Intestinal Circulation during Inhalation Anesthesia

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This study was designed to evaluate the influence of inhalational agents on the intestinal circulation in an isolated loop preparation. Sixty dogs were studied, using three intestinal segments from each dog. Selected intestinal segments were pumped with aortic blood at a constant pressure of 100 mmHg. A mixture of 86Rb and 9-μm spheres labeled with 111Ce was injected into the arterial cannula supplying the intestinal loop, while mesenteric venous blood was collected for activity counting. A very strong and significant correlation was found between rubidium clearance and microsphere entrapment ($r = 0.97, P < 0.0001$), suggesting that the shunting of 9-μm spheres through the intestines reflects the arteriovenous shunting of blood. Nitrous oxide anesthesia was accompanied by a higher vascular resistance (VR), lower flow (F), rubidium clearance (CI-Rb), and microspheres entrapment (CI-Sph) than pentobarbital anesthesia, indicating that the vascular bed in the intestinal segment was constricted and flow (total and nutritive) decreased. Halothane, enfurane, and isoflurane anesthesia were accompanied by a much lower arteriovenous oxygen content difference (AVDO₂) and oxygen uptake than pentobarbital or nitrous oxide. Compared with pentobarbital, enfurane anesthesia was not accompanied by marked differences in VR, F, CI-Rb, and CI-Sph; halothane at 2 MAC decreased VR and increased F and CI-Rb while isoflurane increased VR and decreased F. α-Adrenoceptor blockade with phentolamine (1 mg·kg⁻¹) abolished isoflurane-induced vasoconstriction, suggesting that the increase in VR was mediated via circulating catecholamines. Decreases in mesenteric blood flow, which always have been observed during inhalation anesthesia, primarily are caused by the indirect effects of anesthetics mediated through changes in systemic circulation and the central nervous system. Key words: Anesthetics, gases; nitrous oxide. Anesthetics, volatile: enfurane; halothane; isoflurane. Gastrointestinal tract: intestines, blood flow, metabolism. Measurement techniques: blood flow, microspheres.

The circulatory response to inhalation anesthesia has been studied extensively and involves a decrease in blood pressure and cardiac output.¹ Regional blood flow is regulated by many factors (local, nervous, and humoral) influencing the circulation directly and indirectly.² Changes in regional blood flow during inhalation anesthesia can be mediated through central mechanisms, which may depend on a reduction in cardiac output and changes in vascular tone, due to changes in various humoral substances such as epinephrine, histamine, se-

rerotin, and many others. Finally, these alterations may be induced by a direct influence of an anesthetic on one or another area of the peripheral circulation. The splanchnic circulation may play an important role in alterations and maintenance of homeostasis during anesthesia.³ It has been shown that all inhalational anesthetics decrease blood flow through the gut.⁴–¹¹ A reduction in splanchnic blood flow is associated with a decrease in cardiac output.⁶,¹²,¹³ Therefore, it is not clear as to what extent the observed decrease in splanchnic blood flow depends on a decrease in cardiac output (and/or a reduction in blood pressure), a decrease in metabolism and oxygen requirements with a subsequent decrease in blood flow, or a direct influence of anesthetics on the regional circulation. This study was designed to evaluate the influence of inhalational anesthetics on the intestinal circulation in an isolated loop preparation, allowing determination of the direct and hormonal effects of anesthetics on the peripheral circulation. Another objective of the present study was to compare the clearance of rubidium with the entrapment of 9-μm spheres during inhalation anesthesia in order to verify whether entrapment of 9-μm spheres still would reflect nutritive blood flow under the effects of inhalational anesthetics as it did under different pathophysiological conditions during pentobarbital anesthesia.¹⁴

