KISS: 'keep insulin safe and simple'

Part 1: initiating insulin in type 2 diabetes

Lifestyle change and oral hypoglycaemic agents will initially be effective in achieving stable and on-target blood glucose levels in patients with type 2 diabetes. However, the time will come when insulin therapy has to be started.

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Many patients with type 2 diabetes eventually require insulin therapy for glycaemic control. While the problems of starting insulin are immediate and obvious to both doctors and patients, the problems of not starting are more remote and less perceptible – a progressive increase in the risk of diabetes related complications. However, starting insulin is not hard, not risky and does work.

This article provides a simple six-step guide to starting insulin therapy in patients with type 2 diabetes to achieve stable and on-target blood glucose levels (BGL). The accompanying patient handout provides a guide to the procedure of injection insulin (pages 35 to 37).

Step 1. Is the patient's A_{1c} on target?

Individual glycosylated haemoglobin (A_{1c}) targets will depend on the likelihood of microvascular complications and problems with insulin. However, the United Kingdom Prospective Diabetes Study (UKPDS) has shown that the higher the A_{1c} then the greater the microvascular risks.[1] Usually an A_{1c} above 7% (BGL above 8 mmol/L) and certainly an A_{1c} above 8% (BGL above 10 mmol/L)

IN SUMMARY

- **An A_{1c} above 7% (BGL above 8 mmol/L) and certainly an A_{1c} above 8% (BGL above 10 mmol/L) should prompt consideration of starting insulin therapy.**
- **Before starting insulin check the patient's lifestyle, adherence to diabetes medications, the presence of other conditions and the other medications prescribed.**
- **Choosing the type of basal insulin depends on the pros and cons of the intermediate acting isophane insulin and the long acting insulin analogue and the patient's choice of injection device. If the fasting BGL is high, the insulin should be used at bedtime; if the fasting BGL is on target but the evening BGL is high, the insulin should be used in the morning. The starting dose should be 10 units.**
- **When adjusting basal insulin, approach targets fast and fine tune slowly. 'Going slow' can take too long; 'going fast' can cause hypoglycaemia and weight gain.**
- **Once basal insulin and preprandial blood glucose are on target consider stopping oral hypoglycaemic agents, particularly sulfonylureas, and consider starting quick acting insulin before meals.**
- **Potential problems starting insulin include coping with practical details, hypoglycaemia, weight gain and psychological resistance.**

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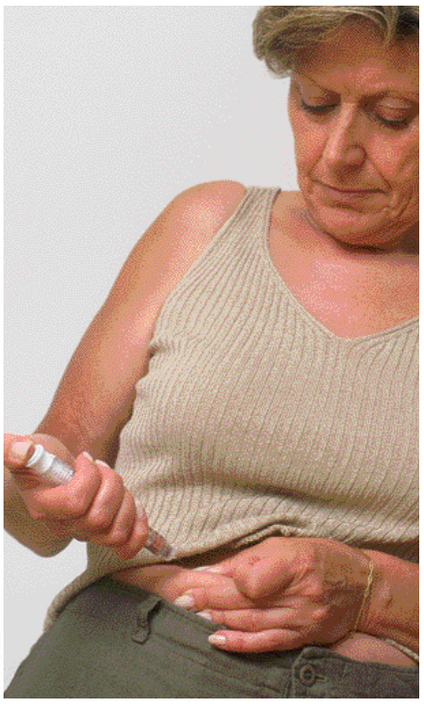


PHOTOLIBRARY

Table 1. Secondary causes of hyperglycaemia*

Medications

Oral contraceptive pill
Oral corticosteroids
Thiazides
Beta blockers
Phenytoin
Antipsychotics
Glucosamine

Medical conditions

Urinary tract infections (including those that are asymptomatic)
Dental infections (including those that are asymptomatic)
Hyperthyroidism
Occult malignancy

* Not an exhaustive list.

should prompt action.[2]

Some people think that the A_{1c} and blood glucose 'numbers' give comparable assessments of glycaemic control – for example, an A_{1c} of 8% corresponds to an average BGL of 8 mmol/L. Some also think '5 to 10' is okay for both numbers. However, this is not so.

