Splanchnic Circulation During Nitrous Oxide Anesthesia and Hypocarbia in Normal Man

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Circulatory effects of nitrous oxide-d-tubocurarine anesthesia with hyperventilation were studied in healthy, young men. Cardiac output, mean arterial blood pressure, and splanchnic blood flow were measured. During anesthesia and hyperventilation with normal \( \text{PCO}_2 \) (CO\(_2\) added to the inspired gases), splanchnic vascular resistance was elevated significantly and the blood flow reduced, but oxygen consumption was unaltered from control values. Cardiac output and total peripheral resistance were unchanged. When \( \text{PCO}_2 \) was not maintained at the normal level, total peripheral resistance and splanchnic vascular resistance were reduced and the respective blood flows augmented compared with the normocarbic period. However, the demand of the splanchnic viscera for oxygen was increased out of proportion to the increase in flow. It is suggested that the nitrous oxide-curare-hyperventilation technique may be a poor choice for patients with marginal levels of splanchnic blood flow.

Carbon dioxide tension profoundly affects vascular tone in both conscious and anesthetized individuals. Controlled studies of the splanchnic circulation made during halothane anesthesia and during nitrous oxide anesthesia have demonstrated that hypocarbia has marked effects on blood flow.\(^1\,^2\) However, hypocarbia produced by artificial hyperventilation of the lungs is a more frequent accompaniment of many techniques of general anesthesia. In particular, the nitrous oxide-relaxant technique commonly utilizes hyperventilation and predictably causes respiratory alkalosis. Since hypocarbia can increase vascular resistance and decrease blood flow in other vascular beds, e.g., cerebral, it seemed important to ascertain the effect of hypocarbia on the splanchnic circulation in man during nitrous oxide anesthesia.

Methods

Six healthy male volunteers to whom the procedures had been explained thoroughly on two prior visits to the laboratory were studied. Their ages ranged from 21 to 30 years. Each reported in the early morning following a 12-hour fast. Under local anesthesia a 100 cm. No. 7 Lehman catheter was introduced into an antecubital vein, and with the aid of image intensification fluoroscopy, advanced into a right hepatic vein. In addition, a Courmand needle was placed into a femoral artery and a 60 cm. radiopaque polyethylene catheter was inserted into an antecubital vein and advanced into the superior vena cava (SVC). The electrocardiogram was recorded from plate electrodes on the skin, using a Grass recorder.

The splanchnic blood flow was measured by the Fick principle using indocyanine green dye (ICG).\(^3\,^4\) A 20 mg. priming dose, also used for cardiac output determination, was followed by a sustaining infusion of dye (stabilized with human albumin) from a constant infusion pump through the SVC catheter. The infusion rate was approximately 1 mg./minute and the concentration of ICG in the arterial plasma averaged 1 mg./liter. Twenty minutes were allowed for stabilization of arterial ICG concentration; sampling of arterial and hepatic venous blood then began. Three observations of flow were made during a 30-minute period in each of three study phases (control, nitrous oxide anesthesia with normal \( \text{PCO}_2 \), and ni-
torous oxide anesthesia with reduced $P_aCO_2$.
Following induction of anesthesia the rate of
ICC infusion was decreased by one-third to
compensate for reduced dye clearance by the
liver.

Femoral arterial and hepatic venous pres-
sures were monitored with Statham strain
gauges and the Grass recorder. Splanchnic
vascular resistance was calculated as perfusion
pressure (mean arterial minus mean venous)
divided by blood flow rate. Hematocrit was
determined in capped hematocrit tubes spun
at 2,300 g for 30 minutes. Arterial $P_{O_2}$, $P_{CO_2}$,
and pH were measured using an IL electrode
assembly. Cardiac outputs were determined in
duplicate using a 5 or 10 mg. injection of ICC,
a Waters' cuvette densitometer, and a Harvard
constant withdrawal pump.

