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THE MANAGEMENT OF DIABETES DURING SURGERY

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"Diabetes offers a serious bar to any kind of operation, and injuries involving open wounds, haemorrhage, or damage to the blood vessels are exceedingly grave in subjects of this disease. A wound in the diabetic patient will probably not heal while the tissues appear to offer the most favourable soil for the development of putrefaction and pyogenic bacteria. The wound gapes, suppurates, and sloughs. Gangrene readily follows an injury in diabetics, and such patients show terrible proneness to the low form of erysipelas, and cellulitis." (Treves, 1896.)

The advent of insulin revolutionized the treatment of diabetic patients undergoing surgery, a revolution that was extended by the discovery of antibiotics. Nonetheless, in unpractised hands surgery can still be disastrous for diabetics in terms of both morbidity and mortality. Even in good centres surgery carries a significant mortality and morbidity. Wheelock and Marble (1971) reported a 3.7% mortality in a series of 2780 patients studied between 1965 and 1969, while Galloway and Shuman (1963) had a 3.6% mortality and 17.2% morbidity in 667 cases. In the same period Alieff (1969) reported a 13.2% mortality. In diabetics undergoing renal transplantation there was two to four times the mortality compared with non-diabetics (Kjellstrand et al., 1972). The major causes of mortality and morbidity were and still are myocardial disease and infection. Obviously these are important in non-diabetics as well as in diabetics, but in the latter, poor control of diabetes with its attendant disturbances of electrolyte and intermediary metabolism will inevitably exacerbate these problems. Myocardial infarction itself is more likely to be mortal in diabetics (Soler et al., 1974) while resistance to infection is diminished in poorly controlled diabetes (Bagdade, Nielson and Bulger, 1972). Wound healing is also said to be impaired.

Diabetics undergoing surgery tend to be a high-risk group. Three-quarters or more of surgical diabetics are likely to be over the age of 50 (Galloway and Shuman, 1963). In this age group obesity is common and there is an increased prevalence of myocardial and peripheral vascular disease, as well as renal impairment, compared with the non-diabetic population. It is obvious from this that problems may arise both during and after operation in diabetics, and that these problems will be exacerbated by poor control of the diabetes. The magnitude of the problem for the anaesthetist and surgeon is demonstrated by the fact that it has been estimated that a diabetic has only a 50% chance of avoiding surgery during his lifetime (Root, 1966).

One further important point is that diabetes often presents *de novo* on surgical wards as a result of the stress either of the surgical condition or of admission to hospital. Beaser (1970) states that 25% of the diabetic patients on a surgical ward may be newly discovered cases. It is thus of paramount importance that surgical cases be screened adequately, as failure to make the diagnosis before operation may lead to a stormy postoperative course.

There is obviously a need for a logical straightforward set of guidelines for the treatment of diabetes during and after surgery. At present there are a multitude of recommended regimens, many of which are irrational if not dangerous. In the following review we shall first discuss the metabolic response of normal man to surgery and starvation (generally the fate of the surgical patient, wittingly or unwittingly) and how this may be modified in the diabetic patient. We shall then review some of the present regimens recommended for the treatment of diabetes in surgery. In the final section we shall discuss the rationale for the use of a simple i.v. regimen which can be applied to all diabetics undergoing surgery regardless of time of day or of severity of operation.

METABOLIC AND HORMONAL RESPONSE TO SURGERY

Metabolism in Normal Man

Fed and fasted states

In normal man anabolism and catabolism are finely balanced. During feeding anabolism predominates with the laying down of food reserves in the form of

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glycogen and triglycerides. At the same time protein synthesis is stimulated. During fasting, as for example during the night, the body switches to catabolism, mobilizing stored fuels. As starvation increases so the pattern of fuels used changes. During short-term starvation there is an obligatory requirement for approximately 180 g glucose per day for nervous tissue and red cell metabolism.

Some of the glucose need is met by mobilization of hepatic glycogen but reserves are relatively small, and a progressively greater proportion of the glucose requirement comes from gluconeogenesis. The major substrates for this are lactate and pyruvate, alanine, glucogenic amino acids and glycerol. Lactate and pyruvate are derived in part in extrahepatic tissues from circulating glucose and as such represent no net gain of glucose. However, a proportion also comes from muscle glycogen, thus creating a means, albeit energetically wasteful, whereby muscle glycogen can be converted into circulating glucose. Alanine is derived in muscle from the amino groups of other amino acids, in particular the branch chain amino acids, and pyruvate. Originally it was thought that the pyruvate was produced not only from glucose but also from the carbon skeletons of the other amino acids. There is now some doubt as to whether the latter occurs. If this is proved correct then no *net* gain of glucose can come from alanine, and other amino acids assume greater importance. These include glutamine which goes from muscle to gut, where it is converted to alanine and thence to the liver for gluconeogenesis. Regardless of the fate of the carbon skeleton there is a net flow of amino acids away from extrahepatic tissues with an overall loss of protein. Glycerol from adipose tissue lipolysis also acts as a glucose precursor, but quantitatively is unimportant.

In short-term starvation there is also increased lipolysis in adipose tissue. The released fatty acids are either used direct as a fuel or are converted by the liver to ketone bodies. These cannot be oxidized by liver and serve as a useful fuel in extrahepatic tissues. It should be remembered that, in resting man, 90% of the energy used by muscle comes not from glucose but from fatty acid and ketone body oxidation.

As starvation continues a major change, termed "ketoadaptation", occurs in nervous tissue. The brain starts to use ketone bodies and the overall glucose requirement decreases by 50%. Renal gluconeogenesis, which normally amounts to only 10% of the total, remains constant and hepatic glucose production decreases dramatically (Owen et al., 1969). Amino acid use for gluconeogenesis and for oxidation decreases at the same time, and urinary urea excretion shows a marked decrease, with ammonia assuming greater importance as a nitrogenous waste product (Cahill, 1970). During this period blood ketone bodies increase to concentrations of 4–6 mmol $litre^{-1}$ from overnight fasted values of 0.05–0.50 mmol $litre^{-1}$. This is associated with a mild acidaemia.

The increase in ketone bodies and fatty acids has a further effect in inhibiting glucose oxidation in muscle and peripheral tissues, thereby preserving glucose and indirectly protein. This is the so-called glucose–fatty acid cycle (Randle et al., 1963). In terms of energy reserve triglycerides are much the most important with 15 000 g or 135 000 kcal in a 70-kg man. Liver glycogen amounts to only 100 g or 400 kcal, while protein can provide up to 25 000 kcal. Metabolism in starvation is, however, geared to protein preservation and the predominant fuel used is fat (Cahill, 1976). At the same time the basal metabolic rate decreases, which decreases the total caloric requirement.