The A_{1c} value reflects the overall average BGL (24 hours per day over several weeks). Within the ideal ranges for both A_{1c} and BGL, values do approximate each other, but at higher than ideal levels, the A_{1c} value is lower than the average BGL, with the difference between the two increasing with increasing values.[3] The formal relation between BGL and A_{1c} can be described by the equation:

$$BGL\ (mmol/L) = 2A_{1c}(\%) - 6$$

where BGL is the average over 24 hours.

Following this formula, an A_{1c} of 8% equates to a BGL of 10 mmol/L.

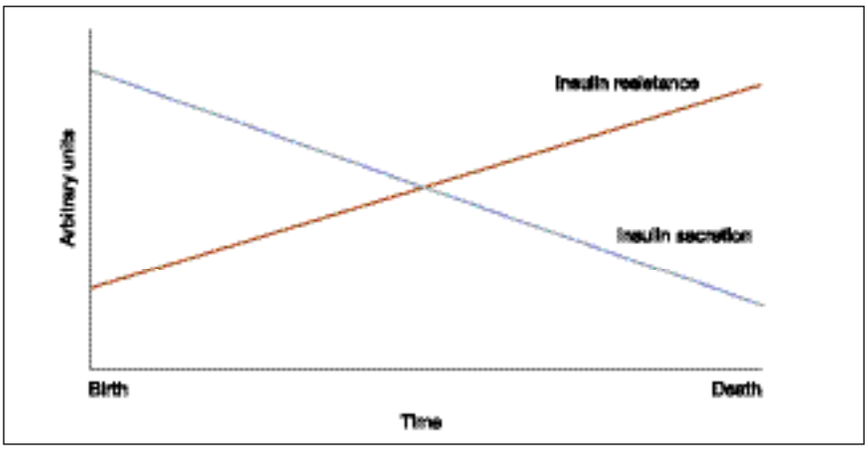


Figure 1. Diabetes progression – insulin resistance and insulin capacity. With progression of disease the capacity of beta cells to secrete insulin and the body's capacity to respond to insulin both decrease. Prediabetes (impaired fasting glucose, impaired glucose tolerance) starts when insulin resistance exceeds insulin secretory capacity (point of intersection). Diabetes progressively worsens with time.

Step 2. Are there potential lifestyle or medication changes, or treatable medical conditions?

Lifestyle

There are two very practical reasons to check lifestyle:

- insulin therapy will not substitute for a healthy lifestyle – starting insulin in people who are overweight, underactive or overeating is likely to increase their weight and may not improve blood glucose control
- many patients gain weight when starting insulin – partly because controlling glycaemia controls glycosuria, thus increasing the amount of glucose available in the body.

Patients considering insulin should be encouraged to 'eat less and walk more',[4] but lifestyle change should not become a reason for the person (and doctor) to delay insulin.

Medication adherence

Most doctors know that many patients do not take their medication as prescribed. We sometimes forget, however, that *our* patients may not perfectly adhere to the treatment schedule we prescribe.

Consider making the comment: 'One reason for your high A_{1c} value could be that you are not getting enough tablets. Most patients forget to take some of their tablets – how often do you miss yours?'

Also consider reviewing the patient's overall medication schedule. Aim for a once or twice daily dosing schedule and a lower number of tablets to be taken (by using higher tablet strengths and combined formulations).

Doctors also sometimes forget to

Table 2. Characteristics of basal insulins

Insulin type	Trade name	Origin	Appearance	Comments
Intermediate acting (12 to 24 hours' duration)				
Isophane	Humulin NPH	Human	Cloudy	Available as vials for use in syringes and disposable cartridges for use in pen injectors
	Protaphane	Human	Cloudy	Available as vials for use in syringes, disposable cartridges for use in pen injectors, disposable pen injectors and a larger disposable injection delivery device (InnoLet)
Long acting (24 to 36 hours' duration)				
Detemir	Levemir	Analogue	Clear	Available as disposable pen injectors
Glargine	Lantus	Analogue	Clear	Available as vials for use in syringes and cartridges for use in pen injectors

increase doses of prescribed oral hypoglycaemic agents or add extra medications to keep the A_{1c} on target. The usual sequence of oral hypoglycaemic agents is: lifestyle +/- metformin +/- sulfonylurea +/- glitazone. At present, rosiglitazone (either as a single agent formulation [Avandia] or combined with metformin [Avandamet]), is eligible for PBS subsidy as dual and triple therapy (i.e. with metformin and/or a sulfonylurea). Pioglitazone (Actos) is only eligible for PBS subsidy as dual therapy (i.e. with metformin or a sulfonylurea).

