The Influence of Dextrose Administration on Neurologic Outcome after Temporary Spinal Cord Ischemia in the Rabbit

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The influence of dextrose administration on neurologic outcome after temporary spinal cord ischemia was examined in New Zealand white rabbits. Spinal cord ischemia was produced by infrarenal balloon occlusion of the aorta in unanesthetized animals. Animals were observed for 3 days for neurologic evaluation. Fasted animals received intravenous dextrose, 0.5 g·kg⁻¹, or placebo before a period spinal cord ischemia. The dextrose was administered as either a bolus of a 50% solution (D50) 15 min before ischemia or as an infusion of a 5% solution (D5W) over 90 min before ischemia. With either mode of administration, preocclusion plasma glucose level was moderately increased as compared with that in animals that received lactated Ringer's solution in equivalent volume, i.e., for the D50 bolus: 291 ± 82 (SD) versus 166 ± 67 mg·dl⁻¹ (P < 0.005); and for D5W infusion: 177 ± 38 versus 137 ± 13 mg·dl⁻¹ (P < 0.01). With either mode of administration, neurologic outcome was poorer (P < 0.025) at 72 h in the animals that had received dextrose. For example, of the 10 animals that received D5W by infusion, nine were paraplegic (unable to walk) 72 h after ischemia, whereas only three of 10 control animals were paraplegic. The adverse effect of an increased blood glucose level has been demonstrated previously for cerebral ischemia. The present results are the first demonstration that increased plasma glucose may result in a worsened neurologic outcome after spinal cord ischemia. Further, they indicate that, in rabbits, the threshold for this effect is low, i.e., dextrose administration sufficient to produce a mean preischemic plasma glucose increase of 40 mg·dl⁻¹ was sufficient to result in an increased frequency of postischemic paraplegia. (Key words: Metabolism, hyperglycemia: spinal cord ischemia. Spinal cord, ischemia: hyperglycemia.)

THE WEIGHT of clinical and laboratory evidence indicates that an increased blood glucose value before ischemia predisposes patients to a poorer neurologic outcome after an episode of cerebral ischemia.[1–10] The favored explanation is that an increased substrate (glucose) supply results in a greater lactic acid accumulation during the period of ischemia and a less favorable intracellular environment during reperfusion.[11–14] Although studies of cerebral ischemia have been numerous, the relevance of increased glucose to outcome after spinal cord ischemia has not been established. The following investigations were undertaken 1) to determine whether an increased plasma glucose value influences neurologic outcome after temporary spinal cord ischemia, and 2) to examine the

serum glucose threshold for a deleterious neurologic effect.

Methods

All protocols were reviewed and approved by the Animal Subjects Committee of the University of California, San Diego.

DESCRIPTION OF THE MODEL

Spinal cord ischemia was produced in New Zealand white rabbits by temporary occlusion of the abdominal aorta.[15] Rabbits of either sex, weighing 2.8–3.5 kg, were studied. Before the study, the rabbits were maintained on a standard light/dark cycle and were fed Universal Rabbit Chow (Universal Feed, Inc., Colton, California). Free access to water was provided during fasting immediately before the study. For preparation, anesthesia was induced by placing the animals in a Plexiglass® box containing 4% halothane in oxygen. After loss of consciousness, the rabbits breathed halothane in oxygen from a face mask. After skin infiltration with 0.25% bupivicaine (0.5–1.0 ml), a 4 Fr., balloon-tipped, pediatric angiography catheter (Critikon Inc., Tampa, Florida) was advanced 15 cm into the abdominal aorta through a femoral arteriotomy immediately distal to the inguinal ligament. Preliminary investigations revealed that this results in a balloon location 0.5–1.5 cm distal to the left renal artery. The groin wound was then loosely approximated, and the halothane was discontinued. Immediately before catheter insertion, intramuscular cephazolin, 25 mg·kg⁻¹, and intravenous heparin, 1,000 units, were administered.

Aortic occlusion was performed 90–120 min after discontinuation of halothane and after confirmation of normal neurologic function. The balloon was inflated until there was a loss of pulsatile distal aortic pressure (as transduced via the dye injection port of the angiographic catheter). In each animal, the rapid (15–25 s) onset of flaccid lower extremity paralysis was confirmed. The duration of aortic occlusion varied (8–30 min) according to the protocols described below.