All these processes are controlled through a delicate interplay between a group of hormones, the anabolic and catabolic hormones (table I). Only one

TABLE I. *Anabolic and catabolic effects of hormones. + + = major stimulatory effect; − − = major inhibitory effect; + / − = stimulation if insulin present, inhibitory if insulin absent; (+) = important only if insulin absent; + ? = selective stimulatory effect. No attempt has been made to indicate tissues where major actions occur. For further details see Alberti* (1979)

	Anabolic effects			Catabolic effects				
	Glyco-genesis	Lipo-genesis	Protein synthesis	Glyco-genolysis	Gluco-neogenesis	Lipolysis	Ketogenesis	Proteolysis
Insulin	+ +	+ +	+ +	−	− −	− −	− −	− −
Glucagon	−	−	0	+	+ +	(+)	+	0
Cortisol	+ / −	+ / −	− −	+ / −	+	+	(+)	+ +
Catecholamines	−	0	0	+ +	+ +	+ +	+	0
Growth hormone	0	0	+ +	0	+	(+)	(+)	0
Thyroid hormone	0	0	+ ?	0	+	+	(+)	+

hormone has an overall anabolic effect and that is insulin. Secretion is stimulated by carbohydrate or protein feeding, or both. It is responsible for directing absorbed fuels into stores, such as glycogen, triglyceride and protein. At the same time it drives glucose into metabolically important tissues such as muscle and adipose tissue, simultaneously sparing other fuels and switching off lipolysis. In the liver, as well as driving lipogenesis and glycogenesis, insulin inhibits gluconeogenesis, even when present in small concentrations, thereby preventing unnecessary wastage of amino acids. One other hormone, growth hormone, has some anabolic effects, but these are all directed at protein preservation. Thus it inhibits glucose uptake by tissue such as muscle and simultaneously has a mild stimulatory effect on alternative fuel production, in the form of fatty acids and ketone bodies. Overall glucose utilization decreases, amino acids are spared and these are driven into cells and into protein synthesis by growth hormone.

The stress hormones, glucagon, cortisol and catecholamines, have combined actions which oppose those of insulin, but none alone has the importance and the unique properties as a catabolic hormone that insulin has as an anabolic hormone. Thus the main actions of cortisol are to cause net protein breakdown in extrahepatic tissues and increase the flow of gluconeogenic precursors to the liver, where it also enhances amino acid degradation and gluconeogenesis. Glucagon has its main effects on the liver, stimulating ketogenesis (when adequate amounts of fatty acids are presented), gluconeogenesis and glycogenolysis. It also specifically increases alanine uptake by the liver. In contrast, catecholamines act mainly on lipolysis and glycogenolysis.

Whether the reaction of the body is anabolic or catabolic depends on the relative amounts present of insulin and the other hormones. In the fed state insulin predominates, although glucagon and growth hormone secretion may increase as well. In starvation the concentrations of insulin slowly decrease, leaving a relative excess of the catabolic hormones and the body switches to catabolism, but in a finely tuned manner. Problems arise if there are sudden large increases in the concentrations of the catabolic hormones—and this is relevant to surgery and will be discussed below—or if insulin is absent as in the insulin-deprived juvenile-onset (Type I) diabetic. In this latter case the restraining effects of even basal concentrations of insulin are lost and catabolism runs riot. We have been able to demonstrate this experimentally in normal man by using somatostatin to inhibit insulin, growth hormone and glucagon secretion, and then selectively replacing or increasing the concentrations of the catabolic hormones (Alberti, Batstone and Johnstone, 1977; Johnston et al., 1979). This problem of total insulin deficiency is obviously of importance in the diabetic.

One hormone, triiodothyronine (T3), which is normally considered to be catabolic, and certainly increases the basal metabolic rate (BMR), shows interesting behaviour in starvation. In this situation concentrations of T3 decrease (and those of rT3 increase) as if in protection against excess caloric expenditure (Portnay et al., 1974) and this correlates with the decrease in BMR. This is also important with regard to nitrogen conservation as administration of T3 to starved subjects increases nitrogen excretion (Carter et al., 1975).

For further details on metabolic regulation in the fed and fasted states, see reviews by Cahill (1976), Newsholme (1976), Garland and Hales (1978), Söling and Seufert (1978) and Alberti (1979).

Response to surgery

Inevitably the fine regulation of metabolism described above is perturbed by surgery. Surgery provides one of the classical "stress" situations and the catabolic response to surgery and injury has been recognized for many years. In particular, it is characterized by increased metabolic rate, increased net protein breakdown with nitrogen loss and glucose intolerance. The extent of the metabolic disturbance is related to the severity of the operation (Allison, Tomlin and Chamberlain, 1969) and the presence of complicating factors such as shock and sepsis (Clowes et al., 1976). In uncomplicated elective surgery, particularly "superficial" operations, there is at most a 10% increase in basal metabolic rate and a very small increase in nitrogen excretion. The main changes will be present during operation, but will be short-lived thereafter. With more severe, complicated operations BMR may be doubled, protein wastage massive and the disturbance prolonged for many days.

The hormonal changes are well recognized (Johnston, 1974). First, there is increased catecholamine secretion and increased ACTH and cortisol secretion. These may indeed precede the actual operation and be a response to fear. There is a further increase during the actual operation, and an increase in plasma cyclic AMP concentrations (Gill et al., 1975). Glucagon (Russell, Walker and Bloom, 1975)

and growth hormone secretion may also be increased, although some authors have found little or no change in glucagon (Giddings et al., 1976; Miyata, Yamamoto and Nakao, 1976). The exact stimulus which causes these increases is not clear. Obviously there is a strong central component and much of the endocrine disturbance, in particular with respect to glucocorticoids and growth hormone, does not occur or is at least modified by extradural anaesthesia (Nistrup-Madsen et al., 1977). The increased glucagon secretion will be contributed to by a direct effect of catecholamines on the pancreatic A cells.

Simultaneous with these changes there is marked inhibition of insulin secretion. This is present during operation, is associated with marked glucose intolerance and has been demonstrated by several authors (Allison, Tomlin and Chamberlain, 1969; Clarke, 1970; Wright, Henderson and Johnston, 1974). This is followed by increased insulin concentrations after operation but still associated with glucose intolerance. The suppression of insulin secretion during surgery is almost certainly a consequence of catecholamine inhibition (Porte et al., 1966).

These hormonal changes are associated with several interesting metabolic changes. Blood glucose concentrations increase during surgery, proportional to the severity and extent of the operation (Weddell and Gale, 1935; Hayes and Brandt, 1952). The increase in blood glucose persists after operation and this, with the hyperinsulinism that follows surgery, suggests a phase of insulin resistance. It was originally considered that extrahepatic glucose oxidation was decreased, but Long and colleagues (1971) showed normal or increased peripheral glucose oxidation. It is worth noting that insulin sensitivity may nonetheless be comparatively decreased as absolute concentrations of insulin are increased. The main defect, however, appears to be inappropriately enhanced gluconeogenesis (Giddings, 1974) which is non-suppressible by glucose (Gump et al., 1974). The cause of this phenomenon and the relative insulin resistance have not been clearly documented. Ross and colleagues (1966) could not correlate the insulin resistance with changes in cortisol and growth hormone concentrations and Clowes and colleagues (1976) have indeed suggested the presence of a "resistance factor" that they have called "lipid plasma A". It seems unnecessary, however, to evoke new factors. As outlined above, there is a complex interplay between different catabolic hormones and the combined increases in circulating concentrations of the different hormones probably account for the glucose changes, growth hormone and cortisol contributing principally in peripheral tissues, and glucagon, catecholamines and cortisol in the liver.

Changes in blood concentrations of gluconeogenic precursors have also been noted. After minor surgery there is little alteration in blood lactate and pyruvate concentration. However, increased concentrations are found after major operations (Schweizer and Howland, 1965; Thomas, Alberti and Platt, 1979, in preparation). This must be a result of increased extrahepatic production, as uptake for gluconeogenesis is simultaneously increased. The increased concentrations of catecholamines (Christensen, Alberti and Brandsborg, 1975) and cortisol (Alberti et al., 1977) are undoubtedly responsible, together with some inhibition of pyruvate oxidation. In some patients hypoxia or hypovolaemic shock, or both, will also contribute. Insulin resistance may contribute to impaired pyruvate oxidation (Ryan, 1976).