When control measurements were completed,
anesthesia was induced with thiopental (2 mg./
kg body weight) given intravenously, followed
by $N_2O-O_2$ in a 2:1 ratio from a nonrebreat-
ching circuit. d-tubocurarine (0.7 mg./kg.) was
given intravenously and the trachea was
tubated with a cuffed Magill tube. Additional
d-tubocurarine was given as needed, the total
dose ranging from 61 to 72 mg. in the six sub-
jects. Mechanical ventilation was maintained
using a Bird Mark IV assistant controller. Respi-
ratory rate and tidal volume were kept con-
stant throughout the anesthetic period. Tidal
volume was monitored with a Wright respi-
rometer. Esophageal temperature was mea-
sured with a thermistor and body temperature
was maintained at the initial level ($\pm 0.5^\circ\text{C}$)
with an electric heating blanket. End tidal
$P_{CO_2}$ was measured using a L-B-1 CO$_2$
analyzer, pressurized with nitrous oxide to elimi-
nate the crossover effect.

A delay of 30 to 45 minutes (average 39)
ensued before establishment of a steady state
of anesthesia with respect to end-tidal $P_{CO_2}$,
pulse rate, and arterial pressure, following
which the measurements made during the con-
trol period were repeated twice more. The
two study periods during anesthesia were com-
parable except for levels of end-tidal and ar-
terial $P_{CO_2}$. During one period, hypocarbia
was produced by hyperventilation whereas
during the other $CO_2$ was added to the in-
spired gas mixture to produce normocarbia.
The order in which the normocarbic and hy-
pocarbic periods were studied was randomized.
The results were analyzed statistically using
Student's $t$ test.

Results

Results are summarized in tables 1 and 2.
Table 1 lists the general conditions and find-
ings; table 2 lists the data pertaining to the
splanchnic circulation. The three observations
of splanchnic blood flow made at ten-minute
intervals in each of the three study periods
have been averaged. In brief, the adminis-
tration of nitrous oxide-oxygen-curare with inter-
mittent positive-pressure ventilation and normo-
carbia was accompanied by significantly in-
creased splanchnic vascular resistance and perfus-
tion pressure. Splanchnic blood flow and
clearance of ICC diminished. There was no
significant change in oxygen consumption or
$P_{CO_2}$ in hepatic venous blood. Cardiac output,
heart rate, and total peripheral resistance were
unaltered.

When $CO_2$ was not added to the inspired nit-
utous oxide-oxygen mixture, hypocarbia (mean
$P_{CO_2} = 18$ mm. Hg) developed. However,
there was no significant change in perfusion
pressure, clearance of ICC, or splanchnic blood
flow when compared with the normocarbic pe-
riod. Splanchnic vascular resistance was de-
creased ($P < 0.03$) though still elevated when
compared with the control period, and the $P_{O_2}$
of hepatic venous blood also was reduced ($P
< 0.01$). Oxygen consumption was increased
in five of six cases, but the change for the
group was only of borderline significance sta-
tistically ($P < 0.08$). Total peripheral resis-
tance was reduced, and cardiac output in-
creased, in three of the four individuals for
whom these data were obtained.

Discussion

The marked increase in splanchnic vascular
resistance observed in the present study was
unexpected, since Epstein and his co-workers
previously had examined the splanchnic circu-
lation during nitrous oxide anesthesia and
found no change provided that $P_{CO_2}$ remained
normal. Differences between their study and
ours with respect to the initial conditions and
to anesthetic technique might account for the
discrepancy. The earlier workers gave nor-
COOPERMAN, WARDEN, AND PRICE

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Mar.- Apr. 1968

TABLE 1. Respiratory and Circulatory Effects of Nitrous Oxide-curarization Hyperventilation Anesthesia

<table>
<thead>
<tr>
<th>Subject</th>
<th>Heart Rate</th>
<th>Cardiac Output</th>
<th>TPR</th>
<th>PaCO₂</th>
<th>V̇E</th>
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<td>H</td>
<td>C</td>
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C = during control period; N = during anesthesia and normocarbia; H = during anesthesia and hypocarbia.

