KISS: 'keep insulin safe and simple'

Part 2: living with insulin and type 2 diabetes

Living with insulin and type 2 diabetes 24 hours a day, seven days a week, can be associated with problems if they are not anticipated and avoided.

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Starting insulin therapy in patients with type 2 diabetes using the KISS approach ('Keeping Insulin Safe and Simple') is not risky, not hard and does work – see the article on initiating insulin therapy in the March 2007 issue of *Medicine Today*.[1] However, problems can arise when patients are living with insulin and type 2 diabetes 24 hours a day, seven days a week, if these are not anticipated and avoided.

This article considers the common problems experienced by people taking insulin and gives practical advice on how to make living with insulin safe and simple.

Weight gain

'In the last eight months I've put on 10 kg. I've tried everything but my weight is like an old TAA (Trans Australian Airlines) flight and going 'up, up and away'. You have got to do something to help me.'

Sue is 54 years old and justifiably worried.

IN SUMMARY

- **Continuing oral hypoglycaemic agents and adding 10 units of basal insulin at bedtime is almost always the best way to start insulin in people with type 2 diabetes. Metformin also helps with weight control.**
- **Patients should 'eat less and walk more' to balance the extra energy available when improved glycaemia reduces glycosuria.**
- **Insulin should be adjusted to fit lifestyle, not vice versa.**
- **Improving glycaemic control comes with the price of hypoglycaemia, weight gain and extra effort by patient and doctor.**
- **Blood glucose measurement results may vary by plus or minus 20%, even after the patient's technique and the testing equipment have been checked.**
- **Eating before physical activity reduces the risk of hypoglycaemia and blunts postprandial hyperglycaemia.**
- **When travelling by air, patients should adjust insulin dosages if the time zone difference between origin and destination is more than four hours. Less insulin is needed for travel eastwards (a shorter day) and more insulin for travel westwards (a longer day).**
- **Patients should carry a full set of diabetes equipment in their hand luggage when flying. Taking a survival kit in the hand luggage and a second full set of diabetes equipment in the check-in luggage is recommended. Airline regulations on the carriage of diabetes equipment should be checked.**

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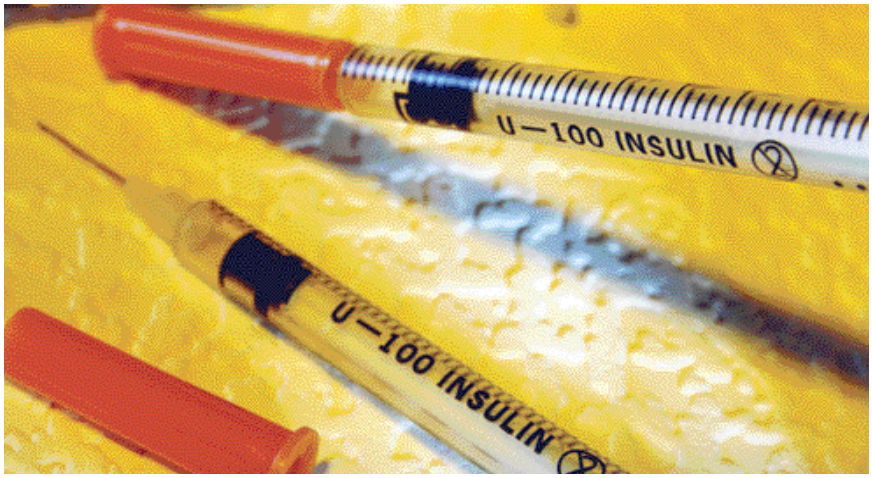

When she started insulin eight months ago, she was slightly overweight at 66 kg (height, 156 cm; BMI, 27.1 kg/m^2). Now she weighs 74 kg, her triglyceride level has increased from 1.5 to 3.2 mmol/L and her blood pressure has also increased despite her taking a higher dosage of ACE inhibitor and adding a low dose thiazide.