After deflation of the balloon, the rabbit was placed in the supine position, the groin wound was reopened, the catheter was removed, and the wound was filled with Betadine® ointment and closed. Rabbits held in the supine position quickly assumed an immobile trance-like state. In addition, all rabbits had at least brief lower-body in-

sensibility after aortic occlusion, and catheter removal was readily accomplished without anesthesia.

The rabbits were observed for 72 h. Antibiotic (cephazolin 25 mg·kg⁻¹, im) was administered once daily, and bladder contents were expressed manually as required. A score of neurologic function (see below) was recorded by a blinded observer 2 h after balloon deflation and on mornings 1, 2, and 3 thereafter. In all of the investigations, any rabbit that died before the conclusion of the 3-day observation period was excluded from analyses and was replaced with an additional animal.

DOSE–RESPONSE (OCCLUSION DURATION VS. NEUROLOGIC OUTCOME) STUDIES IN FASTED ANIMALS

Fifty rabbits were fasted for 16 h before aortic occlusions of 8–30 min. Neurologic scoring was performed according to a four-point scale of motor function: 0 = paraplegic with no lower-extremity motor function; 1 = paraparetic with lower-extremity function but inability to draw legs under body and/or hop; 2 = ability to draw legs under body and hop but not normally; 3 = normal motor function.

An analysis of the relationship between the duration of aortic occlusion and neurologic outcome (score on day 3) was performed in order to determine the ED_{50}, the occlusion duration that would produce a major neurologic deficit (unable to walk/hop) in 50% of animals. The method used was developed by Waud[16] and has been used in similar studies by Zivin et al.[17,18] The approach is analagous to the determination of an LD_{50} for a pharmacologic agent. For the purposes of the present analysis, the animals were segregated into those that had a major neurologic deficit (scores 0 and 1) and those that did not (scores 2 and 3).

MODERATE HYPERGLYCEMIA (D50 BOLUS) STUDIES

Twenty-four rabbits were fasted for 16 h before placement of an aortic balloon catheter as described above. Immediately after induction of anesthesia, a catheter was placed in an ear vein and lactated Ringer' solution was infused at 6 ml·kg⁻¹·h⁻¹. Seventy-five minutes after discontinuation of the halothane anesthetic, the rabbits received intravenously, on a random basis, either 0.5 g·kg⁻¹ of a 50% dextrose solution (Travenol Laboratories, Deerfield, Illinois) or an equivalent volume of saline. Fifteen minutes thereafter, the aorta was occluded for 14 min. Approximately 2 min after deflation of the balloon, the lactated Ringer's infusion was discontinued and the animal was turned into the supine position for catheter removal.

Hemodynamic parameters (mean arterial pressure [MAP] and heart rate [HR]) were recorded and blood analysis for pH, Pa_{CO_2}, Pa_{O_2}, hematocrit, plasma glucose (glucose oxidase method), and plasma osmolality (freezing point depression) were performed before the 50% dextrose/saline bolus, again before aortic occlusion and 1 min after balloon deflation. Comparisons within groups were made by repeated measures analysis of variance. Where significant differences ($P < 0.05$) were identified, pairwise comparisons were performed with a Bonferronni corrected t test for paired data. Comparisons between groups were made with the use of t tests for unpaired data. To determine whether dextrose administration was associated with a worsened neurologic outcome, the neurologic scores recorded on day 3 were compared with the use of a rank-sum statistical technique (Mann-Whitney U-test).

MILD HYPERGLYCEMIA (D5W INFUSION) STUDIES

The strikingly poorer neurologic outcome (see "Results") of the animals that received a 50% dextrose bolus in the initial study prompted further investigation. This series of experiments was performed to examine the effect of a lesser increase in plasma glucose concentration while simultaneously avoiding the undefined influences of a bolus of hypertonic solution.

Twenty-four rabbits were fasted for 21 h before the study. The preparation was identical to that of the preceding series (aortic balloon catheter and peripheral intravenous catheter). At the conclusion of the preparation, halothane was discontinued. When spontaneous movement was noted, on a random basis, an intravenous infusion of either lactated Ringer's solution or 5% dextrose in water was started at a rate of 7 ml·kg⁻¹·h⁻¹. The infusion continued for 90 min (total dextrose dose: approximately 0.5 g·kg⁻¹), at which time the infusion was discontinued and the aorta was occluded for 12 min. The aortic catheter was removed approximately 2 min after deflation of the balloon. MAP and HR were recorded and blood analyses (plasma glucose, osmolality, arterial blood gases [ABGs], Hct, serum lactate) were performed at the end of the preparation, after 60 min of infusion, before aortic occlusion and 1 min after deflation of the aortic balloon.

