Effect of 33% Xenon Inhalation on Whole-Brain Blood Flow and Metabolism in Awake and Fentanyl-Anesthetized Monkeys

Liping Yao, MD; Jesus Bandres, MD; Edwin M. Nemoto, PhD; J. Robert Boston, PhD; Joseph M. Darby, MD; and Howard Yonas, MD

Background and Purpose: Despite the documented diagnostic value of local cerebral blood flow maps by xenon-enhanced computed tomography, reports of cerebral blood flow activation by inhaled 33% Xe raised concerns about the method’s safety and accuracy. We evaluated the effect of 33% Xe inhalation on cerebral blood flow and cerebral metabolic rates for oxygen and glucose in four awake and six fentanyl-anesthetized rhesus monkeys.

Methods: Platinum microelectrodes and catheters in the torcular Herophili were used to measure cerebral blood flow by hydrogen clearance, and oxygen and glucose concentrations. Cerebral variables were measured after 5 and 35 minutes of exposure to room air followed randomly by 67% O₂ in 33% N₂ or Xe. Five- and 35-minute measurements were combined because the duration of exposure had no effect.

Results: In awake monkeys, 33% Xe compared with 33% N₂ reduced (p<0.05) cerebral blood flow from 75±12 to 66±9 (mean±SD) ml · 100 g⁻¹ · min⁻¹ and oxygen consumption from 6.1±0.7 to 5.1±0.6 ml · 100 g⁻¹ · min⁻¹. In fentanyl-anesthetized monkeys, cerebral variables during 33% N₂ versus 33% Xe were cerebral blood flow, 84±26 versus 79±23 ml · 100 g⁻¹ · min⁻¹; oxygen consumption, 5.0±0.7 versus 4.9±0.5 ml · 100 g⁻¹ · min⁻¹; and glucose consumption, 8.4±1.9 versus 7.9±2.0 mg · 100 g⁻¹ · min⁻¹.

Conclusions: In awake monkeys, 33% Xe reduced rather than activated cerebral blood flow and oxygen consumption by 12% and 16%, respectively; it had no effect in fentanyl-anesthetized monkeys. (Stroke 1992;23:69–74)

Xenon-enhanced computed tomographic (CT) measurements of local cerebral blood flow (CBF) have proved valuable in the clinical management of acute and chronic cerebrovascular disorders.¹⁻⁴ This method accurately identifies small brain regions with low or no flow that progress to infarction,⁵ as well as hyperemia following embolus migration and vascular reconstructive surgery.⁶⁻⁷ Because CBF information obtained by xenon-enhanced CT provides direct anatomic reference to the baseline CT with high spatial resolution, the test provides important information about local CBF, the adequacy of collateral flow, the cause of symptoms, and the efficacy of surgical procedures in patients with occlusive vascular disease.⁴

Despite its clinical utility, the safety and accuracy of xenon-enhanced CT have been questioned because xenon is suspected of increasing CBF,⁸⁻¹¹ cerebral blood volume, and, thereby, intracranial pressure (ICP). Increased ICP could be hazardous in patients with head injury, cerebral mass lesions, or stroke.¹² On the other hand, other studies²⁻³⁻⁶⁻¹³⁻¹⁴ demonstrated no CBF increase in humans and nonhuman primates exposed to 30–40% Xe for 4–6 minutes. Nevertheless, some have cautioned that xenon-induced flow activation may cause a “steal” phenomenon.¹² These concerns represent an obstacle to clinical acceptance of the method.

We evaluated the effects of 33% Xe on whole brain CBF and on cerebral metabolic rates for oxygen (CMRO₂) and glucose (CMRG) after 5 and 35 minutes of 33% Xe inhalation in unanesthetized and in fentanyl-anesthetized monkeys.

Materials and Methods

This protocol was approved by the Animal Care and Use Committee of the University of Pittsburgh,
School of Medicine, Pittsburgh, Pa. The rhesus (Macaca mulatta) monkeys were nonferal, young adults (male and female) weighing 4–6 kg.

