

Glucose: A Reevaluation of its Intraoperative Use

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IT IS COMMON PRACTICE for anesthesiologists to administer glucose-containing solutions during the intraoperative period. However, recent evidence suggests that intraoperative glucose may be undesirable in certain circumstances. In view of the emerging knowledge of risks of glucose administration, it is the intent of this

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article to reevaluate the use of glucose in the intraoperative period.

Current Intraoperative Glucose Use

Typically, 50–150 g of glucose is given intraoperatively for the following reasons: to prevent hypoglycemia, to provide energy, to allow free water administration, to conserve protein, and to prevent ketosis. With respect to hypoglycemia (defined in adults as blood glucose concentrations less than $50 \text{ mg} \cdot \text{dl}^{-1}$ or blood plasma glucose concentrations of less than $57 \text{ mg} \cdot \text{dl}^{-1}$), which might occur secondary to fasting, typical values of morning fasting glucose suggest that this is not a significant concern with either male or female surgical patients.¹ However, with increasing length of fasting, the incidence of hypoglycemia increases. Merrimee and Tyson found a prominent sex difference in plasma glucose response to fasting in non-diabetic subjects of normal weight.² The mean (\pm SEM) plasma glucose concentration in men ($N = 12$) decreased from $89.0 \pm 3.5 \text{ mg} \cdot \text{dl}^{-1}$ at the start of the fast to $67.5 \pm 3 \text{ mg} \cdot \text{dl}^{-1}$ at 72 h. On the other hand, fasting women ($N = 45$) showed plasma glucose decreases to $57.7 \pm 1.7 \text{ mg} \cdot \text{dl}^{-1}$ at 24 h. Plasma glucose continued to decrease in these women to $41.3 \pm 2 \text{ mg} \cdot \text{dl}^{-1}$ at 72 h. These results suggest that glucose administration should be considered in women fasted 24 h or longer. However, the response to major surgical stress tends to counter tendencies toward hypoglycemia, most patients showing an increase in plasma glucose during surgery. Intraoperative glucose administration exacerbates this trend.³ In adults and children, there is a positive correlation between glucose infusion rate and intraoperative plasma glucose, regardless of whether or not a patient is diabetic (fig. 1).^{4,5} At rates equal to or greater than $12.5 \text{ g glucose} \cdot \text{h}^{-1}$ (250 ml of 5% dextrose solution per hour), blood glucose is consistently above $200 \text{ mg} \cdot \text{dl}^{-1}$.

It has been suggested that small amounts of glucose are important to maintain myocyte energy levels. Liaw *et al.* have shown that $90 \text{ g} \cdot \text{d}^{-1}$ of glucose given to total hip replacement patients prevents postoperative decreases in ATP, ADP, and phosphocreatine in skeletal

muscle.⁶ The magnitude of this effect intraoperatively is not known, because, in this study, glucose was withheld for about 96 h.

The dose of glucose for protein sparing in the uncomplicated elective surgical patient is controversial. Traditionally, glucose doses in the range of 100–150 g · d⁻¹ were considered adequate for a 50% reduction in protein catabolism during starvation.⁷ In contrast, Askenazi *et al.*⁸ found that 100 g of glucose per day in postoperative patients reduced urinary nitrogen by only 23%. Giddings⁹ found that introducing glucose on the first postoperative day produced no reduction in nitrogen loss for at least 24 h, suggesting that there were effects of glucose on the reversal of the fasting state, but not on the nitrogen loss related to the stress of surgery. Few researchers have analyzed the immediate effects of intraoperative glucose. A recent study suggests, for example, that intraoperative glucose does not produce protein sparing during the intraoperative period.¹⁰ These results merit further investigation, and may re-vamp some of our thinking about intraoperative *versus* postoperative effects of glucose on nitrogen sparing.

Intraoperative glucose infusions at rates of 12.5 g · h⁻¹ decrease blood free fatty acid and ketone levels.¹⁰ This may have beneficial effects upon the myocardium by decreasing oxygen consumption and susceptibility to arrhythmias. Free fatty acids have been shown to increase myocardial oxygen consumption,¹¹ and their presence in elevated amounts following myocardial infarction is associated with an increased incidence of arrhythmias.^{12,13} However, studies reporting intraoperative free fatty acid levels in the range known to enhance arrhythmogenicity (greater than 1200 Meq · L⁻¹) did not report any increased incidence of myocardial arrhythmias.¹⁴

Problems with Intraoperative Glucose Administration

Despite these traditional reasons for giving glucose intraoperatively, there is now an emerging body of evidence that glucose may contribute to an adverse outcome if given inappropriately.