Methods

Experiments were performed on 60 mongrel dogs of either sex, weighing 15–20 kg. Thirty-one dogs (control group) were anesthetized with intravenous pentobarbital sodium 30 mg·kg⁻¹ initially and supplemented as required. The remaining 29 animals (experimental groups) were anesthetized with methohexitol sodium, 4 mg·kg⁻¹. Muscle relaxation was achieved with pancuronium, 0.1 mg·kg⁻¹. Controlled ventilation, adjusted to maintain arterial CO₂ tension at 35–40 mmHg, was provided with an Air Shield® ventilator through an endotracheal tube in all of the animals. Femoral arteries and veins were exposed and cannulated; 100 ml of blood was collected and replaced with 550 ml of Ringer’s lactated solution. This blood was used during the experiment to replace blood taken for analyses. Ringer’s lactated solution was infused through the left femoral vein at a constant rate of 15 ml·kg⁻¹·h⁻¹.
A laparotomy was performed and a segment of the small intestine, supplied by a vascular arcade arising from a single mesenteric artery and vein, was selected. The method of the isolated loop preparation has been described previously. Short segments of the mesenteric artery and vein were dissected free of the mesentry. Heparin, 5 mg·kg⁻¹ iv, was administered. The mesenteric vein was transected and cannulated with polyethylene tubing of appropriate size. Blood from the mesenteric vein was collected in a reservoir placed at the level of the mesenteric vein to achieve a mesenteric venous pressure of 0 mmHg. This blood was pumped back into the dog through a femoral vein. When the venous drainage was established, the artery was transected and cannulated, and arterial blood was pumped from the aorta through the chosen intestinal segment (using a Holter precision roller pump) at a constant pressure of 100 mmHg. The isolated loop with cannulated vessels was completely separated from the animals' body and placed between saline-soaked gauzes and plastic wrap and temperature maintained at 37–38° C with an electrical pad.

Aortic pressure (via a femoral artery cannula) and perfusion pressure (pressure in arterial limb between pump and the intestinal segment) were recorded with Statham® transducers and a Grass® polygraph.

After 30 min of stable perfusion and mean arterial pressures, arterial and mesenteric venous blood samples were taken for pH and oxygen content determinations. A mixture of ⁸⁶Rb and ⁹-μm spheres labeled with ⁴¹Ce was injected within 15 s into the arterial cannula supplying the intestinal loop (the port of injection was placed between the femoral artery and the pump), while mesenteric venous blood was collected in test tubes for 5 min (15 s for each test tube) for activity counting. The collection of mesenteric venous blood was begun 10 s prior to the injection of the rubidium and microspheres. After 3 min of blood collection, pump perfusion was terminated and the intestinal segment was divided into four to six pieces and processed for activity counting. Blood drained from the mesenteric vein was replaced with blood that had been collected at the beginning of the experiment. Then, another intestinal segment was prepared and processed the same way. Three intestinal segments were used from each dog.

Ten to 15 min were required for the preparation of each isolated intestinal segment. An additional 10 to 15 min were needed to stabilize perfusion pressure. This period was followed by 30 min of stable perfusion and mean arterial pressures, and then another 5 min were required for blood sampling and rubidium and microspheres injection. Thus, each stage of the experiment lasted about 1 h, and the measurements of circulatory variables were performed at the end of the hour, which provided sufficient time for tissue saturation with an anesthetic.

The first intestinal segment was studied under nitrous oxide anesthesia (66% N₂O) in the 29 dogs. The second and third loops were studied under isoflurane, enflurane, and halothane anesthesia (eight dogs per group), where 1 or 2 MAC of anesthetic was used in random order and 0.9 end-expired halothane, 2.2% end-expired enflurane, and 1.5% end-expired isoflurane were considered to equal 1 MAC. In the remaining five dogs, similar experiments were performed under isoflurane anesthesia (2 MAC) and α-adrenoceptor blockade. Phenotolamine, 1 mg·kg⁻¹, was injected intravenously and isoflurane, 3–5% inspired, provided for 5 to 7 min to achieve the desired concentration of 3% end-expired. The measurements were performed at 9–12 min after phenotolamine injection when inspired/expired isoflurane concentration ratio approached 0.6. End-expired concentration of isoflurane at the time of measurements was stable for 5 min at 2 MAC, and the flow through the loop was adjusted to achieve perfusion pressure at 100 mmHg.