The monkeys were studied in two conditions: without anesthesia (n=6) and with fentanyl anesthesia (n=6). Three monkeys were studied in both conditions. The monkeys studied without anesthesia were acclimated to restraint chairs. The monkey to be studied was anesthetized with 10 mg/kg ketamine i.m. (Ketalar, Parke-Davis, Morris Plains, N.J.). A peripheral venous catheter was inserted into a hind limb vein and 0.9% NaCl was infused at 5 ml/kg/hr. Rectal temperature was monitored (YSI Telethermometer, Yellow Springs Instrument Co., Yellow Springs, Ohio) and maintained at 37–38°C with a hot-water heating blanket (Gorman-Rupp, Inc., Bellville, Ohio). Cefazolin, 500 mg (Kefzol, Eli Lilly and Co., Indianapolis, Ind.), was injected intramuscularly.

Oxygen, 33% in N$_2$, was provided by face mask during aseptic surgery. Two PE 50 catheters were inserted nonocclusively, one into each femoral artery for blood pressure monitoring and blood sampling. The wounds were treated topically with 2.0% lidocaine jelly and sutured.

A 5 mm x 1 cm craniectomy was made over the torcula, and a PE 50 catheter was inserted for cerebral venous blood sampling. A second craniectomy, 1 cm anterior to the first, was made over the superior sagittal sinus, and a 100-µm platinum microelectrode was inserted to monitor hydrogen clearance for CBF measurements. The catheter and microelectrode were secured with cyanoacrylate glue (Kodak 910, Rochester, N.Y.). Two silastic catheters were inserted into the nasopharynx, one for the administration of hydroxybutyrate and the other for sampling of end-tidal air for monitoring of end-tidal carbon dioxide concentration.

For awake studies, the monkey was secured in the restraint chair while still sedated by ketamine, and allowed to recover from anesthesia. A 5.0-l plastic bell-shaped helmet was placed over the head and either room air or xenon-mixed air flowed through the helmet at 10 l/min for up to 35 minutes during each exposure. The arterial catheters were connected to transducers (Spectramed Inc., Critical Care Division, Oxnard, Calif.) connected to a Model MP-7 Grass polygraph. The platinum microelectrode was connected to a Chemical Microsensor (Transidyne Corp., Ann Arbor, Mich.), and the output connected to the Grass recorder. Rectal temperature, arterial blood pressure, and end-tidal carbon dioxide and sagittal sinus hydrogen concentrations were continuously monitored.

When the study was completed, the monkey was reanesthetized with ketamine, and the catheters and microelectrodes were removed. The cranial defects were sealed with bone wax, and all wounds were closed in several layers. The monkey was allowed to recover from anesthesia and returned to the Central Animal Facility.

For studies with anesthesia, the monkey was intubated with a cuffed endotracheal tube (3.0–4.0 mm i.d., Division of Mallinkrodt, Inc., Glens Falls, N.Y.) and mechanically ventilated (large animal ventilator, Harvard Apparatus, Waltham, Mass.) with 67% O$_2$ and 33% N$_2$. As the monkey recovered from ketamine anesthesia, fentanyl citrate (Elkin-Sinns, Inc., Cherry Hill, N.J.) anesthesia was induced with an intravenous bolus of 50 µg/kg and maintained with a continuous infusion at 10 µg/kg/hr (Rate Infuser, Becton Dickinson, Lincoln Park, N.J.). The monkey was paralyzed with pancuronium bromide (Pavulon, Elkin-Sinns), 0.2 mg/hr i.v. End-tidal carbon dioxide was continuously monitored (model 1620, Novametrix Medical Systems Inc., Wallingford, Conn.) and controlled between 5% and 6%. At the end of the study, fentanyl anesthesia was discontinued; the monkey recovered spontaneously and was weaned from the ventilator and extubated.

In all studies, the monkey breathed room air during two baseline measurements of all variables. Thereafter, the gas mixture was randomly switched to 67% O$_2$ with either 33% N$_2$ or 33% Xe when a second set of two measurements of all physiological variables was made, one at 8 minutes (after 3 minutes of xenon or N$_2$ inhalation) and the other at 28 minutes.