Table 1. Weight gain in type 2 diabetes[2]

- Improved glycaemic control – leads to decreased glycosuria and weight gain (2 kg per 1% decrease in A_{1c})
- Prandial boluses – lead to weight gain independent of glycaemia
- Oral hypoglycaemic agents, sulfonylureas and glitazones, cause weight gain but stopping them and/or metformin is likely to worsen glycaemia
- Use of premixed insulins – hypoglycaemia caused by the short acting component may lead to weight gain
- Overuse of insulin – may cause hypoglycaemia, increased appetite and weight gain

Why has Sue gained weight?

Sue may have developed a medical condition (such as hypothyroidism) or be taking a medication (such as a tricyclic antidepressant) that is causing her to gain weight. Most likely, however, her increased weight has been caused by:

- using the wrong insulin preparation
- stopping her metformin
- not anticipating weight gain with improved glycaemic control (Table 1)[2].

The wrong insulin

Usually the most appropriate starting insulin schedule is to continue oral hypoglycaemic agents and add a bedtime dose of basal insulin – either intermediate acting isophane insulin (Humulin NPH, Protaphane) or long acting analogue insulin.[3,4] Occasionally, the fasting blood glucose level (BGL) will be on target but the BGL before the evening meal will be high: then a morning dose of basal insulin will be appropriate. Starting with a bedtime basal insulin and continuing oral hypoglycaemic agents produces better glycaemic control, less weight gain and less hypoglycaemia than other insulin schedules (twice daily basal, basal/ bolus, twice daily premix), and only needs one injection.[4]

Some practitioners hope that 'one size will fit all' and use premixed insulins, which have basal and bolus insulins in fixed proportions (usually 70%:30%). In clothing, the size XL will fit all but will not do so very comfortably or elegantly. For patients with type 2 diabetes, premixed insulins rarely fit anyone and additionally cause several problems. The quick acting insulin can cause hypoglycaemia and extra weight gain, and the fixed proportions of the two types of insulin can make titration difficult because changing the dose changes both the basal and the bolus components.[4]

Eventually, many people with type 2 diabetes will require quick or very quick acting insulin to achieve the A_{1c} target of less than 7.0%.[5]

Stopping oral hypoglycaemic agents

Generally, oral hypoglycaemic agents should be continued unless there is a reason to stop them (such as renal impairment). Stopping oral hypoglycaemic agents is likely to worsen glycaemia because they were probably having some hypoglycaemic effect. For example, metformin and/or glitazones increase insulin sensitivity (and thereby reduce insulin resistance) and sulfonylureas and glitinides increase insulin secretion. Furthermore, stopping metformin removes its beneficial effects in terms of weight control (Table 1). Metformin as monotherapy for six months is associated with weight loss (about 2 to 3 kg)[6] as opposed to the weight gain associated with monotherapy with both sulfonylureas and glitazones (about 2 to 3 kg the wrong way),[7,8] a net weight advantage of 4 to 6 kg for metformin.

The insulin sensitiser metformin will continue to be useful for as long as it can be safely used and is tolerated because insulin resistance continues and/or worsens with time. However, the effect of insulin secretagogues such as the sulfonylureas progressively decreases as the capacity of the pancreas to secrete insulin decreases.

Not anticipating weight gain with improved glycaemic control

Hyperglycaemia is associated with glycosuria; the potential energy associated

with the glucose is also lost in the urine. Improving glycaemic control will reduce or stop glycosuria and is likely to produce weight gain because the previously excreted glucose now becomes available for metabolism. The greater the improvement in glycaemia, the more the decrease in glycosuria and the greater the weight gain. As a rough rule, 2 kg is gained for each 1% decrease in A_{1c} when insulin is started (Table 1).

Other factors may contribute to weight gain. For example, people may feel like eating more because they feel better when their hyperglycaemia is controlled, and overenthusiastic insulin therapy can produce hypoglycaemia with its associated desire and need for extra food intake.