The animals were observed for 3 days thereafter, and neurologic scoring was performed as described above, with one exception: during the course of our earlier investigations, it became apparent that the original neurologic scoring system failed to distinguish between gradations of neurologic deficit that were readily discernible. Accordingly, the neurologic scoring system was expanded from four grades to five to include a category (new #2) of animals having good lower-extremity strength yet still unable to walk or hop: 0 = paraplegic with no lower-extremity motor function. 1 = poor lower-extremity mo-

TABLE 1. Physiologic Variables Recorded before the Intravenous Administration of a Bolus of 50% Dextrose or Saline, before Aortic Occlusion and Immediately after Reestablishment of Aortic Flow

	Saline				Dextrose				
	Presaline	Preocclusion	Postocclusion	ANOVA	Predextrose	Preocclusion	Postocclusion	ANOVA	Saline Versus Dextrose
Gluc (mg·dl⁻¹)	160 ± 30	147 ± 27	156 ± 37	NS	137 ± 45	291 ± 82	207 ± 70	$P < 0.04*$	$P < 0.004\dagger$
MAP (mmHg)	97 ± 16	97 ± 17	83 ± 17	NS	94 ± 6	93 ± 9	96 ± 18	NS	NS
HR (beats·min⁻¹)	232 ± 28	237 ± 20	258 ± 27	NS	230 ± 40	226 ± 38	283 ± 24	$P < 0.03*$	NS
pH	$7.43 \pm .06$	$7.44 \pm .05$	$7.42 \pm .07$	NS	$7.46 \pm .05$	$7.48 \pm .05$	$7.47 \pm .05$	NS	NS
Pa_{CO_2} (mmHg)	31 ± 2	29 ± 3	23 ± 3	$P < 0.001*$	32 ± 7	27 ± 5	20 ± 6	$P < 0.002$	NS
Pa_{O_2} (mmHg)	86 ± 8	89 ± 11	95 ± 7	NS	85 ± 9	90 ± 5	97 ± 7	NS	NS
HCT (%)	40 ± 5	40 ± 5	42 ± 5	NS	39 ± 5	39 ± 3	41 ± 4	NS	NS
Osm (mOsm·l⁻¹)	293 ± 15	292 ± 16	295 ± 15	NS	289 ± 12	294 ± 14	297 ± 16	NS	NS

Gluc = plasma glucose; MAP = mean arterial pressure; HR = heart rate; Hct = hematocrit; Osm = plasma osmolality. All values are mean $\pm$ SD.

ANOVA = analysis of variance; NS = no significant difference. See text for further information regarding within-group differences.

* A significant $(P < 0.05)$ within-group difference by repeated measures analysis of variance.

† A significant difference between preocclusion plasma glucose values in the saline- and dextrose-treated groups (unpaired t test).

tor function—flicker of movement or weak antigravity movement only. 2 = some lower-extremity function with good antigravity strength but inability to draw legs under body and/or hop. 3 = ability to draw legs under body and hop but not normally. 4 = normal motor function.

The statistical analyses were performed as described above (repeated measures analyses of variance, t tests, Mann-Whitney U-test).

Results

THE MODEL

Our laboratory has performed this spinal cord ischemia technique on more than 200 occasions. There has never been a neurologic deficit that was apparent on the patient's emergence from anesthesia nor has a spontaneous deficit occurred before the time of elective aortic occlusion. With the balloon-tipped catheter placed as described above in rabbits of 2.8–3.5 kg, the cessation of pulsatile pressure in the aorta distal to the inflated infrarenal balloon catheter has invariably resulted in the onset of a flaccid paraplegia within 30 s.

