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Does Halothane Protect Against Hypoxia?

To the Editor.—Hershenson et al.1 confirmed a previous investigation2 that halothane significantly reduces cardiac output and oxygen consumption in normoxic and hypoxic newborn lambs when compared to paral-
yzed, ventilated controls. They conclude that halothane reduces oxygen consumption and delivery, and may be protective in hypoxic patients. One must exercise caution in interpreting these results because of two serious design flaws in this study. Hershenson et al.1 used paralyzed newborn lambs that were anesthetized with fentanyl (30 µg · kg⁻¹ · hr⁻¹) as their control animals. Fentanyl may not be an “anesthetic” in newborn lambs at ten to 100 times this dose.3 Indeed, the ability of fentanyl to anesthetize other species at this dose has been questioned as well.4 We wonder how this may have affected the author’s conclusions. Were the decreases seen in oxygen consumption and delivery the result of halothane per se, or secondary to the reduction of an artificially elevated oxygen consumption and delivery caused by pain or immobilization stress?5 Perhaps any anesthetic agent would produce the same results.

Secondly, all animals were exposed to progressively lower levels of inspired oxygen (100%, 21%, 15%, 10%) in this study without either an intervening return to normoxia or randomization of the sequence of exposure. Were the decreases in oxygen consumption and delivery at the 10% FpO₂ level unduly influenced or exaggerated by the immediately preceding hypoxic exposure?

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In Reply.—We welcome and appreciate Dr. Yaster’s comments concerning experimental design. With regards to the use of fentanyl, we agree that fentanyl alone may not provide surgical anesthesia in the new-
born lamb. We have found that unparalyzed animals given fentanyl alone at 30 µg · kg⁻¹ · hr⁻¹, while able to lie on the operating table without restraint and appearing to have a blunted response to stimulation, continued
to exhibit tachycardia (240 beats·min⁻¹), have occa-
sional spontaneous movements, and respond to noxious
stimuli. We did not, however, observe this in our con-
trol animals, in which anesthesia was induced with thiop-
ental, 10 mg·kg⁻¹. Perhaps thiopental has a longer
half-life in newborn lambs, or has synergistic effects
with fentanyl. Whatever the mechanism, control ani-
mals did not suffer from immobilization stress or pain as
evidenced by mean heart rate (205 beats·min⁻¹), \( O_2 \)
delivery (29.2 cc·kg⁻¹·min⁻¹), and \( O_2 \) consumption
(12.1 cc·kg⁻¹·min⁻¹), all of which were less than or
equal to values obtained in awake newborn lambs.¹ In
fact, we have found that fentanyl reduces total-body \( O_2 \)
consumption in succinylcholine-paralyzed lambs by
about 20%. These data demonstrate that control ani-
mals were, indeed, in an unstressed state, and, there-
fore, we consider the results of our study to be valid.

With regard to the randomization of exposures to
hypoxic gas mixtures, exposure to 10% \( O_2 \) often caused
severe cardiovascular instability or death of the experi-
mental animals. Like Dr. Yaster, we too were concerned
that such exposure would influence subsequent mea-
surements, and, therefore, deemed randomization im-
practical. Instead, as previously stated in the Methods
section, animals were exposed to progressively lower
levels of inspired oxygen, and ventilated with room air
for 30 min between exposure to hypoxic gas mixtures to
allow for recovery from hypoxia.

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