When people with type 2 diabetes start insulin, they should be encouraged to 'eat less and walk more' to balance the expected effects of reduced glycosuria.[9]

Difficulty losing weight

You reintroduce the metformin and switch Sue from twice daily premix to bedtime basal insulin. You also suggest she get some dietetic advice. She returns 10 weeks later.

'Your medication change and the dietary advice seem to be working. Initially my weight went down rather than up. I lost 2 kg in the first six weeks. But now I'm stuck. My weight hasn't changed for the last few weeks.'

Why is Sue no longer losing weight?

Again consider potential complicating conditions and medications. However, the common causes for patients reaching a weight plateau are:

- eating extra carbohydrate to 'balance' the insulin
- patient and/or doctor aiming for 'tight' glycaemic control
- walking 'more' but not enough.

Extra carbohydrate to 'balance' the insulin

Some people on insulin are advised to eat extra complex low glycaemic index (GI) carbohydrate at meals, between meals, before bed and before exercise to 'balance' the hypoglycaemic effects of medication and exercise. The extra snacks are thought to 'spread' the glycaemic load more evenly throughout the day.

This advice may be well intentioned and theoretically sound but it may make it impossible for a person using insulin to control their weight. Asking people taking insulin to increase their carbohydrate intake and eat six times a day is asking them to put on weight.

Extra carbohydrate on its own would not necessarily cause a problem if it were balanced by a lesser intake of other major nutrients, particularly fat. Usually, however, people eat the extra carbohydrate as well as their normal meals. Moreover, they don't just eat extra carbohydrate, they eat extra other energy sources as well – for example, the extra slice of bread might come with butter, cheese, ham or mayonnaise, or all of these.

People with diabetes should adjust their hypoglycaemic medication to suit their lifestyle, rather than vice versa. If hypoglycaemia occurs, they should decrease hypoglycaemic medication rather than increase carbohydrate. If the person is worried about hypoglycaemia when exercising, then the solution is, once again, to decrease hypoglycaemic medication.

If the overnight or fasting BGL is low in a person taking basal bedtime insulin and daytime oral hypoglycaemic agents, decrease the insulin. If the low BGL occurs during the day, decrease the oral hypoglycaemic agents (particularly the sulfonylurea). If the person is on twice daily basal insulin, you will probably have already stopped the sulfonylurea. Hypoglycaemia during the night should prompt a decrease in the bedtime insulin dose, and hypoglycaemia in the day should prompt a decrease in the morning insulin dose.

Aiming for 'tight' glycaemic control

The glycaemic target of A_{1c} below 7% is based on data from the Diabetes Control and Complications Trial (DCCT) for type 1 diabetes and the United Kingdom Prospective Diabetes Study (UKPDS) for type 2 diabetes.[7,10] As seen in Figure 1, the risk of microvascular complications (retinopathy) in type 2 diabetes increases