Fatty acid metabolites also show changes which are clearly distinguishable from those found in starvation. Interestingly, we and others have found that ketone body concentrations following surgery plus starvation are smaller than those found following starvation alone (Clowes et al., 1976; Foster et al., 1979). In our own patients this amounted to 2.94 ± 0.41 *v.* 5.68 ± 0.12 mmol litre^{-1} following a 72-h fast, rather greater than the values of 0.8 ± 0.02 and 2.0 ± 0.5 found by Clowes and colleagues (1976). The latter authors found even smaller values in the presence of sepsis. It can be calculated that utilization of ketone bodies and fatty acids as fuels by peripheral tissues decreases by 10% after uncomplicated surgery. Glucose use is not increased and the implication is that amino acids are being oxidized in increased amounts. This has been confirmed for branched chain amino acids (Ryan, 1976). The question arises as to the mechanism of the decreased fatty acid and ketone body availability. This is perhaps secondary to the increased insulin concentrations following surgery. Adipose tissue is much more sensitive than muscle to insulin and it is possible that, despite obvious insulin resistance in muscle, there is suppression of lipolysis and hence fatty acid and ketone body availability.

These observations fit in with the pattern of protein metabolism following surgery. It was originally assumed that there was increased proteolysis after surgery, but this probably only occurs in cases complicated by sepsis or shock. In uncomplicated cases protein breakdown appears normal but protein synthesis is impaired (O'Keefe, Sender and James, 1974; Crane et al., 1977; Williamson et al., 1977),

although our own data do not support this (Foster et al., 1979). There are two possible mechanisms for this. First, as a result of increased branch chain amino acid oxidation, tissues may lack amino acids essential for protein synthesis. This has been suggested by Ryan (1976). Circulating concentrations of branched chain amino acids tend, however, to be increased (Dale et al., 1977) and Elia, Smith and Williamson (1979) have recently reported a block in tissue uptake of branched chain amino acids after operation. Linked with this is the observation that ketone bodies inhibit alanine output from tissues—an index of amino acid degradation—and it has been noted that severe injury is characterized by small ketone body concentrations and increased alanine values (Smith et al., 1975). The net results are a negative nitrogen balance and the relentless breakdown of tissue protein (although visceral protein tends to be protected) in the days following surgery.

These metabolic changes are also associated with changes in electrolytes. Sodium tends to be retained and intracellular concentrations increase while the reverse happens with potassium, with a resultant loss of potassium in the urine. At the same time there may be loss of calcium, magnesium and phosphate.

Many authorities have attempted to modify the catabolic response to surgery. Thus high protein feeding, amino acid infusions, growth hormone, and full parenteral nutrition have all been tried (Lee, 1974; Richards and Kinney, 1977). Of greatest interest in the present context is that insulin therapy in combination, obviously, with adequate amounts of calories and amino acids, is probably the most effective means available to date for reversing catabolism after operation. Allison and his group (see review in Woolfson, Heatley and Allison, 1977) have pioneered this therapy. Their findings emphasize the unique role of insulin as an anabolic hormone, and the predictable metabolic mayhem that will ensue if insufficient insulin is present. Their most recent report (Woolfson, Heatley and Allison, 1979) suggests that insulin is only really effective in the non-diabetic if the catabolic rate is increased.

Response to anaesthesia

So far all the emphasis has been on the metabolic response to surgery. Anaesthesia itself also has effects, although it has been suggested that waiting for anaesthesia has a greater metabolic effect than anaesthesia itself (Allison, 1971). Nearly all anaesthetics have some metabolic effects, with extradural and spinal anaesthesia having the least effects. This topic has been reviewed in detail many times (Greene, 1972; Petrides and Napp-Mellinghoff, 1978). Ether and chloroform have the greatest effects, causing hyperglycaemia, fatty acid mobilization and inhibition of insulin secretion, all secondary, presumably, to catecholamine discharge and ACTH secretion. The modern inhalation anaesthetic agents such as halothane have some effects, but these are minor compared with the stress of surgery itself (Allison, Tomlin and Chamberlain, 1969; Clarke, 1970; Clarke, Johnston and Sheridan, 1970). There are also few metabolic effects of concern to diabetics of premedication or of muscle relaxants.

Metabolism in the Diabetic

It is obvious that if insulin is totally absent catabolism will predominate and death will ensue. Lipid mobilization is markedly enhanced; fatty acid release from adipose tissue increases; ketogenesis, spurred on by a relative excess of glucagon, accelerates and ketone body supply soon outstrips ketone body utilization with consequent ketoacidosis and severe acidaemia. Similarly, net protein breakdown occurs; gluconeogenic precursors flow to the liver; gluconeogenesis and glycogenolysis, freed from the usual restraint applied by insulin, are increased and hyperglycaemia occurs. This is exacerbated by the inability of muscle and adipose tissue to take up glucose. There is also an inappropriate increase in glucagon, cortisol and eventually catecholamine, all of which accelerate the development of hyperglycaemic ketoacidosis. This is followed by the well-known symptom complex of glycosuria, polyuria, dehydration, hyperosmolality and coma.

Electrolyte changes also occur with loss of sodium, potassium, calcium, magnesium and phosphate because of the diuresis. The loss of potassium is compounded by the acidaemia which drives potassium out of cells and the insulin deficiency which prevents normal intracellular accumulation of potassium (see Alberti and Hockaday (1977) for a more detailed account of the sequelae of insulin deficiency).

In milder insulin deficiency the predominant defect is failure of peripheral tissues to take up glucose properly. There is enough insulin present for control of adipose tissue metabolism and gluconeogenesis. The end result is hyperglycaemia with glycosuria, and some loss of electrolytes in the urine.

Effect of surgery in the diabetic

It is obvious from this account that surgery or a similar stress will tend to worsen the metabolic status

in both insulin-independent ("maturity-onset", Type II) and insulin-dependent diabetics ("juvenile-onset", Type I). In the former, insulin demand will outstrip potential supply from the already compromised pancreas. The usual increase in insulin secretion after operation will not occur, so not only will insulin resistance be present but insulin deficiency will also result. This will lead to a greater impairment of muscle glucose utilization and more rapid gluconeogenesis; severe hyperglycaemia with hyperosmolality will thus ensue. This is obviously to be avoided. In minor surgery where the stress is small the perturbation will be short-lived if no additional therapy is given, but it is questionable whether even this is a permissible risk.

In insulin-dependent diabetes it is obvious that catabolism will predominate if the patient remains on a fixed dose of insulin before operation, with the same caloric input. In practice caloric input decreases to near zero and insulin requirements obviously decline, but again they do not decline to zero, and it is important to match the increased insulin requirement secondary to the stress during and after operation with the correct amount of insulin. Metabolic decompensation must be avoided, but so must hypoglycaemia.

TREATMENT OF DIABETES DURING SURGERY

Aims of treatment

The main aim of therapy must be to achieve rapid recovery from the surgical stress with a minimum of intercurrent problems related directly to the metabolic disturbance, such as ketoacidosis or hypoglycaemia, or those indirectly related such as infection, delayed wound healing or cardiovascular events. The main differences from therapy in the non-diabetic are the use of insulin and the choice of electrolyte and fluid replacement. It is beneficial, if not obligatory, for the diabetic, particularly those taking insulin or those about to have anything but the most minor surgery, to be admitted to hospital for assessment and stabilization of their diabetes at least 24–48 h before operation. If this were done universally morbidity and mortality (and overall hospital stay) would decrease sharply. Sadly this is not universal practice, because the point is often not appreciated and because of shortage of beds.

Insulin therapy for diabetics before, during and after surgery

Many different regimens have been suggested for the treatment of diabetes during surgery. Some of these are summarized in tables II and III. Different treatments have been proposed for Type I and Type II diabetics, for minor and major elective surgery and for emergency surgery. These will be discussed in turn. One of the major problems in assessing these regimens is that no large-scale prospective study of mortality, morbidity and metabolic status in which two or more regimens have been compared has been published. We have performed a small comparative study and results will be drawn freely from this (Thomas, 1978; Thomas, Alberti and Platt, 1979, in preparation).

