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Halothane anesthesia does not suppress sympathetic activation produced by neuroglucopenia

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HAVEL, PETER J., DAVID E. FLATNESS, JEFFREY B. HALTER, JAMES D. BEST, RICHARD C. VEITH, AND GERALD J. TABORSKY, JR. *Halothane anesthesia does not suppress sympathetic activation produced by neuroglucopenia.* Am. J. Physiol. 252 (Endocrinol. Metab. 15): E667–E672, 1987.—To determine the suitability of halothane anesthesia for studies of sympathetic control of the endocrine pancreas in dogs, we assessed the effect of halothane anesthesia (0.8% inspired concentration) on the sympathetic response to central neuroglucopenia. In dogs anesthetized with halothane, intravenous administration of the neuroglucopenic agent, 2-deoxy-D-glucose (2-DG; 100 mg/kg), produced increases of both systemic plasma epinephrine (EPI; $\Delta = 269 \pm 86$ pg/ml, $P < 0.025$) and norepinephrine (NE; $\Delta = 157 \pm 55$ pg/ml, $P < 0.025$) equivalent to those previously observed in conscious dogs. Measurement of plasma NE kinetics revealed that the plasma NE response to 2-DG during halothane was due to an increase in the rate of NE appearance that was identical to that of conscious dogs, rather than to an impairment of NE clearance. In contrast, 2-DG at this dose did not increase plasma EPI or NE levels in dogs anesthetized with pentobarbital sodium (30 mg/kg). Plasma glucose increased modestly after 2-DG (100 mg/kg) in both conscious and halothane-anesthetized dogs but not in the pentobarbital-anesthetized dogs. Although 2-DG at a threefold higher dose (300 mg/kg) caused plasma EPI, NE, and glucose ($\Delta = 12 \pm 3$ mg/dl, $P < 0.001$) to increase in pentobarbital-anesthetized dogs, the responses to this higher dose of 2-DG were all significantly larger in halothane-anesthetized dogs (Δ of plasma glucose = 30 ± 8 mg/dl, $P < 0.005$; $P < 0.0025$ vs. pentobarbital). The catecholamine data demonstrate that halothane is a more suitable anesthetic than pentobarbital for use in experiments studying reflex neuroglucopenic activation of the sympathetic nervous system. The glucose data suggest that certain metabolic responses secondary to sympathetic activation are also preserved in halothane-anesthetized animals.

epinephrine; norepinephrine; norepinephrine kinetics; pentobarbital sodium, plasma glucose; 2-deoxy-D-glucose; dog

WE HAVE RECENTLY DEMONSTRATED that pentobarbital sodium suppresses the plasma epinephrine (EPI), norepinephrine (NE), and glucose responses to the neuroglucopenic agent, 2-deoxy-D-glucose (2-DG) (23). Pentobarbital also suppresses other central reflexes (7, 24, 25) and in addition inhibits axonal conduction (14) and transmission across peripheral autonomic ganglia (10, 21). Such suppression could abolish or obscure the potential contribution of the sympathetic nervous system to the pancreatic endocrine and metabolic responses to autonomic activation that would normally occur in the conscious animal.

The demonstration that halothane is less suppressive than pentobarbital on certain cardiovascular reflexes (6) and on a pancreatic parasympathetic reflex, the pancreatic polypeptide response to neuroglucopenia (11), led us to evaluate the effect of halothane on the sympathetic responses to neuroglucopenia.

To test whether halothane anesthesia is less suppressive than pentobarbital on the sympathetic and metabolic response to neuroglucopenia, we measured the changes of systemic plasma EPI, NE, and glucose levels after the administration of the neuroglucopenic agent, 2-DG, in dogs anesthetized with 0.8% inspired halothane. These responses were then compared with those responses previously measured in both conscious and pentobarbital-anesthetized dogs (23). To verify that the plasma NE response to 2-DG in halothane-anesthetized dogs was due solely to increased NE release, rather than to a reduction of plasma NE clearance, we measured plasma NE kinetics before and during neuroglucopenia in halothane-anesthetized and conscious dogs.

MATERIALS AND METHODS

Animals and surgical procedures. Sixteen dogs of mixed breed weighing from 29 to 42 kg were used in the experiments with halothane anesthesia. Eight other conscious dogs were used in the NE kinetic experiments. Catheters were chronically implanted in the thoracic aorta of these dogs (11). All animals were fasted overnight (18 h) before the experiments were started.

