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### Time of Peak Hypotension during Rapid Induction Approximates Time of Peak Brain Halothane Tension in the Dog

*To the Editor:*—Behnia and Koushanpour<sup>1</sup> conclude that halothane suppresses the baroreceptor reflex by action on the vasomotor center, or perhaps on an inhibitory efferent pathway, rather than by a direct effect on the baroreceptors themselves. Workers in this field may be interested in our data, arising as an aside to an unrelated study,<sup>2</sup> which lend support to this conclusion.

During the testing in dogs of an automatic control system for induction and maintenance of halothane anesthesia, a precipitous decrease in blood pressure invariably was observed during induction. We were not especially surprised at this serious hypotension because, since one of the performance criteria of the study was to see how rapidly the system could increase the animals' brain tension of halothane to the desired level, inspired tension was taken very rapidly to 4% and the arterial tension (computed from a mathematical model) intentionally was driven above the desired brain tension transiently. However, we were interested to note that the peak arterial halothane tension in the model occurred at 85 s (SD 30 s) from start of induction and peak brain tension occurred at 145 s (SD 31 s), while peak depression of blood pressure (to 54% (SD 16%) of the preinduction value) occurred at 129 s (SD 41 s).<sup>2</sup> This peak blood pressure effect is much nearer the time of peak brain tension than to the time of peak arterial tension, which is the opposite of what would be expected if halothane acted directly on the baroreceptors.

Our published conclusions were specific to the aims

of our own study. However, a more general conclusion would be similar to that of Behnia and Koushanpour: that suppression of baroreceptor reflex by halothane is less likely to be a direct effect on the baroreceptors than it is to be a central effect.

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### Postoperative Methemoglobinemia in a Neonate

*To the Editor:*—We feel that the following case report is worthy of your readers' attention.

#### REPORT OF A CASE

The second twin, birth weight 640 g, gestational age 26 weeks, required urgent ligation of a patent ductus arteriosus. When presented for surgery, the baby was 7 days of age and weighed 580 g. He had been on continuous mechanical ventilation for severe respiratory distress syndrome since birth.

The anesthesia was accomplished without incident, and vital signs (ECG, rectal temperature, intraarterial blood pressure) remained stable during an anesthetic based on fentanyl, pancuronium, oxygen, and nitrogen. During surgery, the baby received 0.01 mg of atropine, 10 µg fentanyl, and 100 µg pancuronium. At the end of the procedure, following transfer to the Neonatal Intensive Care Unit, the patient's color was peculiarly dusky, in spite of adequate ventilation with an  $FI_{O_2}$  of 1.

The arterial blood gas analysis at that time revealed the pH to be 7.38,  $P_{CO_2}$ —38 mmHg,  $P_{O_2}$ —112 mmHg, and  $O_2$  Sat—79%.

The discrepancy between the apparent satisfactory  $P_{O_2}$ , the  $O_2$

saturation, and the patient's color prompted an analysis of the blood for methemoglobinemia, the pediatric staff being aware of two similar cases when methemoglobinemia had developed following a similar operation and anesthesia.<sup>1</sup>

The methemoglobin level was 35%—this gradually fell to 12% at 9 h and 1.6% at 24 h. A methemoglobin level was done on the patient's twin, which was normal, and so it was felt a congenital cause could be excluded.

While the methemoglobin could have been reduced by the administration of methylene blue, it was felt that this might result in an undesirable amount of hemolysis, and as the baby had received a not inconsiderable amount of adult red blood cells, that an expectant course could be adopted. The rapid fall in the methemoglobin level and satisfactory oxygenation endorsed this decision.

Methemoglobin is an oxidation product of hemoglobin not capable of reversibly binding oxygen and carbon dioxide. The chemical change involves the oxidation of ferrous to ferric iron in the heme moiety. A vast number of chemicals can precipitate this change—among anesthetic drugs, attention would focus on the active nitrogen atom in the aniline ring, the basis both for the synthetic narcotics of the fentanyl group and the amide local anesthetics.

Our first thought was to indict the fentanyl or one of its degradation products. However, we were not certain that a local anesthetic agent had not been used to lubricate the rectal temperature probe. Premature babies, because of a reduced activity of NADH-methemoglobin reductase, catalase, and glutathione peroxidase in fetal erythrocytes, are at great risk to the action of powerful oxidants in the presence of a high arterial  $P_{O_2}$ .

We are aware of two other similar cases where premature babies developed methemoglobin following anesthesia based on pancuronium, fentanyl, and air.<sup>1</sup> It is clear that in one of them a severe metabolic acidosis might have played a part, and in the other, benzocaine ointment was used to lubricate the endotracheal tube. Reference to the pharmaceutical company and to the FDA failed to reveal any other reported cases of methemoglobinemia in premature infants undergoing anesthesia based on fentanyl.

It appears to be common practice to seize the nearest tube of lubricant when seeking to lubricate endotracheal

tubes, nasogastric tubes, or rectal probes, without reference to the amount of agent that could be absorbed. It is not difficult to persuade 0.5–1.0 ml of anesthetic ointment to cover the surface of a rectal probe, and if this were 20% benzocaine,<sup>2</sup> a commonly used concentration, it would represent a considerable pharmacologic challenge to a 500-g infant. Even the use of commonly available 2% lidocaine also could be responsible, as there are reports in the literature of lidocaine being the cause of methemoglobin.<sup>3,4</sup>

In summary, it would behoove us to be more aware of the pharmacologic effects of lubricants in very small babies and to think of other causes of cyanosis at the end of surgery. Meanwhile, we are attempting to examine the problem *in vitro* using the breakdown products of fentanyl. We would be delighted to hear of the experience of any other physicians that might fall into the above category.

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