INCREASED CARBON DIOXIDE PRODUCTION

Glucose administration increases carbon dioxide production (\dot{V}_{CO_2}). The degree of increase depends on the amount of glucose given, how it is utilized, and on the body's metabolic and nutritional state. Edwards *et al.*¹⁵ found no significant change in alveolar carbon dioxide tension following ingestion of 50, 75, or 100 g of glucose (po), and no change in blood lactic acid or carbon dioxide content was reported after 50 g glucose (po).¹⁶ With higher glucose loads, 920 Kcal (approximately

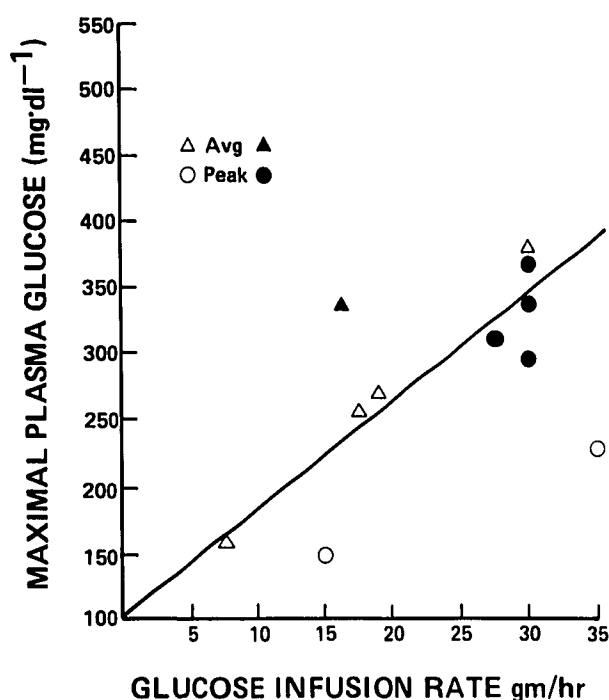


FIG. 1. Correlation of glucose infusion rate with maximal plasma glucose concentration achieved during surgery. Average glucose infusion rates over the total period of surgery are from six patients whose glucose was infused at a constant rate (triangles). In the other four patients, the maximal plasma glucose was related to a period of rapid glucose infusion, and this "peak" glucose infusion rate was used (circles). Open symbols represent normal subjects and closed symbols diabetic subjects. The degree of hyperglycemia obtained was directly proportional to the glucose infusion rate during surgery, as represented by the regression line ($r = 0.78$; $P < 0.01$). Figure from Schwartz SS, Horwitz DL, Zehfus B, Langer B, Moossa AR, Ribeiro G, Kaplan E, Rubenstein AH: Use of a glucose controlled insulin infusion system (artificial beta cell) to control diabetes during surgery. *Diabetologia* 16:157–164, 1979; reprinted with permission.

230 g of glucose), a significant increase in tidal volume, minute ventilation, minute oxygen consumption, and \dot{V}_{CO_2} has been described in normal patients.¹⁷ This 920 Kcal load in patients with chronic obstructive pulmonary disease (COPD) produced no change in arterial carbon dioxide content despite an increase in \dot{V}_{CO_2} .¹⁸ Hagerdal *et al.*¹⁹ found that glucose given intraoperatively does exert a significant effect on postoperative \dot{V}_{CO_2} . In patients receiving approximately 100 g of glucose (iv), a 20% elevation in \dot{V}_{CO_2} was seen accompanied by an increased RQ (RQ; minute CO₂ excretion/minute O₂ consumption). Although respiratory failure has not been reported at common intraoperative glucose doses, several investigators have found that glucose-based hyperalimentation regimens may increase carbon dioxide production enough so that acute respiratory failure has precipitated in some cases.^{20–22}

Individuals with normal cardiopulmonary reserve are able to compensate for glucose induced increases in \dot{V}_{CO_2} by changes in tidal volume and respiratory frequency. Although respiratory compromise is a theoretic possibility, it is unlikely to occur with the glucose doses given intraoperatively unless severe central nervous system and/or pulmonary compromise exists.