Remember though that as type 2 diabetes progresses, the component of insulin deficiency becomes more and more important (Figure 1). Neither insulin secretagogues (sulfonylureas and glitinides) nor sensitisers (glitazones and, to a lesser extent, metformin) will work if there is insufficient insulin.

As for lifestyle change, medication change should not delay initiation of insulin therapy if a patient's A_{1c} value remains above target.

Other medications and medical conditions

Before starting a patient on insulin check that he or she is not taking a medication or has a medical condition that can cause hyperglycaemia (Table 1). Although it may not be possible to change a secondary cause, or changing it may not result in A_{1c} targets being met, it is worth trying.

Step 3. Which basal insulin and which injection device?

In general, once daily basal insulin plus continuing oral hypoglycaemic agents is preferred over other schedules (twice daily basal, basal/bolus, premixed insulin; stopping oral hypoglycaemic agents) because glycaemic control is better and weight gain and hypoglycaemia are less.[5]

There are two types of basal insulin (Table 2):[2]

- the intermediate acting isophane insulin (Humulin NPH, Protaphane), which is cloudy in appearance
- the long acting analogue insulins detemir (Levemir) and glargine (Lantus), which are clear.

Both isophane and analogue insulins will do the job but each has its pros and cons (Table 3).[6] Both the analogues are subsidised by the PBS to treat type 1 diabetes. Currently (March 2007), glargine is subsidised by the PBS for all forms of insulin therapy in type 2 diabetes, but detemir is approved only for use in basal–bolus schedules in type 2 diabetes.

In some patients, the choice of injection device will determine the insulin prescribed. Some patients prefer a particular brand of reusable insulin pen injector, and the use of insulin cartridges of a different brand is not recommended. Other patients prefer the convenience of

Table 3. Basal insulins – pros and cons of analogue compared to isophane insulin

Pros

Consistent profile
Often single daily dose
Less hypoglycaemia than with isophane insulin
No mixing or resuspension needed for injection

Cons

Slower response to dose changes than with isophane insulin
May be confused with bolus insulins as both are clear solutions
Cannot mix with bolus insulins*
Glargine may sting when injected

* Little data on safety or efficacy available.

Basal insulin titration*

Start with 10 units of basal insulin.
Adjust the dose twice weekly, to reach the target fasting blood glucose of <6 mmol/L, using the guidelines below:

Mean fasting glucose over preceding 2 days (mmol/L)	Insulin increase (U/day)
>10	8
8 to 10.0	6
7 to 7.9	4
6 to 6.9	2

- Do not increase the insulin dose if the fasting blood glucose level is <4 mmol/L at any time in the preceding week.
- The insulin dose may be decreased (small decreases of 2 to 4 units) if there is severe hypoglycaemia (requiring assistance) or the blood glucose level is <3.0 mmol/L in the preceding week.

* Adapted from reference 7 (*Diabetes Care* 2003; 26: 3080-3086).

disposable insulin pen injectors or the traditional insulin syringe. Finally, some find the syringes and the fountain pen-like injectors difficult to use and prefer a larger device (InnoLet) where the dose is easily adjusted, the numbers are larger, the device is easier to grasp and the plunger is easily depressed.

While in type 1 diabetes, the flatter profile, longer action and more consistent absorption profile often make analogue basal insulins the better choice, in type 2 diabetes both isophane and the analogue basal insulins are suitable. Whichever basal insulin is chosen, the time of dosage depends on the blood glucose profile. Usually the fasting BGL is high and a bedtime dose is appropriate to control the overnight liver glucose output that causes fasting hyperglycaemia. However, sometimes the fasting BGL is on target but the evening preprandial BGL is high, suggesting that a morning dose is needed.

Having decided the injection device, the type of basal insulin and the timing of the delivery, choosing the initiating dose is easy: start with 10 units.

Step 4. How should the basal insulin dose be adjusted?