Insulin-independent (Type II diabetics)

Table II shows some of the suggestions that have been made for the treatment of insulin-independent diabetics during surgery. If surgery is minor and the patient is on diet alone there is general consensus that no additional therapy is necessary, provided that the patient is well-controlled before operation. Glucose should be monitored after operation both in urine and in blood (see below for details). In patients taking oral antidiabetic therapy there is less general agreement. Older reports tend to suggest continuation of sulphonylureas up to the day before operation. On the day of operation no therapy is given. After operation, subcutaneous insulin may be given depending on urine or blood glucose concentrations.

More recently more emphasis has been given to insulin therapy with a change to insulin before operation often recommended, particularly if major surgery is planned. In view of the predictable metabolic sequelae of surgery, described in detail above, and including insulin resistance and negative nitrogen balance, this seems wise. We have compared the response to surgery of two groups of patients receiving sulphonylureas. Approximately half the patients received no therapy on the day of operation while the other group received insulin–glucose–potassium i.v. This comprised 10% glucose 500 ml containing potassium chloride 10 mmol and insulin 5 units (if blood glucose less than 6 mmol litre^{-1}) before operation) or insulin 10 units (if glucose greater than 6 mmol litre^{-1}). The infusion was given at 100 ml h^{-1} from 30 min before operation until the first oral food was taken. Blood glucose concentration remained stable in patients given the insulin infusion (table IV) while concentrations increased in the "no therapy" group by more than 5 mmol litre^{-1} from 30 min before operation to 4 h after operation. During this period blood glucose concentrations increased by

TABLE II. *Recommended regimens for the treatment of insulin-independent (maturity-onset) diabetes during elective surgery*

Author	Before operation	During operation	After operation
Malins (1968)	(1) Diet alone (2) Omit oral hypoglycaemic agents on day of surgery	(1) Nil (2) Nil (3) Give insulin 10–20 unit s.c. + 50% glucose 50 ml before op. if control poor	Check blood-glucose. Maintain carbohydrate intake
Oakley, Pyke and Taylor (1968)	Omit therapy on day of operation	Nil	Give insulin if glycosuria present according to sliding scale
Beaser (1970)	Soluble insulin to improve control if necessary. Omit insulin or hypoglycaemic agent evening before op. Avoid long-acting agents	Nil	50% preoperative dose of oral agent for 2 days. Then glucose 50–75 g day^{-1} i.v. or orally. Supplementary insulin according to urine tests
Wheelock and Marble (1971)	Change patient's oral agents to isophane insulin if necessary (based on 24-h urine glucose). Else omit therapy	Nil or isophane insulin depending on therapy before op.	Glucose 100–150 g day^{-1} i.v. or orally. Give isophane insulin based on urine and blood glucose
Shuman (1971)	*Minor surgery*: Give usual dose of sulphonylurea. Withhold biguanides. I.v. glucose 150 g day^{-1} if necessary. Add soluble insulin 10 unit per litre of 5% glucose if blood-glucose high	Give insulin and glucose as pre-op if necessary	Give sulphonylureas. Add supplementary insulin s.c. according to urine tests
	Major surgery: I.v. insulin 10 unit per litre of 5% glucose	I.v. insulin 10 unit per litre of of 5% glucose	Continue i.v. insulin–glucose. Increase insulin to 16–20 unit litre according to urine glucose. Give supplementary insulin s.c. if necessary
Steinke and Soeldner (1975)	(1) Diet-treated patients. Nil (2) Oral agent treated patients: change to isophane 10–20 unit day^{-1}	Nil Isophane	Observe closely. Isophane + i.v. glucose. When oral feeding recommenced change to oral agents
Rossini and Hare (1976)	If blood glucose < 150 mg dl^{-1} no therapy. If glucose > 150 < 250 mg dl^{-1} no change in therapy. If glucose > 250 mg dl^{-1} give isophane 16–20 unit day^{-1}. If glucose > 350 mg dl^{-1} give isophane 16–20 unit plus soluble insulin 10–20 unit day^{-1}	Nil, or 50% previous insulin as isophane	I.v. glucose + isophane if necessary
Petrides and Napp-Mellinghoff (1978)	(1) Diet. If post-prandial glucose < 160 mg dl^{-1} leave therapy unchanged	Nil	Observe
	(2) Stop biguanides. Change from chlorpropamide to tolbutamide. Start i.v. tolbutamide 1 g in 5% glucose 500 ml + 5% fructose 1000 ml	Continue tolbutamide–glucose –fructose or no therapy for minor surgery	Continue i.v. if necessary. Restart oral agents with oral feeding

2.4 mmol $litre^{-1}$ in non-diabetic controls. 3-Hydroxybutyrate values were extremely variable, but were nonetheless much smaller in the insulin-treated patients. Plasma non-esterified fatty acids (NEFA) showed a similar pattern. Concentration of lactate and pyruvate tended to be greater in the insulin-treated patients, presumably as a result of the effects of insulin, both inhibiting gluconeogenesis and at the

same time causing increased extrahepatic lactate production from glucose. No symptomatic hypoglycaemia occurred.

Other parameters were also followed. Thus plasma potassium concentration tended to decrease in both groups but urea, perhaps reflecting protein catabolism, increased in the "no therapy" group, but decreased in the insulin infusion group.

Our conclusion was that it was sensible to use the insulin infusion regimen in all sulphonylurea-treated patients except for the well-controlled undergoing minor surgery. Other general guidelines are as follows.

Before operation all biguanides should be stopped because of their known tendency to enhance hyperlactataemia and to cause lactic acidosis (Alberti and Nattrass, 1977). Long-acting sulphonylureas such as chlorpropamide should be stopped at least 3 days before operation and the patient changed to tolbutamide or glibenclamide or, if poorly controlled, to a three-times-daily soluble insulin regimen. On the day of operation the insulin–glucose–potassium regime should be started at 8–9 a.m. If the operation is delayed there is no danger of metabolic decompensation. Once the patient resumes feeding, the infusion is stopped and the patient put on t.i.d. soluble insulin subcutaneously (8–12 unit per dose with further adjustments according to serial blood-glucose estimations) or, if surgery, and therefore the stress, was minor, oral hyperglycaemic agents can be resumed. Further details are shown in the Appendix.

Insulin-dependent diabetes

An equally large number of regimens have been proposed for insulin-dependent as for the insulin-independent diabetics (table III).

The "no insulin—no glucose" regimen has enjoyed some favour. In Fletcher, Langman and Kellock's early report (1965) an impressively small deterioration in glucose control was noted.

