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Are Effects of Halothane on Hepatocytes "Pathologic"?

To the Editor:—As an author of an article that was cited in the recent special article by Chang and Katz,¹ I wish to raise some concerns regarding interpretation of our studies related to the liver. In our paper we reported hepatic morphologic changes after repeated exposures of rats to halothane, .25 per cent.² In hepatocytes of treated rats, smooth endoplasmic reticulum, lipid droplets and microbodies increased, in addition to other minor alterations. None of these alterations was regarded as a "lesion" or "hepatic damage," nor were they described as such in our paper. Therefore, I should like to record my objection to the reference by Chang and Katz that we reported halothane induced "lesions." In my opinion, the changes we recorded should be regarded as reversible and as an adaptation to the administration of the xenobiotic.

Another area of concern is that of cell sampling. In their original report, Chang *et al.* showed electron micrographs of abnormal hepatocytes at moderately high magnification.³ In the text of that paper they made several references to "many" relatively normal cells. In their special article, Chang and Katz published micrographs that are also at moderately high magnification, and all clearly show the existence of abnormal cells. The reader is unable to gain an impression of the frequency of abnormal cells. Since, in any tissue, some cells that are abnormal, dying or poorly fixed, are always found, the omission of any mention of sampling methods or number of cells sampled is disturbing. One way to deal with this problem is to use lower magnification or even light microscopy for orientation of the reader. A good example of the effective use of light microscopy appears in the same issue of ANESTHESIOLOGY in the report by Sipes and Brown.⁴ The light micrographs presented there provide clear evidence of the extent of cellular damage.

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In studies of the effects of anesthetics on organ function or organ change, the effects of the anesthetic state should be separated from the effects of the anesthetic drug *per se* to the extent that this is possible. Could the observed cellular effects be due to the effects of altered feeding, intestinal absorption, etc.? Were the terminal weights of the treated animals comparable to the terminal weights of the untreated controls? Data to answer these questions are not provided. Finally, most morphologic studies can be considerably strengthened and interpretation simplified when they are accompanied by simultaneous measurement of other indices (*e.g.*, correlation of biochemical and structural changes).

In their conclusion, Chang and Katz acknowledge that their findings are still subject to critical debate. I agree.

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