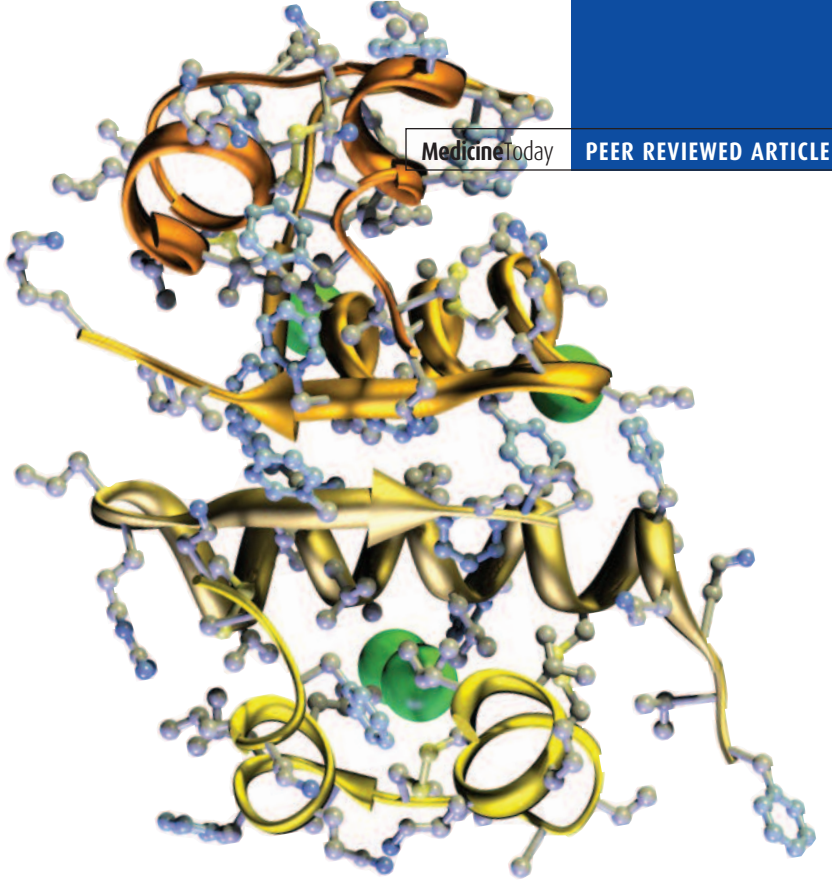


Insulin in type 2 diabetes: which to use and when

In most patients with type 2 diabetes, a night-time dose of basal insulin is the starting point of insulin therapy. With time, a morning dose may also be required, and also the addition of bolus insulin to control postprandial hyperglycaemia.

PAT PHILLIPS
MB BS, MA(Oxon), FRACP, MRACMA, GradDipHealthEcon(UNE)

Dr Phillips is Senior Director, Endocrinology, at the North Western Adelaide Health Service, The Queen Elizabeth Hospital, Adelaide, SA.

IN SUMMARY

- When maximum therapy with oral hypoglycaemic agents (OHAs) does not achieve the desired level of glycaemic control in a patient with diabetes, it is important to review adherence to appropriate lifestyle and OHA therapy and to confirm the absence of medical conditions or medications that can cause hyperglycaemia.
- Generally a night-time dose of basal insulin with continuation of OHA therapy achieves glycaemic targets. Sometimes an initial morning dose and/or a second dose is required.
- With time, further and higher doses of insulin may be required to control preprandial blood glucose levels. Excessive mealtime glycaemic increments should prompt review of the amount and type of carbohydrate eaten and consideration of mealtime acarbose and/or bolus prandial insulin.
- The choice of insulin and the method of injection are often linked. Sometimes a patient will use the same injector type for both basal and bolus insulins. The advantages that analogue insulins offer over traditional insulins are more clinically relevant in type 1 than type 2 diabetes.
- Once glycaemic control is achieved, reducing or stopping OHAs should be considered.
- Although premixed insulins are widely used and convenient for patients, the fixed proportions make dose titration difficult and may mean that controlling hyperglycaemia at one part of the day causes hypoglycaemia at another. Separate basal and bolus insulins makes insulin titration simpler, safer and more flexible.

MODEL OF HUMAN INSULIN. © ISTOCKPHOTO/MARTIN MCCARTHY.

Type 2 diabetes is a progressive disease and maintaining glycaemic control requires progressive treatment. Although lifestyle may control glycaemia at diagnosis, patients and their doctors can expect to progress to one and then additional oral hypoglycaemic agents (OHAs) and finally insulin. In the United Kingdom Prospective Diabetes Study (UKPDS), 50% of patients required insulin therapy to maintain glycaemic control (glycosylated haemoglobin, HbA_{1c} – shortened to A_{1c} – below 7%) within six years of diagnosis.[1] (A patient's A_{1c} value reflects his or her average blood glucose level [BGL] over several weeks.)