GLUCOSE-INDUCED HYPOGLYCEMIA: GLUCOSE ADMINISTRATION IN OBSTETRICAL PATIENTS

As blood glucose levels rise following intravenous glucose administration, insulin secretion is stimulated. As a result, the carrier-mediated transport of glucose into peripheral cells is accelerated. When glucose levels begin to decline, glucagon levels may increase, enhancing liver glycogenolysis and gluconeogenesis. The falling insulin levels augment these processes. Thus glucagon acts to prevent the hypoglycemia which might ensue secondary to insulin. In situations where glucagon secretion is inadequate but there are elevated insulin levels, a risk of hypoglycemia is present. During labor and delivery, such a clinical circumstance may present itself, as the neonate has a delayed glucagon response to falling blood glucose levels. Thus, any treatment which might increase neonatal insulin secretion could significantly increase the risk of hypoglycemia.

Glucose passively crosses the placenta, and maternal values exceed those of the umbilical vein by approximately $15 \text{ mg} \cdot \text{dl}^{-1}$.²³ Insulin does not cross the placenta, and, thus, the fetus is responsible for mounting its own response to glucose. Evidence of fetal insulin production is found as early as 11 weeks of gestation,²⁴ but the fetal pancreas responds rather slowly, if at all, to hyperglycemia.²⁵ Milner and Hales²⁶ observed that increases in fetal insulin occurred 20 min after a 25-g maternal glucose load, and fetal insulin concentration continued to rise for an additional 60–100 min. Tobin *et al.*²⁷ found that greater than 30 min were required to produce an elevated fetal insulin level following glucose $0.5 \text{ g} \cdot \text{kg}^{-1}$, iv, which was given 60 min prior to delivery. Thomas *et al.*²⁸ explored the lower limits of insulin secretion. Glucose was administered, $5 \text{ g} \cdot \text{h}^{-1}$, during labor. It was observed that maternal and fetal blood glucose increased, while fetal insulin did not. Higher and longer rates of glucose infusion (mothers receiving greater than $10 \text{ g} \cdot \text{h}^{-1}$ for more than 4 h prior to delivery) were required for the fetus to have an increase in insulin levels.²⁹ From the above studies, it appears that glucose in doses of 25 g or more to the mother will produce a small, but clinically significant, increase in fetal insulin.³⁰

Similarly, maternally administered glucose given during cesarean section influences neonatal insulin

levels. Kenepp *et al.*³¹ showed that intravenous glucose (100 g) given during pre-epidural hydration for cesarean section produced maternal and fetal glucose values greater than $200 \text{ mg} \cdot \text{dl}^{-1}$. Two hours postpartum, these neonates showed precipitous declines in blood glucose to $35 \pm 4.7 \text{ mg} \cdot \text{dl}^{-1}$ (less than $40 \text{ mg} \cdot \text{dl}^{-1}$ is considered hypoglycemic in full-term infants); however, no signs of neonatal hypoglycemia were noted. During the postpartum period, insulin secretion decreased with the declining plasma glucose concentrations. At the same time, neonatal glucagon levels showed only a small response to declining glucose values, possibly explaining the observed decrease in blood glucose levels. Other investigators have documented impaired neonatal glucagon secretion in infants of diabetic mothers, a group particularly susceptible to hypoglycemia.³² The lower limit of this response is such that, if greater than 25 g of glucose are given during prehydration for cesarean section, fetal hyperinsulinemia is induced.³³ In addition, infants whose mothers received more than 25 g of glucose during cesarean section had a higher incidence of neonatal jaundice, although an explanation for the cause of increased jaundice is not possible from current data.³³

Several patient groups, including preterm infants, infants small for gestational age, infants with erythroblastosis fetalis, and infants of mothers with gestational or insulin-dependent diabetes have a higher risk for neonatal hypoglycemia. For example, newborns of mothers with untreated gestational diabetes have a more profound insulin response to hyperglycemia, and may manifest marked hypoglycemia in the early newborn period (fig. 2).²⁸ The initial rate of decrease in blood sugar level is determined by the maternal blood sugar level at the time of delivery.³⁴ The higher the umbilical cord glucose concentration, the more likely it is that an infant of a diabetic mother will develop hypoglycemia during the first few hours of life.

