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Detection of Carbon Monoxide with Mass Spectroscopy during Anesthesia

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To the Editor:—I read with interest the case report in which Woehlck *et al.*[1] proposed that the detection of mixed halogenated agents during isoflurance anesthesia is a clinically useful sign to suggest the presence of carbon monoxide. The authors correctly note that clinical mass spectrometry cannot directly measure carbon monoxide because its molecular weight is the same as nitrogen and its fragmentation products are similar to those of carbon dioxide.

Yet, mass spectrometry may be helpful in the direct detection of changing carbon monoxide fractions in respiratory gas. In canine studies in which carbon monoxide poisoning was induced by injection of a molar amount of the gas into the inspired limb during closed-circuit anesthesia,[2] we monitored complete uptake of carbon monoxide from the circuit by mass spectrometry (model 6000, Ohmeda, Madison, WI). In that study, carbon monoxide in the circuit was qualitatively detected as spillover into and increase of the nitrogen channel (same molecular weight) and the carbon dioxide channel (conversion to C^{12} fragment). As complete pulmonary uptake of carbon monoxide occurred, the nitrogen and carbon dioxide mass spectrometry signals decreased to baseline levels.

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In Reply:—I agree with Breen that carbon monoxide may be detected and quantitated directly by mass spectrometry in certain situations. However, significant human toxicity may result from less than 1,000 ppm carbon monoxide.[1] This may be as much as 100 times less than the amount administered in the study by Breen *et al.*[2] The potential sources of interference with the technique of direct measurement of carbon monoxide by mass spectrometry includes changing levels of nitrogen and carbon dioxide as well as the presence of anesthetic agents and other gases. The changes in concentrations of nitrogen and carbon dioxide found in breathing circuits are likely to be many times greater than the amounts of carbon monoxide, which may result from anesthetic breakdown. An increase in indicated nitrogen may be due to the presence of carbon monoxide or the presence of nitrogen from air leaks, patient denitrogenation, or the

use of air as part of the respiratory gas mixture. Increased inspired carbon dioxide may be due to the presence of carbon monoxide or the presence of carbon dioxide due to carbon dioxide absorbent exhaustion or leaking valves in a circle system. If 500 ppm (0.05%) carbon monoxide was present in a patient's breathing circuit and was displayed as an increase of either 0.05% nitrogen or 0.05% inspired carbon dioxide, I speculate that this increase would not be distinguishable from innocuous fluctuations of these gases. Therefore, I suggest that, before direct detection of carbon monoxide by mass spectrometry can be used to warn of a patient's exposure to carbon monoxide during anesthetic breakdown, studies must be conducted to show the validity of this technique with clinically relevant concentrations of carbon monoxide.

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Binding of Halothane to Serum Albumin: Relevance to Theories of Narcosis

To the Editor:—The report by Johansson *et al.* provides further insight into the molecular site at which general anesthetics act.[1] The investigators found that halothane quenches the tryptophan fluorescence of bovine serum albumin in a concentration-dependent manner with a dissociation constant of 1.8 mM. They also reported that diethyl ether competes with halothane with a 50% inhibition concentration of 39 mM.

These concentrations surpass those required for anesthesia. At 1.8 mM, halothane equals a partial pressure at 37°C of 0.06 atm (1.8 mM = $(1.8 \times 10^{-6}$ mol/ml) $(2.5436 \times 10^{4}$ ml/mol)/0.75, where 0.75 is the partition coefficient for halothane in Krebs' solution at 37°C.[2] This exceeds the anesthetizing partial pressure of halothane in humans by a factor of 8.[3] Similarly, the partial pressure of ether at 39 mM equals 0.76 atm, assuming a partition coefficient of 13.[4] This exceeds the anesthetizing partial pressure of ether in humans by a factor of 40.[5]

Although Johansson *et al.* performed their studies at 25°C, the above ratios (8 for halothane and 40 for ether) for 37°C will approximate ratios at 25°C because of the counterbalancing changes in solubility and potency of anesthetics with decreasing temperature.[6] Furthermore, the dissociation constant of 1.8 mM for halothane quenching found by Johansson *et al.* is also an order of magnitude greater than the anesthetic potency of halothane measured in animals at lower temperatures: The righting reflex EC_{50} of halothane in tadpoles is approximately 0.1 mM at 20°C.[7] The calculations of partial pressure also assume that the solution used in the experiment was equivalent to an isotonic salt solution. If the albumin added appreciably to the solubility of halothane, this would lower the partial pressure calculated for halothane but not that for ether, whose solubility in blood scarcely differs from that in water.[8,9]

Even allowing for these factors, it appears that the partial pressures applied exceed those that produce anesthesia. If so, can the results provide us with insights into mechanisms of anesthetic action? Does the five-fold difference in the ratios for ether and halothane (8 *vs.* 40) mean that the finding for halothane does not apply equally to all anesthetics, and thus that the tryptophan site is not representative of a relevant anesthetic site of action? Finally, do results obtained at 25°C apply at the higher temperatures sustained by homeotherms?

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