Inhalational anesthetics were administered through a Forreger® Copper Kettle with a North American Drager anesthesia machine. End-expired concentrations of inhalational anesthetics were measured constantly with an Engren® Multigas Monitor for Anesthesia (EMMA). With a 30-min warm-up period, the EMMA was zeroed against room air. A humidity retaining device, “artificial nose,” separated the EMMA sensor from the animals' humidified air. In this case, water vapor values consistently showed 0.5%; therefore, the actual value of end-expired isoflurane concentration was equaled to a read-off value minus 0.5%. The EMMA was calibrated with a calibration transducer provided by the Engren Company. Thirty random EMMA measurements were compared with measurements obtained with the Perkin-Elmer® Medical Gas Analyzer, Model 1100, and the values were found to be identical.

Oxygen tension and pH were measured with an Instrumentation Laboratories model 818 pH/blood gas analyzer. Oxygen content was measured with an Instrumentation Laboratories CO-oximeter 282. Each shipment of microspheres (purchased from 3M Co.) was checked for size of spheres (determined with a standard Coulter Counter® routinely used for determination of red blood cell size), fragmentation, and status of aggregation. Microspheres were used only when size variations did not exceed standard deviations of 1 μm. Microspheres were labeled with ⁴¹Ce and suspended in a 10% dextran solution with polysorbate (Tween 80). Microspheres were mixed in a special injector with ⁸⁶Rb and diluted in 3 ml of normal saline. Each injection contained about 10⁶ of spheres and approximately 300
μCi of rubidium. Each of the isotopes generated approximately 0.5 × 10^6 counts/min.

Radioactivity in the intestinal segment and mesenteric venous blood samples was analyzed with a Tracer 2250 gamma counting system (Tracer Northern). This system utilizes the least-squares “fitting” technique to resolve the amount of radioactivity contributed by each isotope (141Ce and 86Rb in this case) in gamma ray spectra obtained by an NaI detector for the individual tissue and blood samples. 14,16,17 The method employs an isotope calibration file that contains the decay rate, the number of counts per microspheres, and the spectral definition of each isotope used in the study. Once loaded into memory, this calibration file was used by the Microsphere Analysis Program to conduct a comparison of the spectra contained in the file (standard spectra) and the spectra of the blood or tissue sample.

Total blood flow for each intestinal segment was measured directly by the amount of blood drained from the mesenteric vein. Each segment was weighed after the experiment and blood flow (F), calculated in ml · min⁻¹ · g⁻¹. Vascular resistance (VR) was calculated as follows:

\[
VR \text{ (dyn} \cdot \text{s} \cdot \text{cm}⁻² \cdot \text{g}) = \frac{\text{Perfusion pressure (mmHg)}}{\text{blood flow (ml} \cdot \text{min}⁻¹ \cdot \text{g}⁻¹)} \times 1,333
\]

Arteriovenous oxygen content difference was calculated and expressed in ml/dl of blood. Oxygen uptake was calculated by multiplying intestinal blood flow by arteriovenous oxygen content difference. Rubidium and 9-μm sphere clearances were calculated as follows: Cl-Rb = F × (Rb injected – Rb venous)/Rb injected, and Cl-Sph = F × (Sph injected – Sph venous)/Sph injected, where F is intestinal blood flow in ml/min · g⁻¹; Rb injected and Rb venous are rubidium activity injected into and recovered from the intestinal segment, respectively, and Sph injected and Sph venous are numbers of 9-μm spheres injected into and recovered from the intestinal segment, respectively. 14 The activity injected into the segment was compared with activity found in the blood and intestinal segment.

Data were summarized as the mean ± standard error of the mean. Differences between groups and control values (pentobarbital or nitrous oxide) were tested by the use of a one-way analysis of variance. Differences between levels of the same drug were tested by use of a randomized block analysis. Individual comparisons between pairs of means were performed using Fisher’s protected least significant difference test. 18 Pearson’s correlation coefficient and the corresponding least-squares regression equation were used as the measure of association when comparing two response measurements. Differences were considered significant if P < 0.05. All computations were performed with the aid of the Statistical Analysis System. 19

**Results**

The amount of activity found in the intestinal segment and mesenteric venous blood did not differ from the injected activity by more than 10%. The difference in the activity of 141Ce and 86Rb (calculated per gram of tissues) between samples of one intestinal loop never exceeded 10%. A very strong and significant correlation was found between rubidium and microsphere clearances, r = 0.97, P < 0.0001 (fig. 1).