Protocols. To determine the effects of halothane anesthesia on reflex activation of the sympathetic nervous system produced by 2-DG, dogs bearing previously implanted catheters were anesthetized with halothane. An ultrashort-acting barbiturate, thiamylal sodium (18 mg/kg, Surital, Parke, Davis), was used for induction. Then an endotracheal tube was inserted and the animal was ventilated with an air-driver respirator connected to a vaporizer (Draeger, FRG) supplying halothane (0.8%

inspired concentration) in oxygen. At least 45 min was allowed for the short-acting barbiturate to be redistributed and for stable halothane anesthesia to be achieved. As in the previously reported experiments in conscious and pentobarbital-anesthetized dogs, the 2-DG was administered as a bolus of either 100 or 300 mg/kg into the cephalic (foreleg) vein and flushed in rapidly with saline. Blood samples were drawn from the implanted catheter at 0 min before and at 5, 15, 30, 45, 50, and 60 min after the 2-DG injection. In selected experiments, tritiated NE ([^{3}H]NE) was infused to determine the rate of NE appearance in and clearance from plasma. In these experiments a bolus of 30 μCi of [^{3}H]NE was administered intravenously into the cephalic vein followed by an infusion of 2 μCi/min. The infusion was run for 30 min to achieve a steady state; then samples were drawn from the aortic catheter at −15, −10, −5, and 0 min before and at 5, 15, 30, 35, 40, and 45 min after the 2-DG injection.

Assays and data analysis. Blood samples for glucose determination were drawn and put into tubes containing EDTA. Blood samples for catecholamine measurement were drawn and put into tubes containing EGTA and glutathione. All blood samples were centrifuged at 4°C and frozen at −20°C until assayed. Plasma glucose was measured by the glucose-oxidase method using a Technicon AutoAnalyzer (Technicon Instruments, San Francisco, CA). This method measures 2-DG in plasma with 35% cross-reactivity relative to glucose. Plasma 2-DG concentrations after the injection of 100 and 300 mg/kg into dogs have been previously determined (24). To calculate the plasma glucose response to the sympathetic activation induced by 2-DG, the measured values in plasma (glucose + 0.35 2-DG) were corrected by subtracting 35% of the previously measured average value of 2-DG in plasma.

Plasma epinephrine and norepinephrine were measured in duplicate using a highly specific and sensitive single-isotope radioenzymatic method (9). The intra- and interassay coefficients of variation for the plasma catecholamine assay in this laboratory are 9 and 12%, respectively.

The concentration of plasma [^{3}H]NE, required for the calculation of specific activity, was determined by liquid scintillation counting of radiolabeled NE after extraction of the plasma with alumina to remove all NE metabolites. Because the [^{3}H]NE infusion rate is constant and known and the specific activity of [^{3}H]NE can be measured, the endogenous plasma norepinephrine appearance rate can be calculated as follows

$$\text{NE appearance} = [^3\text{H}]\text{NE infusion rate} \times \frac{[\text{NE}]}{[[^3\text{H}]\text{NE}]}$$

This formula is valid only at steady state, i.e., when the [^{3}H]NE infusion rate, the [NE] and the [[^{3}H]NE] are constant. At steady state, the NE clearance rate can be calculated by dividing the plasma NE removal rate (equal to the appearance rate) by the plasma NE concentration (4)

$$\text{NE clearance} = \frac{\text{NE removal (appearance)}}{[\text{NE}]}$$

The change of plasma concentrations of glucose were calculated by subtracting the 0-min value from the corrected 60-min peak value after the injection of 2-DG. The changes of plasma concentrations of EPI and the changes of plasma NE in the experiments with the 100 and 300 mg/kg doses of 2-DG were calculated by subtracting the 0-min value from the 30-min value following 2-DG. The changes of NE appearance rate were calculated by subtracting the mean of the −15-, −10-, −5-, and 0-min values from that of the 30-min value after 2-DG. The 5- and 15-min values were not used for this calculation because [NE] was not constant.

The data reported in the results are means ± SE. Statistical comparisons of means within a group were made with a paired t test; statistical comparisons of means of different groups were made with a two-sampled t test. Dunnett's test was used for multiple comparison between more than two groups.

