

from isolated episodes usually present a fallacious association drawn between the administration of a drug and the subsequent development of hepatic damage. Then to compound the problem, the association is then misconstrued as "due to" and comes to be cited by other individuals as essentially proving a causal relationship between the drug and the hepatic damage.

Surveys have failed in the past to implicate the halogenated anesthetics in current use in postoperative hepatic damage. In fact, most relevant retrospective studies show no difference in the incidence of postoperative hepatitis following any of the commonly used anesthetic agents.

This reported case has failed to disprove the existence of a coincidental viral hepatitis, drug interaction, or other reasonable, possible causes for a postoperative jaundice. The allergic theory of the halogenated anesthetics toxicity also becomes less and less tenable in this or any other case of a like gender.

I plead with my fellow physicians to report a case of this type as one of postoperative jaundice alone, and to desist in stating such an untenable diagnosis as "enflurane, halothane, or methoxyflurane hepatitis" in medical writing or in patients' hospital records!

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To the Editor.—It would, indeed, be singular if hepatic necrosis did not follow enflurane anesthesia on rare occasions, as it has occurred after all other anesthetics known to man that have achieved widespread use. This report was, therefore, not surprising but disturbing when one realized that a causal rather than a temporal relationship was being implied. It is notoriously misleading to arrive at such conclusions from an isolated case.

Nevertheless, this case does, perhaps, illustrate two salient facts that ought to be better known by anesthesiologists and surgeons nationwide. First, Mushin et al,¹ despite questionable conclusions, did demonstrate an incidence of postoperative hepatic necrosis nine times greater than the expected figure in patients who had been given two anesthetics in a four-week period. The London Hospital Study has confirmed this and, second, has stressed that this consequence occurs *regardless of the anesthetic used*.² Although the choice of anesthetic may not have been influenced by the fear of postoperative hepatitis in this

case, it does illustrate the futility of avoiding a halogenated agent in these circumstances.

Potent causes of hepatic necrosis that tend to be more common in patients undergoing multiple operations include sepsis, shock, hypoxia, blood transfusions, malnutrition, and the intake of known hepatotoxic drugs.

The former two may have been operative in this patient. It is also unwise to rule out a coincidental viral hepatitis merely because no history of a contact was elicited. Only one third of viral hepatitis cases do recall being exposed to the disease.

It would be better to reserve speculation and judgment on the hepatotoxic potential (if any) of enflurane until the results of extensive clinical trials proceeding at present are forthcoming.

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1. Mushin WW, Rosen M, Jones EV: Post-halothane jaundice in relation to previous administration of halothane. *Br Med J* 3:18-22, 1971.

2. Simpson BR, Strunin L, Walton B: Halothane hepatitis: Fact or fallacy. *Proc R Soc Med* 66:56-63, 1973.

The patient died 20 days after the first operation (enflurane), nine days after the second (no enflurane). THE JOURNAL's editorial error, for which we apologize, has been excluded as a possible factor within the comments presented here.—ED.

Overdose of Tetanus Toxoid

To the Editor.—I would like to report a patient who received an overdose of "tetanus toxoid, fluid." A total dose of 3.8 ml (2.0 ml intramuscularly in one buttock, 1.6 ml in the other, and 0.2 ml subcutaneously in the left deltoid region) was inadvertently administered to a 32-year-old female employee. The patient was to have received prophylactic γ -globulin (0.02 ml/lb of body weight) because of a puncture wound of her little finger by a hypodermic needle in a contaminated disposal box. Based on her report of localized reactions to tetanus toxoid in the past, the 0.2-ml dose rather than the standard 0.5 ml of tetanus toxoid, fluid was ordered.

There was no immediate local or systemic response. The patient refused hospitalization for observation. Fifty milligrams of diphenhydramine hydrochloride (Benadryl) orally every four hours was prescribed for three days. A local reaction manifested by mild erythema, heat, induration, slight tenderness, and pain developed at each injection site in the buttocks, with a peak at about 48 hours followed by gradual diminution and

complete disappearance in five days. There was no reaction at the injection site in her arm at any time. There were no systemic symptoms or other signs noted during this period or over the next five weeks.

The medical departments of three major drug companies who manufacture tetanus toxoid were consulted and were not aware of any patient receiving a dose comparable to that given this patient.

The patient demonstrated a typical delayed hypersensitivity with no serum sickness or significant complications. The wide margin of safety of tetanus toxoid, fluid in this case was appreciated by all.

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As Directed

To the Editor.—Dr. Lerman (227:204, 1974) suggests that when he writes a prescription with the directions "Sig: With manufacturer's directions," the pharmacist should label all dispensed drugs with proper individualized instructions. He also recommends that the pharmacist should give the patient the package insert and underline the dosage instructions!

As Dr. Lerman is aware, manufacturer's instructions contained in package inserts frequently list several different regimens that are dependent on many specific patient factors. If the pharmacist has access to the patient's record, he can assist the physician in determining the most suitable dosage for a specific patient. However, without this information it is dangerous as well as illegal for the pharmacist to determine the dosage.

I agree with Dr. Lerman that verbal instructions are usually unreliable, and it has been demonstrated in the pharmaceutical literature that written instructions in common patient language are much more effective in improving patient compliance and reducing medication errors.^{1,2} I completely disagree with his statement that the patient should be given the package insert. The package insert is designed for professional information, and the patient does not have the medical knowledge to understand what is meant by such terms as "cardiotonic glycoside," "agranulocytosis," or "extrapyramidal reactions."

In conclusion, I agree that the pharmacist should never type "Take as directed" on the label. If there is any question concerning the dosage, he should contact the physician. In