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Correspondence

Fluroxene in the Rat and Man

To the Editor:—Harrison and Smith, in the article, "Massive Lethal Hepatic Necrosis in Rats Anesthetized with Fluroxene, after Microsomal Enzyme Induction" (ANESTHESIOLOGY 39:619–625, 1973), draw rather sweeping, and what I consider inaccurate, conclusions from their data. These investigators note that in rats fluroxene caused hepatic damage which was increased by pretreatment with the enzyme-inducing drug, phenobarbital. From this they concluded, "Speculation aside, the clinical implication of our observation is clear. Fluroxene anesthesia should not be used for any patient who is on a regimen of treatment with a drug that has enzyme-inducing properties."

I believe the point at which Drs. Harrison and Smith have erred is in making a direct transposition of the results of an animal study to clinical practice. It is well known that there are great variations in the metabolism and pharmacologic effects of many drugs among different species of animals. For this reason, it is an accepted pharmacologic principle that animal toxicity studies have relevance for investigation of drug toxicity in man only if the animal model and man share similar metabolic pathways and toxic manifestations. Specifically, with regard to fluroxene anesthesia in man, there does not appear to be a higher incidence of hepatic dysfunction following its administration than with any other anesthetic agent. Also, it is known that there are major differences in the products of its metabolism between dogs, mice, and rats on the one hand and man on the other; the markedly hepatoxic substance, trifluoroethanol, is a major end-product of the metabolism of fluroxene in the animal species but not in man. Therefore, it is not unexpected that treatment with an enzyme-inducing drug would increase the amount of toxic metabolite in the animals and would exacerbate any adverse reaction the metabolite might produce. Since trifluoroethanol is only a very minor product of the metabolism of fluroxene in man, there is no reason to suspect that enzyme induction would lead to hepatic damage in man. Therefore, it is apparent that the animal model proposed by Harrison and Smith is inappropriate, *i.e.*, the metabolic pathways are different and the toxic manifestation is not common to both species. Their conclusion, then, is speculation, and almost certainly incorrect.

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To the Editor:—I have every sympathy with the views expressed by Dr. Mazze, for I confess my own initial reaction to the observations reported in our paper[1] were similar. Indeed, this crucial question of the applicability to man of drug research in animals was extensively discussed with particular reference to fluroxene in a recent Editorial in ANESTHESIOLOGY.[2]

However, I thought that we had made it clear in our paper that we considered that the publication of a report of a human fatality from a similar lesion following fluroxene anesthesia[3] and in circumstances analogous to that pertaining in our experimental animals gave our observations immediate clinical relevance. Since that time ANESTHESIOLOGY has published another report of a similar fatality.[4] In addition, there have been two recent reports of postoperative jaundice immediately following fluroxene anesthesia, although in these circumstances no cause–effect relationship can be strictly validated.[5,6]

In the circumstances we still feel that exposing to fluroxene anesthesia patients whose levels of microsomal enzyme activity may have been increased by previous medication is exposing such patients to an unwarranted hazard, a hazard over which the clinician in the present state of knowledge has no control. The drug armamentarium of the anaesthetist is sufficiently wide and versatile today to allow adequate alternate choice where use of a particular agent might be hazardous to the patient.

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REFERENCES

1. Harrison GG, Smith JS: Massive lethal hepatic necrosis in rats anesthetized with fluroxene, after microsomal enzyme induction. ANESTHESIOLOGY 39:619–625, 1973
2. Wardell WM: Fluroxene and the penicillin lesson (editorial). ANESTHESIOLOGY 38:309–312, 1973
3. Reynolds ES, Brown BR, Vandam LD: Massive hepatic necrosis after fluroxene anesthesia. N Engl J Med 286:530–531, 1972
4. Tucker WK, Munson ES, Holaday DA, et al: Hepatorenal toxicity following fluroxene anesthesia. ANESTHESIOLOGY 39:104–107, 1973
5. Harris JA, Cromwell TH: Jaundice following fluroxene anesthesia. ANESTHESIOLOGY 37:462–463, 1972
6. Wallman SB, Surks SN: Hepatic damage after fluroxene anesthesia. Anesth Analg (Cleve) 52:942–945, 1973

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Overinflating Low-pressure Cuffs to Prevent Aspiration

To the Editor:—Our department has switched to the newer high-volume, low-pressure cuffed Portex endotracheal tubes. When we inflate these cuffs, we add air until reaching the point of no "leak" with positive pressure applied to the airway. When testing for respiratory force and vital capacity in awake intubated patients in the recovery room, I have noticed on several occasions that there has been an apparent discrepancy in test measurements, that is, a very poor (only slightly negative) inspiratory force, but a good (expired) vital capacity. I believe that when these patients inspire, the dilation of the trachea normally seen with inspiration seems to allow them to breathe around as well as through the tube. In fact, when the tube was deliberately occluded, they were able to get some air in, but rarely could force air out around the cuff.

In light of this, I have been deliberately overinflating the cuff in patients who are prone to aspirate during the intra- or postoperative period.

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