In the present investigations, the comparisons of neurologic outcome have been based on day 3 neurologic scores. In the course of our use of this model, 58 animals with abnormal scores on day 3 have been observed for additional periods of 1–6 days. In five, the final neurologic score differed from that on day 3. The condition of two rabbits that were paraparetic and unable to walk deteriorated to complete paraplegia. Two paraparetic but walking animals lost the ability to walk but did not become completely paraplegic. One paraparetic nonwalking animal recovered the ability to walk. Ten animals that were normal on day 3 have also been observed for an additional 4 to 10 days. None has changed neurologic status.

OCCLUSION DURATION VERSUS NEUROLOGIC OUTCOME

The ED_{50}, *i.e.*, the duration of aortic occlusion that resulted in the inability to walk, was 13.73 ± 1.29 (SE) min. There were 10 deaths among the 50 animals before the end of the 3-day observation period, and the ED_{50} is based on the remaining 40 animals. The deaths generally occurred in the first 18 h (nine of 10) and occurred predominately in the animals that sustained longer occlusions (15–19 min—three animals; 20–25 min—seven animals). Premortem ABGs obtained in several of these animals revealed a profound metabolic acidosis and normoxemia. Limited postmortem examinations revealed no abnormalities of the abdominal aorta or its major branches.

MODERATE HYPERGLYCEMIA (D50 BOLUS) STUDIES

There were four deaths after occlusion. All occurred in animals that received dextrose. Two died within 3 h of deflation of the aortic balloon after episodes of intense myoclonus-like activity that began in the lower extremities and spread variably in a rostral direction. Two additional animals were killed to relieve apparent distress related to similar episodes. The abdominal aortas of all four animals were patent.

The hemodynamic and blood analysis data are presented in table 1. The preocclusion plasma glucose level was 291 ± 82 (SD) mg·dl⁻¹ in the animals that received the 50% dextrose bolus 15 min before spinal cord ischemia and 147 ± 27 mg·dl⁻¹ in the control group $(P < 0.005)$. In animals receiving dextrose, the plasma glucose level decreased significantly between the preocclusion and postocclusion determinations $(P < 0.005)$. There was no difference between the postocclusion plasma glucose concentration in the control rabbits and in those receiving dextrose.

TABLE 2. Physiologic Variables Recorded in Animals That Received a 90-Minute Infusion at $7\ ml \cdot kg^{-1} \cdot min^{-1}$ of Either Lactated Ringer's Solution or D5W before Temporary Aortic Occlusion

	Lactated Ringer's Solution					D5W				
	Postprep	60 Minutes	Preocclusion	Postocclusion	ANOVA	Postprep	60 Minutes	Preocclusion	Postocclusion	ANOVA
Gluc $(mg \cdot dl^{-1})$	167 ± 30	141 ± 15	137 ± 13	151 ± 19	$P < 0.006$	146 ± 35	$186 \pm 33*$	$177 \pm 38*$	148 ± 24	$P < 0.002$
MAP (mmHg)	82 ± 8	99 ± 13	99 ± 13	94 ± 21	$P < 0.003$	75 ± 5	98 ± 10	95 ± 8	85 ± 17	$P < 0.0002$
HR (beats $\cdot min^{-1}$)	276 ± 21	256 ± 35	260 ± 28	278 ± 27	NS	277 ± 28	266 ± 19	244 ± 31	292 ± 33	$P < 0.002$
pH	7.35 ± 0.08	7.39 ± 0.09	7.39 ± 0.09	7.39 ± 0.09	$P < 0.05$	7.37 ± 0.07	7.45 ± 0.06	7.45 ± 0.08	7.44 ± 0.08	$P < 0.0003$
Pa_{CO_2} (mmHg)	35 ± 6	27 ± 5	26 ± 5	22 ± 5	$P < 0.0002$	35 ± 2	28 ± 3	27 ± 3	22 ± 2	$P < 0.0002$
Pa_{O_2} (mmHg)	93 ± 8	91 ± 9	90 ± 8	97 ± 8	$P < 0.02$	88 ± 7	89 ± 6	84 ± 7	95 ± 5	$P < 0.0002$
Hct (%)	42 ± 3	40 ± 3	39 ± 3	41 ± 3	$P < 0.0003$	42 ± 3	40 ± 3	40 ± 3	41 ± 3	$P < 0.02$
Osm $(mOsm \cdot l^{-1})$	288 ± 3	283 ± 6	282 ± 3	285 ± 4	$P < 0.0002$	290 ± 4	285 ± 6	282 ± 6	285 ± 6	$P < 0.0002$

Data were recorded immediately after surgical preparation (Postprep), after 60 min of infusion (60 Minutes), after 90 min of infusion (preocclusion), and 1 min after reestablishing aortic flow (postocclusion).