Adjusting the basal insulin dose slowly could mean it would take many months to achieve optimal control. For example, it could take 15 months or more for those patients needing 50 to 100 units of basal insulin per day if the dose was increased by 2 units every two weeks from the starting dose of 10 units – both you and the patient would have given up by then.

However, increasing the dose too fast may cause hypoglycaemia and weight gain. The last thing you want for an apprehensive patient (and family) is to cause hypoglycaemia and/or dramatic weight gain because of excess hunger.

The answer is *festina lente* – hasten slowly. An example of an appropriate insulin titration protocol is given in the box on this page. The principles are:[7]

- when blood glucose is well above target, increase by larger amounts than when blood glucose is close to target
- adjust doses every two to three days; even better, encourage the patient to change the dose following an agreed protocol, perhaps with advice from your practice nurse.

Note that the BGL target in the example protocol can be changed, with corresponding changes in the dosage adjustment.

Following such an insulin titration protocol will enable targets to be achieved more quickly than going slowly (in our example, eight to 12 weeks rather than 15 months) but with less risk of hypoglycaemia and weight gain than going fast.

Once the fasting preprandial BGL is on target, check the other (the evening) preprandial BGL. For those patients who have fasting BGL on target but high evening BGL, once the evening preprandial BGL is on target, check the fasting preprandial BGL. In both instances, if the other preprandial BGL is not on target then add a second dose of basal insulin (10 units) and adjust according to the agreed protocol to achieve target preprandial blood glucose control.

Step 5. Should oral hypoglycaemic agents be stopped and/or quick acting bolus insulin started?

Should oral hypoglycaemic agents be stopped?

Stopping an oral hypoglycaemic agent would mean fewer tablets to be taken but may also mean that the daily insulin dose would have to be increased or a second dose added. The sulfonylurea may no longer be able to increase insulin secretion. The insulin sensitisers will continue to work since insulin resistance remains a problem, but the risk of serious side effects progressively increases with the patient's age and the duration of diabetes (with metformin, lactic acidosis; with the glitazones, fluid overload and cardiac failure).

What is the patient's A_{1c}?

A_{1c} values reflect BGLs over the past few weeks and therefore provide a check that a patient's BGL records are giving an accurate view of overall blood glucose control.

The target A_{1c} value can usually be achieved using a bedtime and/or morning basal insulin dose with or without metformin or a glitazone. If a patient's A_{1c} is not on target with this schedule, check the following items.

- **The patient's reported blood glucose results are accurate.** If the patient's average BGL is very different from that predicted by the A_{1c} (the average BGL should be $2A_{1c} – 6$, as mentioned earlier) then his or her blood glucose measurements and/or records may not be accurate or adequate.

Blood glucose results may be misleading because the glucose meter, glucose strip or patient technique is faulty. Patients may not be conducting regular quality control checks to ensure that their technique is accurate, and they may be getting incorrect high or low readings. Occasionally patients do not record high or low values because they 'know what caused them' and 'it was an unusual event'. Rarely, patients will enter incorrect results or results of nonexistent tests. This may be to give a 'good' report to the doctor because the doctor clearly wants certain tests to be done and certain results to be obtained.

- **The patient's BGL results are similar to laboratory results.** Compare the laboratory BGL measurement of a fasting blood sample against the patient's BGL measurements immediately before and after the blood is taken. This will give an idea of the variability between the patient's values and between the mean of the patient's values and the actual (laboratory) value.
- **The reported A_{1c} results accurately reflect glycaemia.** Ask the laboratory if there is a possibility that their A_{1c} assay is giving misleading results (e.g. with a haemoglobinopathy or uraemia). Ask yourself if red blood cell turnover could be increased (due to, for example, haemolysis or blood loss) as the A_{1c} value depends on the average BGL during the lifetime of the red cell.
- **There is no 'hidden hyperglycaemia'.** Assuming reported blood glucose and A_{1c} values are accurate, preprandial BGLs are on target and A_{1c} is off target, check postprandially and during the night (at, for example, 3.00 a.m.) for 'hidden hyperglycaemia'. Usually discrepancies between preprandial BGL and A_{1c} can be resolved but occasionally hyperglycaemia can 'hide' postprandially and/or during the night.