TABLE III. *Recommended regimens for the treatment of insulin-dependent (juvenile onset) diabetes during elective surgery*

Author	Before operation	During operation	After operation
Izzo (1965)	Stop long-acting insulins. Start on 6-hourly soluble insulin s.c. based on urine "sliding scale" with spot checks of blood-glucose 2 h after meals	Continue 6-hourly insulin based on "sliding scale". Give glucose as i.v. infusion. Use i.v. fructose for extra calories	Continue 6-hourly insulin based on "sliding scale". 10% glucose 500 ml or 5% glucose + 5% fructose 6-hourly. Change to oral feeding as soon as possible. When insulin requirements stable change to pre-admission insulin
Fletcher, Langman and Kellock (1965)	Usual therapy	Withhold insulin	Give soluble insulin s.c. according to "sliding scale" based on glycosuria
Malins (1968)	Control ketosis. Change to b.d. soluble insulin	Soluble insulin i.v. + glucose 25 g 2 h before operation	Check blood-glucose frequently, soluble insulin accordingly
Oakley, Pyke and Taylor (1968)	Control carefully	Omit insulin if well-controlled, give glucose 10–20 g i.v. if urine glucose free. In "ketosis-prone" give 50–70% usual morning dose of insulin 30 min before op. + 50% glucose 20 ml. For afternoon operations give 80–90% morning insulin s.c. + breakfast. Check blood-glucose in long operations—give insulin if glucose increases > 100 mg dl^{-1}.	S.c. insulin + i.v. glucose depending on blood and urine tests
Beaser (1970)	75% usual total daily dose, all in morning or 25% usual total dose as soluble insulin with each meal	Give up to 25 units insulin in 5% or 10% glucose 50 g	Continue i.v. insulin in glucose; glucose 150–200 g day^{-1}. Supplementary s.c. insulin depending on blood- and urine-glucose

Continued on next page

TABLE III *Continued*

Author	Before operation	During operation	After operation
Wheelock and Marble (1971)	Stabilize on isophane or soluble + isophane	I.v. glucose 5% + 50% usual daily insulin dose s.c. Glucose 100–150 g on day of operation	Isophane b.d. ± soluble insulin. I.v. glucose if necessary—oral feeding as soon as possible
Shuman (1971)	Control	Usual dose of insulin morning of operation, 5% glucose i.v. containing electrolytes	If on isophane, increase dose slightly. Supplement with soluble insulin 6–20 unit based on blood- and urine-glucose
Steinke and Soeldner (1975)	Control on isophane or lente + supplemental soluble insulin	One-third usual total dose before op. as isophane, one-third after op.	Continue isophane. Supplementary soluble insulin if glycosuric or hyperglycaemic
Rossini and Hare (1976)	Stabilize carefully. If blood glucose 250–350 mg dl^{-1}, increase isophane insulin 10–20%. If blood glucose > 350 mg dl^{-1} add soluble insulin 10–20 unit	Give half total daily insulin as isophane a.m. and half immediately after op.	Give isophane with supplementary soluble insulin as before op. based on blood-glucose
Taitelman, Reece and Bessman (1977)	Control on isophane	Continuous i.v. insulin: 1 unit h^{-1} if preop. requirement ⩽ 20 unit day^{-1}, 2 unit h^{-1} if preop. requirement > 20 unit day^{-1}. 5% glucose 500 ml/4 h	
Bacchus (1977)	Control	(1) I.v. 5% glucose in 0.9% saline + normal daily dose insulin as s.c. NPH or Lente. Immediate after op. 25% as soluble insulin s.c. (2) I.v. infusion of insulin in 5% glucose: soluble insulin 1 unit per 3–4 g glucose. Monitor blood-glucose concns	(1) 4–6 h post-op. 25% usual dose as soluble insulin s.c. depending on blood glucose (2) Continue i.v. infusion then change back to preop. therapy
Petrides and Napp-Mellinghoff (1978)	Control with intermediate or slow-acting insulins	Give 5–10% glucose infusion to make up usual calories, soluble insulin i.m. before op. according to blood-glucose	Immediately after op. measure blood-glucose 2–3 hourly, soluble insulin i.m. accordingly. 5% glucose 2–3 litre day^{-1}. Intermediate insulin + supplementary soluble insulin according to blood-glucose
Oakley, Pyke and Taylor (1978)	Soluble insulin b.d.	(1) Morning operations—omit breakfast and insulin (2) Afternoon operations—decrease morning insulin + breakfast. I.v. glucose at induction if blood-glucose low	5% glucose from time of operation. Soluble insulin with pump, 1–3 unit h^{-1}. Otherwise insulin 20 unit in 1 litre 5% glucose in 8 h. Continue until patient eating

Unfortunately, this gives a misleading picture of the metabolic status of the patient. The effect of starvation on an insulin-deprived diabetic is to cause a moderate decrease in blood-glucose concentration (Alberti et al., 1975). Simultaneously, blood ketone body concentrations increase sharply and acute metabolic decomposition begins with increases in plasma glucagon and cortisol concentrations. Because of the stress of operation, blood glucose concentration does not actually decrease with the "no therapy" regimen. Indeed, in our patients there was a 5.6-mmol $litre^{-1}$ increase in glucose (table IV). Ketone body concentrations were variable, but six of nine patients showed marked increases during and following operation (table V) and mean plasma NEFA increased significantly. In addition there was a marked increase

TABLE IV. *Blood-glucose concentration (mmol litre^{-1}) in normal subjects, insulin-independent and insulin-dependent subjects during and after surgery. Insulin-independent subjects were given either (a) an insulin infusion until the first meal or (b) no therapy until after the operation. Both groups received soluble insulin t.i.d. after operation based on plasma-glucose and "Dextrostix" readings. Preoperative therapy was reinstituted as soon as possible. Glucose was given as 5% glucose i.v. until oral feeding recommenced. Insulin dependent subjects were treated by one of four regimens. Groups (c) received insulin–glucose–potassium from 30 min before operation until normal feeding resumed. If operations were scheduled for the afternoon patients took breakfast with their normal insulin. Group (d) comprised four subjects from group (c) where the insulin–glucose–potassium infusion was continued for 72 h. Group (e) patients were given no insulin or glucose before or during operation. Groups (f) received half the usual morning dose of insulin s.c. together with glucose 25 g given i.v. over 4 h. *Samples taken 30 min after breakfast on the 1st, 2nd and 3rd days after operation. Results obtained at a District General Hospital and taken from Thomas, Alberti and Platt (1979). Number of subjects in parentheses. Results given as mean ± SEM*

	Before op.	15 min after induction	After operation 1 h	4 h	24 h*	48 h*	72 h*
Insulin-independent							
(a) Insulin infusion (9)	10.3 ± 1.1	11.6 ± 1.0	9.5 ± 1.1	10.1 ± 0.9	12.3 ± 1.2	11.9 ± 1.2	10.3 ± 1.3
(b) No therapy (11)	8.9 ± 0.8	8.8 ± 0.9	10.3 ± 1.1	14.2 ± 1.3	12.4 ± 1.1	12.7 ± 1.2	11.6 ± 1.8
Insulin-dependent							
(c) Insulin-infusion (short) (12)	9.1 ± 1.9	9.0 ± 1.8	8.8 ± 1.2	9.6 ± 1.3	12.7 ± 1.2	11.6 ± 0.8	6.3 ± 0.6
(d) Insulin-infusion (long) (4)	12.5 ± 3.8	—	—	14.1 ± 3.0	9.7 ± 2.0	7.8 ± 1.5	9.2 ± 2.2
(e) No insulin or glucose (10)	9.0 ± 1.1	8.7 ± 1.2	12.4 ± 1.6	14.8 ± 1.2	12.7 ± 1.3	14.7 ± 1.8	14.7 ± 1.8
(f) S.c. insulin + i.v. glucose (11)	9.3 ± 1.0	8.6 ± 1.3	11.3 ± 1.6	14.9 ± 1.2	13.9 ± 1.2	13.5 ± 1.2	17.3 ± 1.9
Non-diabetic (7)	5.1 ± 0.3	5.7 ± 0.5	6.8 ± 0.4	7.5 ± 0.4	7.0 ± 0.8	5.8 ± 0.2	5.0 ± 0.3

TABLE V. *Blood 3-hydroxybutyrate concentration (mmol litre^{-1}) in normal subjects, insulin-independent and insulin-dependent subjects during and after surgery. Groups and therapy as described in legend to table IV. Results are given as means ± SEM. Distribution of results was often grossly abnormal and this method of expression has been used simply for clarity*