Measurements were initiated by bleeding hydrogen gas into the nasopharynx of the unanesthetized monkeys or via a needle into the endotracheal tube of the fentanyl-anesthetized monkeys (Figure 1). Hydrogen was administered until cerebral venous blood and brain concentrations equilibrated as indicated by a plateau in the hydrogen level detected in the torcula. After about 10 minutes of equilibration, arterial and cerebral venous oxygen contents were simultaneously withdrawn (1 ml/min) for measurements of arterial blood gas tensions, arterial and cerebral venous oxygen contents (IL Co-Oximeter, model 482, Instrumentation Laboratory, Lexington, Mass.), and glucose content (YSI model 23A glucose analyzer, Yellow Springs Instrument Co.). On-line data acquisition on an IBM AT computer was begun to acquire the baseline hydrogen level. The inspired hydrogen was abruptly discontinued and its clearance

![Figure 1](image-url). The experimental protocol timing of arterial blood sampling and cerebral blood flow (CBF) measurements.
recorded until the level returned to zero over about 10 minutes.

In a few studies, arterial hydrogen clearance was monitored. Arterial hydrogen cleared to 5% of the initial level within 20 seconds after hydrogen delivery was discontinued (Figure 2). However, to ensure complete elimination, t1/2 in seconds was measured 40 seconds after zero time as described by Martins et al.15 Cerebral blood flow was then calculated from the equation: 

\[ \text{CBF (ml} \cdot 100 \text{g}^{-1} \cdot \text{min}^{-1}) = 0.693 - 60 - 100/(t_{1/2} \text{seconds}) \]

Although it is implicit in this equation that clearance curves are monoexponential and our curves were monoexponential (Figure 2), Waltz et al16 showed that practically, there is a good correlation between CBF calculated by the T1/2 method, the stochastic method, and exponential analysis. Cerebral blood flow calculated by the three methods differed. Cerebral blood flow values calculated by T1/2 were higher than values calculated by the height/area and exponential analysis methods. Cerebral oxygen consumption and CMRG were calculated from the following equations:

\[ \text{CMRO}_2 (\text{ml} \cdot 100 \text{g}^{-1} \cdot \text{min}^{-1}) = \text{CBF} \cdot \overline{\text{A-V}} \text{vol} % \text{O}_2 / 100, \]

\[ \text{CMRG (mg} \cdot 100 \text{g}^{-1} \cdot \text{min}^{-1}) = \text{CBF} \cdot \overline{\text{A-V}} \text{mg} % \text{glucose} / 100. \]

The oxygen-glucose index was calculated as the ratio of CMRO2:CMRG x 6 in \( \text{mmol} \cdot 100 \text{g}^{-1} \cdot \text{min}^{-1} \).

The data were analyzed by one-way analysis of variance for repeated measures and the two-tailed paired or unpaired Student-Newman-Keuls test

with a minimum acceptable value of 0.05. Within-group and between-group comparisons were made for each variable.

**Results**

Two monkeys studied unanesthetized had high cerebral venous oxygen contents resulting in CMRO2 values that were half the normal value. The data from these monkeys were discarded. Arterial PCO2, pH, and mean arterial pressure (MAP) were similar after 5 and 35 minutes of xenon inhalation and did not differ with the inhaled gas mixture; therefore, the data were combined (Table 1). Mean Paco2 ranged from 86 to 90 mm Hg during room air breathing and from 223 to 273 mm Hg with 67% O2. Mean arterial pressure ranged from 109 to 113 mm Hg, while Paco2 was spontaneously regulated at about 35 mm Hg. Arterial pH remained well within normal limits.

In unanesthetized monkeys, cerebral variables did not change with duration of xenon inhalation but differed with time between the different gas mixtures (Table 2). After 5 minutes, CBF, CMRO2, and oxygen-glucose index were significantly less during xenon inhalation than during nitrogen inhalation. After 35 minutes, these cerebral variables were similar between gas mixtures. At 35 minutes, CMRG and oxygen-glucose index did not differ with the inhaled gas mixture. (An oxygen-glucose index consistently greater than 1.0 indicates cerebral metabolism of substrates other than glucose.) Cerebral variables did not change over time. Therefore, values measured at 5 and 35 minutes were combined for each gas mixture.

When the data were compared between inhaled gas mixtures, most of the differences were observed between nitrogen or xenon and air (Table 3). However, the control for xenon effects was 33% N2/67% O2 and comparison with this group showed that xenon reduced CBF by 12% and CMRO2 by 16% whereas CMRG and oxygen-glucose index were unaffected.

