

the hemoptysis.<sup>3</sup> If hemoptysis occurs or new pulmonary changes near the catheter tip are seen, the catheter should be removed without delay.

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### Reductive Metabolism of Halothane and Hepatotoxicity

*To the Editor:*—Eger<sup>1</sup> rightly points out that the currently identified reductive metabolites of halothane have not been shown to be toxic in themselves. However, we have recently reported hepatic functional and morphologic abnormalities that accompany increases in concentrations of volatile reductive halothane metabolites in Fischer 344 rats subjected to enzyme induction and hypoxia.<sup>2-5</sup> Specifically, concentrations of 1,1-difluoro-2-chloroethylene (CDF) and 1,1,1-trifluoro-2-chloroethane (CTF) were low in the absence of abnormalities in hepatic function or morphology. However, a four- to eightfold increase in reductive metabolism of halothane resulted from enzyme induction and moderate hypoxia (oxygen, 14 per cent) and this was associated with hepatic necrosis in all animals at 24 hours after anesthesia; appropriate controls showed no such abnormalities. These findings satisfy accepted criteria for hepatic damage due to direct cellular injury. The formation of CDF and CTF could only proceed via an intermediate free radical or carbanion,<sup>4</sup> so it is most likely that these metabolites merely serve as a "marker" of reductive metabolism and that hepatic cellular injury results from the intermediate carbanion or free radical. These observations were made in an animal model with oxidative and reductive halothane metabolism similar to that of man, and the lesion described was similar to that previously reported in cases of presumed halothane hepatitis. Thus, the findings in our animal model have pertinence to the important question of hepatic effects of halothane in man.<sup>3,4</sup>

We found in man that reductive halothane metabolites were present in the exhaled air during halothane anesthesia with 100 per cent oxygen at concentrations

higher than those reported after anesthesia by Sharp *et al.*<sup>6</sup> Our studies also show that concentrations of volatile reductive halothane metabolites rapidly increase from the start of anesthesia, reach a plateau after one hour, and decline rapidly after anesthesia. In conclusion, there seems little doubt that the reductive metabolism of halothane has significance for human hepatic toxicity of halothane, and that the volatile reductive metabolites CDF and CTF are useful markers for reductive metabolism.

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