Gluc = plasma glucose; MAP = mean arterial pressure; HR = heart rate; Hct = hematocrit; Osm = plasma osmolality. All values are mean

$\pm$ SD.

ANOVA = analysis of variance; NS = no significant difference. See text for further information regarding within-group differences.

* A significant $(P < 0.007)$ difference between the corresponding values in the lactated Ringer's- and D5W-treated groups.

Pa_{CO_2} was significantly less at the postocclusion determination $(P < 0.002)$ in both groups, reflecting a well-compensated metabolic acidosis. The Pa_{CO_2}s did not differ between groups.

Heart rate increased significantly $(P < 0.03)$ after occlusion in those receiving dextrose. This increase was not observed in the saline-treated animals, however, the postocclusion HRs did not differ significantly $(P = 0.08)$ between groups. MAP, pH, Pa_{CO_2}, hematocrit, and serum osmolality did not differ significantly within or between groups.

The neurologic status was significantly (Mann-Whitney test, $P < 0.025$) poorer on days 1, 2, and 3 in the animals that received dextrose. Four of 10 animals that received saline and 10 of 10 that received dextrose were unable to walk or hop.

MILD HYPERGLYCEMIA (D5W INFUSION) STUDIES

There were two deaths after occlusion. Both occurred in the first 12 h in animals that received lactated Ringer's solution. The abdominal aortas were patent at postmortem examination.

The hemodynamic and blood analysis data are presented in table 2. Plasma glucose concentration increased significantly in the animals that received D5W by infusion, and plasma glucose values were significantly greater $(P < 0.007)$ after 60 and 90 min of infusion than were the values in animals receiving lactated Ringer's solution.

In both groups (animals receiving D5W and animals receiving lactated Ringer's solution), MAP was significantly less at the immediate postpreparation determination (animals still lightly anesthetized) than at the subsequent measurement intervals. However, there were no between-group differences in MAP at any interval. HR

was significantly increased after deflation of the aortic balloon in animals receiving D5W. There were no other within- or between-group differences in HR.

In both groups, pH was significantly less and Pa_{CO_2} was significantly greater immediately after preparation than at subsequent measurement intervals. Pa_{CO_2} was significantly less after occlusion (reflecting respiratory compensation for a postdeocclusion metabolic acidosis) in both groups. There were no between-group differences for pH and Pa_{CO_2}. Pa_{O_2} increased significantly in both groups at the postocclusion determination (in concert with the reduction in Pa_{CO_2}). There were no intergroup differences in Pa_{O_2}. Hematocrit and serum osmolality decreased during the period of infusion in both groups. There were no differences between groups.

The final neurologic status was significantly poorer in animals that received D5W before spinal cord ischemia. Nine of the 10 animals that received D5W and three of 10 control animals were unable to walk or hop at the final evaluation (fig. 1). The median neurologic scores (range in parantheses) at the assessments performed at 2 h after deflation of the aortic balloon and on mornings 1, 2, and 3 thereafter were, respectively: for the animals that received lactated Ringer's solution: 3.5 (1–4), 3.5 (0–4), 3.5 (0–4), and 3.2 (0–4); and for those receiving D5W: 2.3 (1–4), 1.8 (0–4), 1.2 (0–4), and 1.2 (0–4). (0 = complete paraglegia; 4 = normal). These neurologic scores differed significantly (Mann-Whitney U-test, $P < 0.025$) on days 2 and 3.