Heart rate = beats per minute; cardiac output = liters per minute; TPR = total peripheral resistance, mm Hg/liter per minute; PaCO₂ = mm Hg; V̇E = respiratory minute volume during anesthesia in liters per minute.

Perfusion pressure = mean arterial minus mean hepatic venous pressure; SVR = splanchnic vascular resistance (splanchnic perfusion pressure in mm Hg/splanchnic blood flow in liters per minute); SBF = splanchnic blood flow in liters per minute; O₂c = splanchnic oxygen consumption in ml per minute; CICG = ICG clearance of plasma in ml per minute; PVo₂ = oxygen tension of hepatic venous blood in mm Hg.

* P < 0.05.
** P < 0.01.
*** P < 0.001.

Sign. = Significance referred to column at left.

Phenobarbital and scopolamine for preanesthetic medication, used succinylcholine instead of d-tubocurarine to produce muscular flaccidity, and studied male and female patients rather than healthy, young men. In addition, the initial level of splanchnic blood flow was significantly higher in our subjects than in theirs. However, the most important difference between their study and ours is the manner in which the subjects' lungs were ventilated. Epstein et al. maintained a normal PaCO₂ with a "servorespirator" in which end-expired carbon dioxide tension automatically regulated the inflating pressure. We, on the other hand, intentionally hyperventilated our subjects, producing tidal volumes which averaged 1.3 l and minute volume approximating 15 l/minute. It is well recognized that the motions of the diaphragm have important effects upon the hepatic circulation. In addition, the peripheral pooling of blood caused by elevated airway pressure is capable of inducing vasoconstriction reflexly by way of the barostatic mechanisms and this could further increase splanchnic vascular resistance.

Another possible cause for splanchnic vasoconstriction observed during anesthesia and normocarbia in the present study is that oxygen consumption was diminished. Since the tissues (except muscle) have no significant capacity for storing oxygen, the steady-state oxygen consumption is identical with oxygen demand. It is well recognized that local metabolic demand regulates vascular resistance in many areas. However, the change in oxygen requirement (about 20 per cent) is far too small to account for either the increase in resistance or the reduction in blood flow.

Therefore, the question arises whether hyperventilation of the magnitude employed in this study can reduce splanchnic blood flow sufficiently to interfere with tissue oxygenation. We have no direct information on this point; however, the oxygen tension in hepatic venous blood was unaffected by hyperventilation at normal PaCO₂.

The same cannot be said for the situation during hypocapnea, for the shift from normal to reduced PaCO₂ increased splanchnic oxygen demand by 50 per cent while increasing splanchnic blood flow only half as much. From the standpoint of availability of oxygen in rela-
tion to demand, this situation is the least favorable of those studied by us though there still was no evidence for splanchic hypoxia. The measured reduction in hepatic venous oxygen tension (table 2) merely reflected the Bohr effect, and the oxygen content of the hepatic venous blood was not reduced during hypocarbia. The increase in oxygen demand during hypocarbia probably underlies the increase in splanchic blood flow which was observed. However, the effect itself is inexplicable in terms of mechanism and, to our knowledge, has not been reported previously.

The general circulatory changes induced by hypocarbia—that is, increased cardiac output and reduced peripheral resistance—have been reported previously⁵,⁶ and are well documented. Our findings, however, are dissimilar to those of Pryv-Roberts and his coworkers¹⁰ who found that cardiac output and PaCO₂ were correlated directly. We have no explanation for this discrepancy; however, we consider their “eucapnic” level (48 mm Hg) to be hypercarbic.