This article reviews the factors influencing the use of insulin in type 2 diabetes and outlines the KISS approach (Keep Insulin Safe and Simple) to insulin therapy in patients with type 2 diabetes.[2-5]

Two important factors affect decisions on which insulin(s) to use:

- the type of diabetes – type 1 or type 2 – the patient has
- the appropriate level of glycaemic control – the target A_{1c}.

Once the decision to use basal or bolus insulin is made, there are two further issues to consider:

- the form of basal and/or bolus insulin – traditional or analogue
- the delivery device – injection by syringe, pen, a larger injecting device (Innolet) or pump.

Type 1 versus type 2 diabetes

In type 1 diabetes and the related late onset autoimmune diabetes of adults, there is an absolute insulin deficiency. Insulin is used to mimic the normal diurnal insulin profile as closely as possible (Figure 1).[6] There are two major components to this insulin profile: a continuous background (basal) level of insulin and mealtime increments when extra insulin is required to match the mealtime nutrient influx.

We are a long way from achieving the ideal of delivering insulin into the portal circulation, anticipating and controlling nutrient input and integrating insulin delivery with the other physiological responses to food intake. However, we are getting closer with modern insulin delivery systems, which now include affordable, reliable and user-friendly external insulin infusion pumps.

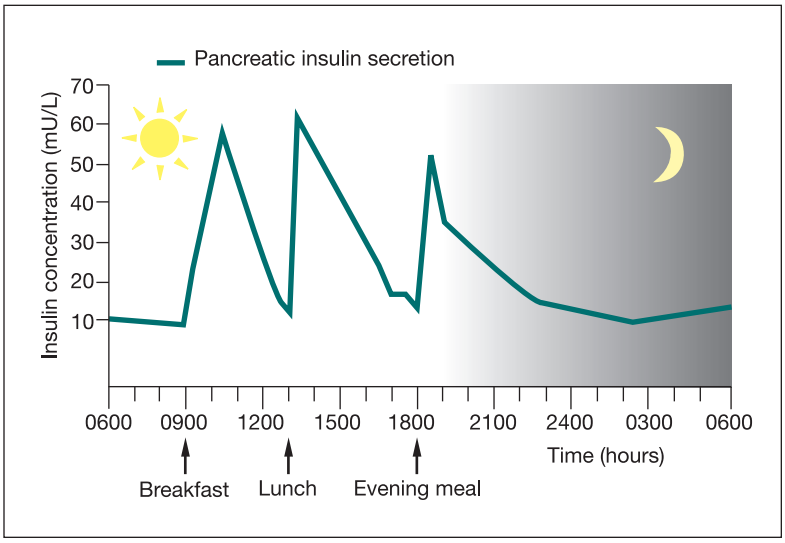
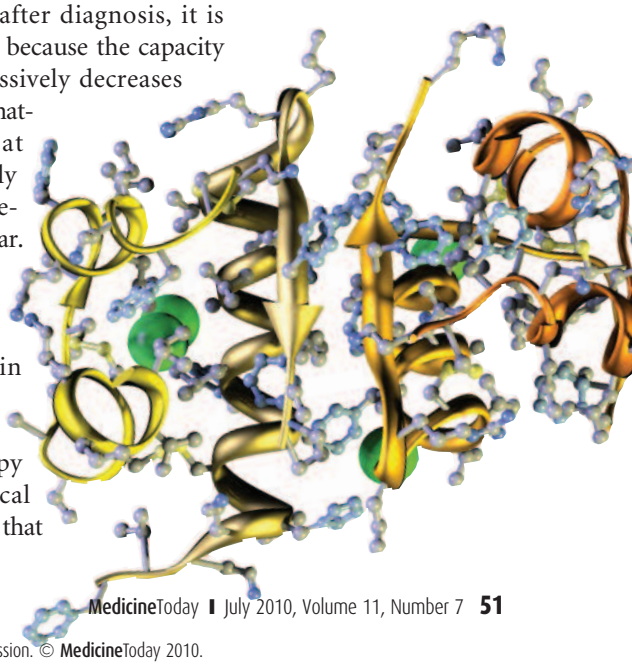


Figure 1. Normal 24-hour profile of insulin secretion.

In type 2 diabetes, the problem is relative rather than absolute insulin deficiency. The patient's insulin secretion capacity progressively declines and although background and mealtime insulin secretion continues it is not enough to control blood glucose because increasing hepatic and peripheral insulin resistance has the effect of making the insulin relatively deficient. Interestingly, absolute insulin levels may exceed those in people without diabetes, particularly early in the course of type 2 diabetes, but insulin resistance reduces the effect of the insulin. Oral hypoglycaemic therapy aims to reduce insulin resistance and, if necessary, to increase insulin levels.

