20 studies of 95,783 individuals followed for 12.4 years. *Diabetes Care* 1999;**22**: 233–40.
11 Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;**360**: 7–22.
12 Rubins HB, Robins SJ, Collins D, Nelson DB *et al.* Diabetes, plasma insulin, and cardiovascular disease: subgroup analysis from the Department of Veterans Affairs high-density lipoprotein intervention trial (VA-HIT). *Arch Intern Med* 2002;**162**: 2597–604.
13 Winocour PH, Fisher M. Prediction of cardiovascular risk in people with diabetes. Review. *Diabet Med* 2003;**20**:515–27.
14 Chen J, Marciniak TA, Radford MJ, Wang Y, Krumholz HM. Beta-blocker therapy for secondary prevention of myocardial infarction in elderly diabetic patients. Results from the National Cooperative Cardiovascular Project. *J Am Coll Cardiol* 1999;**34**: 1388–94.
15 Colwell JA; American Diabetes Association. Aspirin therapy in diabetes. *Diabetes Care* 2003;**26**(Suppl 1):S87–8.
16 Williams B, Poulter NR, Brown MJ, Davis M *et al.* British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary. *BMJ* 2004;**328**: 634–40.

Diabetes in hospital

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As diabetes is becoming more prevalent, the number of diabetic patients admitted to hospital is rising. Some admissions are directly due to diabetes but diabetic adults are also six times more likely than non-diabetic adults to be admitted for other reasons.[1] This is a worldwide and large-scale problem. Up to 10% of UK hospital inpatients[2] and six million people hospitalised each year in the USA are diabetic.[3] Patient associations identify hospitalisation as a priority time in diabetic life for better care because poor glycaemic control increases susceptibility to complications and lengthens hospital stay.[4] It is also an unhappy time if, as too often happens, patients who are experts in self-care are denied information, support and autonomy.[5]

Why glucose control destabilises in hospital

Stress causes an outpouring of counter-regulatory hormones including adrenaline, glucagon, cortisol and growth hormone. These accelerate catabolism, hepatic gluconeogenesis and lipolysis, and raise blood glucose, fatty acids and ketone bodies. In acute myocardial infarction (AMI), for example, there is a direct correlation between plasma adrenaline and glucose concentrations. Hospitalised patients are physically inactive – another potent reason for hyperglycaemia. Blood glucose rises, but in an unpredictable way because other factors favour hypoglycaemia. Ill people may not be able to eat as normal and, at least in the UK, their hospital diet is often unsatisfactory.[6] They may be unable to call for extra food when hypoglycaemic because they are physically incapable or cognitively impaired.

Most unsatisfactory of all, they may be 'treated' in an authoritarian way by people who know less about diabetes than they do. This was graphically illustrated by a UK trial in which a diabetes specialist nurse shortened hospital stay by 27% through supervising and coordinating diabetes care.[7]

Does good glycaemic control really matter?

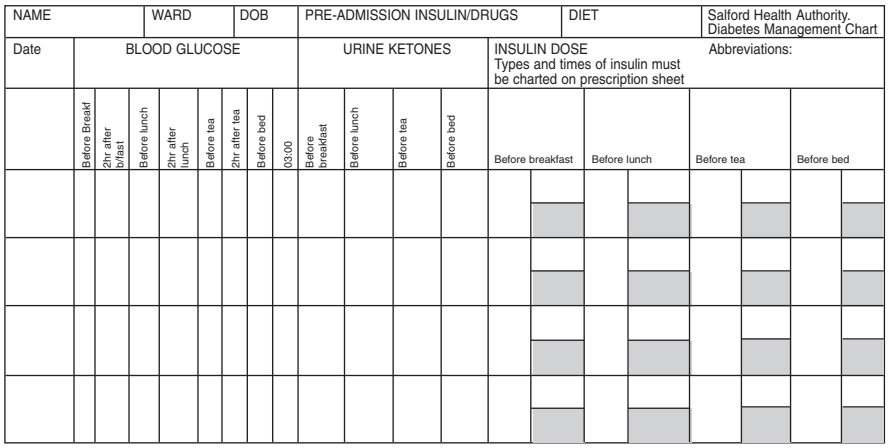
Logically, good control might be expected to improve well-being, prevent postoperative infection, hasten the resolution of infection, facilitate wound healing and prevent severe hyperglycaemia. A turning point in hospital care was the Dextrose Insulin and Glucose in Acute Myocardial Infarction (DIGAMI) study, which showed that tight control at the time of MI and over