	Before op.	15 min after induction	After operation 1 h	4 h	24 h	48 h	72 h
Insulin-independent							
(a) Insulin infusion (7)	0.21 ± 0.08	0.14 ± 0.08	0.02 ± 0.01	0.05 ± 0.02	0.03 ± 0.01	0.18 ± 0.11	—
(b) No therapy (9)	0.13 ± 0.04	0.20 ± 0.05	0.26 ± 0.07	0.25 ± 0.07	0.13 ± 0.06	0.08 ± 0.03	—
Insulin-dependent							
(c) Insulin infusion (short) (8)	0.24 ± 0.14	0.19 ± 0.04	0.11 ± 0.04	0.13 ± 0.04	0.13 ± 0.04	0.40 ± 0.29	0.30 ± 0.18
(d) Insulin infusion (long) (3)	0.13 ± 0.15	0.08 ± 0.02	0.13 ± 0.15	0.13 ± 0.13	0.05 ± 0.02	0.15 ± 0.10	0.24 ± 0.13
(e) No insulin or glucose (9)	0.40 ± 0.21	0.51 ± 0.23	0.57 ± 0.22	0.56 ± 0.17	0.43 ± 0.20	0.58 ± 0.30	0.44 ± 0.19
(f) S.c. insulin + i.v. glucose (8)	0.17 ± 0.07	0.19 ± 0.07	0.33 ± 0.17	0.58 ± 0.19	0.42 ± 0.20	0.50 ± 0.35	0.32 ± 0.19
Non-diabetic (6)	0.09 ± 0.04	0.15 ± 0.04	0.21 ± 0.06	0.33 ± 0.07	0.19 ± 0.13	0.08 ± 0.03	0.27 ± 0.21

in plasma urea concentration and urine urea excretion during the day before operation and the first day after operation. There were also markedly negative potassium, phosphate, calcium and magnesium balances. This should emphasize the need to examine parameters other than glucose when assessing the efficacy of a regimen.

Other suggested regimens advocate giving a fraction of the usual dose of insulin as a subcutaneous bolus followed by an infusion of i.v. glucose. We have found little benefit of such a regimen (tables IV and V) compared with no therapy at all. Undoubtedly reasonable results have been achieved with many of these regimens, but most of them are based on habit and practice rather than logic.

Since continuous i.v. insulin therapy was introduced for the treatment of diabetic ketoacidosis (Page et al., 1974) there has been a resurgence of interest in

the use of this type of therapy in all diabetic emergencies (Leslie and Mackay, 1978). Many groups now use continuous insulin infusion for the treatment of diabetics during surgery, but few proper studies have been reported. Taitelman, Reece and Bessman (1977) compared results obtained with their usual therapy or two-thirds of the usual dose of isophane insulin subcutaneously with a regimen in which insulin 2 unit h^{-1} was given continuously with 5% glucose 125 ml h^{-1}. Patients usually receiving isophane 20 unit per day or less were given insulin 1 unit h^{-1}. The patients were undergoing elective orthopaedic operations. Control of blood-glucose was better on the insulin infusion regimen than on isophane insulin, but it should be noted that two patients out of eight receiving 2 unit h^{-1} showed rapidly decreasing blood-glucose concentrations. Woodruff and colleagues (1977) using a 1-unit h^{-1} regimen also showed reasonable glycaemic control, but stopped the infusion 1 h after the end of operation.

We have looked at two regimens with continuous insulin infusion. In the first the infusion was commenced 30 min before operation and was as described above (insulin 2 units – glucose 10 g – potassium 2 mmol per hour) and continued until the first oral feeding. In four patients the infusion was continued for 72 h. In the main group, glucose control was improved over the "traditional" therapies up to 4 h after operation (table IV) and ketone body concentrations were decreased. In the group with a 72-h infusion, glycaemic and ketone body control was improved for the whole 72 h compared with all other groups. It is important at this point to distinguish between the apparently poor prognostic sign of a low ketone body response to surgery in non-diabetics (Smith et al., 1975; see above) and the control of ketosis in a diabetic by the use of insulin. In the latter case insulin has beneficial effects on protein metabolism as well as on carbohydrate and lipid utilization. The so-called protein-sparing effect of ketosis as popularized by Blackburn and colleagues (1973) is irrelevant in the diabetic patient. We noted, indeed, that plasma urea concentrations decreased and that calculated nitrogen balance in the infused patients was more positive than, not only "traditional" therapies, but the non-diabetic group as well. Similarly, plasma potassium concentration remained stable and potassium balance was considerably improved compared with other regimens. Clinical episodes of hypoglycaemia did not occur, although periodic adjustment to the insulin infusion rate was made with the rate increasing to 10 unit h^{-1} in one extremely ill, infected patient.

Our recommendation would be to use the insulin infusion regimen in all insulin-dependent diabetics undergoing any form of surgery. The insulin dose can be adjusted according to blood-glucose measurements. Continuation of the infusion until the patient is eating normally would seem desirable, at which time a return can be made to the preoperative insulin regimen. Alternatively, the patient can be treated with a Soluble or Actrapid or Leo Neutral insulin regimen starting at 12–16 units t.i.d. with further doses based on blood-glucose concentrations.

Method of administration of insulin

I.v. infusion of mixtures of glucose, insulin and potassium have been used clinically for nearly 20 years (Sodi-Pollares et al., 1963). The first major advocants for its use in surgery were Galloway and Shuman (1963), although they tended to reserve it for milder cases. One main argument about the use of insulin infusions concerns the method of delivery. Sönksen and colleagues (1968) and Weisenfeld and colleagues (1968) both showed clearly that insulin adsorbs to glass, with the latter authors finding the same for plastic tubing. This has led many authorities to reject the use of insulin added to standard i.v. solutions. The problem can be obviated by adding albumin, polygeline (Kraegen et al., 1975) or a small volume of the patient's own blood (Sönksen, 1976) to the infusion. Alternatively, it has been suggested that flushing the giving-set with 25–50 ml of the insulin solution in the infusion bag prevents further loss (Petersen, Caldwell and Hoffman, 1976). We found 72–90% insulin recovery from a glucose–potassium–insulin mixture of the composition used in our treatment regimen. This was considered clinically acceptable.

The alternative is to use a concentrated solution of insulin in a small volume. This may be done using an infusion pump with a plastic syringe. Taitelman, Reece and Bessman (1977) reported 90% recovery of insulin with this system and it has been advocated for therapy after surgery by Leslie and Mackay (1978) with insulin at a concentration of 1 unit ml^{-1} in saline 0.154 mol $litre^{-1}$. An interesting recent development is the use of the pump to infuse insulin 0.5 unit h^{-1} i.v. in patients not otherwise receiving i.v. therapy and having relatively minor procedures. Excellent preliminary results have been obtained (Barnett, Pyke and Watkins, personal communication). In well-staffed centres where care before and after operation is

meticulous, insulin infusion with a pump is the treatment of choice, but even so Leslie and Mackay reported two pump failures. In our own District General Hospital we felt strongly that the insulin and glucose infusions should not be divorced. I.v. infusions from bags often run at varying rates, or stop altogether, while infusion pumps can occasionally fail. By combining insulin and glucose in the same infusate we feel that the added safety, in the average hospital and recovery ward, more than compensates for the somewhat variable loss of insulin through adsorption.

Recently, publications have appeared in which a glucose-controlled insulin infusion system (the so-called artificial endocrine pancreas) has been used to control diabetes during and after surgery (Pfeiffer et al., 1976; Schwartz et al., 1979). This is an ideal system, in that normoglycaemia can be maintained throughout regardless of i.v. fluid replacement and surgical manoeuvres. However, it is costly, as yet a research tool, and in the majority of cases quite unnecessary.

