

sponsible for reversal of epidural narcotic tachyphylaxis in the case reported by McCoy and Miller and, more importantly, my failure to obtain this outcome following epidural local anesthetic in the majority of cases in whom I have attempted it. Rather, it has been my experience that either a protracted series of epidural local anesthetic blocks or continuous epidural infusion often is required. The resultant duration of analgesia is usually consistent with the duration of local anesthetic blockade. The efficacy of epidural local anesthetic injections for relief of cancer pain is well appreciated.² The resulting analgesia may be short-lived or in some cases quite sustained for as long as several weeks or more. The latter response may occur because of an underlying reflex sympathetic dystrophy.² Given the likely biochemical basis for opiate tolerance^{5,6} and the time frame required to reverse this effect in animal models (1–2 weeks), it would be naive to simply assume that responsiveness to epidural narcotics had returned following epidural injection of a local anesthetic. Rather, the response in such patients is likely singularly due to the effects of the epidural local anesthetic, *i.e.*, sympathectomy. This issue is of major importance, because spinal narcotic tolerance seems to be the limiting factor in successful application of chronic epidural narcotic therapy. This also accounts for the interest in other forms of epidural therapy, given the multiple receptors, modulators, and substrates involved in spinal nociceptive pathways.⁷ Perhaps a trial of epidural local anesthetic therapy should precede attempts to use

epidural narcotics, because some patients may have protracted pain relief following epidural local anesthetic therapy alone.

DENNIS W. COOMBS, M.D.
*Director, Clinical Investigations
Department of Surgery (Anesthesia)
Dartmouth-Hitchcock Medical Center
Hanover, New Hampshire 03756*

REFERENCES

1. McCoy D, Miller ME: Epidural morphine in a terminally ill patient. *ANESTHESIOLOGY* 57:427, 1982
2. Bonica JJ: Cancer pain, Pain, Research Publications: Association for Research in Nervous and Mental Disease, vol. 58. Edited by Bonica JJ. New York, Raven Press, 1980, pp 335–362
3. Woods WA, Cohen SE: High dose epidural morphine in a terminally ill patient. *ANESTHESIOLOGY* 56:311–312, 1982
4. Yeung JC, Rudy TA: Multiplicative interaction between narcotic agonisms expressed at spinal and supraspinal sites of antinociceptive action as revealed by concurrent intrathecal and intracerebroventricular injections of morphine. *J Pharmacol Exp Ther* 215:633–642, 1980
5. Takemori AE: Neurochemical basis for narcotic tolerance and dependence. *Biochem Pharmacol* 24:2121–2126, 1975
6. Martin WR, Eades CG: A comparison between acute and chronic physical dependence in the chronic spinal dog. *J Pharmacol Exp Ther* 146:385–395, 1964
7. Yaksh TL: Spinal opiate analgesia: Characteristics and principles of action. *Pain* 11:293–364, 1981

(Accepted for publication April 25, 1983.)

Anesthesia-induced Hepatotoxicity

To the Editor:—The letter by Strunin and colleagues¹ proposing abandonment of the rat model of anesthesia-induced hepatotoxicity invites further comments. The rat model has certain problems that Strunin *et al.*¹ have emphasized. However, one should not expect from a model more than the model can give. Obviously, the rat model cannot solve all problems related to the whole spectrum of liver injuries. I think that there are at least three different types of postoperative liver dysfunction in humans. One of these is fulminant halothane-induced hepatitis; there are some old² and some very important recent^{3,4} data strongly suggesting that this form of hepatitis is mediated immunologically. Another form of postoperative hepatitis is viral hepatitis, which coincides with the perioperative period.^{5–7} Finally, liver damage can develop in response to intermediates of reductive metab-

olism of halothane and/or a substantial decrease in oxygen availability to the liver *per se* due to respiratory and/or circulatory (systemic or regional splanchnic) depression.⁸

The rat model has not been very helpful in elucidating the first two forms of liver injury; however, it seems to be suitable for the last one. The article by Plummer *et al.*,⁹ which evoked the letter to the editor,¹ is a good example of the fruitfulness of the rat model in elucidating a metabolic etiology of anesthetic hepatic toxicity. Many recent publications have shown the usefulness of the model in evaluation of oxygen availability to the liver.^{8,10,11}

I think the rat model is still in its infancy; the model actually was born only 4 years ago, when liver injury could be reproduced regularly.^{12,13} Since then, many factors have been shown to influence liver damage in the

rat (Strunin *et al.* accurately listed some of them¹). I believe that as research with the model matures, investigators will find the rat model instrumental in discovering the link between anesthetic effects and hepatotoxicity. Furthermore, the mechanisms of hepatic damage in the rat indeed may be similar to those in at least one form of human postoperative hepatic dysfunction. Therefore, I cannot agree that the time for the rat's retirement has come.