Although exogenous insulin is usually not required for some time after diagnosis, it is usually needed eventually because the capacity to secrete insulin progressively decreases with time. It has been estimatedthat insulin capacity at diagnosis is approximately 50% of normal, and thereafter declines by 3% per year. It is therefore no surprise that so many people with type 2 diabetes require exogenous insulin to achieve A_{1c} targets. Adherence to appropriate lifestyle and OHA therapy and the absence of medical conditions or medications that



continued

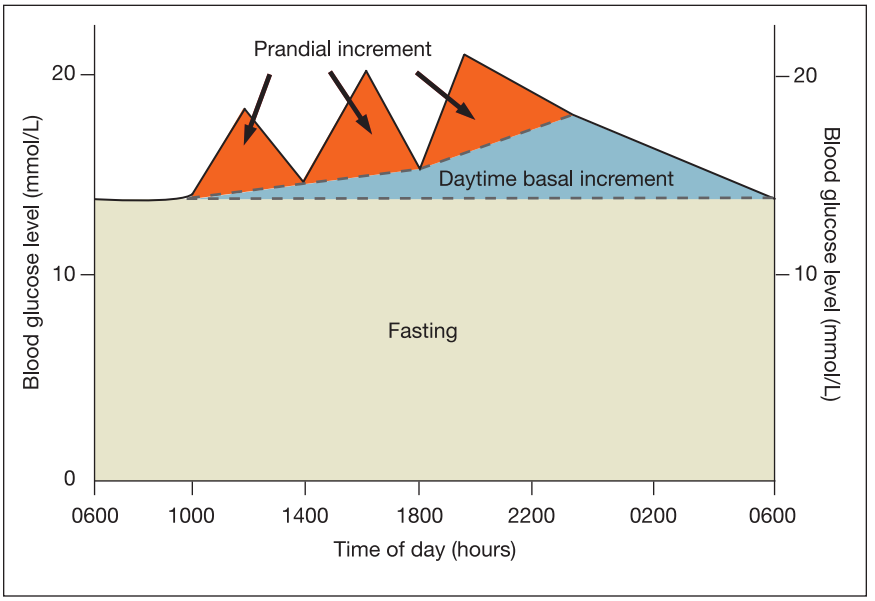


Figure 2. Blood glucose profile in a patient with diabetes (average blood glucose level, 16.9 mmol/L), showing the three components of total blood glucose.

can cause hyperglycaemia should, of course, be reviewed before initiating insulin therapy in a patient in whom glycaemic control is not being achieved despite maximum therapy with OHAs.

Initially, the requirement is to increase the background insulin levels (basal insulin); later, it becomes necessary to also increase mealtime increments (bolus insulin). Continuing endogenous insulin secretion, even though relatively inadequate, makes the use of insulin in patients with type 2 diabetes much safer and simpler than in those with type 1 diabetes. Recent changes in the structure of many Australian general practices have made initiating and titrating insulin in patients with type 2 diabetes much easier because the therapy can now be co-ordinated by practice nurses.

When glycaemic control has been achieved with the use of insulin, it has to be decided which OHAs to reduce or stop and when to do so. Reducing the number, administration frequency and cost of medications is welcomed by patients, in addition to the improved sense of wellbeing associated with improved glycaemic control.

Table 1. Blood glucose levels and type 2 diabetes*

Preprandial blood glucose level (mmol/L)	Postprandial blood glucose level (mmol/L)	Comment
4 to 6.0	4 to 7.7	Ideal level – normoglycaemia
6.1 to 6.9	7.8 to 11.0	Moderate level – minimises microvascular problems
7.0 and above	11.0 and above	High level – consider more active treatment; associated with micro- and macrovascular complications

* As recommended by Diabetes Australia and the RACGP.[8] The International Diabetes Federation suggests a postprandial target <7.8 mmol/L (two hours postprandial)

The 24-hour glycaemic profile

There are three components to an individual's glycaemic profile over the day and night.[7] The major contributor is the baseline set by the fasting BGL; the second contributor is the daytime increment, or less commonly, decrement, in the baseline during the day; and the third contributor is the prandial increase. Figure 2 illustrates the blood glucose profile of a patient with diabetes. A basal (i.e. preprandial) BGL of 4 to 6 mmol/L is considered normoglycaemic (Table 1).[8]

Hypoglycaemic therapy targets both the basal and prandial blood glucose components. Most non-insulin OHAs control both basal and prandial glycaemia but some (and especially acarbose and repaglinide) specifically control prandial glycaemia (Table 2). The currently available insulins are broadly divided into basal and bolus (prandial) insulins. The analogue insulins come closest to meeting the criteria of being truly basal (i.e. long-acting with a relatively flat time–action profile – detemir and glargine) or prandial (i.e. rapid onset, high peak, rapidoffset of action – aspart, glulisine and lispro). The older traditional basal insulin isophane (or NPH) has a definite 'hump' in its time–action profile six to 10 hours after injection and usually a duration of action of less than a full 24 hours. The older traditional neutral bolus insulin is both slower and longer acting than the bolus analogues and has a lower peak.