Key Points

- **Up to 10% of NHS inpatients have diabetes**
- **It is unrealistic to expect every patient to have normal blood glucose all the time; we define good control as four out of five preprandial glucose values in the range 4–10 mmol/l**
- **Acutely ill patients should be managed with intravenous insulin/dextrose**
- **Patients well enough to eat should be treated with subcutaneous insulin; a four times daily 'basal-bolus' regimen reduces the glucose rise after meals and is flexible enough to be adjusted within-day to correct for any upwards or downwards trend**
- **Analogues are showing promise as the insulins of choice for patients in hospital**

KEY WORDS: Diabetes mellitus, inpatient management

Fig 1. Integrated monitoring and prescribing, organised around meal times, not 'by the clock'.



the next three months reduced three-year mortality by 11%.[8] Benefit has since been shown for deep sternal wound infections after coronary artery bypass graft and nosocomial infections.[9] Even people without diabetes can benefit from insulin infusions. In critically ill, mainly post-cardiac surgical patients, an insulin infusion given if plasma glucose was over 6 mmol/l reduced overall mortality, the duration of stay in the intensive care unit (ICU), the incidence of septicaemia and critical illness polyneuropathy, and the requirement for blood transfusion or dialysis.[10]

Monitoring and targets

Haemoglobin A1c, and even short half-life analytes like fructosamine and glycated albumin, are not sufficiently responsive to be of value. Using electrochemical sensing technology, beta-hydroxybutyrate can now be measured in a few seconds at the bedside – of value in the management of ketoacidosis but hopefully unnecessary in other hospitalised patients.[11] Continuous glucose sensing is showing promise, but monitoring by finger-prick glucose measurements is the standard of care at present. Timing of blood tests that takes no account of meal times is valueless because plasma glucose can double in the two hours after a meal even in well controlled diabetes. The time axis of our hospital's monitoring chart is marked by meal times, not clock time, to reinforce the simple message that measuring blood glucose by the clock will produce chaotic and uninterpretable results whatever the patient's level of control. We recommend blood tests up to four times per day: before each main meal and a bedtime snack (Fig 1).

Treatment should aim to avoid symptomatic hyper- and hypoglycaemia, although doctors' and nurses' exaggerated fear of hypoglycaemia tends to condemn patients to unnecessary hyperglycaemia. In the absence of a clear evidence base, our definitions are:

- *good control:* four out of five preprandial glucose values in the range 4–10 mmol/l
- *poor control:* one or none of the preprandial glucose values in the target range
- *suboptimal control:* scores in between those of good and bad control.

By those criteria, there is substantial room for improvement in both Salford and Bangalore, with about one-third of patients poorly controlled and no more than half well controlled.[6,12]

In both our institutions, urine is regarded as of value only in detecting ketosis and, even then, as a poor second best to finger-prick betahydroxybutyrate measurement.

Treatment regimens

Answers to frequently asked questions about the management of diabetes in hospital are summarised in Box 1 (published in detail elsewhere;[13] an excellent, practical handbook is also available[2]).

Some general points may be made:

- There is no evidence that sulphonylureas are unsafe, but insulin is the preferred treatment for acutely ill people because of its short half-life and responsiveness to fast-moving situations.
- Hospitalised patients are candidates for permanent conversion from tablets to insulin because type 2 diabetes is a progressive disease.

Box 1. Answers to FAQs on management of diabetes.

1 Listen to the views of your patients and be ready to take their advice; they may be much more expert than you.
2 Pay close attention to how they respond to your regimen; learn insulin dosing from someone more expert than you, then learn from experience.
3 If you withhold insulin from a patient because their blood glucose level is normal, it will not stay normal for long! A major cause of instability is undue fear of hypoglycaemia (often on the part of nursing staff, projected on to a junior doctor summoned to see their patient).
4 Do not expect blood glucose levels to be completely normal; 'good control' in hospital is four out of five glucose levels in the target range 4-10 mmol/l.
5 Involve the diabetes advisory team as soon as possible but learn from them; do not just pass responsibility on to them.
6 Do not give metformin to an 'ill' patient in hospital (eg on a coronary care unit) because of the risk of lactic acidosis.
7 There are three levels of intensity of insulin treatment for hospitalised patients:
- an intravenous insulin/glucose regimen for acutely ill (non-eating) patients
- four times daily insulin for the patient who is unstable but well enough to eat
- a maintenance regimen (which may or may not be four times daily) for all other patients.