RESULTS

Plasma EPI, NE, plasma glucose, and NE kinetic responses to 2-DG (100 mg/kg) in halothane-anesthetized dogs. Base-line plasma NE averaged 161 ± 28 pg/ml in halothane-anesthetized dogs, increased to 318 ± 63 pg/ml 30 min after 2-DG (Δ = 157 ± 55 pg/ml, $P < 0.025$), and remained elevated for the next 0.5 h (Fig. 1). These data are compared in Table 1 to the previously reported responses in pentobarbital-anesthetized and conscious dogs (23). The NE response to 2-DG was identical to that of conscious dogs and significantly larger than that of pentobarbital-anesthetized dogs ($P < 0.05$; Fig. 1).

Base-line NE appearance in halothane-anesthetized dogs was 7 ± 1 ng·kg^{-1}·min^{-1}. Base-line NE appearance was somewhat higher in conscious dogs, 13 ± 1 ng·kg^{-1}·

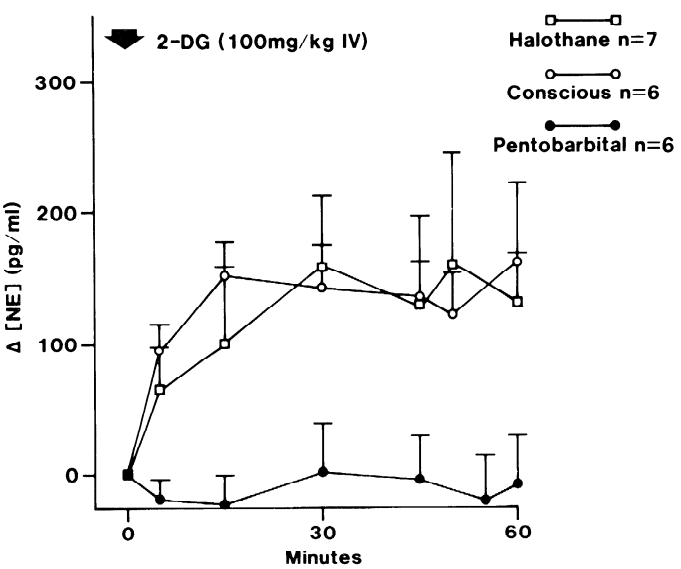

FIG. 1. Change of plasma norepinephrine (NE) in response to 2-deoxy-D-glucose (2-DG; 100 mg/kg) in 7 dogs anesthetized with halothane (0.8%), in 6 dogs anesthetized with pentobarbital (30 mg/kg), and in 6 unanesthetized dogs.

TABLE 1. *Basal and 2-DG-stimulated NE, EPI, and glucose levels in halothane-anesthetized, conscious, and pentobarbital-anesthetized dogs*

Anesthesia	2-DG (100)			2-DG (300)	
	Halo ($n = 7$)	Pento* ($n = 6$)	Cons* ($n = 6$)	Halo ($n = 6$)	Pento* ($n = 14$)
Basal [NE], pg/ml	161±28	118±41	138±18	63±22	166±38
Δ [NE], pg/ml	157±55	3±37†	143±28	262±33	126±28‡
Basal EPI, pg/ml	55±21	46±12	128±51	17±8	35±8
Δ [EPI], pg/ml	269±86	5±9†	145±58	707±212	161±34‡
Basal glucose, mg/dl	96±6	107±3	107±3	103±4	111±2
Δ Glucose, mg/dl	19±6	4±3†	13±4	30±8	12±3§

Values are means ± SE. 2-DG, 2-deoxy-D-glucose; NE, norepinephrine; EPI, epinephrine; Halo, halothane (0.8%); Pento, pentobarbital (30 mg/kg); Cons, conscious, no anesthesia. * Previously published data included for the purpose of comparison with halothane data. † $P < 0.05$ vs. halothane; ‡ $P < 0.0005$ vs. halothane; § $P < .0025$ vs. halothane.