Glucose administration in obstetrics, then, is a double-edged sword. It is important to prevent neonatal hyperglycemia of a degree that will stimulate neonatal insulin production. Yet, evidence suggests that maternal ketosis might also harm the fetus. Churchill *et al.*,³⁵ for example, found a significant difference in neurologic outcome in terms of the Bayley Scale at 8 months, posturing factors at 1 yr, and IQ at 4 yr when comparing infants of diabetic mothers with third-trimester ketonuria versus non-diabetic, non-ketonuric controls. A study by Churchill and Berendes³⁶ found a difference in IQ when the children of non-diabetic ketonuric women in the third trimester were compared with those of non-diabetic non-ketonuric women (89 versus 98.7). However, the above-mentioned studies did not separate the effects of ketosis from those of diabetes or nutrition.

Thus, it is difficult to know whether it was the ketosis or other disturbances which were responsible for these results. Other investigators have shown no IQ impairment in military recruits who were exposed *in utero* to severe maternal food restrictions during the Holland famine of 1944–1945.³⁷ However, in this study, no data concerning maternal ketonuria are available. Although results are inconclusive, the possible link between ketosis and detrimental neonatal outcome and the pregnant woman's predisposition towards ketosis suggests that glucose should be given during labor and delivery.

The question is what dose of glucose to use. This is particularly important since pregnancy is characterized by an accelerated starvation pattern. Hypoglycemia, hyperketonemia, and hypoalaninemia occur within 16 h of fasting, as opposed to 24–36 h in the non-pregnant individual.³⁸ As noted earlier, doses of greater than 10 g·h⁻¹ cause increases in fetal insulin. Kenep *et al.*³⁹ have shown that rates of 75 mg·kg⁻¹·h⁻¹ are sufficient to prevent the accumulation of acetoacetate, and recommend glucose infusions of 3.5–7 g·h⁻¹ as appropriate during labor. With cesarean section, large glucose loads should be avoided. With epidural anesthesia or other procedures, fluid loading, when needed, should be done with non-glucose-containing solutions, and the amount of glucose given should be less than 25 g.

HYPERGLYCEMIA-ASSOCIATED INTRACELLULAR LACTIC ACIDOSIS

Background. Recent animal studies have shown that hyperglycemia existing prior to a severe ischemic or hypoxic event will enhance the ischemic damage.^{40,41} The most accepted hypothesis of the mechanism of this observation is that, in the presence of ischemia or hypoxia, oxidative metabolism of glucose fails and glycolysis with its end product of lactate increases. With sufficient intracellular lactate accumulation, intracellular pH falls, and this may lead to compromised cellular function and, possibly, cell death.⁴² A recent study suggests an alternative hypothesis that, in awake animals, hyperglycemia may decrease cerebral blood flow, and thus place these animals at greater risk than normoglycemic controls;⁴³ however, changes in cerebral blood flow have not been noted by other groups reporting glucose-related brain damage.⁴¹

Despite controversy concerning mechanisms, the observations are important. Meyers and Yamaguchi⁴⁴ found that, in juvenile monkeys, glucose infusion prior to cardiac arrest increased neurologic damage. Siemkowicz and Hansen⁴⁵ observed similar findings in rats after 10 min of ischemia. In that study, neurologic recovery and mortality in the rats bore a direct relation to

