) have a more rapid onset and offset and a higher peak than neutral insulins (actrapid, Humulin R) and can control blood glucose before lunch and after the evening meal. Bolus insulin may be needed when overall night and day time glycaemia is on target (fasting and before the evening meal blood glucose) but A1C is too high.

First check that the blood glucose values you are seeing are a true and complete record. Patients have been known to put in numbers that will make you feel better and/or omit high values as they ‘know what caused them and I don’t usually do that’. Ask the diabetes nurse to check blood glucose testing and insulin injection techniques.⁴

If fasting and evening blood glucose are on target, records are complete and correct and

Table 3. Adjusting basal doses

BGL*	Insulin dose
>10	8 units more
8–10	6 units more
6–8	2 units more
3.5–6.0	No change
<3.5	4 units less

* This algorithm can be used to titrate bed time or morning doses basal insulin

Usually the BGL target before breakfast or the evening meal is <6. If targets are different, adjust the algorithm accordingly

A1C is high, it’s time to find the hidden ‘hypers’. These are often in the middle of the day, late morning or midday before lunch, or at the end of the day after a large meal and an evening with the remote in front of the television! If so, adding quick acting insulin before breakfast or the evening meal respectively will get the blood glucose back under control.

Once again, start low (eg 4. units) and increase doses to bring 2 hour postprandial blood glucose values under 15. Then recheck the A1C and overall glycaemia. Don’t aim to get postprandial glucose too low. The ‘quick acting’ insulins are not all that quick and aiming for a 2 hour postprandial glucose in the ideal range of <8 mmol/L is asking for hypoglycaemia later on.

8. Using a bolus insulin to fix a problem with the basal insulin

‘I use a sort of sliding scale of regular – my blood glucose before meals plus two. That usually seems to work okay but just recently things are seesawing. High blood glucose before

breakfast, low before lunch, high before tea. Plus a few hypos at night. It really is a mess’.

Indeed it is. Sliding scale insulin is obsolete. Sliding scale uses something that will work in the future (the bolus insulin) to control something that happened in the past (and caused the high blood glucose). Sliding scale insulin is a convenient way of not having to think too much but frequently causes problems.

The problem here is that more bedtime basal insulin is needed. Taking extra regular at breakfast won't fix the problem but may cause blood glucose to be low before lunch. Then, less regular insulin may be given at lunchtime causing the evening blood glucose to be high. The sliding scale insulin dose before the evening meal is increased and overnight hypoglycaemia occurs. The next morning, blood glucose may be even higher because of the extra carbohydrate consumed during the 'hypo' and the ongoing deficit of basal insulin.

A basal insulin problem must be fixed with the appropriate basal insulin. It's a temptation for patients to fix blood glucose 'right now' but they will be tempting fate if they do. One day they'll find themselves on the seesaw. Patients should learn to identify the problem that is causing current blood glucose to be high. Then they can correct the underlying problem and not just try to fix the blood glucose value at that time.

9. Prescribing carbohydrate snacks between meals or before activity to avoid hypoglycaemia

'The dietician told me that now I'm on insulin I need to have morning tea, afternoon tea and a bedtime snack to spread my carbohydrate over the day and to stop my blood glucose falling between meals. She also said I should have a snack before I exercise so I don't get a 'hypo'. I've not had any hypos but I'm really stacking on the weight – 5 kg since I started insulin 2 months ago. I feel like I'm eating all day. Do I really need all that food?'

No. Asking people with diabetes to have extra carbohydrate and to eat six times per day is asking them to get fatter.

Activity is important to use extra energy and control weight. Extra food beforehand negates this and may actually provide more energy than the activity uses. Remember when starting

insulin people need to 'eat less and walk more'. Hypoglycaemia between meals indicates either too much insulin or too little available glucose. Reduce the dose of the appropriate insulin and/or modify the composition of the preceding meal.

Hypoglycaemia during activity doesn't usually occur with 'walking more' but if it does, adjust the preceding dose of insulin. Don't use extra food to correct a problem caused by the preceding insulin dose or the preceding meal. Fix them instead.

10. Not progressively increasing insulin doses or not adding new doses of insulin

'I've just got a quick clinical question. I started insulin in a 56 year old woman some 18 months ago. Just like you said – start with 10 units at bedtime and increase the dose. It worked well but now she's on 85 units per day and has to dial her pen injector twice to give the dose. She's asking why she needs all this insulin. Her daughter is a nurse and said she knows lots of people who only need 30–40 units per day. Her A1C is 8.7% but she's resisting any increased insulin dose. What do you advise?' Increase the dose and/or add metformin if you stopped it (as long as it is safe).

When delaying insulin the temptation was to accept the 'reasons' for the high A1C. But blood glucose progressively increases because of the various insulin resistances in the patient and doctor. The situation now is similar. At diagnosis lifestyle may well control blood glucose. Later tablets will be needed and then more tablets. The UKPDS found that approximately 50% of people needed insulin within 5 years of diagnosis to maintain glycaemic control (A1C <7%).⁵

The patient is a long way from 7% and her A1C has probably been well above target and climbing for several years. She may need a second shot of basal insulin and the doses at morning and bedtime may need to be increased to get blood glucose before breakfast and before the evening meal under control. If A1C is still above target, find the 'hidden hypens' and fix them.

An A1C of 8.7% doesn't sound very high when you are used to dealing with blood glucose values. However, the A1C is equal to the average blood glucose only at 6 mmol/L (6% at 6 mmol/L). Thereafter the blood glucose and

A1C progressively diverge.

Average BGL = (2A1c-6) mmol/L. An A1C of 7% equates to average blood glucose of 8 mmol/L; 8% to 10 mmol/L and 8.7% to 11.4 mmol/L. At 8.7% the patient is spending most of her time in the double figures. Expect insulin requirements to progressively increase as the insulin resistance progressively increases and the insulin capacity progressively decreases (*Figure 1*).

It's true that some people may need only 30–40 units per day but others will need 100–200 units per day. When the A1C starts climbing, 'don't just sit there doctor, do something'... increase the insulin.

The bottom line

The KISS method is safe and simple but mistakes are easy to make. Most result from not recognising the true progressive nature of type 2 diabetes and not feeling comfortable about starting and increasing insulin. Insulin is just one step in the diabetes pathway, it's not the end of the road for the patient and it's not hard for the doctor to use. Remember, insulin is your friend. Insulin is good. Insulin works.

Conflict of interest: Dr Phillips has provided advice, participated in company sponsored meetings and clinical trials and received honoraria from all three companies marketing analogue insulins: Lilly, Novo Nordisk, Sanofi-Aventis. Dr Phillips does not believe that these associations have influenced the content of this article.

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