TABLE 2. *Plasma NE kinetics in halothane-anesthetized, conscious, and pentobarbital-anesthetized dogs*

	Halo ($n = 6$)	Cons ($n = 8$)	Pento* ($n = 6$)
Basal NE appearance, $ng \cdot kg^{-1} \cdot min^{-1}$	7±1	13±1†	2±1‡
2-DG-stimulated NE appearance, $ng \cdot kg^{-1} \cdot min^{-1}$	17±15	24±3	NM
Δ at 30 min, $ng \cdot kg^{-1} \cdot min^{-1}$	10±4	11±2	NM
Basal NE clearance, $ml \cdot kg^{-1} \cdot min^{-1}$	46±3	70±2§	16±6§
Clearance during 2-DG, $ml \cdot kg^{-1} \cdot min^{-1}$	52±4	76±5§	NM

Values are means ± SE. NE, norepinephrine; 2-DG, 2-deoxy-D-glucose; Halo, halothane anesthesia (0.8%); Pento, pentobarbital anesthesia (30 mg/kg); Cons, conscious, no anesthesia; NM, not measured. * Previously published data included for the purpose of comparison. † $P < 0.025$ vs. halothane; ‡ $P < 0.001$ vs. halothane; § $P < 0.0025$ vs. halothane.

min^{-1} ($P < 0.025$ vs. halothane) but was markedly lower in pentobarbital-anesthetized dogs (4), 2 ± 1 $ng \cdot kg^{-1} \cdot min^{-1}$ ($P < 0.001$ vs. halothane). Thirty minutes after 2-DG, NE appearance in halothane-anesthetized dogs increased to 17 ± 5 $ng \cdot kg^{-1} \cdot min^{-1}$ (Δ = 10 ± 4 $ng \cdot kg^{-1} \cdot min^{-1}$; $P < 0.05$). In conscious dogs, 2-DG caused NE appearance to increase to 24 ± 3 $ng \cdot kg^{-1} \cdot min^{-1}$ (Δ = 11 ± 2 $ng \cdot kg^{-1} \cdot min^{-1}$; $P < 0.0005$). This increment was indentical to that measured in the halothane-anesthetized dogs (Table 2). NE appearance after 2-DG was not measured in pentobarbital-anesthetized dogs. NE clearance in halothane-anesthetized dogs was 46 ± 3 $ml \cdot kg^{-1} \cdot min^{-1}$ before and 52 ± 4 $ml \cdot kg^{-1} \cdot min^{-1}$ after 2-DG. In conscious dogs NE clearance was greater, both before, 70 ± 2 $ml \cdot kg^{-1} \cdot min^{-1}$, and after 2-DG, 76 ± 5 $ml \cdot kg^{-1} \cdot min^{-1}$ (both $P < 0.0025$ vs. halothane) (Table 2). We have previously demonstrated that pentobarbital decreased basal NE clearance to 16 ± 6 $ml \cdot kg^{-1} \cdot min^{-1}$ ($P < 0.0025$ vs. halothane) (4). NE clearance was not measured in pentobarbital-anesthetized dogs receiving 2-DG.

In dogs anesthetized with halothane, base-line EPI averaged 55 ± 21 pg/ml. EPI increased to 324 ± 102 pg/ml by 30 min after the injection of 100 mg/kg of 2-DG (Δ = 269 ± 86 pg/ml, $P < 0.025$); EPI remained elevated during the next 0.5 h. Compared with the previously reported data (Table 1) obtained from pentobarbital-anesthetized and conscious dogs (23), the EPI response to 2-DG in halothane-anesthetized dogs was significantly greater than in pentobarbital-anesthetized dogs ($P < 0.05$) and not significantly different from that in conscious dogs (Fig. 2).

Basal plasma glucose in halothane-anesthetized dogs was 96 ± 6 mg/dl and increased to 115 ± 4 mg/dl 60 min after 2-DG (Δ = 19 ± 6 mg/dl, $P < 0.01$). These data are compared in Table 1 with the previously reported glucose responses of conscious and pentobarbital-anesthetized dogs. The plasma glucose response to 2-DG in halothane-anesthetized dogs was significantly greater than that of pentobarbital-anesthetized dogs ($P < 0.05$; Fig. 3).