During each stage of measurements, analysis of arterial blood samples showed PaO₂ to be above 100 mmHg, PaCO₂ between 35 and 40 mmHg, and hematocrit values between 30 and 35%. Observations with values not within these ranges were excluded from the study.

The main variables observed during various conditions of the experiments are presented in table 1. Nitrous oxide anesthesia was accompanied by significantly lower F, Cl-Rb, Cl-Sph, and higher VR values than pentobarbital anesthesia.

One MAC of halothane anesthesia was accompanied by a significantly lower arteriovenous oxygen content...
<table>
<thead>
<tr>
<th></th>
<th>Pent</th>
<th>N2O</th>
<th>H1-1</th>
<th>H1-2</th>
<th>E1-1</th>
<th>E1-2</th>
<th>I-1</th>
<th>I2bd</th>
<th>I-2bd</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>0.56 ± 0.01</td>
<td>0.49 ± 0.01*</td>
<td>0.51 ± 0.03</td>
<td>0.70 ± 0.09†</td>
<td>0.50 ± 0.04</td>
<td>0.58 ± 0.02‡</td>
<td>0.44 ± 0.03*</td>
<td>0.38 ± 0.02*‡§</td>
<td>0.68 ± 0.08*†***</td>
</tr>
<tr>
<td>VR</td>
<td>243 ± 6.0</td>
<td>286 ± 8.5*</td>
<td>299 ± 19.3</td>
<td>198 ± 12.9†</td>
<td>283 ± 27.3*</td>
<td>255 ± 11.7†</td>
<td>317 ± 24.8*</td>
<td>352 ± 28.0*‡§</td>
<td>207 ± 23.6*†***</td>
</tr>
<tr>
<td>AVDO2</td>
<td>3.64 ± 0.10</td>
<td>3.79 ± 0.14</td>
<td>2.38 ± 0.24†</td>
<td>1.41 ± 0.23*‡</td>
<td>2.21 ± 0.46‡</td>
<td>1.28 ± 0.24*‡§</td>
<td>2.59 ± 0.19†</td>
<td>2.50 ± 0.28*‡§</td>
<td>1.34 ± 0.19†***</td>
</tr>
<tr>
<td>O2 upt</td>
<td>2.0 ± 0.0</td>
<td>1.8 ± 0.1</td>
<td>1.2 ± 0.1†</td>
<td>0.9 ± 0.1‡</td>
<td>1.0 ± 0.1†</td>
<td>0.7 ± 0.1‡</td>
<td>1.1 ± 0.0†</td>
<td>1.0 ± 0.1*†</td>
<td>0.9 ± 0.0*†***</td>
</tr>
<tr>
<td>Cl Rb</td>
<td>0.47 ± 0.01</td>
<td>0.41 ± 0.01*</td>
<td>0.45 ± 0.02</td>
<td>0.57 ± 0.02*‡</td>
<td>0.43 ± 0.04</td>
<td>0.51 ± 0.02*‡§</td>
<td>0.39 ± 0.02*</td>
<td>0.55 ± 0.02*‡§</td>
<td>0.55 ± 0.05**‡***</td>
</tr>
<tr>
<td>Cl Sph</td>
<td>0.52 ± 0.01</td>
<td>0.45 ± 0.02*</td>
<td>0.49 ± 0.03</td>
<td>0.63 ± 0.03*‡</td>
<td>0.47 ± 0.04</td>
<td>0.52 ± 0.02*‡§</td>
<td>0.41 ± 0.02*</td>
<td>0.37 ± 0.02*‡§</td>
<td>0.60 ± 0.07**‡***</td>
</tr>
<tr>
<td>MAP</td>
<td>130 ± 4.1</td>
<td>135 ± 3.1</td>
<td>73 ± 4.0†*</td>
<td>36 ± 5.4*‡</td>
<td>66 ± 6.2*‡</td>
<td>37 ± 4.4*‡</td>
<td>87 ± 6.9†*</td>
<td>49 ± 5.0*†***</td>
<td>32 ± 4.7**†***</td>
</tr>
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</table>