Monitoring insulin therapy

The keystone of all forms of management of diabetes during surgery is measurement of blood-glucose concentration. Urine glucose measurement is retrospective with a long time delay and is too insensitive. It provides information on whether blood-glucose concentrations are increased, but when values are negative does not distinguish between severe hypoglycaemia and values just below renal threshold (9–12 mmol $litre^{-1}$).

Ideally, blood-glucose concentrations should be measured before operation, once or twice during the operation (depending on the duration of surgery) then 2–3-hourly after operation until the patient is feeding again or at least until the morning after operation. Thereafter 3–4-hourly measurements are required if the patient continues to be fed i.v. It is vital that results should be available rapidly. In many hospitals 4- or 5-h delays in reporting results occur, and this is unacceptable. If a speedy service is not available then a rapid method should be available for use on the ward. Sophisticated apparatus such as the Yellow Springs Analyser, which can be used with whole blood, are advisable for this purpose but are expensive and susceptible to clinician abuse. Careful use of Dextrostix or Reflotest with a reflectance meter is more than adequate for surgical purposes. The new cheaper forms of reflectance meter, such as Glucochek, seem ideal and should be within the budget of all surgical units. It cannot be emphasized too much that proper staff training is required if these machines are to give accurate results.

The following simple guidelines can be used to modify insulin therapy if blood-glucose measurements are available. If blood-glucose before operation is less than 6 mmol $litre^{-1}$, start with insulin 5 unit per 500 ml of 10% glucose + potassium 10 mmol. If the value increases to more than 10 mmol $litre^{-1}$, double insulin content. If glucose value before operation is more than 6 mmol $litre^{-1}$, start with insulin 10 units per 500 ml of glucose. If in any subsequent measurement the value is greater than 10 mmol $litre^{-1}$, replace infusion with insulin 15 units per 500 ml of glucose and 20 unit if blood glucose is greater than 20 mmol $litre^{-1}$. Occasionally, further increases may be necessary. Halve the dose to 5 unit/500 ml if there has been a decrease to less than 5 mmol $litre^{-1}$. In practice, frequent adjustment is unnecessary after the acute phase when, on average, 4 unit h^{-1} were needed following major operations. It is worth noting that this regimen uses more glucose than that of Taitelman, Reece and Bessman (1977), with which rapidly decreasing glucose concentrations were noted in two of eight patients given insulin 2 unit h^{-1}.

It is pertinent to mention so-called "sliding scales" for insulin administration based on urine-glucose. These are used as security blankets by the nervous or ignorant. Their use encompasses comforting numerical guidelines, but they are based on false logic. The limitations of sliding scales in patient management are manifold. First they are always retrospective. This may be harmless in a stable situation, but after surgery blood-glucose concentrations can change sharply. A patient may thus have urine containing 2% glucose (because blood-glucose was high some hours previously) at a time when blood-glucose concentrations are near normal or decreasing rapidly. Second, urine may not be available at the desired time, which in many wards would mean that no insulin was given at all. Third, urine volumes and glucose thresholds may change after surgery. *In toto*, the effect of using sliding scales is often to induce glycaemic instability of roller-coaster proportions.

Factors influencing insulin requirement

Many factors may influence requirement during and following surgery. Awareness of these may pre-empt possible problems in metabolic regulation. Obviously the stress of surgery induces some degree of insulin resistance and this is proportional to the

severity of surgery. The hormonal basis for this has been described above. Infection also may cause a dramatic increase in insulin requirement. This is probably caused by increased glucagon (Rocha et al., 1973) and cortisol (Beisel et al., 1967) secretion. Approximately 13% of Galloway and Shuman's series (1963) had infections, with similar figures reported by Beaser (1970), so that infection is not an uncommon complication after operation. In particular, urinary tract infections should be sought and treated.

Several drugs may increase insulin requirement including steroids, catecholamines and propranolol. In addition it should be remembered that infusion of blood increases insulin need in that, even when glucose content is small, contents of lactate and pyruvate are high and these precursors will stimulate gluconeogenesis, particularly in diabetics. One final and common situation in which additional insulin may be needed is that of the obese patient. Such patients are classically insulin-resistant as a result of "down regulation" of insulin receptors. If diabetics are more than 50% heavier than ideal body weight it is advisable to double the usual insulin dose and even greater amounts may be necessary.

Intravenous fluids and electrolyte replacement for diabetics during and after surgery

So far we have considered only the use of 10% glucose as an i.v. replacement fluid for diabetics. "Normal" saline (0.154 mmol litre^{-1}) has no particular hazards for the diabetic, but one or two commonly used replacement fluids such as Hartmann's solution are less desirable. We have noted a sharp increase in blood-glucose concentration in diabetics when given Hartmann's solution during or after operation (Thomas and Alberti, 1978). This may be caused by the lactate component being converted readily to glucose. Other lactate-containing solutions should also be avoided. If alkalinization is desired there seems little objection to bicarbonate.

Fructose administration has enjoyed intermittent favour in the treatment of diabetics after operation (Halmagyi and Israng, 1968; Mehnert, 1970). It is metabolized rapidly to glucose and lactate, with the latter predominating. If the circulation is compromised or there is abnormal liver function, lactic acidosis may ensue (Woods and Alberti, 1972).

Potassium therapy has been referred to above. Moderate replacement, together with i.v. insulin infusion, results in only small total body losses compared with most other treatment regimens. In the longer term significant decreases in plasma phosphate and magnesium occur with surgery, and replacement should be considered if patients have prolonged periods of i.v. alimentation after operation.

Emergency surgery and diabetes

Diabetics are as likely to require emergency surgery as the rest of the population: 5% (33) of Galloway and Shuman's operations (1963) in diabetics were of this type. Eighty per cent of these were the result of infection. In such cases we again would use the glucose–insulin–potassium infusion. If initial assessment indicated co-existent diabetic coma, precoma or severe metabolic decompensation, then surgery should be delayed until the metabolic status of the patient has improved. This is particularly true for conditions associated with severe abdominal pain, as this may be caused purely by the ketoacidosis and disappear completely with appropriate treatment of the ketoacidosis (Campbell et al., 1975). The converse is also true, however; that is, severe peritonitis may be present with minimal pain, perhaps as a result of autonomic neuropathy (Wheelock and Marble, 1971). This is exceedingly rare.

Postoperative complications in diabetics

Diabetics may develop any of the usual complications after operation. The commonest relate to infection (see above) which must be sought assiduously and suspected in any patient showing an increased insulin requirement after operation.

Cardiovascular complications. A disproportionate number of operations in diabetics are for cardiovascular disease—either myocardial, or of the legs. In such cases diffuse disease is almost always present. In a series of 100 diabetic patients undergoing lower limb surgery for gangrene or infection Kahn, Wagner and Bessman (1974) noted cardiac disease in 63%, peripheral vascular disease in 44% and cerebrovascular disease in 24%. There was a 9% mortality with six of the deaths caused by myocardial infarction. Higher mortality rates have been reported by others (Ecker and Jacobs, 1970).

Lower limb amputations are still unfortunately common in diabetics. In 1968 Warren and Kihn found that half of their major lower limb amputations were performed on diabetics. Undoubtedly this figure can be improved upon with intensive education and care, but cases still occur with distressing regularity. The overall outcome is poor in diabetics, as shown for example for transmetatarsal amputations by Effeney and Lim (1977). Similarly, when major

vessel grafting is undertaken results are poorer in diabetics than in non-diabetics. LoGerfo, Corson and Mannick (1977) found a 72% graft patency after 5 years in their group as a whole, but only 45% in diabetics. Similar experiences occur with cardiac surgery.