A_{1c} targets

Setting a target for the A_{1c} level in an individual balances the benefit of improved glycaemic control in reducing the likelihood of future microvascular complications against the costs of achieving

that control in terms of side effects (particularly weight gain and hypoglycaemia) and the effort and cost of more intense therapy. The general goal of an A_{1c} below 7% has been recommended by Australian and many other authorities but as the RACGP diabetes guidelines point out: 'Over-zealous management can result in severe hypoglycaemia and may be associated with increased mortality.'[8]

Patients who are likely to get most benefit at least cost are those with a high A_{1c} level and therefore a high risk of future complications. The benefit in terms of relative risk reduction may be the same at all levels of A_{1c} but the absolute risk reduction is higher at higher levels of absolute risk. Similarly, the relative cost increase of improving glycaemic control may be the same at all levels of A_{1c} but the absolute cost progressively increases at lower A_{1c} levels.

For some groups of patients, the benefits are systematically lower and the costs systematically greater for the same degree of improved glycaemic control. For example, the biologically old (i.e. people older than about 65 years whose biological age is 10 or more years older than their chronological age) may not reap the long-term benefits of reduced microvascular complications but do experience the immediate higher costs of intensive control. In such patients, glycaemic targets might be set higher and the insulin schedule kept as safe and simple as possible.

Traditional versus analogue insulin

There are pros and cons for the traditional and the analogue forms of both basal and bolus insulins.

Basal insulins

The major advantages of analogue basal insulins (detemir and glargine) compared to traditional basal insulin (isophane) are that their absorption profile is more consistent, they last longer (about 24 hours) and no mixing is required. The latter can be a major advantage in situations where the patient or carer administering the insulin cannot be relied on to thoroughly mix the cloudy solution of isophane insulin (a suspension of insoluble neutral insulin–protamine crystals) and may therefore give variable amounts of insulin each time. (Thorough mixing involves rocking the pen or vial backwards and forwards end to end and then rolling between the hands.)

The major disadvantages of the basal analogues can actually be their very advantage – their flat, extended profile. Sometimes there is a daytime decrement in basal glycaemia (rather than an increment), with the BGL before the evening meal being lower than the fasting BGL. In such situations, with a basal analogue insulin at night (bedtime), giving more insulin to control the fasting BGL will result in hypoglycaemia the next evening but using a lower dose to control the next evening's preprandial BGL will result in fasting hyperglycaemia. So either the fasting BGL or the next evening's preprandial BGL is controlled, not both. Here the shorter duration of isophane is actually an advantage because the bedtime dose can be titrated to control the fasting BGL and/or the breakfast dose can be titrated to control the evening preprandial BGL. Switching the basal analogue dose to the morning does not solve the problem and may even make things worse.

Table 2. Effectiveness of non-insulin oral hypoglycaemics

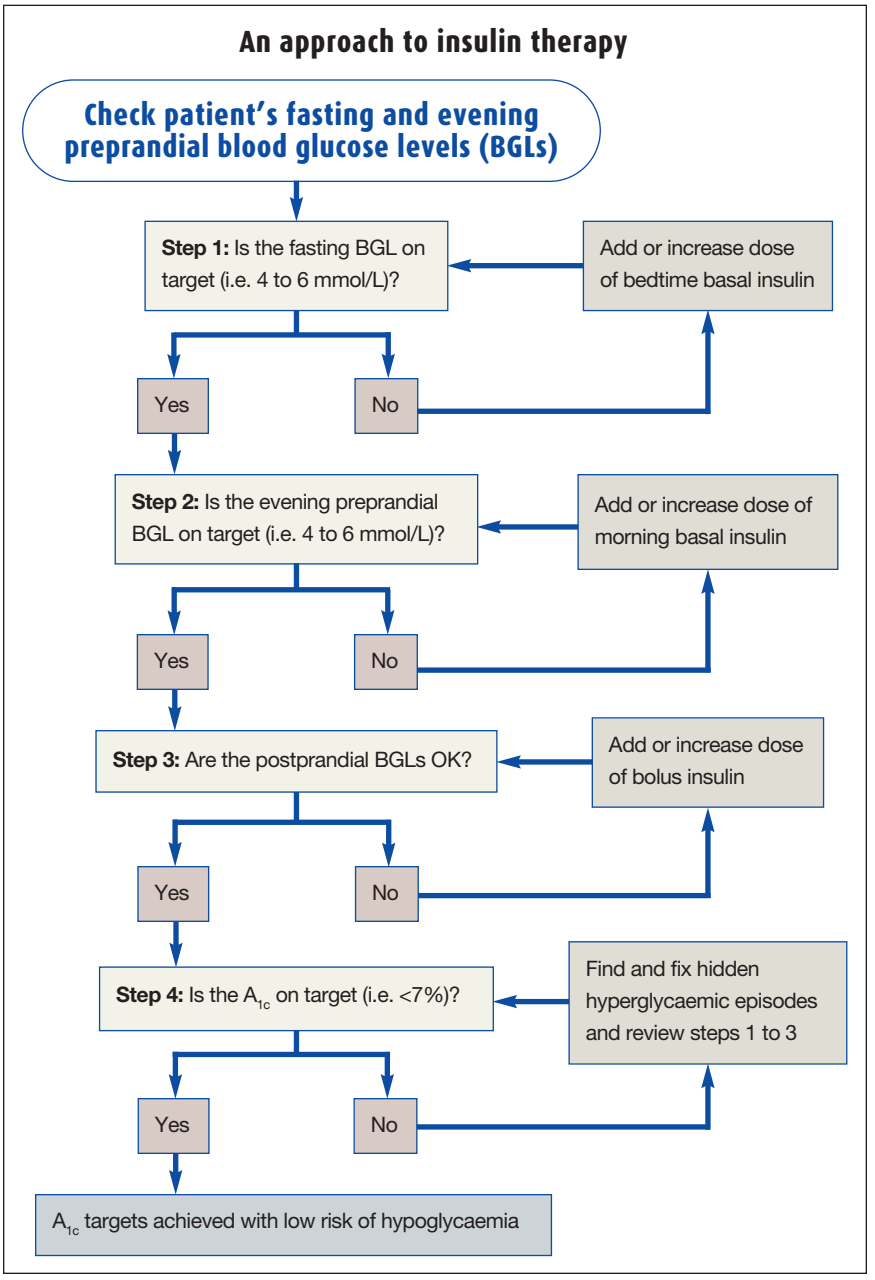
Non-insulin oral hypoglycaemic agent	Basal blood glucose control	Prandial blood glucose control
Acarbose	–	++
Glitazones	++	+
GLP agents*	+	++
Metformin	++	+
Repaglinide	–	++
Sulfonylureas	++	++