F = flow in ml·min⁻¹·g⁻¹; VR = vascular resistance in the intestinal segment in dyn·s·cm⁻²·g⁻¹; AVDO₂ = arteriovenous blood oxygen content difference in ml·dl⁻¹; O₂ upt = oxygen uptake in ml·oxygen·min⁻¹·100 g⁻¹; Cl Rb and Cl Sph = rubidium clearance and microsphere clearance, respectively, in ml·min⁻¹·g⁻¹; MAP = mean aortic pressure in the dog in mmHg (blood pressure of the intestinal loop contained at 100 mmHg); Pent = pentobarbital anesthesia; N₂O = nitrous oxide 66% inspired; H-1 and H-2 = 1 and 2 MAC of halothane anesthesia, respectively; E-1 and E-2 = 1 and 2 MAC of enflurane anesthesia, respectively; I-1 and I-2 = 1 and 2 MAC of isoflurane anesthesia; respectively; I-2bd = 2 MAC of isoflurane with α-adrenoceptor blockade with phenolamine 1 mg·kg⁻¹.

* P < 0.05 versus pentobarbital.
† P < 0.05 versus N₂O.
‡ P < 0.05 versus 1 MAC of the same inhalational anesthetic.
§ P < 0.05 versus corresponding level of halothane.
¶ P < 0.05 versus corresponding level of enflurane.
** P < 0.05 versus 2 MAC of isoflurane.
with phentolamine, VR and AVDO₂ were significantly lower and F₁, rubidium, and microsphere clearances were significantly higher than corresponding values observed at 2 MAC of isoflurane without blockade (table 1, figs. 2–5).

Discussion

Rubidium clearance was chosen for the experiments as an index of nutritive flow.₁⁴,₂₀ Rubidium is highly diffusible across exchange vessels, which means that most of the substance presented in the exchange vessels is absorbed by tissues. Consequently, the ratio of absorbed to nonabsorbed rubidium represents the ratio of the blood flow through nutritive vessels to flow through nonnutritive vessels. Previous studies have demonstrated in some pathophysiologic conditions that 9-µm spheres and rubidium behave in the vascular bed in a similar way, i.e., spheres are trapped and rubidium is absorbed in the nutritive exchange vessels and shunted through nonnutritive vessels where exchange does not occur, or occurs to a limited extent.₁⁴ The results of the present study (a strong correlation between microspheres and rubidium clearances) confirm that 9-µm spheres can be used as a tool to study nutritive blood flow in tissues also during inhalation anesthesia.

The perfusion of the intestinal segment by a pump with constant pressure assured independence of the intestinal circulation from the systemic circulation, while...
increases intestinal blood flow in dogs\textsuperscript{21,22} but to a much lesser extent than other studied anesthetics.\textsuperscript{23} Therefore, pentobarbital was chosen for the control group of animals. In the experimental group, methohexitol, a barbiturate with a relatively short half-life,\textsuperscript{24} was selected for induction of anesthesia. Barbiturates can decrease MAC values of inhalational anesthetics for a long time.\textsuperscript{25} It must be kept in mind that methohexitol and nitrous oxide had certain residual effects on the following stages of the experiment, but the effects were probably minimal and, more important, all three groups of animals receiving inhalational anesthetics apparently experienced similar residual effects of methohexitol and nitrous oxide. All of the animals had the same fluid management, surgical preparation, and similar hematocrit values, which probably means that animals had similar sympathetic stimulation throughout the experiments. Therefore, differences between groups can be attributed to the influence of the anesthetic resulting from the following: the anesthetic's direct effect on the intestinal circulation, and/or from the anesthetic's effect on hormonal factors (e.g., release of epinephrine from adrenal glands).