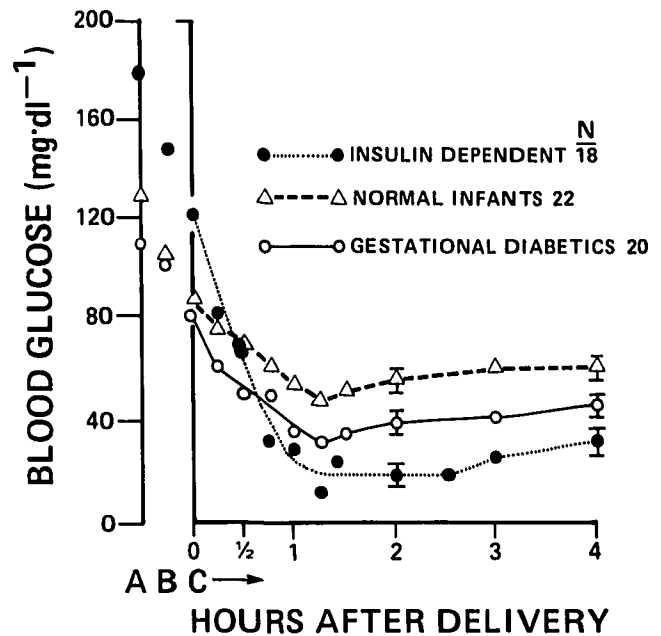


FIG. 2. Serial changes in the concentration of glucose in the blood of infants immediately and up to 4 h following delivery. The group denoted "gestational diabetics" are infants from mothers who had abnormal intravenous glucose tolerance tests during pregnancy but received no insulin therapy. The group denoted "insulin dependent" had mothers who were taking insulin. Error bars denote standard error of the mean. Mean glucose levels are from maternal vein (A), umbilical vein (B), and umbilical artery (C) from the three groups. N denotes number of infants in each group. At 2 and 4 h, the blood glucose levels of infants of insulin dependent mothers and mothers with gestational diabetes were significantly different from normal infants ($P < 0.001$ and $P < 0.01$, respectively). Figure from McCann ML, Chen CH, Katigbak EB, Kotchen JM, Likly BF, Schwartz R: Effects of fructose on hypoglycemia in infants of diabetic mothers. *N Engl J Med* 275:1–7, 1966; reprinted with permission.

the pre-ischemic blood glucose level, with normoglycemic animals having the best outcome as compared to hyper- or hypoglycemic animals. In followup studies, it was shown that the damage in this model was not related to changes in cerebral blood flow or alterations in ion distribution.^{46,47} Ginsberg *et al.*,^{48,49} using a cat model, showed inhibition of restitution of brain high-energy metabolite levels (ATP and phosphocreatine) and impairment of local cerebral blood flow in glucose-pretreated animals. Welsh *et al.*⁵⁰ showed that mice had a pre-ischemic threshold blood glucose value (approximately 225 mg·dl⁻¹), above which significant impairment in recovery of brain energy metabolites occurred. Pulsinelli *et al.*⁴⁰ observed that the timing of hyperglycemia is crucial, as the greatest neurologic damage occurred when rats were made hyperglycemic prior to the ischemic event. Kagstrom *et al.*⁵¹ examined cerebral blood flow following severe incomplete ischemia, and showed differences in recovery of regional cerebral

TABLE 1. Admission Blood Glucose Levels and Neurological Recovery after Out-of-hospital Cardiac Arrest

Group	Number of Patients	Glucose Level (mg · dl ⁻¹)*
Never awakening	154	341 ± 13†
Ever awakening	276	262 ± 7
Persistent deficits	90	286 ± 15‡
No deficits	186	251 ± 7

* Values are expressed as mean ± standard error of the mean.

† Significantly different from mean glucose level in patients who did awaken ($t = 5.9$; $P < 0.0005$).

‡ Significantly different from mean glucose level in patients without persistent deficits ($t = 2.4$; $P < 0.02$).

Data from Longstreth WT, Inui TS: High blood glucose level on hospital admission and poor neurological recovery after cardiac arrest. *Ann Neurol* 15:59-63, 1985; reprinted with permission.

blood flow between fed and fasted rats. Fasting was associated with a higher local cerebral blood flow after 60 min of recirculation. These results were similar to Ginsberg *et al.*'s data,⁴⁸ however, Kagstrom *et al.*⁵¹ examined much lower blood glucose levels. Work by Rehncrona *et al.*,^{42,52,53} in rats, supports the suggestion that hyperglycemia exacerbates the effects of brain ischemia by causing tissue lactate accumulation. Studies using deprivation of oxygen without ischemia (hypoxia) have also demonstrated that energy recovery after reoxygenation is related to the pre-insult glucose levels.⁴¹ Recent studies in primate models involving complete ischemia have shown that administering glucose approximately 30 min prior to the onset of the insult results in a significant increase in cerebral injury, even when the blood glucose at the time of insult is not significantly elevated (181 ± 19 vs. 140 ± 6 mg · dl⁻¹ in glucose- and non-glucose-treated animals, respectively).⁵⁴