- Metformin should be avoided in the acute phase of any illness because of the risk of lactic acidosis; it is absolutely contraindicated in renal failure, liver disease and severe heart failure.

There are three levels of intensity of insulin treatment:

- intravenous infusion therapy
- a four times daily 'basal-bolus' regimen, and
- a patient's 'usual' therapy.

Intravenous infusion therapy

Unless there is a need to limit the volume of administered fluids, the patient receives an infusion of (usually isotonic) dextrose with added potassium. Dextrose gives something for insulin to 'work against', damping out swings in plasma glucose. Potassium prevents hypokalaemia caused by insulin driving potassium into cells. Intravenous insulin may be added to the dextrose and potassium ('GKI' regimen) or infused through a syringe driver, with the rate of insulin administration adjusted according to hourly near-patient glucose measurements. Syringe drivers have become more widely used than GKI as pumps have become generally available in hospitals and are widely used in ICUs and coronary care units. Figure 2 shows how staff in one hospital are advised to set and adjust the rate of insulin infusion.

Basal-bolus therapy

Insulin need can be divided into 'boluses' matched to the timing and size of (usually three) meals, and a 'basal' (long-acting insulin before bed) requirement that is not. Well motivated ambulatory patients use basal-bolus therapy to maintain euglycaemia and avoid hypoglycaemia in day-to-day life – qualities even more important at times of illness. Subcutaneous insulin infusion pumps are an even better means of meeting basal-bolus needs. They are unproven in acute illness and too sparsely available to be included in this review, but anyone on a pump should be encouraged to use it during hospital admission unless too ill to take responsibility for themselves.

Insulin analogues are often used for basal-bolus therapy:

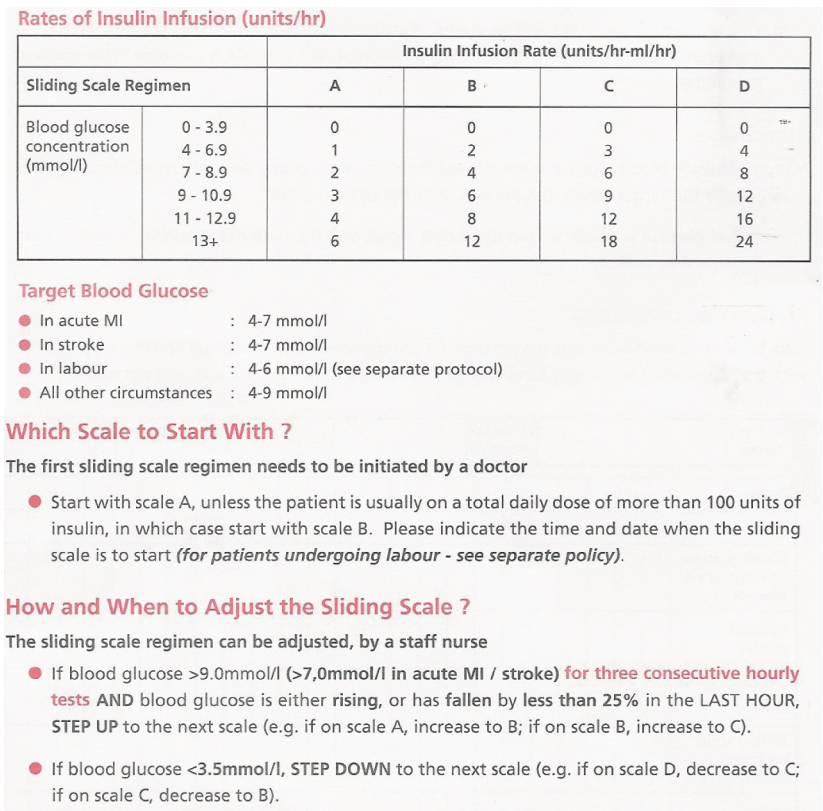
- lispro or insulin aspart, because it is even more rapidly absorbed than soluble insulin and can be given when food is served, and
- glargine, which is a more predictably absorbed long-acting insulin.