Total blood flow, determined directly, and nutritive flow, evaluated indirectly by CI-Rb and CI-Sph, were lower during nitrous oxide than pentobarbital anesthesia (table 1, figs. 2, 5). The observed vasoconstriction can be related to the direct influence of nitrous oxide or to an increase in the concentration of vasoconstricting substances (e.g., catecholamines), which resulted from the influence of nitrous oxide on adrenal glands and/or from light anesthesia. Nitrous oxide anesthesia in the whole animal was accompanied by a decrease in blood flow through the preportal area\textsuperscript{11,26} and an increase in mesenteric vascular resistance.\textsuperscript{26} These changes in splanchnic circulation (described in the literature and also observed in this study) may be the result of an increase in catecholamine levels observed during nitrous oxide anesthesia.\textsuperscript{27} Therefore, our results in this regard supplement previously reported data.

Halothane, enflurane, and isoflurane anesthesia were accompanied by a much lower AVDO\textsubscript{2} and oxygen uptake than pentobarbital and nitrous oxide. It appears that the decrease in oxygen uptake by these inhalational agents depends on the direct influence of anesthetics on metabolism. It has to be realized that the effect of inhalational anesthetics on intestinal oxygen uptake was compared with the effect of pentobarbital and nitrous oxide rather than with the awake state. The three studied inhalational anesthetics affected intestinal circulation differently: compared with pentobarbital, enflurane anesthesia was not accompanied by remarkable differences in VR, nutritive blood flow (evaluated by CI-Rb and CI-Sph), and total blood flow (measured directly); halothane at 2 MAC decreased VR and increased total and nutritive blood flow (CI-Rb increased), while isoflurane increased VR and decreased total and nutritive blood flow through the intestinal segments.

During halothane anesthesia, mesenteric vascular resistance in the whole body was unchanged\textsuperscript{5,8} or increased,\textsuperscript{7} while mesenteric blood flow always decreased.\textsuperscript{4,11} Obviously, changes in mesenteric vascular resistance in the whole body depend not only on direct and humorally mediated factors but on changes in primary systemic circulatory variables and nervous control. A decrease in intestinal blood flow usually is associated with a reduction in cardiac output during barbiturate\textsuperscript{12} and halothane\textsuperscript{13} anesthesia. Thus, it appears that the direct effect of halothane at 2 MAC is vasodilation, while in the whole body a decrease in cardiac output leads to a compensatory increase in mesenteric vascular resistance and a decrease in blood flow. Apparently, direct vasodilatory action of halothane does not seem to interfere with this vasoconstricting response.

Isoflurane led to an increase in VR and a decrease in flow, total and nutritive. Phenylephrine completely abolished the vasoconstricting effect of isoflurane. It is well-known that regional blood flow is controlled mainly by local metabolic factors.\textsuperscript{2} Isoflurane, as well as halothane and enflurane, reduced oxygen demand of the intestinal loop. An autoregulatory-mediated increase in resistance and a decrease in flow followed the decrease in oxygen uptake only during isoflurane but not during halothane and enflurane anesthesia. The data could have suggested that this metabolic autoregulation was preserved during isoflurane and lost during enflurane (blood flow did not change) and especially during halothane anesthesia (blood flow even increased). However, a statistical analysis
showed that a reduction in oxygen uptake during iso-
flurane anesthesia did not correlate at all with the
changes in resistance, flow, and clearances. Therefore,
the data do not support the "autoregulatory" explanation
of the constricting effect of isoflurane on the intestinal
vasculature. On the other hand, disappearance of the
isoflurane-induced vasoconstriction in conditions of α-
adrenoceptor blockade suggests that the effect is medi-
ated through circulating catecholamines. Evidence
concerning the influence of isoflurane on catecholamines
is conflicting but suggests some sympathoadrenal stimu-
lation.26,29 Preganglionic sympathetic activity is inhibited
to a lesser extent than vagal activity during isoflurane
anesthesia,30 suggesting that the increase in circulating
catecholamines might result from the relatively high
preganglionic sympathetic activity. The reported effects
of isoflurane on plasma catecholamines are not consistent
within the literature. Perry et al. did not observe an
increase in catecholamines during isoflurane anesthesia.31
Dobkin et al. observed increased catecholamine levels
during isoflurane anesthesia.32 Additionally, a significant
increase in plasma epinephrine and a decrease in the
concentration of norepinephrine also has been demon-
strated clearly, suggesting that the increase in plasma
epinephrine results from an action of isoflurane on
adrenal epinephrine release.33 Our study employed ex-
tensive surgical preparation, which alone could result in
a substantial release of catecholamines. Thus, it seems
that the direct influence of isoflurane on the intestinal
vasculature is vasodilation, which is overridden by the
vasoconstricting effect of circulating catecholamines.
Apparently, catecholamine concentration did not in-
dcrease during halothane and enflurane, as it did during
isoflurane anesthesia.