To examine the relationship between preocclusion plasma glucose level and final neurologic deficit score, the Spearman rank correlation coefficient was calculated for the combined lactated Ringer's solution- and D5W-treated groups. There was no apparent correlation ($r_s = 0.334$).
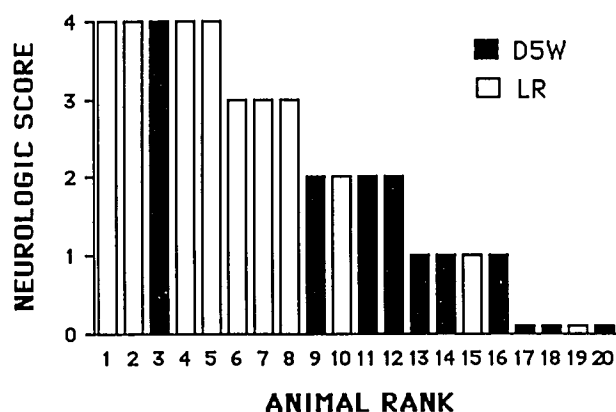
FIG. 1. Neurologic score 72 h after spinal cord ischemia for fasted rabbits that received either lactated Ringer's solution (LR) or 5% dextrose in water (D5W) at 7 ml·kg^{-1}·h^{-1} for 90 min before aortic occlusion; 4 = normal; 3 = can walk/hop but not normally; 2 = cannot walk/hop, but moderate strength; 1 = flicker of leg movement; 0 = complete paraplegia. Function was significantly poorer ($P < 0.025$) in animals that received D5W.

Discussion

A strong, though not undisputed, case[19-21] has been built that an increased plasma glucose level before an episode of cerebral ischemia results in a greater lactic acid accumulation during ischemia and poorer cellular recovery thereafter. The issue of whether this same phenomenon occurs in spinal cord has not been examined previously. Although the physiologic similarities between the brain and spinal cord are numerous, it is reasonable to wonder whether the impact of increased glucose availability would be apparent in the lesser metabolic rate environment of the spinal cord. The present data indicate that despite metabolic differences, increased glucose availability is deleterious and they suggest that the threshold for this effect is quite low in the rabbit. Specifically, the administration of sufficient D5W to result in a mean plasma glucose increase of approximately 40 mg·dl^{-1} at the time of temporary aortic occlusion resulted in a significantly poorer neurologic outcome. The plasma glucose levels achieved as a consequence of dextrose infusion in this study are well within ranges commonly seen after routine clinical administration of dextrose-containing solutions.[22,23]

We considered the possibility that factors other than the metabolic consequences of an increased plasma glucose level were responsible for the results. There were no between-group differences in osmolality, blood pressure, or hematocrit. However, no measurements were made during the period of ischemia or after catheter removal (which occurred immediately after reestablishment of aortic patency), and unrecognized variations of these or other variables may have occurred and contributed to

the final outcome. Hyperglycemia has been reported to cause reductions in cerebral blood flow (CBF) by unidentified mechanisms.[24] Accordingly, a decrease in spinal cord blood flow (SCBF) may have been a factor in determining neurologic outcome. However, the magnitude of the previously reported hyperglycemia-related changes in CBF was small (i.e., a decrease of CBF in rats of approximately 7% from control for each plasma glucose increment of 180 mg·dl^{-1}. Therefore, it seems likely that the changes in SCBF, if any, were small.

After, completion of the series in which hyperglycemia was produced by bolus administration of 0.5 g·kg^{-1} of D50, we wished to exclude the possibility that the initial neurologic observations were in some way an artifact of the method of dextrose administration. Specifically, the concern was that the adverse neurologic outcome was related to either 1) persistent vascular and/or rheologic effects of an osmotic transient caused by 50% dextrose, or 2) to the very high peak serum glucose levels (not measured) that were inevitably achieved immediately after D50 administration. The latter might conceivably result in a more substantial labile intracellular supply of glucose than would be inferred from a plasma glucose analysis made some minutes later. The second study sought to obviate these potential problems by administration of the same dextrose load over 90 min as a 5% solution. Despite lesser maximum measured plasma glucose levels, the adverse neurologic effect was again demonstrated.

There are limited data that suggest that hyperglycemia during reperfusion also contributes adversely to neurologic outcome.[25] Although hyperglycemia during reperfusion may have been a factor in the first series of studies (D50 bolus), in the final series (D5W infusion) the animals that received dextrose before aortic occlusion were normoglycemic with respect to control animals at the end of the period of aortic occlusion. Accordingly, we conclude that persistent hyperglycemia during the reperfusion period is not a necessary condition for the adverse influence of dextrose administration.