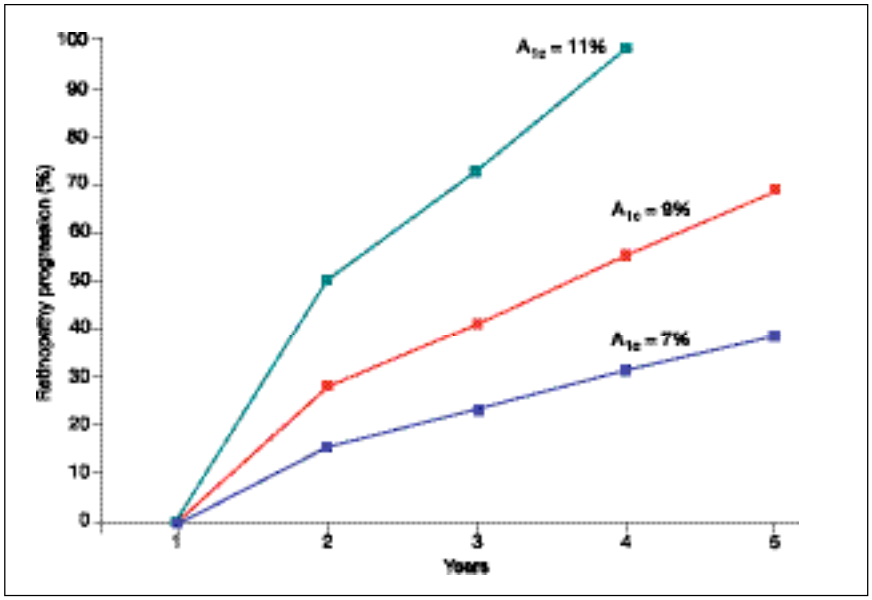

Figure 1. Retinopathy increases with time and with increasing A_{1c} levels. (Retinopathy progression defined as a two-step change in grade of the condition.)[7]

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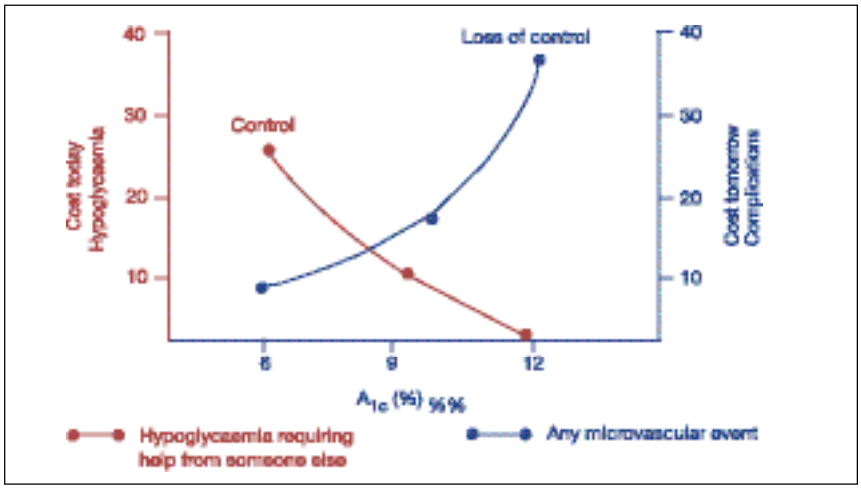

Figure 2. The person with diabetes is faced with a choice between the risk of diabetes complications with worsening control and the cost of extra self and medical care plus the risks of hypoglycaemia and weight gain.[7]

progressively with time, and more rapidly as the A_{1c} rises. Even at an A_{1c} of 7.0%, there is progression (35% progression of retinopathy over five years). This has led some people to propose lower A_{1c} targets (below 6.5%, for example)[11,12] and others to point out that the ideal target is normoglycaemia (that is, A_{1c} below 6.0%).

The 'price' to be paid for minimising the future risk of complications is weight gain, hypoglycaemia and patient effort and expense (Figure 2).[7] For each 1% decrease in A_{1c}, the progression of microvascular complications decreases by about 30%; however, the risk of hypoglycaemia increases by 25%, weight is gained (about 2 kg per 1% decrease in A_{1c}) and the patient (and doctor) have to work harder.

Obviously glycaemic targets must be individualised. While 'tight' glycaemic control may be an appropriate target for a young woman planning a pregnancy, less 'tight' control would seem more appropriate for an octogenarian with newly diagnosed diabetes who lives alone and whose memory is failing.

The current A_{1c} target of below 7.0% is the generally accepted compromise between the benefits and costs of improving glycaemic control.

Walking more but not enough

Objectively measuring physical activity can give people an unpleasant surprise. Many of us are busy all day and feel physically and mentally exhausted when we get home to relax in front of the TV with the remote control. If we were to wear a pedometer to measure our steps, we might find we had walked fewer than 3000 steps during the day. We would not be alone; half of Australian adults are not engaging in regular physical activity.[13]

Adding objectivity has two advantages:

- it can provide a baseline at the start of activities so realistic targets are set
- it provides feedback to monitor progress.

Activity can be measured in various ways, such as pedometers, time, number of blocks or meters on gym equipment.