These multiple observations from several laboratories are, however, not without controversy. Ibayashi *et al.*⁵⁵ used a model of bilateral carotid ligation for 3 h in spontaneously hypertensive rats, and failed to show differences in metabolic recovery between normo- and hyperglycemic animals, despite differences in brain lactate levels. However, their initial blood glucose levels of 160 ± 12 mg · dl⁻¹ seems high compared to those reported by Rehncrona *et al.*⁵² of 108 ± 13 mg · dl⁻¹, and this may be a factor in their findings.

Studies in humans have also examined the effects of hyperglycemia on neurologic outcome after ischemia. The results of these studies at present are inconclusive. Longstreth and Inui,⁵⁶ in a retrospective study of 430 patients, observed that high blood glucose levels on hospital admission correlated with poorer neurologic recovery following cardiac arrest (table 1). However, this same group of investigators examined blood glucose levels obtained during cardiopulmonary resuscitation

(pre-hospital) in a different patient sample, and that data suggested that the blood glucose level was a function of the duration of the resuscitation. Thus, people with more prolonged cardiopulmonary resuscitation had higher blood glucose levels. Mortality and failure to awaken in this second study was correlated best with duration of cardiopulmonary resuscitation, and not with the value of the blood glucose. However, in this group of patients, admission blood glucose levels were not available, so that the findings of the first and second study cannot be directly compared.⁵⁷ Pulsinelli *et al.*,⁵⁸ in a retrospective study of diabetic and nondiabetic stroke patients, found a poorer neurologic outcome in patients with diabetes. A second group of nondiabetic stroke patients was examined prospectively. This sample was divided into hyper- and normo-glycemic groups using 120 mg · dl⁻¹ as the upper limit of normoglycemia. A trend (not statistically significant) toward poorer neurologic outcome was found in the hyperglycemic group. However, these human studies are difficult to interpret because reactive hyperglycemia often occurs in the context of brain ischemic events.⁵⁹ It is possible, for example, that the reactive hyperglycemia to the stress of injury may, in fact, provide the glucose level that contributes to the poorer outcome.⁶⁰ On the other hand, the degree of hyperglycemia is often related to the severity of the diabetes. Severe diabetes has a high level of associated complications, such as vascular disease, which can certainly contribute to the association between hyperglycemia and poorer outcome. Of greater importance are the recent observations by Riddle and Hart⁶¹ showing a marked association between chronic hyperglycemia (as estimated by glycosylated hemoglobin concentration) and stroke, even in patients with no known history of diabetes. The association between diabetes and stroke has long been recognized,⁶²⁻⁶⁴ and the current studies suggest that the glucose level may be important, though the role of vascular disease cannot be ruled out. Clearly, the role of glucose concentration and neurologic damage during ischemia in humans has not yet been completely defined.

Intraoperative glucose in neurosurgical patients. Metabolic studies in patients receiving preoperative steroids who underwent supratentorial craniotomy showed that hyperglycemia occurred when glucose was given intraoperatively at rates approximating 12.5 g · h⁻¹ (250 ml · h⁻¹ of 5% dextrose solution).¹⁰ In the absence of glucose, intraoperative plasma glucose never decreased below 86 mg · dl⁻¹, suggesting little risk of significant hypoglycemia in this group of patients. In patients not given glucose, ketone body concentrations gradually increased over the 4-h intraoperative period. However, these elevations were not severe enough to alter acid-base status. No difference in protein sparing as mea-

sured by urinary nitrogen excretion was observed in patients who received intraoperative glucose. Although no significant neurologic complications were observed in patients receiving intraoperative glucose, the blood glucose levels obtained (greater than $200 \text{ mg} \cdot \text{dl}^{-1}$) were similar to those in many of the experimental studies described in the previous section.