Plasma EPI, NE, and glucose responses to 2-DG (300 mg/kg) in halothane-anesthetized dogs. In dogs anesthetized with halothane, plasma NE averaged 63 ± 22 pg/ml and increased to 325 ± 22 pg/ml 30 min after the injection of 300 mg/kg 2-DG. This response (Δ = 262 ± 33 pg/ml, $P < 0.0005$) was significantly larger than that

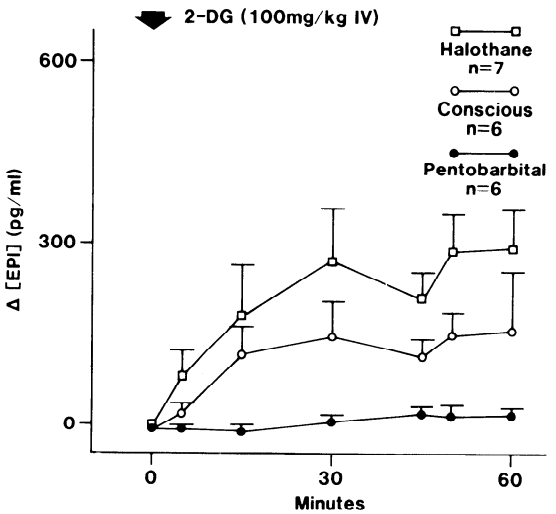

FIG. 2. Change of plasma epinephrine (EPI) in response to 2-deoxy-D-glucose (2-DG; 100 mg/kg) in 7 dogs anesthetized with halothane (0.8%), in 6 dogs anesthetized with pentobarbital (30 mg/kg), and in 6 unanesthetized dogs.

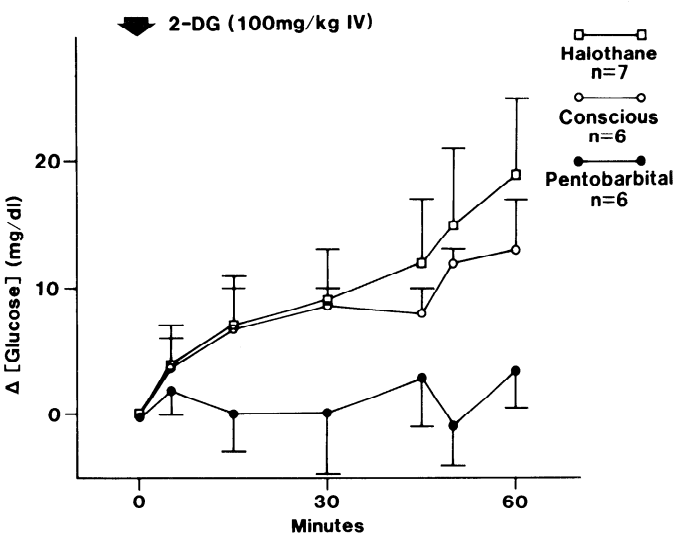

FIG. 3. Change of plasma glucose in response to 2-deoxy-D-glucose (2-DG; 100 mg/kg) in 7 dogs anesthetized with halothane (0.8%), in 6 dogs anesthetized with pentobarbital (30 mg/kg), and in 6 unanesthetized dogs.

in the dogs anesthetized with pentobarbital ($P < 0.005$; Fig. 4; Table 1). Plasma EPI increased from 17 ± 8 pg/ml to 723 ± 206 pg/ml 30 min after injection of 300 mg/kg 2-DG into halothane-anesthetized dogs. This response ($\Delta = 707 \pm 212$, $P < 0.025$) was significantly larger than the EPI response to 300 mg/kg of 2-DG in pentobarbital-anesthetized dogs ($P < 0.0005$ (Fig. 5; Table 1. In halothane-anesthetized dogs, base-line plasma glucose averaged 103 ± 4 mg/dl and increased to 133 ± 10 mg/dl, 60 min after 2-DG ($\Delta = 30 \pm 8$ mg/dl, $P < 0.005$). This glucose response was significantly larger than that in pentobarbital-anesthetized dogs ($P < 0.0025$; Fig. 6; Table 1). In conscious dogs, 2-DG at a dose of 300 mg/kg caused convulsions that were quickly terminated by pentobarbital injection. Therefore, the comparable data from conscious dogs are not available.

The mean changes of plasma glucose in the five groups of dogs administered 2-DG (100 mg/kg or 300 mg/kg) correlated with the mean plasma NE and EPI responses ($r = 0.97$, $P < 0.005$, and $r = 0.97$, $P < 0.005$, respectively, $n = 5$).