Walking suits most people, and walking with a companion (human, canine or music) makes it enjoyable. People can add extra incidental activity into their day – for example, taking the first car parking space rather than cruising to find the closest one and taking the stairs rather than the lift.[9] The long term goal might be 30 to 40 minutes or 10,000 steps per day, and could be achieved in a series of steps from the baseline (e.g. 10% increments every one to two weeks). The message is to 'walk more, walk each day, and walk more each week'.

The general practitioner has a key role in prescribing, encouraging and monitoring activity for people like Sue who find it difficult to control their weight.

BGL and exercise

'I've done as you suggested and I'm up to 4000 steps a day. But my blood glucose goes up when I walk, not down. This morning I started at 6.2 and when I got back I was 8.3. I thought exercise was supposed to help me control my diabetes, not make it worse!'

Why does exercise make Sue's blood glucose go the wrong way?

Sue's raised BGL when she exercises may be caused by:

- blood glucose results not being totally reproducible
- her eating before she walks
- blood glucose initially increasing and then decreasing as activity continues.

Reproducibility of blood glucose results

Blood glucose meters are now smaller, faster, easier to use and more accurate, reliable and reproducible than ever before. But they are not perfect, nor people-proof.

Technique is important when using meters, and mistakes are easily made (Table 2). Some mistakes may be detected by watching the person do a test, others when the meter and strips are checked. Arrange for quality control tests (using a quality control fluid for the meter); this service may be available at some diabetes centres or branches of Diabetes Australia. Alternatively, ask Sue to perform blood glucose measurements immediately before and immediately after providing a blood sample for a laboratory glucose measurement – checking her results against the laboratory result will show the accuracy (how close her mean value is to the laboratory result) and reproducibility (how much

her blood glucose results differ) of her measurement.

Even with meticulous technique, BGL readings may be plus or minus up to 20% of the mean value; in Sue's case, 6.2 and 8.3 may be variations around a mean of 7.2 mmol/L. However, if Sue repeatedly measures her BGL as increasing then it is probably a real phenomenon.

Eating before walking

Blood glucose levels rise after meals regardless of whether people have diabetes but the increase is much more in those with the condition (for example, by up to 8 mmol/L compared with about 3 mmol/L). If Sue had eaten breakfast before her morning walk, her BGL would be expected to increase, the degree of increase depending on the glycaemic index and amount of carbohydrate she ate (the glycaemic load) as well as the other nutrients consumed (particularly fat).[14] The values of 6.2 and 8.3 mmol/L could simply be part of Sue's blood glucose profile after breakfast.

Sue may be wise to eat her usual breakfast before she walks, particularly if she plans to walk briskly and for a long time. She then won't have to worry about hypoglycaemia or to eat extra food, which would counteract the beneficial effect of the walking on her weight. The activity may also limit the blood glucose rise after breakfast.

Blood glucose may increase initially then decrease with activity

The blood glucose response to physical activity depends on the insulin levels, food intake and intensity and duration of exercise. In people without diabetes, activity triggers a sympathetic response (catecholamines) that increases hepatic glucose output to provide the muscles with glucose; insulin secretion in response to the increased blood glucose prevents any 'overswing' to hyperglycaemia. In people with diabetes, particularly type 1 diabetes, beta cells have partially or totally lost the capacity to control hepatic glucose output. If insulin levels are low, a sympathetic response triggers excessive hepatic glucose output, leading to hyperglycaemia. On the other hand, if insulin levels are high (from insulin secretagogue or injection), hepatic glucose output is reduced and blood glucose will fall, leading to hypoglycaemia.

As activity progresses in a person without diabetes, the tendency for blood glucose levels to fall is countered by decreasing insulin levels leading to lesser inhibition of hepatic glucose output and, therefore, a continuing glucose supply maintaining normoglycaemia.