Operations with ischemia risks. In neurosurgery, hypotension,⁶⁵ increased intracranial pressure,⁶⁶ hypoxia, and brain retraction^{67,68} may result in brain ischemia. Carotid endarterectomy and coronary artery bypass grafting represent other types of surgical procedures where brain ischemia can occur.⁶⁹ Further research is necessary to delineate the effects of hyperglycemia on intraoperative events related to brain ischemia in these clinical situations. However, in view of the findings in animal studies, the trends seen in human studies, and the fact that intraoperative glucose appears to have minimal beneficial effects, withholding glucose from the intraoperative fluid regimen should be considered for patients undergoing the above-mentioned procedures. Glucose can always be given postoperatively. If one is anxious about intraoperative hypoglycemia, occasional glucose levels by capillary blood glucose analysis can be done in the operating room quickly and inexpensively. Others have expressed agreement with this approach.⁷⁰

Most studies of adult inpatients undergoing operations of short duration (up to 4 h in length) suggest that intraoperative hypoglycemia is not a concern.^{3,10} However, with surgery of greater than 4 h, the effects of withholding glucose in the face of surgical stress, intraoperative starvation, and the long-term effects of ketosis are not known. Therefore, until further information is available, glucose administration is probably warranted during surgical procedures longer than 4 h. Alternatively, periodic measurement of blood glucose can be done. On the basis of studies in fasting subjects, 100–150 g glucose may be given intraoperatively during prolonged surgery. Glucose levels over $200 \text{ mg} \cdot \text{dl}^{-1}$ will usually not be attained in nondiabetic subjects if glucose is given slowly (fig. 1).

MISCELLANEOUS PROBLEMS

Aylett⁷¹ reported that glucose, 25 g iv, could significantly slow the rate of gastric emptying. MacGregor *et al.*^{72,73} used an intestinal perfusion technique to show that hyperglycemia ($160 \text{ mg} \cdot \text{dl}^{-1}$) delays gastric emptying of meals containing fat and protein or protein alone. MacGregor *et al.*⁷⁴ also found a delay in stomach emptying when patients on total parenteral nutrition received solid food. This observation has considerable import for the anesthesiologist. If total parenteral nu-

trition is used to supplement oral nutrition prior to elective surgery, an increased risk of aspiration from a full stomach may be present. Additional studies involving gastric residuals on the morning of surgery need to be performed on this group of patients to better define the problem.

Postinfusion thrombophlebitis at the intravenous site has been associated with the acidic pH of 5% dextrose solutions (pH range 4.2–5.3).⁷⁵ Fonkalsrud *et al.*⁷⁶ reported that neutralization of 5% dextrose solutions caused a threefold decrease in phlebitis during the first 24 h postoperatively. However, the incidence of postinfusion thrombophlebitis with 5% glucose solutions given during the intraoperative period is not known.

Intravenous carbohydrate infusions may cause postoperative decreases in serum phosphate concentration.⁷⁷ A reduction in serum phosphate of $0.20\text{--}0.30 \text{ mM} \cdot \text{l}^{-1}$ may occur, regardless of the type of infusion (10% or 20% solutions), infusion rate ($0.15\text{--}0.50 \text{ g glucose} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$), or amount of glucose infused (55–100 g glucose).⁷⁸ Experiments in hypophosphatemic dogs have shown reduced chemotactic mobility of leukocytes.⁷⁹ Other studies have suggested that a decrease in serum phosphate of $0.22 \text{ mM} \cdot \text{l}^{-1}$ that occurs with infusion of 1 l 10% glucose may be associated with reduced phagocyte function, as estimated by engulfment of *Candida albicans*, intracellular killing of *Candida albicans*, oxygen consumption during phagocytosis, and generation of superoxide ions during standard stimulation tests.⁷⁸

Indications for Glucose Administration

Despite these concerns about intraoperative glucose use, glucose administration is indicated during clinical circumstances where hypoglycemia is likely to occur.

Intraoperative hypoglycemia is an important consideration in diabetics on oral hypoglycemic or insulin regimens who have received their medications up until the time of surgery (or who are receiving pm Lente or NPH insulin). In this situation, the elevated insulin levels in the face of inadequate blood sugar concentrations and blunted catecholamine response, the risks of withholding glucose far outweigh those of giving it.⁸⁰ Even so, occasional spot glucose levels during prolonged procedures provide greater insurance against hypoglycemia than glucose administration alone.