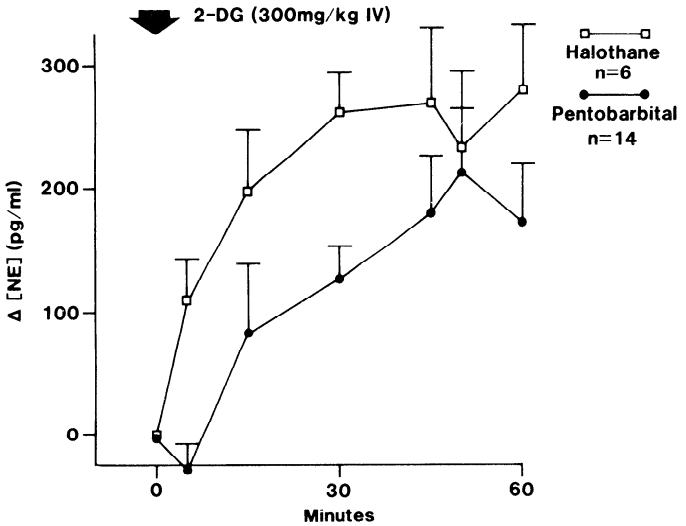

FIG. 4. Change of plasma norepinephrine (NE) in response to 2-deoxy-D-glucose (2-DG; 300 mg/kg) in 6 dogs anesthetized with halothane (0.8%) and in 14 dogs anesthetized with pentobarbital (30 mg/kg).

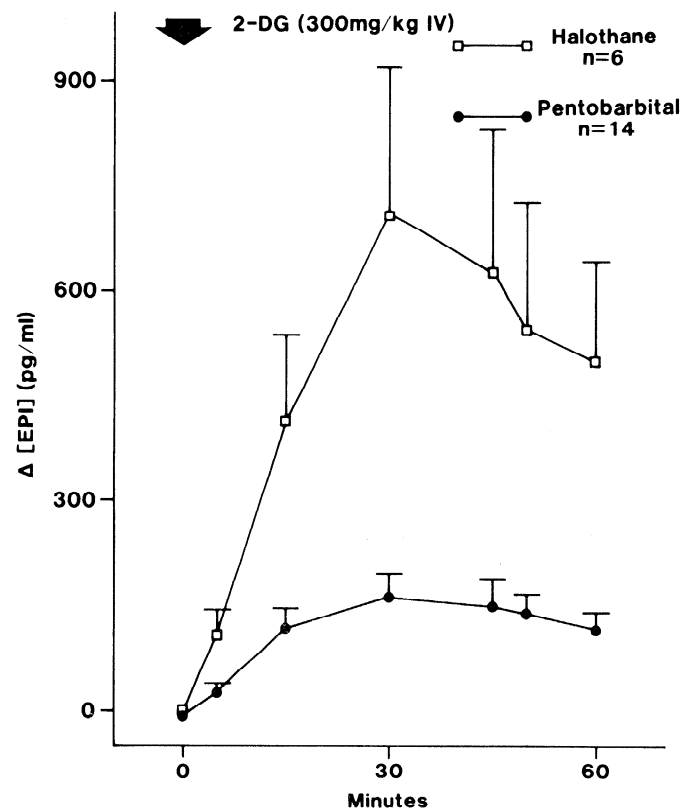

FIG. 5. Change of plasma epinephrine (EPI) in response to 2-deoxy-D-glucose (2-DG; 300 mg/kg) in 6 dogs anesthetized with halothane (0.8%) and in 14 dogs anesthetized with pentobarbital (30 mg/kg).

DISCUSSION

The present studies were designed to determine whether halothane anesthesia suppresses the adrenergic activation induced by central neuroglucopenia. Finding an anesthetic that does not suppress autonomic reflexes is of critical importance for studies of reflex neural control of pancreatic islet function, because many such studies require acute surgical access to the superior pancreatic vein. For example, the sampling of pancreatic venous blood is necessary for the measurement of pancreatic somatostatin output, because neither portal venous nor peripheral somatostatin levels are indices of pancreatic somatostatin secretion (22).

We chose to evaluate halothane anesthesia, because it has been shown to be less inhibitory than other anesthetics on certain cardiovascular reflexes (6) and because we have demonstrated that low levels of halothane anesthesia (0.8% inspired) allow parasympathetic responses to neuroglucopenia that are equivalent to those observed in conscious dogs (11). This dose of halothane would usually be considered inadequate to produce surgical anesthesia in dogs (17), but the use of thiamylal sodium for the induction anesthesia lowers the minimum alveolar concentration value for halothane (8) and enables an inspired concentration of 0.8% to produce surgical anesthesia in over 90% of the dogs we have studied.