We can now compare the effects of seven different anesthetic techniques in relation to splanchic oxygen uptake and blood flow. Table 3 summarizes the results which have been obtained previously by ourselves and others.⁵,¹¹,¹² It can be seen that spinal anesthesia resembles halothane anesthesia in its action on the splanchic circulation whereas the nitrous oxide-curare-hyperventilation technique resembles cyclopropane anesthesia. Although there is a similar change in splanchic blood flow in all cases, splanchic vascular resistance is little changed in the former group and greatly increased in the latter. In addition, the variations in oxygen consumption are not nearly as marked as are the changes in splanchic blood flow, implying that even a reduced blood flow will provide adequate oxygenation. However, these studies were conducted in healthy, young individuals. It might well be that in the patient with marginal circulatory inadequacy in the splanchic viscera, an anesthetic technique which does not increase vascular resistance would be preferable.

### Table 2. Splanchic Circulation and Metabolism Before and During Nitrous Oxide Anesthesia

<table>
<thead>
<tr>
<th>Subject</th>
<th>Perf. Pres.</th>
<th>SVR</th>
<th>SBF</th>
<th>QO₂</th>
<th>CICG</th>
<th>PVO₂</th>
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<td>80</td>
<td>81</td>
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</table>

Mean Sign. **85** **92** **85** **44** **96** **77** **2.06** **1.12** **1.40** **(P=0.09)** **76** **59** **88** **(P=0.08)** **0.74** **0.47** **0.51** **No** **No** **No** **No** **No** **No** **No**

See footnotes to Table 1 for explanation of symbols.

### Table 3. Comparison of Effects of Anesthetic Techniques on Splanchic Circulation and Oxygen Consumption

<table>
<thead>
<tr>
<th>Anesthetic Technique</th>
<th>Ventilation</th>
<th>PacO₂</th>
<th>SVR</th>
<th>SBF</th>
<th>QO₂</th>
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<td>High spinal</td>
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<td>Normal</td>
<td>+7</td>
<td>-29</td>
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<td>11</td>
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<tr>
<td>Halothane</td>
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<tr>
<td>Cyclopropane</td>
<td>Controlled</td>
<td>Normal</td>
<td>+9</td>
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<td>2</td>
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<tr>
<td>Nitrous oxide-curare-hyperventilation</td>
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<tr>
<td>Nitrous oxide-succinylcholine</td>
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<td>Normal</td>
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Present study
Summary

1. The splanchnic circulation and metabolism were studied in six normal male volunteers during anesthesia with nitrous oxide, d-tubocurarine, and hyperventilation. P_{aCO_2} was controlled by adding CO_2 to the inspired gases.

2. During hyperventilation with normal P_{aCO_2}, splanchnic vascular resistance more than doubled and blood flow was reduced by a corresponding amount; however, the demand of the splanchnic viscera for oxygen was unaltered.

3. When P_{aCO_2} was permitted to fall (CO_2 not added) there was a marked increase in oxygen demand but only a small increase in blood flow, and the splanchnic vascular resistance remained significantly elevated above normal.

4. With respect to its effects on the splanchnic circulation, the nitrous oxide hypocarbic technique resembles cyclopropane, whereas halothane resembles spinal anesthesia.

5. It is concluded that the nitrous-oxide-d-tubocurarine-hyperventilation technique may be a poor choice for clinical use in patients with marginal levels of splanchnic circulation.

References


Anesthesia

INTRAUTERINE HEPATITIS Fetal erythroblastosis frequently is treated by intravenous transfusion. Donor cells are injected into the peritoneal cavity of the unborn, where they are absorbed. Probably it was inevitable that serum hepatitis would be transmitted in this way. A case is presented in which a fetus, transfused on four occasions, was delivered by cesarean section after meconium was found in amniotic fluid. The infant, jaundiced at birth, was given four exchange transfusions in the first four days of life, but died on the 16th day of life. Autopsy revealed active hepatitis. Neither the mother nor other recipients of the donor blood developed hepatitis. (Mandelbaum, B., and Brough, J. A.: Hepatitis Following Multiple Intravenous Transfusions, Obstet. Gynec. 30: 188 (Aug.) 1967.)