SIMON GELMAN, M.D., PH.D.
Professor of Anesthesiology
Department of Anesthesiology
The University of Alabama in Birmingham
619 South 19th Street
Birmingham, Alabama 35233

REFERENCES

1. Strunin L, Harrison LJ, Davies JM: Etiology of halothane hepatotoxicity. *ANESTHESIOLOGY* 58:391, 1983
2. Dykes MHM, Gilbert JP, McPeck B: Halothane in the United States. An Appraisal of the literature on "halothane hepatitis" and the American reaction to it. *Br J Anaesth* 44:925-934, 1972
3. Vergani D, Mieli-Vergani G, Alberti A, Neuberger JM, Eddelston ALWF, Davis M, Williams R: Antibodies to the surface-altered

4. Neuberger J, Gimson AES, Davis M, Williams R: Specific serological markers in the diagnosis of fulminant hepatic failure associated with halothane anaesthesia. *Br J Anaesth* 55:15-19, 1983
5. Dougherty WJ, Altman R: Viral hepatitis in New Jersey 1960-1961. *Am J Med* 32:704-716, 1962
6. Johnstone M: Halothane hepatitis. *Lancet* 2:526, 1978
7. Johnstone M: Liver injury in the surgical patient. A critical review. *Br J Anaesth* 36:718-729, 1964
8. Shingu K, Eger EI, II, Johnson AB, Van Dyke, RA, Lurz FW, Harper MH, Cheng A: Hepatic injury induced by anesthetic agents in rats. *Anesth Analg* 62:140-145, 1983
9. Plummer JL, Beckwith ALJ, Bastin FN, Adams JF, Cousins MJ, Hall P: Free radical formation *in vivo* and hepatotoxicity due to anesthesia with halothane. *ANESTHESIOLOGY* 57:160-166, 1982
10. Shingu K, Eger EI, II, Johnson BH: Hypoxia per se can produce hepatic damage without death in rats. *Anesth Analg* 61:820-823, 1982
11. Shingu K, Eger EI, II, Johnson BH: Hypoxia may be more important than reductive metabolism in halothane-induced hepatic injury. *Anesth Analg* 61:824-827, 1982
12. McLain GE, Sipes IG, Brown BR Jr: An animal model of halothane hepatotoxicity: Role of enzyme induction and hypoxia. *ANESTHESIOLOGY* 51:321-326, 1979
13. Ross WT Jr, Daggy BP, Cardell RR: Hepatic necrosis caused by halothane and hypoxia in phenobarbital-treated rats. *ANESTHESIOLOGY* 51:327-333, 1979

(Accepted for publication April 26, 1983.)

Anesthesiology
59:488-489, 1983

Safety Check for the CPRAM Circuit

To the Editor:—In the October 1982 issue of *ANESTHESIOLOGY*, KHI Anesthesia and Resuscitation (Frazer, Pennsylvania) advertises its coaxial Mapleson D circuit, the CPRAM™ (Controlled Partial Rebreathing Anesthesia Method) Breathing System. It differs from the Bain circuit, another coaxial circuit, by having two sideholes at the patient end of the inner (fresh gas) hose (fig. 1). The manufacturer claims that this results in "vortex dynamics," which provides better humidification of fresh gases and efficient removal of carbon dioxide. We believe that the design of this circuit creates a possible hazard for the patient. Accordingly, we have devised a technique to protect against this risk.

If the inner hose within a coaxial Mapleson D circuit is partially or completely fractured or disconnected, fresh gas can enter the circuit in a proximal portion of the outer tube rather than at the patient connection. This increases dead space and may result in hypercapnia and possibly hypoxemia. Malfunctioning of the fresh gas hose occurred with early models of the Bain circuit,¹ leading Pethick² to suggest a way to detect proximal disconnection of the inner tube. Oxygen is flushed through the circuit with the patient end of the circuit open. If the inner hose

is intact, the high flow through the inner hose will create a Venturi effect, drawing gas from the outer hose and collapsing the reservoir bag. In contrast, if the inner hose is disconnected or has a fracture, gas will escape to the outer hose and inflate the reservoir bag.

Unfortunately, when this test is performed with the

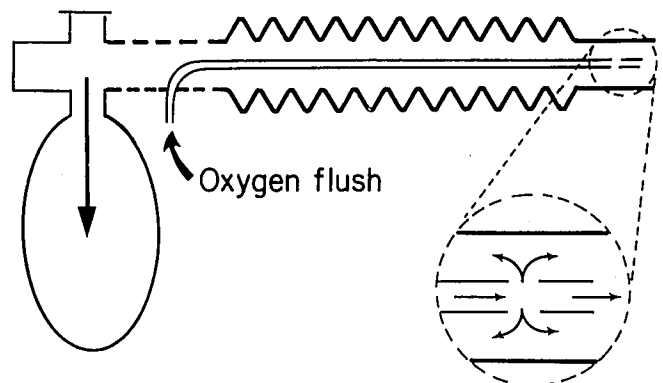


FIG. 1. When the CPRAM™ circuit is flushed with high-flow oxygen, gas exits through the side holes and the reservoir bag always fills, regardless of the integrity of the inner hose.