Physiological variables in the fentanyl-anesthetized monkeys were constant during the 35-minute exposure to the various gas mixtures and were similar at 5

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**Table 1. Physiological Variables Measured After Inhalation of Various Gas Mixtures in Rhesus Monkeys**

<table>
<thead>
<tr>
<th></th>
<th>Air</th>
<th>Nitrogen/oxygen</th>
<th>Xenon/oxygen</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pHa</strong></td>
<td>7.41±0.05</td>
<td>7.38±0.04</td>
<td>7.38±0.05</td>
</tr>
<tr>
<td><strong>Paco2 (mm Hg)</strong></td>
<td>86±6</td>
<td>256±34*</td>
<td>252±25*</td>
</tr>
<tr>
<td><strong>MAP (mm Hg)</strong></td>
<td>110±14</td>
<td>117±7</td>
<td>111±13</td>
</tr>
<tr>
<td><strong>PacO2 (mm Hg)</strong></td>
<td>33±5</td>
<td>34±5</td>
<td>37±4</td>
</tr>
<tr>
<td><strong>Anesthetized monkeys (n=6)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>pHa</strong></td>
<td>7.34±0.03</td>
<td>7.32±0.03</td>
<td>7.34±0.05</td>
</tr>
<tr>
<td><strong>Paco2 (mm Hg)</strong></td>
<td>93±13</td>
<td>294±15*</td>
<td>272±47*</td>
</tr>
<tr>
<td><strong>MAP (mm Hg)</strong></td>
<td>114±8</td>
<td>109±11</td>
<td>105±13</td>
</tr>
<tr>
<td><strong>PacO2 (mm Hg)</strong></td>
<td>40±2</td>
<td>36±7</td>
<td>38±3</td>
</tr>
</tbody>
</table>

Unanesthetized values represent mean±SD of eight measurements. Anesthetized values represent average of 12 measurements. MAP, mean arterial pressure.

*p<0.05 compared with air.
and 35 minutes. Therefore, the two sets of data were pooled (Table 1). Only 
\( \text{PaO}_2 \) was affected by gas exposure (Table 1), increasing from about 90 mm Hg 
during air inhalation to about 300 mm Hg with 67% 
\( \text{O}_2 \). Arterial \( \text{PCO}_2 \) was controlled at about 40 mm Hg, 
and MAP at about 100 to 115 mm Hg. Arterial pH 
remained within normal limits.

Cerebral variables were unaffected by the duration of 
\( \text{Xe} \) inhalation (Table 2). Values at 5 and 35 
minutes were similar for each gas mixture and therefore, 
the data were combined.

Xenon had no effect on cerebral variables in the 
anesthetized monkeys (Table 3). Differences in 
\( \text{CMRO}_2 \) were observed between air and the other 
two gas mixtures. Oxygen-glucose index was unaltered 
by xenon compared with air or nitrogen.

Cerebral blood flow and \( \text{CMRO}_2 \) values on the 
different gases were similar in fentanyl-anesthetized 
and awake monkeys (Table 3). However, \( \text{CMRG} \) was 
41% higher with fentanyl and the oxygen-glucose 
index was about 30% lower (0.90 versus 1.28), 
indicating a shift toward increased glucose relative to 
oxygen utilization which may indicate increased anaerobic 
metabolism or simply increased glucose utilization. On 
room air, there were no differences between 
anesthetized and unanesthetized values in 
any of the cerebral variables (Table 3).

### Discussion

Xenon is a physiologically active gas whose minimum 
\( \text{alveolar anesthetic concentration} \) (i.e., \( \text{MAC} \)), 
the anesthetic concentration at which 50% of the 
subjects respond to a painful stimulus and 50% do not) is 71% in humans\(^1\) 
and unknown in monkeys. Although we expect that the two \( \text{MAC} \) values are 
similar, without precise knowledge, we cannot be 
certain where 33% \( \text{Xe} \) falls in monkeys. A general 
estimate of \( \text{MAC} \) in monkeys can be determined on 
the basis of their reaction to different doses of xenon.

