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Are Additional Cancer Studies Justified?

To the Editor:—Dr. Eger's excellent editorial on Dragons and Other Scientific Hazards[1] prompts me to write about a different but related dragon—the one that has to do with the alleged carcinogenicity of inhalational anesthetics in general, and isoflurane in particular.

I would like to state my opinion that the Commissioner of the Food and Drug Administration should not only stay, as has already been done, but in addition should also revoke the section of the regulations calling for teratogenicity and carcinogenicity studies of halothane, methoxyflurane, enflurane, and isoflurane. This opinion is based on several considerations. First, it is to be expected that fat-solvent inhalational anesthetics will alter the function of lipid membranes. That is the medical reason why they are administered. In addition to their desired effect on neural tissue, there will be undesired effects on other tissues. Embryonic tissue, if present, will be affected, as well as maternal tissue. This effect can be expected not only from inhalational anesthetics, but also from other fat solvents such as ethanol. Equieffective doses of various inhalational anesthetics seem to have about the same damaging effects on developing embryos. Extensive proposed studies would probably add little to what is already known.

Second, the alleged carcinogenic potential of isoflurane is based on its structural similarity to chloromethyl methyl ether, a known carcinogen.[2,3] However, their chemical activities are markedly different. Chloromethyl methyl ether is an active aklylating agent, and isoflurane is not.[4] The activity is the important factor, and the structure can only suggest the activity. How much money should be spent to prove the nonexistence of significant carcinogenicity from isoflurane?

Third, improper analogies have been adduced in the comparison of halothane, methoxyflurane, enflurane, and isoflurane with such compounds as vinyl chloride,[5,6] orally administered carbon tetrachloride, and orally administered trichloroethylene.[7] All of the latter group of compounds are extensively metabolized to compounds that are toxic.[8] Chloromethyl methyl ether, as previously mentioned, is an alkylating agent. Isoflurane, with which it has been inappropriately compared, is not; furthermore, it is less metabolized than any other inhalational anesthetic tested to date. In addition, data of questionable relevance have been generated by such practices as the oral feeding of trichloroethylene in large doses. The information gathered from the second group of compounds has little or no predictive value for the substances in the first group of compounds.

In conclusion, I believe that we should get rid of this dragon before it devours the emperor's new clothes.

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REFERENCES

1. Eger EI II: Dragons and other scientific hazards. ANESTHESIOLOGY 50:1, 1979
2. Van Duuren B: Biological effects of alkylating agents. Ann NY Acad Sci 163:580–1029, 1969
3. Van Duuren B, Goldschmidt BM, Katz C, et al: Carcinogenic activity of alkylating agents. J Natl Cancer Inst 53:695–700, 1974
4. Vitcha JF: The history of Forane. ANESTHESIOLOGY 35:4–7, 1971
5. Haddow A: On the biological alkylating agents. Persp Biol Med 16:503–524, 1973
6. Saffiotti U: Carcinogenesis 1957–77. Notes for a historical review. J Natl Cancer Inst 59:617–622, 1977
7. Fishbein D: Potential Industrial Carcinogens and Mutagens. Environmental Protection Agency, Washington, D.C., 1977
8. Arcos JC: Criteria for selecting chemical compounds for carcinogenicity testing: An essay. J Environ Pathol Toxicol 1:433–458, 1978

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Minimizing Sore Throat

To the Editor:—I do not agree with some of the conclusions drawn from Loeser *et al.*[1] The statement that changes in cuff volume and pressure from nitrous oxide diffusion are similar in low-residual-volume, high-pressure cuffs as in high-residual-volume, low-pressure cuffs is, in my experience, only partly true.