Review BGLs before lunch and before bedtime to check for morning and evening postprandial glycaemia. Postprandial hyperglycaemia should prompt review of the amount and glycaemic index of the food eaten at that meal (i.e. the glycaemic load).[8] A dietitian will be able to advise on the glycaemic load and on strategies to reduce postprandial glycaemia.

If changes in carbohydrate intake are not needed, practical or effective, then quick acting insulin, in addition to basal insulin, should be considered.

Even if fasting glycaemia is under control, night-time glycaemia can occur because the evening basal isophane insulin dose is given too early. For example, a basal insulin dose with the evening meal at 5.00 p.m. may not provide enough insulin next morning before a late breakfast at 9.00 a.m. Shifting the insulin dose to bedtime may control both BGL and A_{1c}. This is less of a problem with the longer acting analogue basal insulins.

Which quick acting bolus insulin is appropriate?

A quick acting bolus insulin should be considered if preprandial BGLs are on target but A_{1c} and postprandial BGL are not.

Table 4. Characteristis of bolus insulins

Insulin type	Trade name	Origin	Appearance	Comments
Rapid acting (also known as very quick acting)*				
Insulin aspart	NovoRapid	Analogue	Clear	Available as vials for use in syringes, disposable cartridges for use in pen injectors and as disposable pen injectors
Insulin lispro	Humalog	Analogue	Clear	Available as vials for use in syringes and disposable cartridges for use in pen injectors
Short acting (also known as quick acting)†				
Neutral insulin	Actrapid Humulin R	Human Human	Clear Clear	Available as vials for use in syringes and cartridges for use in pen injectors Available as vials for use in syringes and disposable cartridges for use in pen injectors

* Onset, 5 to 15 minutes; peak, 30 to 90 minutes; duration, 4 to 6 hours † Onset, 30 to 60 minutes; peak 2 to 3 hours; duration, 8 to 10 hours.

As for basal insulins, there are traditional and analogue bolus insulins (Table 4):

- the rapid acting (or very quick) analogue insulins aspart (NovoRapid) and lispro (Humalog)
- the short (or quick) acting neutral insulin (Actrapid, Humulin R).

Both analogue and neutral insulins are clear solutions but each has its pros and cons (Table 5). A neutral (human) bolus insulin may act too slowly to control postprandial hyperglycaemia and may act for so long that hypoglycaemia before the next meal becomes a risk. Analogue bolus insulins are faster in starting and stopping, and may control postprandial hyperglycaemia with lesser risk of hypoglycaemia before the next meal. However, the analogues may increase the risk of hypoglycaemia if the meal is not eaten promptly or if enough carbohydrate is not eaten with the meal (the Australian steak and salad is a classic for hypoglycaemia as it contains no carbohydrate). The rapid acting insulin analogues may also 'run out' before the next meal, causing preprandial hyperglycaemia.

Once again the choice may be determined by the choice of basal insulin injection device and insulin. The patient may choose the same type of injection device for convenience, but it should be made clear which device has which insulin. Remember that both basal and bolus insulins can be clear and that the pen injectors for both clear insulins may be confused if they are not different brands and/or colours.

For patients on isophane basal insulin, quick acting analogue bolus insulin may control postprandial blood glucose and the isophane insulin control blood glucose before the next meal. For patients on analogue basal insulin, neutral (human) bolus insulin may be better to control the blood glucose before the next meal (especially if the next meal is more than 6 hours after the bolus insulin, when an analogue might 'run out').

What dose of bolus insulin to use?

As with the basal insulin, choosing the initiating dose of bolus insulin is easy: use one-third of the corresponding morning or evening basal insulin dose. The usual recipe is two-thirds basal insulin and one-third bolus insulin.

Adjust the starting dose according to the blood glucose profile. *Festina lente* still applies – not too slow and not too fast, get it 'just right'. Increase the dose by 20% if BGLs are well off target and by 10% when they are closer to target. Figure 2 shows which BGL through the day is controlled by which type of insulin.

Don't aim too low. The major side effect of quick acting insulin is hypoglycaemia (and weight gain because of the associated hunger symptoms). Hypoglycaemia is less likely in patients with type 2 diabetes than in those with type 1 diabetes, but can still be a problem with both quick acting and basal insulins.

