Correspondence

Halogenated gas embolism prevention by Intralipid™

To the Editor:

The apparent safety and utility of an experimental infusion of isoflurane in Intralipid™ has been announced by Drs. Eger and MacLeod.[1] These investigators cited "relative overdosing at various tissue levels with subsequent direct toxic sequelae"[1] as the consequence of an intravenous injection of plain halothane described in earlier reports.[2-4] However, "The aetiology of the damages described is conjectural," "possibly being due to direct capillary damage or to embolization."[4]

Eger and MacLeod referred to a case of human self-poisoning by 3 ml liquid halothane *iv* producing acute hypoxia, acute right heart strain pattern by ECG, pulmonary artery pressure of 30/16 mmHg with pulmonary artery occluding pressure of 8 mmHg.[2] The selected commentary[5] on that Case Report[2] offers that "This is more consistent with ... a manifestation of hypoxic pulmonary vasoconstriction."[5] Certainly at body temperature a 3 ml *iv* injection of halothane instantaneously converts to 720 ml of halothane gas. A gas embolism of this magnitude likely would produce an acute morbidity or mortality directly on the basis of embolism. Pulmonary haemorrhage seen on autopsy[2,4] could be secondary to embolism.

The success of Eger and MacLeod's mice in well tolerating emulsified isoflurane[1] is attributable to the strong partitioning of the isoflurane into the Intralipid™ while in intravascular circulation, safety and slowly releasing the isoflurane while preventing gross gas embolism. This new method[1] should hold promise for simplified circuit anaesthesia with emulsified volatile agents.

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REFERENCES

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2 *Dwyer R, Coppel DL.* Intravenous injection of liquid halothane. Anesth Analg 1989; 69: 250–5.

3 *Kawamoto M, Suzuki N, Takasaki M.* Acute pulmonary edema after intravenous liquid halothane in dogs. Anesth Analg 1992; 74: 747–52.

4 *Sandison JW, Sivapragasam S, Hayes JA, Woo-Ming MO.* An experimental study of pulmonary damage associated with intravenous injection of halothane in dogs. Br J Anaesth 1970; 42: 419–24.

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REPLY

I wish to thank Dr. Gould for his interest and enthusiasm in the use of iv emulsified isoflurane. I would like to address his comments regarding the possible cause of the cardiopulmonary toxicity seen with the iv use of pure halothane. It remains my feeling that the pathology reported in these case reports[1-2] and studies[3-5] is likely the effects of direct toxicity of either a very high concentration of agent or that of a liquid halothane embolism that created the toxicities described.

Halothane's boiling point is 50.2° C. Consequently, at 37° C halothane exists primarily as a liquid. Were halothane injected into the bloodstream there would likely initially exist a liquid halothane bolus. Equilibration would occur with time into four compartments: undissolved liquid halothane, dissolved liquid halothane, dissolved gaseous halothane and as a vapour pressure the halothane creates. Multiple factors may well come into play concerning the speed at which equilibration occurs. These include the size and shape of the halothane liquid bubble, blood flow characteristics, the blood solubility of the halothane, the blood:gas coefficient and time for equilibration. Given enough time for total equilibration a small halothane bolus of 3 ml would only yield a concentration of the equivalent of <1% end tidal concentration. However, if insufficient time passes for equilibration before the bolus reached a vessel of a critically small diameter then there might exist an embolism of liquid halothane. It is possible that this scenario could occur in the lungs' capillary network and create tissue toxicity. Even if the liquid could totally dissolve, there would likely not be time for sufficient mixing with the entire intravascular compartment and local concentrations of the agent might rise to very high levels creating tissue damage.

I feel it unlikely that a halothane gas embolism could form at 37° C. The system of halothane liquid in blood is really a mixture of a solute and a solvent. In such a mixture when increasing concentrations of a solute are added, eventually the concentration exceeds that which the solvent can accommodate. At this critical point "rain out" of the liquid solute occurs at a sub-boiling point temperature. Consider an analogy of a mixture of gasoline and water at 37° C in a sealed container. In this system the gasoline exists in four compartments: as a liquid layer undissolved in the water, a dissolved liquid component within the water layer, as dissolved gas and as an exerted vapour pressure. There are no undissolved gaseous gasoline bubbles present. Rather, the gasoline that can not dissolve in the water layers out as a liquid.

We speculate that by emulsifying the volatile agents in Intralipid™ micelle-like microbubbles of liquid agent might be created. This thesis would suggest that the Intralipid™ acts