Usual insulin therapy

Practice varies by district and patient, but some broad generalisations may be made:

- Most people take two doses, though some with type 2 diabetes take a single basal dose combined with metformin.
- Pre-mixed combinations of short- and medium-acting insulin are popular for twice daily regimens.
- Basal bolus treatment is reserved for highly motivated (usually) type 1 patients who self-monitor regularly and make day-by-day adjustments to their doses.

Fig 2. A family of 'sliding scales' to maintain euglycaemia in ill, non-eating patients on dextrose infusions.



Rates of Insulin Infusion (units/hr)

		Insulin Infusion Rate (units/hr-ml/hr)			
Sliding Scale Regimen		A	B	C	D
Blood glucose concentration (mmol/l)	0 - 3.9	0	0	0	0
	4 - 6.9	1	2	3	4
	7 - 8.9	2	4	6	8
	9 - 10.9	3	6	9	12
	11 - 12.9	4	8	12	16
	13+	6	12	18	24

Target Blood Glucose

- In acute MI : 4-7 mmol/l
- In stroke : 4-7 mmol/l
- In labour : 4-6 mmol/l (see separate protocol)
- All other circumstances : 4-9 mmol/l

Which Scale to Start With ?

The first sliding scale regimen needs to be initiated by a doctor

- Start with scale A, unless the patient is usually on a total daily dose of more than 100 units of insulin, in which case start with scale B. Please indicate the time and date when the sliding scale is to start *(for patients undergoing labour - see separate policy)*.

How and When to Adjust the Sliding Scale ?

The sliding scale regimen can be adjusted, by a staff nurse

- If blood glucose >9.0mmol/l **(>7,0mmol/l in acute MI / stroke)** for three consecutive hourly tests **AND** blood glucose is either **rising**, or has **fallen** by **less than 25%** in the LAST HOUR, **STEP UP** to the next scale (e.g. if on scale A, increase to B; if on scale B, increase to C).
- If blood glucose **<3.5mmol/l, STEP DOWN** to the next scale (e.g. if on scale D, decrease to C; if on scale C, decrease to B).

A simple conceptual framework and classification

Insulin treatment can be thought of as *anticipating* or *following* a patient's glycaemic control:

- A patient tailoring short-acting insulin doses before each meal to the amount they expect to eat is *anticipating* the effect of the food on plasma glucose.
- At the other extreme, an insulin infusion adjusted hour-to-hour according to bedside glucose measurements is *following* and correcting for whatever glucose excursions may occur.

Our classification is into '*non-eating*' and '*eating*' patients:

- *Eating* patients are subclassified into 'unstable' and 'stable'.

- A *non-eating* patient is so unwell that their insulin requirement is unpredictable. Swings in blood glucose must be damped by a continuous glucose infusion, with the rate of insulin infusion 'following' hourly blood glucose measurements.

Thus, an insulin and glucose ('sliding scale') regimen or GKI is well suited to surgery, labour and intensive care. Once the patient is well enough to start eating, the regimen will fail because it will always be 'chasing its tail' as plasma glucose rises after meals. At that time, an anticipating regimen is needed.

A basal-bolus regimen, by its nature, anticipates the rise in plasma glucose after meals, but it can also follow. Insulin doses can be varied on the experience of previous doses/meals, both to anticipate insulin need and to correct hyper- or hypoglycaemia. Basal-bolus therapy is a logical step for patients coming off insulin infusions, who are eating but unstable, because it combines the principles of anticipating and following. The first bolus dose should be given 30 minutes before stopping the infusion. Box 2 gives an example, in the absence of general and well-validated rules for calculating insulin doses.

A detailed consideration of 'usual' insulin therapy is beyond the scope of this article, but suffice it to say that basal-bolus therapy is a 'bridge' between infusion and usual therapy.

Conclusions

Generalists are often called on to care for diabetes in hospitalised patients. They could do so more effectively with the support of a liaison diabetes specialist nurse. Most preprandial glucose measurements should be in the range 4–10 mmol/l. Ill, 'non-eating' patients need intravenous glucose and insulin infused by a syringe driver, adjusted according to hourly near-patient glucose measurements. Patients well enough to eat do not need an infusion regimen; if one is used, plasma glucose will swing widely as the regimen 'chases its tail'. A basal-bolus regimen, used by well motivated ambulatory patients, should be the standard of care for eating but unstable patients before transfer to their usual regimen and discharge.