In lower limb surgery the situation is complicated by the presence of microvascular disease and neuropathy as well as large vessel disease. In the myocardium there may also be small vessel disease (Ledet et al., 1979). The presence of this diffuse vascular disease affecting both small and large vessels undoubtedly contributes to the morbidity and mortality of diabetics undergoing surgery for any cause.

Other problems specific to diabetes. A significant number of diabetics coming to surgery will have some degree of renal disease. Hypertension, oedema and proteinuria should be sought. If diabetic nephropathy with clinical sequelae is present, special care must be taken with respect to parenteral feeding, and the use of drugs which are normally excreted in the urine.

The other major symptom complex likely to afflict diabetics is neuropathy. Somatic neuropathy should not complicate general surgery. However, autonomic neuropathy can present real problems. A neuropathic bladder can present with retention after operation. Postural hypotension may also cause problems. The most dramatic of the probable complications attributable to autonomic neuropathy has been pointed out recently by Page and Watkins (1978). They reported 12 episodes of sudden cardiorespiratory arrest, three of which occurred during anaesthesia, in patients with severe autonomic neuropathy. They suggested that arrests were caused by respiratory rather than cardiovascular causes. Anaesthetists should be alerted to this possibility and proper assessment of autonomic nervous function performed before operation in all long-standing diabetics.

CONCLUSIONS

In conclusion, much has been written in the past on surgery in diabetic patients, but there are few objective reports and comparisons of the different recommended regimens. Many of these are complicated and invite error. We have used a regimen which we have found safe, simple and easy to manage in an average hospital. This involves the i.v. administration of insulin, glucose and potassium as a single infusion. This is commenced from the morning of the day of operation and continued until normal feeding is reinstituted. The regimen is applicable to insulin-independent and insulin-dependent diabetics alike. Problems with severe hypoglycaemia or hypokalaemia have not been encountered and positive benefits with respect to blood-glucose stability, and nitrogen and potassium balance have been noted. Frequent monitoring of blood glucose is necessary for all regimens but can be achieved with simple bedside methods. In well-staffed centres insulin can be given with more precision and less adsorptive losses using an infusion pump. The increase in insulin requirement after operation, caused by infection and certain drugs, has been emphasized. Finally, the possibility of morbidity or mortality from cardiovascular causes should be remembered.

APPENDIX

GUIDELINES FOR CARE OF DIABETIC PATIENTS DURING AND AFTER OPERATION

(A) *Maturity-onset diabetics: minor operations*

Assuming well-controlled; if not change to insulin preoperatively and treat as in (C).

(i) *Before operation.* If on a long-acting sulphonylurea (e.g. chlorpropamide) change to tolbutamide or glibenclamide 1 week before operation. Stop all biguanides.

(ii) *During operation.* No sulphonylurea on day of operation. Treat as non-diabetic if blood-glucose < 7 mmol litre^{-1}. Check blood-glucose before operation and 4 h after operation.

(iii) *After operation.* Recommence sulphonylurea with first meal. Use i.v. glucose with caution, if at all.

(B) *Maturity-onset diabetics: major operations*

If badly controlled, change to insulin and treat as in (C).

(i) *Before operation.* As for (A) above.

(ii) *During operation.* As for insulin-dependent diabetics (see below).

(iii) *After operation.* As for insulin-dependent diabetics (see below). Once the patient is eating, treat with t.i.d. Actrapid or Leo Neutral insulin—about 8–12 units before each main meal is a rough starting guide, but more will be needed in those who are obese, are infected, have hepatic disease or are receiving steroids. The dose should be adjusted as necessary, and once it decreases to less than 20 units per day, transfer back to oral agents or diet.

(C) *Insulin-dependent diabetics: all operations*

(i) *Before operation.* Stabilize as carefully as possible for 2–3 days before operation. All patients should be on at least twice-daily insulin (e.g. Actrapid and Retard, Soluble and Isophane.) On the day preceding operation give short-acting insulin only (i.e. Actrapid, Soluble or Leo Neutral t.i.d.).

(ii) *During operation.*

a. Give *no* subcutaneous insulin on day of operation, even if the surgery is planned for the afternoon (although this should be avoided if at all possible).

b. Set up an infusion of 10% glucose 500 ml containing Actrapid or Leo Neutral insulin 10 units plus KCl 1 g at 8–9 a.m. Run through in 4–5 h.

c. Check blood-glucose and plasma potassium before infusion and after 2–3 h. If the latter blood-glucose is between 5 and 10 mmol litre^{-1} then continue the infusion as before. If the blood-glucose is outside this range, change the insulin as follows:

If glucose < 5 mmol litre^{-1} change to 10% glucose 500 ml + insulin 5 units + KCl 1 g.

If glucose > 10 mmol litre^{-1} change to 10% glucose 500 ml + insulin 15 units + KCl 1 g.

If glucose > 20 mmol litre^{-1} change to 10% glucose 500 ml + insulin 20 units + KCl 1 g.

d. Thereafter check blood-glucose 2–4-hourly using Dextrostix, preferably with the aid of a Reflectance Meter or Glucocheck machine. N.B. Meticulous technique is required if useful results are to be obtained —in particular ensure that the Dextrostix are not old or discoloured. If bedside machines are not available then read the "stix" by eye. If the value by this method is less than 6 mmol litre^{-1} or greater than 11 mmol litre^{-1} send a sample to the laboratory for accurate measurement.

e. Continue to adjust insulin and potassium doses according to results (e.g. if plasma $K^+ > 4$ mmol litre^{-1} then stop the KCl, if plasma K is < 4 mmol litre^{-1} increase to 2 g per 500-ml bottle).

(iii) *After operation*

a. Continue with 4–5 hourly infusions of 10% glucose–insulin–potassium, checking blood-glucose 4-hourly, and plasma K^+ 8-hourly. If fluid needs to be restricted for any reason, then equivalently smaller volumes of 20% or 50% glucose can be used, though these should be given via a central line.

b. Stop infusions when oral feeding is recommenced, and give t.i.d. Actrapid or Leo Neutral (daily total dose to equal the normal preoperative dose, adding an extra 20% if infection is present, and an extra 20% if the patient is receiving steroids).

c. Adjust dose as necessary and return to original preoperative regimen (i.e. short-acting/long-acting insulin combination) in 2–3 days.

d. If oral feeding cannot be restarted 48 h after surgery, consider parenteral nutrition.

(D) *Intravenous fluids*

These can be as for non-diabetics, except that lactate containing fluids should be avoided.

Special Notes

Cardiac operations. Note that patients on cardiac by-pass receive considerable extra glucose from the "deadspace" of the machine. In such patients insulin 20 units per 500 ml of 10% glucose should be used as soon as they are put on by-pass. If volumes need to be restricted 50% glucose 100ml or 20% glucose 250 ml are equivalent in glucose content to 10% glucose 500 ml.

Sepsis. Sepsis will always greatly increase insulin requirements.

Continuous therapy. If the infusion stops, the patient's extracellular fluid will contain no effective insulin within *30* min. Therefore ensure that treatment is *continuous.*

Normoglycaemia. Aim to maintain blood-glucose between 5 and 10 mmol litre^{-1}. The only possible benefit of a greater concentration is an osmotic diuresis.

Common sense. These are guidelines. The starting regimen (glucose 500 ml + insulin 10 units + KCl 1 g) is based on experience and a comparative study, but it is not meant to be unthinkingly adhered to. Patients will always vary, so therapy must be flexible and common sense applied.

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