KEY: – indicates not effective; + indicates effective; ++ indicates more effective.
* Exenatide (a GLP mimetic), and sitagliptin and vildagliptin (GLP enhancers). ABBREVIATION: GLP = glucagon like peptide.

Bolus prandial insulins

The major advantages of analogue bolus insulins (aspart, glulisine and lispro) compared to traditional bolus insulin (neutral insulin) are their speeds of onset and offset and the higher insulin levels achieved. The profiles of bolus analogues after injection mean that patients can inject them immediately before eating, postprandial glycaemic excursions are lower and hypoglycaemia before the next meal is less likely. In contrast, it is recommended that neutral insulin be administered 30 to 40 minutes before eating. Moreover, the lower peak and longer duration of traditional bolus insulin may not control postprandial glycaemia and cause hypoglycaemia before the next meal.

Once again the major disadvantage of the bolus analogues can be their very advantage – the rapid onset and offset and their high peak. Once the injection is given, a meal containing adequate carbohydrate must be eaten promptly or hypoglycaemia will occur. Their short duration of action means that hyperglycaemia may occur before the next meal, especially if that meal is eaten many hours later.



Choosing an insulin

In practice, the advantages of the analogue insulins are more clear-cut in type 1 diabetes than in type 2 diabetes and the choice of basal insulin in patients with type 2 diabetes is often based on the advantages of the injection device for that insulin. The choice of the form of bolus insulin may be made so that the same injector type is used for both basal and bolus insulins because the patient is familiar with the device (see later in this article for a discussion of the available delivery devices). Alternatively, different device types may be chosen to clearly differentiate the basal and bolus analogue preparations, which are both clear (in contrast to the traditional preparations where the basal insulin, isophane, is cloudy and the bolus insulin, neutral insulin, is clear).

GPs inexperienced in insulin therapy often decide to use the same basal and bolus insulins and their respective injectors for all their patients requiring insulin therapy. That way they can become familiar with the pros and cons of those particular insulins and their injectors. As they become more familiar with insulin therapy they may prescribe a wider range of insulins and injectors.

There are two clinical scenarios where there are clear advantages of one basal insulin type over the other:

- for patients with limited manual dexterity, visual acuity or cognition, the Innolet injection device, which is prefilled with isophane insulin, is often preferable; this large disposable device is easily adjusted, has large numbers that are easy to see, is easy to grasp and has a plunger that is easily depressed
- for patients in whom more than one insulin injection a day is difficult (e.g. when administered by a visiting carer), the basal analogues (detemir, glargine) are often preferable because they can be given at any time of the day (as long as they are given at the same time each day) and usually last the full 24 hours.

The KISS approach (Keep Insulin Safe and Simple) to insulin therapy

Just as there are three components to the glycaemic profile there are three considerations in initiating insulin therapy for type 2 diabetes.

- Is the fasting BGL high?
- Is there a daytime increment or decrement? That is, is the evening preprandial BGL higher or lower than the fasting BGL?
- Is/are the prandial increments excessive?

These considerations are discussed

below and the KISS approach to insulin therapy is summarised in the flowchart on page 56.[5]

Preprandial glycaemia

Almost always the fasting BGL is high.

Generally for both analogue and traditional basal insulins:

- a bedtime dose controls the overnight (fasting) BGL
- a morning (breakfast) dose controls the evening preprandial BGL.

An analogue basal insulin, however, may control both the overnight (fasting) BGL and the evening preprandial BGL whether it is given as a bedtime dose or a breakfast dose.