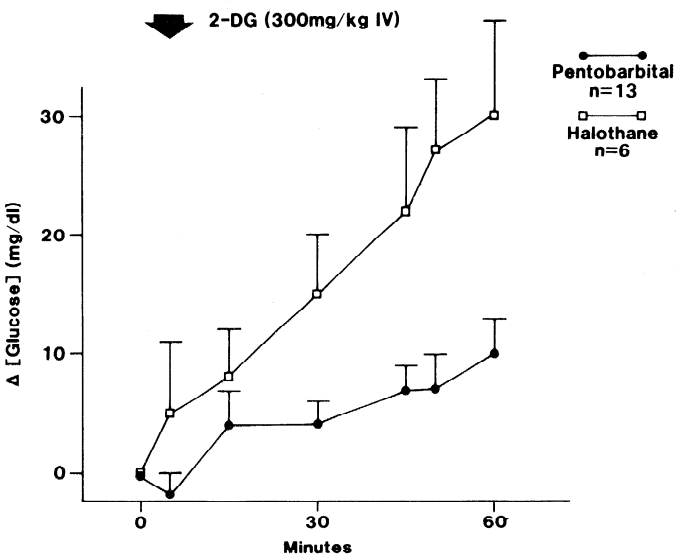

FIG. 6. Change of plasma glucose in response to 2-deoxy-D-glucose (2-DG; 300 mg/kg) in 6 dogs anesthetized with halothane (0.8%) and in 13 dogs anesthetized with pentobarbital (30 mg/kg).

The first set of studies demonstrated that halothane anesthesia allows a modest plasma norepinephrine response to 100 mg/kg of 2-DG that is equivalent to the response observed in conscious dogs (23). To verify that the plasma NE response to 2-DG in halothane-anesthetized dogs was due solely to increased NE release, rather than to a reduction of plasma NE clearance, we compared plasma NE kinetics before and during neuroglucopenia in halothane-anesthetized and conscious dogs by the isotope-dilution technique. For the measurement and calculation of NE kinetics to be valid, it is necessary to have reached a steady state. In this study, from 30 to 45 min after the injection at 2-DG, all of the components used to calculate NE appearance and clearance (see MATERIALS AND METHODS) had reached a plateau and remained constant, thus the required steady state was achieved. Although both base-line NE clearance and the base-line NE appearance rate were somewhat lower in the halothane-anesthetized animals, the increment of the NE appearance rate after 2-DG in halothane-anesthetized dogs was identical to that of the conscious dogs. Thus, the plasma NE response to 2-DG in halothane-anesthetized dogs does reflect an increase of noradrenergic outflow equivalent to that observed in unanesthetized animals. Likewise, the EPI response to 100 mg/kg of 2-DG was not significantly different from that of normal conscious dogs (23). Thus, the adrenomedullary response to neuroglucopenic stress, like the systemic noradrenergic response, is not suppressed by this level of halothane.

Halothane is much less suppressive on autonomic activity than pentobarbital, the anesthetic most commonly used in animal experimentation. For example, both the norepinephrine and epinephrine responses to 2-DG (100 mg/kg), which were preserved under halothane, were absent under pentobarbital anesthesia (30 mg/kg) (23). When a threefold higher dose of 2-DG (300 mg/kg) was administered to pentobarbital-anesthetized dogs, modest norepinephrine and epinephrine responses did occur, yet both NE and EPI responses were significantly larger when this same dose of 2-DG was administered to halothane-anesthetized dogs. Thus, even when the stimulus was increased to allow an adrenergic response to neuroglucopenia in pentobarbital-anesthetized animals, this anesthesia was still clearly suppressive relative to halothane.

Other data also suggest that pentobarbital inhibits neurally mediated events. Certain cardiovascular reflexes, with both sympathetic and parasympathetic components, are impaired in pentobarbital-anesthetized animals (6, 7). More direct measurements demonstrate that pentobarbital anesthesia suppresses the plasma catecholamine responses to hemorrhage (25) and the pancreatic polypeptide response to 2-DG (24). The former is a sympathetically mediated reflex response to hypotension; the latter is a parasympathetically mediated reflex response to central neuroglucopenia (12, 24).