It appears that effects of isoflurane on regional cir-
culation are rather complex: It dilates cerebral and
coronary vessels disproportionately to the metabolic needs
of the brain34 and the myocardium,35,36 it dilates hepatic
arterial vasculature and increases hepatic arterial blood
flow despite a decrease in blood pressure and cardiac
output,11,13 and it constricts intestinal vasculature in the
whole body,11,13,36 as well as in the isolated intestinal
loop preparation (present study).

In summary, compared with pentobarbital anesthesia,
halothane, enflurane, and isoflurane decreased oxygen
uptake in the intestinal segment, probably influencing
tissue metabolism. Enflurane did not significantly influ-
ence the intestinal vascular tone; halothane at 2 MAC
decreased vascular resistance and increased total and
nutritive blood flow, while isoflurane increased vascular
resistance and decreased total and nutritive blood flow.
The data suggest that this increase in VR was mediated
via catecholamines. Decreases in mesenteric blood flow,
which always have been observed during anesthesia with
these agents, is related mainly to the indirect effects of
anesthetics mediated through changes in systemic cir-
culation and the central nervous system.

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References

1. Hickey RF, Eger EI II: Circulatory effects of inhaled anesthetics,
The Circulation in Anaesthesia. Applied Physiology and
Pharmacology. Edited by Prys-Roberts C London, Blackwell
2. Granger DN, Richardson PDI, Kvietys PR, Mortillaro NA:
3. Gelman S, Reves JG, Harris D: Circulatory responses to mida-
zolam anesthesia: Emphasis on canine splanchnic circulation.
4. Gelman S: The effect of enteral oxygen administration on the
hepatic circulation during halothane anesthesia: Experimental
5. Theunin L, Andreen M, Irestedt L: Effect of controlled halothane
anesthesia on splanchnic blood flow and cardiac output in
6. Andreen M, Irestedt L, Zetterstrom B: The different responses
of the hepatic arterial bed to hypovolemia and to halothane
7. Ahlgren I, Aroksen F, Bjorkman L, Wetterlin S: The hemody-
namic effect of halothane in the normovolemic dog. Acta
8. Irestedt I, Andreen M: Effects of enflurane on haemodynamics
and oxygen consumption in the dog with special reference
to the liver and preportal tissues. Acta Anaesthesiol Scand
23:15–26, 1979
and halothane on liver blood flow and oxygen consumption
10. Tranquilli WJ, Manohar M, Parks CM, Thurmon JC, Theodorakis
MC, Bemon GJ: Splanchnic and regional blood flow distribution
in anesthetized swine and swine anesthetized with halothane
+ nitrous oxide, halothane, or enflurane. ANESTHESIOLOGY
56:369–379, 1982
11. Lundeen G, Manohar M, Parks C: Systemic distribution of blood
flow in swine while awake and during 1.0 and 1.5 MAC
isoflurane anesthesia with and without 50% nitrous oxide.
12. Bulky GB, Kvietys PR, Perry MA, Granger DN: Effects of
cardiac tamponade on colonic hemodynamics and oxygen
during isoflurane and halothane anesthesia. ANESTHESIOLOGY
61:84–88, 1984
μm spheres and Rb in the intestinal circulation. Am J Physiol
247:G13–G18, 1984
flow measurements with radionuclide-labeled particles. Prog
Cardiovasc Dis 20:55–79, 1977


34. Newberg LA, Michenfelder JD: Cerebral protection by isoflurane during hypoxemia or ischemia. Anesthesiology 59:29–35, 1983