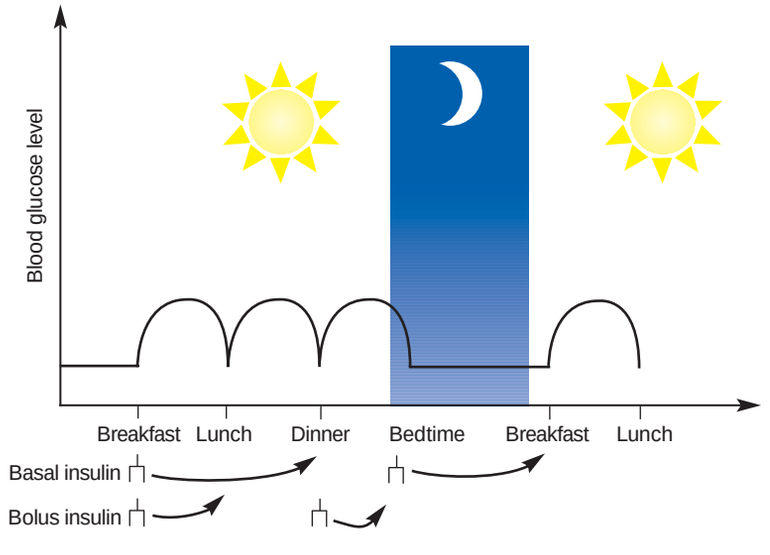
Table 5. Bolus insulins – pros and cons of analogue compared to neutral insulin

Pros	Cons
Inject when eat	Need to eat promptly after injection
Less hypoglycaemia than with neutral insulin	Possible insulin 'run out' before next meal
Better postprandial glycaemic control than with neutral insulin	Need adequate carbohydrate in meal

Step 6. Are problems with insulin likely?

There are two classes of potential problems:[9]

- medical – coping with injection and



Insulin injection	On target blood glucose level
Morning basal	Evening preprandial (pre-dinner)
Morning bolus	Midday preprandial (pre-lunch)
Evening bolus	Pre-bedtime
Bedtime basal	Fasting (pre-breakfast)

Figure 2. Blood glucose profile on basal plus bolus insulin schedule.

monitoring techniques (both the patient and the doctor) and risk of hypoglycaemia and weight gain (patient)
- psychological (both the patient and the doctor).

Medical problems

There are very few patients who cannot manage to administer their own insulin or monitor their BGL using the insulin injectors and blood glucose meters available now. For these few, a relative, carer or visiting nurse could help. The basal insulin injection and the preprandial blood glucose measurement are the most important daily activities.

The timing of the basal insulin is often not critical, particularly for the long acting insulin analogues, as long as the dose is given at approximately the same time each day. Blood glucose testing is most important when starting insulin and, for safety, should be determined several times each day when insulin therapy is being initiated.

Initially BGL targets will not be too ambitious (e.g. preprandial targets of 8 mmol/L). Long term monitoring can be by measuring A_{1c} and the occasional preprandial BGL.

Once doctors are convinced that starting insulin is safe and simple, most can refer patients to a nurse experienced in diabetes care who can help the patient choose and use an appropriate insulin injection device and can check blood glucose monitoring technique. If such a nurse is not available, an approach is to choose one basal insulin preparation and injection device and arrange for a nurse in the practice, hospital or community to become familiar with them. A relevant pharmaceutical representative may be prepared to visit the area and teach the nurse (or the doctor). A similar approach could be adopted when bolus insulin before meals is required. Such a system might take some time to set up but it will enable you and your patients to start insulin simply, safely and sooner.

Psychological problems

As noted, the progressive rise of A_{1c} is caused by defects in insulin resistance and insulin capacity. Often the 'failure' to meet A_{1c} targets is also explained by resistance and capacity factors: psychological resistance on the part of the patients and doctors, and lack of capacity in healthcare systems.[9,10] These lead to delay in starting insulin therapy.

A patient says, 'Just one more try, doctor – I know my blood glucose has been high over Christmas but my New Year's resolution is to lose the 2 kg I gained over

the festive season and get back to my regular walks. My wife wants to start walking too and we'll keep each other motivated.' You think, 'Thank goodness, I really didn't want to start insulin right now. The waiting room is packed, I really need to get away soon and I could do without writing scripts, referrals and all the rest of the paraphernalia. However, I must dig out those notes I made so I know which insulin to use and what dose to start with next time it comes up'.