Although dextrose administration per se was clearly associated with a worsened neurologic outcome, there was no obvious correlation within individual treatment groups between preocclusion plasma glucose concentration and final neurologic score. This observation was unexpected. However, our review of the literature revealed that although numerous studies have demonstrated that neurologic, histologic, or biochemical outcome is poorer in animals treated with glucose before cerebral ischemia than in fasted controls, only two reports provide data regarding the correlation between plasma glucose level and the outcome of glucose-treated animals. Lanier et al.[2] found a good correlation between plasma glucose level and neurologic outcome after global cerebral ischemia (neck tourniquet) in monkeys. Nedergaard[4] measured infarct

volume after focal ischemia (temporary middle cerebral artery occlusion) in rats and his data reveal no apparent correlation between infarct volume and plasma glucose levels. The obvious difference between the study of Lanier *et al. versus* the present data and those of Nedergaard is that the former involved complete ischemia and in the latter two studies there was probably residual flow (*i.e.,* incomplete ischemia). However, it is not clear how this might account for the differences among these studies. The present observations and the data of Nedergaard raise the possibility that plasma glucose level may be an unreliable marker of the amount of intracellular glucose available for conversion to lactic acid. Alternatively, hyperglycemia *per se* may not be solely responsible for modifying neurologic outcome, but rather specific hormonal and/or metabolic consequences of hyperglycemia may be involved. For instance, it is possible that insulin is involved in the adverse effects of dextrose administration. In rats, hyperglycemia will cause a transient increase in net glucose uptake by the brain, but insulin is required for the net uptake of glucose to be sustained.[26] Measurements of serum insulin concentration were not performed in the present study.

We believe that the present model of spinal cord ischemia is relevant to human spinal cord ischemia. It probably produces incomplete rather than absolute ischemia.[18] The distinction between the two circumstances may be important because it has been suggested that incomplete ischemia may be the more deleterious because of the potential for continued substrate supply.[27] Values for SCBF have not been determined during human spinal cord ischemia occurring as a result of aortic occlusion or spinal distraction. However, the clinically recognized relevance of perfusion pressure in these situations suggests that there is at least the potential for some persistent flow.

After reperfusion an initial neurologic recovery was frequently followed by some deterioration. In the moderate and mild hyperglycemia studies there were 33 animals with abnormal final neurologic scores. Twenty-two of these had deteriorated before the final evaluation, with the best scores seen commonly at 2 h, or occasionally 1 day after occlusion. Delayed deterioration has been observed by others using this model[17,28] and it has been speculated that it is the result of a cascade of "secondary insult" processes[28-30] initiated by the original ischemic insult. In the present study this phenomenon was more evident in the animals that received dextrose. (The neurologic scores were not significantly different at the earlier postdeocclusion evaluations in either study.) The explanation for this phenomenon is obscure. However, it implies that the adverse effects of an increased plasma glucose level are not entirely realized immediately after a period of ischemia. Accordingly, it is possible that elucidation of the important secondary processes will allow

development of postischemic therapies that will attenuate the ultimate neurologic deficit.

Intraoperative spinal cord ischemia is a predictable risk of specific surgical procedures. Accordingly, an understanding of the factors that contribute to outcome after spinal cord ischemia, especially those factors that can be manipulated or controlled in the operating room, is relevant. The present investigations indicate that, in the rabbit, dextrose administration before an episode of temporary spinal cord ischemia can contribute to more severe neurologic sequelae. Further, the threshold for this effect may be reached with quantities of dextrose sufficient to produce a mean plasma glucose increase (*vs.* fasted control animals) of as little as 40 mg $\cdot$ dl^{-1}. There is no assurance that the present observations are relevant to human spinal cord ischemia. The extent to which the SCBF and metabolism characteristics of experimental animals approximate those of the human spinal cord are not well defined because of the difficulties inherent in studying the latter. However, the obvious cytoarchitectual similarity between human[31] and animal spinal cords[32,33] leads one to suspect some similarity of metabolic function. Therefore, in the absence of a cogent reason for administering dextrose during the intraoperative period, it would seem prudent to withold these solutions in most cases and to monitor plasma glucose levels during the intraoperative period to avoid hypoglycemia. Whereas witholding glucose to prevent plasma glucose increases may have some justification, there are no data to support a practice of decreasing blood sugar level (*e.g.,* by insulin administration) in the event that a spontaneous or iatrogenically increased plasma glucose level occurs during the intraoperative period. The question of how quickly neurologic risk is reduced when plasma glucose level is decreased by either endogenous or exogenous insulin has not been examined experimentally.

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