In people with diabetes, this normal response to continued activity may be disturbed. In those receiving insulin or insulin secretagogues, the capacity to decrease insulin levels in response to falling blood glucose is reduced or absent, with the result that blood glucose progressively decreases with continuing activity as glucose is taken up by cells. People with diabetes who take insulin or insulin secretagogues are 'between a rock and a hard place': too little insulin, and blood glucose initially increases and may continue to increase; too much insulin, and blood glucose initially decreases and will continue to decrease.

Many people with type 2 diabetes have some residual beta cell function and the blood glucose response to activity is controlled to some degree. However, in type 1 diabetes and type 2 diabetes of long duration, the beta cell response is absent or inadequate and the blood glucose response to activity can be difficult to control.

Summarising the above, there is a biphasic response because:

- there is an initial increase in blood glucose as hepatic glucose output increases excessively because beta cells do not respond normally, and
- with continuing activity, blood glucose progressively falls because insulin levels do not fall (insulin continues to be absorbed from an injection site or secreted by the beta cell under the influence of a secretagogue).

Table 2. Blood glucose monitoring: tips and traps

Tips	Traps
Clean the sample site	Dirty meter
Use enough blood	Expired battery/strip
Maintain the meter	Incorrect strips, calibration or code
Check meter accuracy	Insufficient or smeared blood on strip

Travel

Sue is flying from Sydney to Los Angeles to visit Disneyland, Hollywood and the Universal Studios and then go on a bus tour to Las Vegas. She wants advice on how to handle her medication.

She is currently taking intermediate insulin (isophane) 35 units at breakfast and 16 units at bedtime and metformin 850 mg twice daily.

What should she do?

Adjusting insulin dosages

When travelling by air it may be necessary to adjust insulin dosages on the day of travel to allow more easy synchronisation of meal and injection times with 'local' time on arrival at a destination. Adjustment is advisable if the time zones of the departure and destination points differ by more than four hours (more than four time zones crossed).

If patients keep following the local time of the place of departure until their arrival at the destination (i.e. they don't change their wristwatch until the destination is reached), they can keep track of their insulin injections and meals. The time difference they will experience in changing to the local time on arrival at the destination

Useful resources for type 2 diabetes

- **Diabetes Australia.** Comprehensive series of consumer information resources including multilingual resources. www.diabetesaustralia.com.au/education_info/sheets.html and www.diabetesaustralia.com.au/multilingualdiabetes/HealthPros/index.htm
- **Diabetes Centre.** Professional and consumer resources. www.diabetes.org.au
- **National Diabetes Services Scheme.** Services available include subsidised blood glucose testing strips, free syringes and pen needles, and subsidised insulin pump consumables. Registration forms available from Diabetes Australia, phone 1300 136 588, or via the website, www.diabetesaustralia.com.au
- **RACGP.** *Diabetes Management in General Practice Guidelines 2006/7* available through regional divisions of general practice and at www.racgp.org.au

is the time difference between the place of departure and the destination, i.e. the number of time zones travelled across. The duration of the flight has no effect on the time difference because that time will pass whether the local time at the place of departure or the destination is followed.

The general rules for air travel are:

- if the day of travel is shorter – as it will be if travelling to a time zone 'ahead' of the local time, i.e. travelling east (in this case, Australia to USA) – then less insulin is needed
- if the day of travel is longer – as it will be if travelling to a time zone 'behind' the local time, i.e. travelling west (USA to Australia) – then more insulin is needed.

The changes in insulin doses are roughly proportional to the amount of time by which the day of travel is shorter or longer but, to be on the safe side, slightly lower (see Table 3).

It is not usually necessary to adjust for time zones when flying within Australia as time differences are less than four hours.

Travel across the Pacific Ocean involves crossing the International Date Line and patients may wonder if this will affect the adjusting of insulin dosages. It doesn't, because insulin dosages are considered over 24-hour periods so the 'gain' or 'loss' of a day involved crossing the Line becomes irrelevant.

The day Sue is travelling to California, which is six time zones to the east of Australia's eastern seaboard, her day will effectively be six hours shorter (although it will be 18 hours longer according to the calendar) – if she arrives at 6.00 a.m. in Los Angeles it will be midnight in eastern Australia. She will therefore need less insulin the morning before departure because this is the insulin that will be working during her travel.