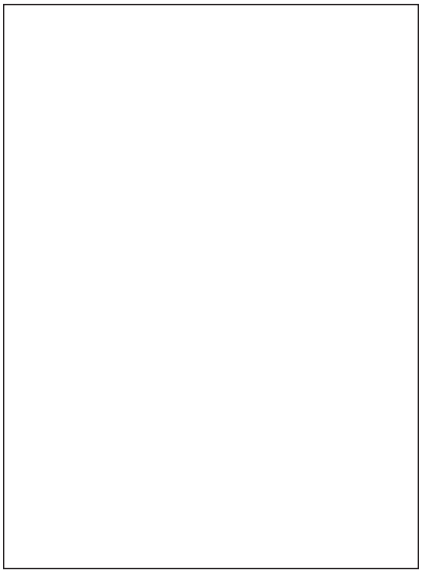
As GPs often use one form of basal insulin, there are two general approaches:

- for a basal analogue, the choice between a morning or bedtime dose might be guided by the presence of a daytime increment (where a morning injection might be preferable) or a daytime decrement (where a bedtime injection might be preferable)
- for isophane, the recommendation is to start with a bedtime dose.

Whether a basal analogue or isophane is being used, the starting dose should be low (e.g. 10 units) and titration should occur frequently (e.g. twice weekly) to bring the blood glucose under control (see the box on basal insulin titration on page 58). If titration increments are small and titration is infrequent, it may be months before an adequate insulin dose is reached; for example, at a titration increment of 2 units per week it would take 15 weeks to get from 10 units to the average required dose of 40 units.

As the target BGL (usually the fasting BGL but occasionally the evening preprandial BGL) comes under control, it is time to check the other basal BGL (breakfast or evening preprandial, respectively) to see if hyperglycaemia or hypoglycaemia is occurring at that time. Usually the second BGL is on target but sometimes it is too high or too low.

- If too low, switch the timing of the basal insulin injection (bedtime to breakfast, or vice versa).
- If too high, add a second dose of basal insulin (add a breakfast dose to a bedtime dose, or vice versa).



Once the indicators of the major contributors to the glycaemic profile (i.e. the fasting BGL and evening preprandial BGL; indicators respectively of the baseline set by the fasting blood glucose and the daytime increment or decrement) are under control, the other preprandial blood glucose (before lunch) should be considered. It should be near target but may be either too high or too low.

- If too high, check whether the patient is eating a morning snack at a reasonable time between breakfast and lunch and whether he or she is being reasonably active between these meals. Suggest to the patient that the snack is omitted, reduced or modified (thereby reducing the glycaemic load), the time between breakfast and lunch is extended or physical activity is increased, whichever is most appropriate. If hyperglycaemia persists, consider adding a breakfast dose of acarbose; start low (e.g. 25 mg when starting breakfast) and go slow (e.g. increments of 25 mg at one to two-weekly intervals to a maximum dose of 100 mg). Acarbose slows carbohydrate digestion, blunting the peak blood glucose concentration and flattening the postprandial BGL profile. If hyperglycaemia still persists, consider adding a dose of bolus insulin (e.g. 5 units) at breakfast and titrating it to control the lunchtime preprandial BGL. The recommended safe and simple guide is to start with 10% of the total daily basal insulin dose and to increase or decrease the dose by 20% when the postprandial BGLs are well off target and by 10% when values are closer.[2]
- If too low, once again check whether the patient is eating any snacks between breakfast and lunch, and the time and activity between the two meals. In this case, suggestions include encouraging an interprandial snack or increasing its size, shortening the gap between breakfast and lunch or decreasing interprandial activity.

If these factors are addressed and hypoglycaemia continues, the type and dose of the basal insulin may need review because the 'hump' of a morning isophane dose may be causing hypoglycaemia before lunch or too much basal insulin is being used.

Prandial glycaemia

Authorities used to recommend focusing on the fasting BGL and the evening postprandial BGL. Strategies included bedtime basal insulin to control the fasting BGL and, if necessary, evening preprandial bolus insulin to control the evening postprandial BGL; alternatively an evening preprandial premix insulin provided both the basal insulin and bolus insulin in one injection.

More recently these authorities have recognised that the evening postprandial blood glucose is made up of at least two components: the preprandial blood glucose that sets the baseline and the prandial

Basal insulin titration[2]

Start with 10 units of basal insulin at bedtime, or in some patients in the morning. Adjust the dose twice weekly, to reach the target fasting blood glucose level (BGL) of <6 mmol/L, using the schedule below:

Mean fasting glucose over preceding two days (mmol/L)	Insulin increase (U/day)
>10	8
8 to 10.0	6
7 to 7.9	4
6 to 6.9	2
3.5 to 5.9	No change
<3.5	-4

- Do not increase insulin dosage if the BGL 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 BGL is <3.0 mmol/L in the preceding week. Titration must be reviewed by healthcare professional at each contact.
- Continue to monitor A_{1c} and regularly review patient risk factors.

increment. Bolus insulin may control the postprandial BGL but does not address any preprandial hyperglycaemia. The focus now is on controlling the preprandial BGL and only then considering the prandial BGL increase.