Meyer et al\(^1\) reported that \( \text{CBF} \) decreased and the 
electroencephalogram slowed markedly when ketamine-sedated 
baboons breathed 80% \( \text{Xe} \), suggesting an 
anesthetic effect at this dose. This might be 
expected if the \( \text{MAC} \) for xenon in monkeys is similar 
to that in humans. Xenon 30–50% had no effect on 
\( \text{CBF} \).

Our results provide no evidence of \( \text{CBF} \) activation 
by 33% \( \text{Xe} \). In fact, xenon depressed \( \text{CBF} \) and 
\( \text{CMRO}_2 \). Residual ketamine may contribute to 
this depression, although 2–3 hours should be sufficient 
time for recovery from ketamine anesthesia. Residual 

edative effects could persist and account for 
\( \text{CBF} \) and \( \text{CMRO}_2 \) depression by 33% \( \text{Xe} \).

Local \( \text{CBF} \) values obtained by xenon-enhanced CT 
correlate well with measurements obtained by other 
methods such as microspheres,\(^8\)9,19–21 but shed no light 

### Table 2. Cerebral Variables Measured After 5 and 35 Minutes of 
Inhalation of Various Gas Mixtures in Rhesus Monkeys

<table>
<thead>
<tr>
<th></th>
<th>5 Minutes</th>
<th>35 Minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unanesthetized monkeys (n=4)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \text{CBF} ) (ml/100 g/min)</td>
<td>81±12</td>
<td>79±5</td>
</tr>
<tr>
<td>( \text{CMRO}_2 ) (ml/100 g/min)</td>
<td>7.2±0.8</td>
<td>6.5±0.4</td>
</tr>
<tr>
<td>( \text{CMRG} ) (ml/100 g/min)</td>
<td>8.1±1.2</td>
<td>7.5±2.0</td>
</tr>
<tr>
<td>( \text{CMRO}_2/\text{CMRG} \times 6 )</td>
<td>1.21±0.18</td>
<td>1.26±0.41</td>
</tr>
<tr>
<td><strong>Nitrogen/oxygen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \text{CBF} ) (ml/100 g/min)</td>
<td>73±11</td>
<td>78±13</td>
</tr>
<tr>
<td>( \text{CMRO}_2 ) (ml/100 g/min)</td>
<td>7.2±0.8</td>
<td>6.4±0.4</td>
</tr>
<tr>
<td>( \text{CMRG} ) (ml/100 g/min)</td>
<td>5.1±0.8</td>
<td>6.9±1.7</td>
</tr>
<tr>
<td>( \text{CMRO}_2/\text{CMRG} \times 6 )</td>
<td>1.51±0.23</td>
<td>1.34±0.27</td>
</tr>
<tr>
<td><strong>Xenon/oxygen</strong></td>
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<td></td>
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<tr>
<td>( \text{CBF} ) (ml/100 g/min)</td>
<td>63±8*</td>
<td>69±9</td>
</tr>
<tr>
<td>( \text{CMRO}_2 ) (ml/100 g/min)</td>
<td>4.9±0.5*</td>
<td>5.2±0.6</td>
</tr>
<tr>
<td>( \text{CMRG} ) (ml/100 g/min)</td>
<td>5.7±1.4</td>
<td>5.5±1.7</td>
</tr>
<tr>
<td>( \text{CMRO}_2/\text{CMRG} \times 6 )</td>
<td>1.21±0.22*</td>
<td>1.35±0.33</td>
</tr>
<tr>
<td><strong>Anesthetized monkeys (n=6)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \text{CBF} ) (ml/100 g/min)</td>
<td>88±19</td>
<td>93±26</td>
</tr>
<tr>
<td>( \text{CMRO}_2 ) (ml/100 g/min)</td>
<td>6.1±1.4</td>
<td>6.6±1.3</td>
</tr>
<tr>
<td>( \text{CMRG} ) (ml/100 g/min)</td>
<td>9.2±3.0</td>
<td>9.4±2.6</td>
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<tr>
<td>( \text{CMRO}_2/\text{CMRG} \times 6 )</td>
<td>0.86±0.14</td>
<td>0.98±0.22</td>
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<tr>
<td>Nitrogen</td>
<td></td>
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<tr>
<td>( \text{CBF} ) (ml/100 g/min)</td>
<td>81±26</td>
<td>86±24</td>
</tr>
<tr>
<td>( \text{CMRO}_2 ) (ml/100 g/min)</td>
<td>4.8±0.6</td>
<td>5.1±0.9</td>
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<tr>
<td>( \text{CMRG} ) (ml/100 g/min)</td>
<td>7.6±1.3</td>
<td>9.1±2.2</td>
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<tr>
<td>( \text{CMRO}_2/\text{CMRG} \times 6 )</td>
<td>0.87±0.14</td>
<td>0.78±0.20</td>
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<tr>
<td>Xenon</td>
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<tr>
<td>( \text{CBF} ) (ml/100 g/min)</td>
<td>79±20</td>
<td>77±25</td>
</tr>
<tr>
<td>( \text{CMRO}_2 ) (ml/100 g/min)</td>
<td>4.9±0.5</td>
<td>4.8±0.6</td>
</tr>
<tr>
<td>( \text{CMRG} ) (ml/100 g/min)</td>
<td>7.9±2.0</td>
<td>7.8±1.7</td>
</tr>
<tr>
<td>( \text{CMRO}_2/\text{CMRG} \times 6 )</td>
<td>0.90±0.30</td>
<td>0.86±0.16</td>
</tr>
</tbody>
</table>