The mechanisms by which pentobarbital suppresses and halothane fails to suppress these autonomic reflexes is not known. However, pentobarbital is known to depress central synaptic transmission (18), and presumably halothane has a similar effect related to its ability to produce central anesthesia. Thus, perhaps the "higher" areas of the central nervous system are equally suppressed by halothane and pentobarbital, allowing both to produce anesthesia, but the "lower" brain areas responsible for autonomic reflexes may be less susceptible to halothane at the dose used for these studies. Pentobarbital has also been demonstrated to block transmission across peripheral parasympathetic and sympathetic synapses (10, 21) as well as to inhibit axonal conduction (14).We have previously demonstrated that halothane (0.8%) is less suppressive than pentobarbital (30 mg/kg) on peripheral parasympathetic neurotransmission (11). Therefore, it is probable that both central and peripheral neural communications are less suppressed by halothane anesthesia.

Although the data presented here indicate that halothane is superior to pentobarbital for the preservation of sympathetic responses, other studies of the effect of halothane show progressive suppression of cardiovascular reflexes in proportion to the concentration of halothane administered (3). It is therefore important to recognize that the difference between halothane and pentobarbital may be less marked at a higher concentration of halothane.

In these studies, we also measured the plasma glucose response to neuroglucopenia as one possible index of the metabolic effects of the catecholamines released by stress. The glucose response to 100 mg/kg of 2-DG in halothane-anesthetized dogs, like the plasma catecholamine response, was equivalent to that of conscious dogs; pentobarbital anesthesia abolished both responses (23). However, when the stimulus was increased to 300 mg/kg of 2-DG, there was a modest plasma glucose response in the pentobarbital-anesthetized dogs (23). However, this response, like the plasma catecholamine response, was significantly smaller than that observed during halothane anesthesia. Indeed, the plasma glucose response was largest when 300 mg/kg of 2-DG was given to halothane-anesthetized dogs, an experiment that also produced the largest catecholamine responses. The close correlations between changes of plasma glucose and plasma catecholamines suggest that these moderate adrenergic activations are responsible for the plasma glucose response. Indeed, circulating catecholamines can produce these effects because infusions of either NE or EPI increase plasma glucose (16, 20). Alternatively, locally released NE may be responsible for the plasma glucose response, because electrical stimulation of the adrenergic nerves to the liver increases plasma glucose levels (18). Finally, the effect of more severe neuroglucopenic stress on plasma glucose can be indirect (2), because marked sympathetic activation can inhibit insulin (1, 15) and stimulate glucagon (1, 13), which in turn would stimulate hepatic glucose production (5). Thus, it is likely that the adrenergic response to 2-DG causes the plasma glucose response, however, the demonstration that halothane allows the plasma glucose response to 2-DG does not rule out a possible suppressive effect of halothane on other metabolic responses to neuroglucopenic stress.

In summary, the plasma NE level, the NE appearance,

EPI, and glucose responses to 100 mg/kg of 2-DG in halothane-anesthetized dogs were indistinguishable from those of unanesthetized dogs, whereas in pentobarbital-anesthetized dogs, plasma NE, EPI, and glucose responses were abolished. A threefold larger dose of 2-DG did produce plasma NE, EPI, and glucose responses in pentobarbital-anesthetized dogs, but in halothane-anesthetized dogs all of these responses were significantly larger. Thus, halothane anesthesia is much less suppressive than pentobarbital anesthesia and is therefore the preferred anesthesia for studying the adrenergic response to neuroglucopenic stress and at least one metabolic consequence of that response.

The authors thank Rix Kuester for surgical assistance. We also thank David Federighi and Susan Soper for assistance with the assays and Louise Parry for secretarial assistance with the manuscript.

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None of the data from the experiments with halothane anesthesia or the norepinephrine plasma kinetic data in conscious dogs have been presented before, even in abstract form. Some data from experiments in pentobarbital-anesthetized or conscious dogs in Table 1 and in Figs. 1–6, which are included for purposes of comparison with the halothane data, have been published in *Am. J. Physiol.* 247 (*Regulatory Integrative Comp. Physiol.* 16): R905–R910, 1986. The norepinephrine kinetic data in pentobarbital-anesthetized dogs in Table 2 have been published in *Endocrinology* 115: 853–857, 1984.

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