If the three preprandial BGL values are on target (e.g. 4, 5 and 6 mmol/L), the A_{1c} value, which is a measure of overall average glycaemia (24 hours per day over several weeks) will check that there is no hidden postprandial hyperglycaemia. In type 2 diabetes, if preprandial BGLs are on target then the A_{1c} usually will be too. If it is not, the strategy is similar to that when the lunchtime preprandial BGL is high, that is:

- review, reduce and/or change the amount and type of carbohydrate eaten at the preceding meal and interprandially
- consider adding mealtime acarbose to blunt the mealtime glycaemic increment
- consider adding and titrating a preprandial dose of bolus insulin to control the prandial increment.

Targets for postprandial blood glucose control are not evidence based; however, the epidemiological evidence that is available suggests the same two-hour blood glucose targets as apply to the oral glucose tolerance test (see Table 1).[8] (In the oral glucose tolerance test, a two-hour BGL of less than 7.8 mmol/L indicates diabetes is unlikely, 7.8 to 11.0 mmol/L that there is impaired glucose tolerance and 11.0 mmol/L or above that diabetes is likely.)

Syringe versus injector

Syringes have the advantage of being widely available both in Australia and worldwide but require the person to carry both syringes and the insulin vial and to draw up the insulin into the syringe. Insulin pen injectors are like large fountain pens with cartridges of insulin rather than ink. These injectors can be preloaded and disposable when the cartridge is empty or reusable with insulin cartridges loaded by the patient. The Innolet device is bigger than the other injectors, with a large dial similar to an eggtimer to set the dose and large, easily seen numbers; it is easier to grasp and has a large plunger that is easier to depress than those on pen injectors. The Innolet is available prefilled with isophane or a neutral insulin and isophane insulin mix and is disposable.

Most patients choose to use a pen injector rather than syringes when starting insulin, but those already using syringes often continue to do so. The choice between disposable or reusable pen injectors depends on their availability for the particular insulin and on the balance between the convenience of a disposable injector versus the larger amount of space required for their storage and their larger carbon imprint (production, transport and disposal). Patients with limited vision or manual dexterity find the Innolet device much easier to use than a pen injector. Table 3 lists the injectors available for different insulins.

If the same type of injection device is used for both basal insulin and bolus insulin, it is important that the two devices are easily distinguishable to minimise the risk of the incorrect insulin being injected by mistake. This is particularly important if an analogue basal insulin and a bolus insulin are being used as both will be clear solutions. However, easily distinguished injection devices are still important if traditional basal insulin is being used, the cloudiness of isophane making it more easily distinguished from clear bolus insulin.

Reducing OHAs

Metformin, pioglitazone and the sulfonylureas are effective with insulin and are subsidised by the PBS for use with insulin.

- Metformin will continue to reduce

insulin resistance and to help weight control. However, it may be convenient to stop any midday dose and prudent to reduce the total daily dose.
- Pioglitazone will also continue to reduce insulin resistance. However, it may be prudent to reduce the dose or cease the medication because both insulin and glitazones increase renal retention of sodium and the risk of future cardiac failure.
- The sulfonylureas glibenclamide, gliclazide, glimepiride and glipizide may still increase endogenous insulin secretion despite the need for exogenous insulin. However, sulfonylureas can be expected to become progressively less effective as the patient's insulin secretion capacity progressively declines. If a trial of stopping the sulfonylurea means that further or higher doses of insulin are required to maintain glycaemic control, the patient can decide whether to restart the sulfonylurea.

As acarbose works independently of insulin by slowing carbohydrate digestion, it can be effective at all stages of diabetes.

Table 3. Insulins and their delivery devices

Basal insulin
- Analogue basal insulins
  - Vials for syringes – glargine
  - Prefilled multidose disposable pens – detemir, glargine
  - Reusable pens (loadable cartridges) – detemir, glargine
- Isophane insulin
  - Vials for syringes
  - Prefilled multidose disposable pens
  - Reusable pens (loadable cartridges)
  - Large reusable device (Innolet)

Bolus insulin
- Neutral insulin, human
  - Vials for syringes
  - Reusable pens (loadable cartridges)
- Analogue bolus insulins
  - Vials for syringes – aspart, glulisine, lispro
  - Prefilled multidose disposable pens – aspart, glulisine, lispro
  - Reusable pens (loadable cartridges) – aspart, lispro

Premixed insulin
- Neutral insulin/isophane insulin mixes
  - Vials for syringes – neutral insulin 30%/isophane insulin 70%
  - Prefilled multidose disposable pens – neutral insulin 30%/isophane insulin 70%
  - Reusable pens (loadable cartridges) – neutral insulin 30%/isophane insulin 70%, neutral insulin 50%/isophane insulin 50%
  - Large reusable device (Innolet) – neutral insulin 30%/isophane insulin 70%
- Analogue bolus insulins/protamine mixes
  - Prefilled multidose disposable pens – aspart 30%/aspart protamine 70%, lispro 25%/lispro protamine 75%, lispro 50%/lispro protamine 50%
  - Reusable pens (loadable cartridges) – aspart 30%/aspart protamine 70%, lispro 25%/lispro protamine 75%, lispro 50%/lispro protamine 50%

A word about premix insulins

Premixed insulins are preparations of fixed proportions of basal (isophane) and bolus insulins (with the exception of glulisine). At present there are no premixes including analogue basal insulins.