\( ^* \)p<0.05 compared with corresponding value at 5 minutes with 
in nitrogen in unanesthetized monkeys.

### Footnotes

\(^{22}\) Love et al reported bilateral internal carotid
artery blood flow with Doppler flow probes in unanesthetized monkeys (also post ketamine anesthesia) exposed to 33% Xe and failed to observe even a transient effect on CBF. Darby et al25 monitored ICP in 17 head-injured patients and observed an increase of 1 mm Hg (p<0.05) late during xenon inhalation. These results were corroborated by Marion et al.24 Darby et al25 also measured ICP during 33% xenon-enhanced CT regional CBF measurements in monkeys; intracranial hypertension induced by a cortical freeze injury and observed no increase in ICP, suggesting no flow activation.

The CBF activation by 33% Xe, however, does occur in the unanesthetized, unsedated patient. Obst et al26 reported CBF activation by xenon of about 37% with CO2 correction and about 17% without correction. More recently, CBF measured by xenon-133 clearance and by transcranial Doppler ultrasonography showed that xenon consistently activated CBF by 12% to 20% with CO2 correction (W.D. Obrist, unpublished results). In 1989, Giller et al27 reported variable increases in CBF, averaging from 36% with 25-35% Xe inhalation in unsedated volunteers. The reason for the discrepancy of these results with previously cited data is unknown. However, we speculate that it may be attributable to the absence of sedation. The discrepancy might be resolved by studying the effect of xenon on CBF in sedated volunteers. The impact of xenon CBF activation on xenon-enhanced CT CBF values is calculated to be maximally less than 5%.28

Whereas CBF and CMRO2 were depressed by 12% and 16%, respectively, with 33% Xe inhalation in awake monkeys, it had no effect in fentanyl-anesthetized monkeys. Thus, xenon's effects on CBF and CMRO2 are sensitive to anesthetics. At the low dose of fentanyl we used, 10 µg/kg per hour, we observed no effect of fentanyl on CBF, CMRO2, CMRG, or oxygen-glucose index when the monkeys were breathing room air. On the other hand, in monkeys anesthetized with fentanyl, 33% Xe inhalation caused a significant increase in CMRG and the oxygen-glucose index, indicating greater glucose utilization or anaerobiosis. Cerebral blood flow and CMRO2 were unaffected. Freeman and Ingvar29 reported that in cats 20 µg/kg i.v. fentanyl reduced CBF by 11-27%, whereas 10 µg/kg had no effect. Carlsson et al30 reported that with increasing doses of fentanyl of 25-100 µg/kg in rats, CBF and CMRO2 progressively declined. Michenfelder and Theye,31 on the other hand, reported that fentanyl 6 µg/kg had no significant effect on CMRG or oxygen-glucose index. Thus, there is some disagreement on the specific effects of fentanyl on the oxygen-glucose index, but all studies show clear-cut depression of CBF and CMRO2 with increasing doses.

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### References


**KEY WORDS** • cerebral blood flow • fentanyl • xenon • monkeys
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