Individuals receiving glucose-based total parenteral hyperalimentation who have their infusions suddenly stopped prior to surgery show an immediate fall in blood sugar. In this circumstance, hypoglycemia may be anticipated,⁸¹ and glucose solutions should be continued intraoperatively. This post-infusion "rebound hypoglycemia" appears to be secondary to persistent en-

ogenous insulin production stemming from the prolonged stimulation of the pancreatic islet cells during carbohydrate infusion.⁸²

Some groups of reasonably healthy patients may have a special risk of hypoglycemia. Doze and White⁸³ found that a sample of 50 young women fasted about 17 h had average preoperative blood glucose values of only 54 mg · dl⁻¹. Twenty-five of these women underwent minor gynecologic procedures (average duration 23 min), and received no intraoperative glucose. Postoperative glucose values in this group were 57 ± 14 mg · dl⁻¹ (mean ± SD). Some of these patients had postoperative glucose levels of only 33 mg · dl⁻¹. These results agree with other studies showing little or no increase in blood glucose during minor surgical procedures.^{84,85} The fasting glucose levels reported in this study are similar to those reported by Merimee and Tyson² for women who were fasted for 24 h. Recognize that these values are considerably lower than overnight fasting glucose values reported in other studies of surgical patients.¹ One major difference between the studies of Doze⁸³ and Merimee² compared to other studies is the duration of fast. In view of this, it would be prudent to administer glucose to patients who have been fasted for longer than 24 h, particularly if female and undergoing relatively minor procedures.

Young children, particularly infants, have a greater tendency to become hypoglycemic, especially with fasting. In 1974, Thomas⁸⁶ showed a 15.2% incidence of hypoglycemia (defined in children by blood glucose less than 40 mg · dl⁻¹) in fasting children who were inpatients. The length of fast was 8–10 h. When the patient group was narrowed to include only those subjects less than 15.5 kg and 47 months, the incidence of hypoglycemia was found to be 28%. These results were not replicated in a later (1979) study of outpatients where no patients under 5 yr of age were found to be hypoglycemic.⁸⁷ Another study combining inpatients and outpatients aged 6 months to 9 yr showed a 1% incidence in all patients and a 2% incidence with inpatients.⁸⁸ The most recent studies, from 1985 and 1986, have not demonstrated frequent occurrences of hypoglycemia in fasting pediatric outpatients.^{5,89,90} These findings suggest that hypoglycemia may not be as common an occurrence in pediatric patients as was previously thought. Since the incidence of hypoglycemia in pediatric patients remains controversial, glucose administration should be continued until more data become available.

Propranolol has been reported to cause spontaneous hypoglycemia. However, during a 48-h fast, no increased incidence of hypoglycemia could be found in patients taking propranolol.⁹¹ Calcium channel blockers (verapamil) have been shown to enhance glucose tolerance in patients with non-insulin-dependent diabetes.

This effect has not been reported in non-diabetic subjects. Therefore, glucose may be withheld in patients on verapamil.⁹²⁻⁹⁴

Postoperative hypoglycemia has been reported following pheochromocytoma removal.⁹⁵ The mechanism is a reactive increase in insulin secondary to the removal of the inhibitory effects of catecholamines on the pancreatic islet cells. It is recommended that patients undergoing pheochromocytoma removal receive glucose-containing solutions and have their blood glucose carefully monitored perioperatively.

Roizen⁹⁶ has listed several causes of hypoglycemia during the fasting state, including pancreatic islet cell adenoma or carcinoma, large hepatoma, large fibroma or sarcoma, alcohol ingestion, hypopituitarism, and adrenal insufficiency. Surgical patients with any of these conditions should receive intraoperative glucose while undergoing close perioperative monitoring of blood glucose levels.

Summary and Recommendations

In certain instances, the adverse effects of glucose may outweigh the potential benefits obtained from glucose administration. Withholding glucose or giving it in moderation so as to keep the blood glucose level below 200 mg · dl⁻¹ is recommended whenever brain ischemia may occur intraoperatively. One may also wish to decrease the intraoperative glucose dose during labor and delivery. In addition, decreased gastric motility must always be kept in mind when caring for patients exposed to prolonged periods of hyperglycemia. In most patients, not administering glucose presents little risk.

In many circumstances, intraoperative glucose administration may be advantageous. However, only with a thorough knowledge of the benefits of glucose and its possible complications can the anesthesiologist rationally administer glucose in the intraoperative setting.

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