Table 3 gives some examples of insulin adjustments. From this, it can be seen that the action required for travel east from Sydney to Los Angeles is a 20% decrease in insulin. So Sue should be advised to reduce her breakfast dose from 35 to 28 units on the day of travel, and to adjust the dose and time of her bedtime insulin to 80% of the usual dose (13 units, instead of

Table 3. Examples of insulin dosage adjustments for different time zones

Destination (from Sydney)	Destination time zone	Local destination time at noon Sydney time (+10 hours GMT)	Length of day of travel	Recommended insulin dosage change*
Honolulu	–10 hours GMT	4 pm	4 hours shorter†	No change necessary
London	GMT	2 am	10 hours longer‡	Increase neutral insulin by 10% before extra meals
New York	–5 hours GMT	9 pm	9 hours shorter†	Reduce insulin by 25% on day of departure
Los Angeles	–8 hours GMT	6 pm	6 hours shorter†	Reduce insulin by 20% on day of departure
Tokyo	+9 hours GMT	11 am	1 hour longer‡	Eat an extra 15 g of carbohydrate 1 hour before next insulin dose, destination local time
Wellington	+12 hours GMT	2 pm	2 hours shorter†	No change necessary

* Adapted from *Diabetes and You – the Essential Guide*, published by Diabetes Australia, 1999, revised 2002. † Flight eastwards, crossing the International Date Line. ‡ Flight westwards.

16) taken six hours earlier than she would normally (at, say, 4 p.m. Sydney time rather than 10 p.m. Sydney time).

When she arrives in California, Sue should adopt the local time for meals and medication. She should take her usual medication (insulin and metformin) when she has her breakfast on the morning of arrival (flights from Sydney to Los Angeles arrive in the early to mid-morning Los Angeles local time). Las Vegas is in the same time zone as Los Angeles so Sue will be able to keep to her new local time when she travels there by bus.

On her return journey to Australia, Sue's day will be six hours longer so she will need extra meals with short acting insulin (one-third of her usual morning basal insulin dose [35 units], i.e. 12 units) to cover the extra time. When she arrives home she should once again adopt local time for medication and meals.

The patient handout on page 53 gives some guidelines on air travel for people taking insulin.

Other travel considerations

In addition to advice on adjusting her hypoglycaemic medications, there are some general tips you can give Sue to help her enjoy her long distance flight without hassles. These include:

- she should eat regular meals and snacks and make time for physical activity
- most agencies will make special arrangements for food for people with diabetes, but Sue should carry her survival kit, including extra food, just in case (see the patient handout on page 53)
- she should take several copies of a letter from you stating that she has diabetes, takes insulin (and other medications), needs to do blood tests and may need special arrangements for food and activity (she should carry one copy of this in her hand luggage)
- she should carry a full set of diabetes supplies (blood glucose monitor and strips, insulin injectors and insulin) in her hand luggage and also pack extra insulin and, if possible, a spare set of the other equipment in her check-in luggage. It is advisable to check the particular airline's regulations regarding the carrying of diabetes supplies early in the planning of a trip.

Further information

Diabetes Australia has produced information sheets for patients on various aspects of living with diabetes, including travelling – see the box on page 50.

Conclusion

Problems can occur in people who are managing their type 2 diabetes with insulin and oral hypoglycaemic agents. However, many of these can be avoided. Improved glycaemic control comes with the risks of hypoglycaemia and weight gain, but these problems can be avoided if the patient and doctor are aware of the risks and know the appropriate countermeasures. Patients need to be aware of the need for adequate physical activity, appropriate food intake and meticulous blood glucose monitoring.

When travelling, people with diabetes should carry a diabetes survival kit containing a full set of their diabetes medication and monitoring equipment, a letter from their doctor stating they have diabetes, and some carbohydrate-rich food. Long distance air travel is likely to involve adjustment of insulin dosages if more than four time zones are crossed. MT

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