Box 2. Post-illness regimen.

Problem:
A 60-year-old woman with type 2 diabetes normally takes 32 units of a 30%/70% short/medium-acting premixed insulin before breakfast and 28 units before tea. Admitted with gastroenteritis, her vomiting has settled and she is hungry, but she has not yet been out of bed. Her total intravenous insulin dose over the last 24 hours was 48 units.

What we would do:

- If she was normally well controlled, we would expect her to go back on to her usual insulin doses on the day of discharge; we would certainly not detain her in hospital for her usual doses to be adjusted.
- However, we do not yet know whether she is fully recovered and able to eat normally, so for the next 24 hours we would prescribe an ultra short-acting analogue insulin before breakfast, dinner and tea, and a long-acting insulin before bed, using the prescription chart shown in Fig 1.
- Splitting her usual insulin into four doses and rounding up to even numbers of units, we would suggest 14 units at each of those four time points (56 units). If we had divided the previous 24 hours' insulin doses into four, it would have come to 12 units qds, which seems too little because it is considerably less than her usual total dose and she is now eating.
- It is impossible to predict accurately what doses she will need, so we would ask the ward staff to review her four times daily blood glucose measurements, and be ready to adjust those suggested doses upwards or downwards depending on her response.
- If she responded well on this regimen and was well enough for discharge the next day, we would continue the qds regimen up to (and including) the lunchtime dose, ask her to resume normal insulin at teatime, monitor frequently, and call our diabetes specialist nursing team for advice if she had difficulty regaining control.

Conflict of interest

Neither author has any conflicting interest.

References

1 Metchick LN, Petit WA Jr, Inzucchi SE. Inpatient management of diabetes mellitus. *Am J Med* 2002;**113**:317–23.

2 Page SR, Hall GM. *Diabetes: emergency and hospital management*. London: BMJ Books, 1999.

3 Levetan CS, Passaro M, Jablonski K, Kass M, Ratner RE. Unrecognized diabetes among hospitalized patients. *Diabetes Care* 1998; **21**:246–9.

4 American Diabetes Association. Hyperglycaemia risk in patients with diabetes mellitus. *Diabetes Care* 2003;**26**(Suppl):S109–17.

5 *What diabetes care to expect*. London: Diabetes UK, 2000.

6 Bhattacharyya A, Christodoulides C, Kaushal K, New JP, Young RJ. In-patient management of diabetes mellitus and patient satisfaction. *Diabet Med* 2002;**19**: 412–6.

7 Davies M, Dixon S, Currie CJ, Davis RE, Peters JR. Evaluation of a hospital diabetes specialist nursing service: a randomized controlled trial. *Diabet Med* 2001;**18**:301–7.

8 Malmberg K. Prospective randomised study of intensive insulin treatment on long term survival after acute myocardial infarction in patients with diabetes mellitus. DIGAMI (Diabetes Mellitus, Insulin Glucose Infusion in Acute Myocardial Infarction) Study Group. *BMJ* 1997;**314**:1512–5.

9 Furnary AP, Zerr KJ, Grunkemeier GL, Starr A *et al*. Continuous intravenous insulin infusion reduces the incidence of deep sternal wound infection in diabetic patients after cardiac surgical procedures. *Ann Thorac Surg* 1999;**67**:352–60; discussion 360–2.

10 van den Berghe G, Wouters P, Weekers F, Verwaest C *et al*. Intensive insulin therapy in critically ill patients. *N Engl J Med* 2001; **345**:1359–67.

11 Byrne HA, Tieszen KL, Hollis S, Dornan TL, New JP. Evaluation of an electrochemical sensor for measuring blood ketones. *Diabetes Care* 2000;**23**:500–3.

12 Deepak PJ, Sunitha K, Nagaraj J, Sanjukta K, Bhattacharyya A. Inpatient management of diabetes: survey in a tertiary care centre. *Postgrad Med J* 2003;**79**:585–7.

13 Bhattacharyya A, Kaushal K, Dornan TL. Glucose control in in-patients. *Diabet Med* 2002;**19**(Suppl 1):4–7.