

Anesthesiology
58:391, 1983

Etiology of Halothane Hepatotoxicity

To the Editor:—The paper by Plummer and his colleagues¹ concerning a rat model draws attention once again to halothane hepatotoxicity. Although it is our impression that the incidence in humans of this often fatal complication has decreased, possibly due to the use of other anesthetic agents, cases still occur. Indeed, in our own institution, we have had three instances, two adults (both female) and one female child, in the past two years. All three patients had severe hepatitis, all reasonable causes were excluded, and it was assumed that halothane was responsible. Fortunately all three patients survived. We question, however, whether further study of the rat hepatotoxicity model will be fruitful in elucidating the cause of halothane-associated hepatitis in humans.

Our reasons for expressing doubt relate to the many variables which seem to affect the rat model. For example, in addition to the anesthetic, severe hypoxia and enzyme induction,² hyperthyroidism,³ starvation,⁴ male sex,² and strain specificity,⁵ are required in some combination before liver damage is seen. In addition, we understand the experimental rat may exhibit unreasonableness in refusing to become hepatotoxic during the summer months or when purchased from a different supply house. Furthermore, during some of our own laboratory studies, we have noted marked decreases in plasma glucose, osmolality and albumen, as well as body weight, in rats subjected to 24-hour periods of starvation. It is not too surprising that, under these conditions, the general anesthetic state rather than the specific anesthetic agent might result in liver damage. The initial studies of the rat model indicated that only halothane seemed to be hepatotoxic and there was a tendency to ignore the plethora of variables. Now it is becoming clear that other volatile and nonvolatile anesthetics⁶ also can cause liver damage, and the specificity of the preparation for halothane seems to us to be in doubt.

A simple metabolic explanation for halothane hepatotoxicity may still be relevant in the rat model, but when one considers humans, the factors operating in the rat have yet to be demonstrated. No clear association

with hypoxia, anesthetic dose, enzyme induction, hyperthyroidism, starvation, or male sex has been established⁷; the only genetic link is tenuous⁸ and requires further study. Perhaps the Pied Piper should be summoned to call the rats away to their well-deserved rest and a more suitable model be sought.

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Buffering Capacity of Citrate Antacids

To the Editor:—Administration of oral antacids to reduce the risk of aspiration pneumonitis in obstetric patients is a widespread practice. Many authors have re-

cently recommended the use of sodium citrate instead of emulsified (particulate) antacids since the former agent exhibits less pulmonary toxicity if aspirated.¹ Al-

though sodium citrate is an effective antacid,² its palatability is low (thus, a flavoring is usually added) and a commercial preparation is not available for this use.

Citrate preparations, however, are commercially available, and although their primary use has been as systemic alkalizers, they are also effective antacids. These clear, non-particulate preparations are Polycitra® and Bicitra® (Willen Drug Company). Polycitra-LC is a sugar-free preparation containing 0.34 M potassium citrate, 0.34 M sodium citrate, and 0.32 M citric acid, whereas Bicitra contains 0.34 M sodium citrate and 0.32 M citric acid. These agents are more palatable than 0.33 M sodium citrate (possibly due to their lower pH: 5.2 for Polycitra-LC; 4.5 for Bicitra), and can be administered orally without a flavoring or other additive. Comparing their effectiveness as antacids (by our measurements), 1 ml of Polycitra-LC or Bicitra will buffer, to pH 2.5, 18 ml and 8 ml of 0.1 N hydrochloric acid, respectively, whereas 1 ml of 0.33 M sodium citrate will buffer 9 ml of 0.1 N hydrochloric acid to the same pH. Therefore, Polycitra-LC should be twice as effective, and Bicitra nearly as effective as 0.33 M sodium citrate in achieving a safe gastric pH (>2.5) in a patient with

a full stomach. Bicitra is also safer than emulsified (particulate) antacids if aspirated.³

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Rebreathing and the Bain Circuit

To the Editor:—The article by Dean and Keenan¹ on spontaneous breathing with the T-piece (Bain) circuit implies that rebreathing is minimal or "prevented" so

long as the carbon dioxide tension of the inspired gases, P_{CO_2} , is less than 10 mmHg (1.4%). This level would surely represent rebreathing and is more than many

BAIN

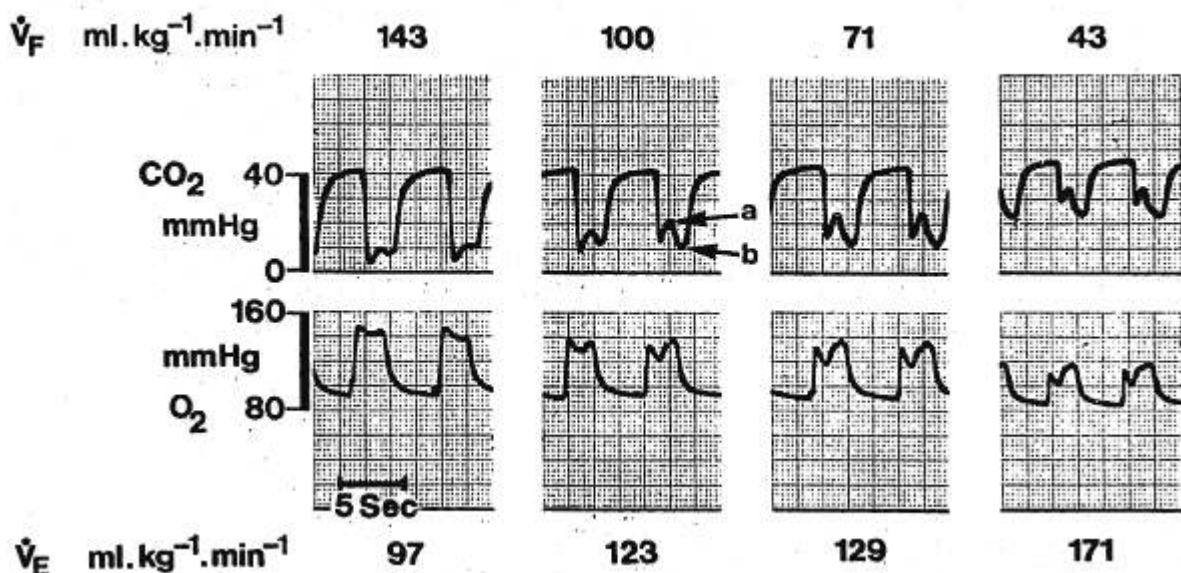


FIG. 1. Respiratory gases in a subject breathing air with a Bain circuit (by permission of *Anaesthesia and Intensive Care*).