In Australia, premixes account for about half of the insulin used in schedules where basal insulin (with or without bolus insulin) is required. Premixed insulins are included in the insulin preparations recommended by the NHMRC for starting insulin in type 2 diabetes.[9]

Premixes are very convenient for patients because only one device and one injection is needed for both basal and bolus insulins. However, the fixed proportion of bolus and basal insulin in each premix formulation means that the proportion of the two components can only be changed in a limited number of ways (from 30:70 to 50:50 for neutral insulin/isophane insulin mixes or from 25:75 to 50:50 for analogue bolus insulin/protamine mixes, or vice versa). Often too much bolus insulin is given in association with the right amount of basal insulin, or vice versa. Doctors and patients may be between the rock of hyperglycaemia because of too little of one insulin and the hard place of hypoglycaemia and weight gain because of too much of the other.

A particular premix may suit a particular person at the particular stage of their diabetes progression, but it is likely that the patient will require different proportions and different amounts of the insulins in the future as their diabetes progresses. Moreover, while diabetes thrives on routine, there may not be a daily routine that applies every day or in the long term.

Sometimes the ease of use of premixes outweighs the disadvantages of a fixed proportion of basal insulin and bolus insulin. However, if it proves difficult to control hyperglycaemia without causing hypoglycaemia, it may be appropriate to change to the more flexible and easily titrated schedule of basal insulin with a separate bolus insulin.

Conclusion

Type 2 diabetes is a progressive disease and progressive treatment, including insulin, can be expected. When maximum

therapy with OHAs does not achieve the desirable level of glycaemic control, it is important to review adherence to appropriate lifestyle and OHA therapy and to confirm the absence of medical conditions or medications that can cause hyperglycaemia.

Generally a night-time dose of basal insulin with continuation of OHA therapy achieves glycaemic targets. Sometimes an initial morning dose and/or a second dose is required. With time, further and higher doses of insulin may be required to control preprandial blood glucose. Excessive mealtime glycaemic increments should prompt review of the amount and type of carbohydrate eaten and consideration of mealtime acarbose and/or bolus insulin. Once glycaemic control is achieved, the stopping or reducing of OHAs should be considered.

Analogue insulins offer some advantages over traditional insulins but these advantages are more clinically relevant in type 1 than type 2 diabetes. Sometimes the choice of insulin and injector are linked because some GPs prefer to use a single injector type or the same basal and bolus insulins for all patients, or because a particular injector suits a particular patient (e.g. the Innolet device for older people).

Premixed insulins are widely used and convenient for patients. However, the fixed proportions make dose titration difficult and may mean that to control hyperglycaemia at one part of the day causes hypoglycaemia at another. A schedule of separate basal insulin and bolus insulin makes insulin titration simpler, safer and more flexible. MT

References

1. United Kingdom Prospective Diabetes Study (UKPDS) Group. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in people with type 2 diabetes (UKPDS 33). Lancet 1998; 352: 837-853.

2. Phillips P. KISS: 'keep insulin safe and simple'. Part 1: initiating insulin in type 2 diabetes. Medicine Today 2007; 8(3): 23-34.

3. Phillips P. KISS: 'keep insulin safe and simple'. Part 2: living with insulin and type 2 diabetes. Medicine Today 2007; 8(4): 43-54.

4. Phillips P. KISS: 'keep insulin safe and simple'. Part 3: troubleshooting insulin problems in type 2 diabetes. Medicine Today 2007; 8(5): 47-55.

5. Phillips P. KISS: 'keep insulin safe and simple'. Part 4: titrating insulin in type 2 diabetes. Medicine Today 2007; 8(6): 43-52.

6. Phillips P. Insulin analogues: what do they offer to the insulin KISS ('keep insulin safe and simple')? Medicine Today 2008; 9(11): 22-34.

7. Phillips P. Getting A1c under 7%. The KISS ('keep insulin safe and simple') approach in type 2 diabetes. Medicine Today 2008; 9(10): 43-48.

8. Harris P, Mann L, London J, Phillips P, Webster C; RACGP, Diabetes Australia. Diabetes management in general practice. Guidelines for type 2 diabetes, 2009/10. 15th ed. Canberra: Diabetes Australia; 2009. Available online at: http://www.racgp.org.au (accessed June 2010).

9. Diabetes Australia, NHMRC. Section 5: What lifestyle modification and therapeutic interventions can be used to improve blood glucose control in people with type 2 diabetes? In: National evidence based guideline for blood glucose control in type 2 diabetes. Canberra: Commonwealth of Australia; 2009. p. 98-179.

COMPETING INTERESTS: Dr Phillips has received research and travel grants, acted on advisory boards and been involved with clinical trials and seminars sponsored by a range of pharmaceutical companies. He does not think these associations have influenced the content of this article.