Both patient and physician are showing the psychological insulin resistance that stops or delays people starting insulin (Table 6). Neither wants to take the next step; the problems of starting insulin are immediate and obvious to both. The problems of not starting are more remote and less obvious – a progressive increase in the risk of diabetes related complications.

Many patients and their healthcare providers prefer to delay insulin therapy until it is 'absolutely essential'. However, some of the concerns can be easily resolved, for example:

- demonstrate that injections are virtually painless with a 'dry' injection
- introduce the person to a successful patient
- explain that the risk of hypoglycaemia is remote (1/20th that in type 1 diabetes)[9]
- explain that 'eating less and walking more' will limit or prevent weight gain.[4]

Some concerns are less easy to resolve: some employers do discriminate against people with diabetes (even though this is illegal), and access to some jobs is more difficult for those with diabetes (e.g. airline pilots and the active armed forces). Overall, though, insulin does not limit opportunity much.

Table 6. Causes of psychological insulin resistance

Patients	Doctors
Insulin therapy will be painful and difficult	Patients do not want insulin therapy
Fear of weight gain and hypoglycaemic episodes	Difficult, extra time needed
'End of the road', diabetes worse	Patients need referrals
Employment, dependency	Hypoglycaemic episodes, weight gain
	Insulin therapy will not work and is costly

Conclusion

Doctors should 'just do it!' Nothing is so persuasive as seeing that starting insulin

is not hard, not risky and does work.

The KISS approach – summarised in the box on this page – really does work. Most patients (and their doctors) will feel better and wonder why they didn't start insulin much earlier. A patient might say, 'I feel great. I have more energy and don't need daytime naps. If I had known how easy it was to start insulin, I would have done it years ago'. A doctor might say, 'But I thought you had to use a basal bolus schedule with four shots a day. I had no idea how to start, which insulin to use and what doses'.

Remember 'Insulin works, insulin is good, insulin is your friend'.[11] MT

Six steps to initiating insulin therapy for type 2 diabetes

The KISS – or 'Keep insulin safe and simple' – approach involves the six steps to stable sugars outlined below.

Before starting a patient with type 2 diabetes on insulin

- Step 1. A_{1c} levels indicating insulin therapy
  - If A_{1c} >7% (which indicates average blood glucose level (BGL) >8 mmol/L), consider starting insulin.
  - If A_{1c} >8% (which indicates average BGL >10 mmol/L), strongly consider starting insulin.
- Step 2. Making lifestyle or medication changes, and treating other medical conditions

  Check whether making lifestyle or medication changes or treating other medical conditions might get the patient's A_{1c} closer to target; insulin may still be necessary.

When starting a patient with type 2 diabetes on insulin

- Step 3. Selecting the basal insulin and the injection device
  - Choose between isophane or analogue insulin.
  - Choose between syringe, pen or other injector.
- Step 4. Adjusting the basal insulin dose
  - Start with 10 units at bedtime if fasting BGL is high, or 10 units in the morning if fasting BGL is on target but evening preprandial BGL is high.
  - Increase doses every two to three days using agreed protocol.
  - Consider adding a second basal insulin dose if the other preprandial BGL remains high.
- Step 5. Stopping oral hypoglycaemic agents and/or starting quick acting bolus insulin
  - Consider stopping sulfonylurea and decreasing metformin and/or glitazone dose(s).
  - If preprandial BGLs are on target and A_{1c} is high, check that BGL and A_{1c} measurements are accurate and for 'hidden' hyperglycaemia.
  - Consider starting quick acting bolus insulin if preprandial BGLs are on target but A_{1c} and postprandial BGL are not. Use a neutral or analogue bolus insulin; start with one-third of the corresponding morning or bedtime basal dose and increase by 10 to 20% depending on closeness to BGL target.
- Step 6. Coping with potential problems when starting insulin
  - Educate the patient regarding injection technique and blood glucose monitoring and how to cope with hypoglycaemia and weight gain.
  - Discuss psychological insulin resistance with the patient.

Remember: 'Insulin works, insulin is good, insulin is your friend'.

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