CORRESPONDENCE

References

(accepted for publication November 2, 1992.)

In Reply:—Johnstone’s letter concerns our Fluro-Ethyl® spray, (a nonflammable prescription topical anesthetic or skin refrigerant) and chlorofluorocarbons (CFCs) implicated in stratospheric ozone depletion.

Fluro-Ethyl contains 75% (by volume) dichlorotetrafluoroethane (114), a CFC also known as Freon® 114 or Dymel® 114, and 25% ethyl chloride. Johnstone is incorrect in stating that dichlorotetrafluoroethane is Freon 12. The chemical name for Freon 12 is dichlorodifluoromethane.

Freon 114 has been identified as a stratospheric ozone-depleting chemical. An accelerated phase-out is in progress for this chemical and for the other class 1 chemicals listed in the Clean Air Act Amendments of 1990, Title VI-Stratospheric Ozone Protection. The original phase-out, once set to be January 1, 2000, has been accelerated by Executive Order of President Bush. By the end of 1995, there will be no production of most class 1 chemicals; dichlorotetrafluoroethane is included in this phase-out. It also should be noted that this phase-out is far more strict than the United Nations-sponsored Montreal Protocol.

Johnstone states that other products, such as ethyl chloride, are available to anesthetize skin. However, ethyl chloride is flammable; Fluro-Ethyl® is not. Ethyl chloride, therefore, is sometimes not permitted in hospitals if not stored according to the recommendations of the Joint Commission on Accreditation of Hospitals.

It also should be noted that the current U. S. production of 114 is 50% of the 1986 volume, 360 million pounds. Fluro-Ethyl® uses 0.04% of this amount.

Gebauer is complying with the phase-out schedule. Regardless of the fact that we have no replacement at present for Fluro-Ethyl®, there will be no production of 114 in 1995; therefore, there will be no product.

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Risk of Ischemia in Patients Receiving Desflurane Versus
Sufentanil: Sample Size and Clinical Significance

To the Editor:—Anticipating the arrival of desflurane into our clinical armamentarium, I eagerly read Helman et al.’s randomized trial of sufentanil versus desflurane in patients with documented coronary artery disease. Helman et al. performed what appears to be a methodologically exacting study demonstrating that desflurane, like the other potent inhalational agents, can be used, with appropriate adjuncts, without unacceptable hemodynamic consequences in this patient population.

What is unclear to me as a clinical reader is their discussion directed at differences between the sufentanil and desflurane groups relative to adverse cardiac outcomes. First we are informed that “our sample size was insufficient to detect a significant difference, and that even a ‘10-fold’ increase in sample size would have been unable to detect a difference. But then the authors conclude that on the basis of a “relative risk” calculation, we should not rule out that desflurane could be associated with more prebypass ischemia than sufentanil in these patients.

What does ‘not significant’ mean to the clinical reader? To me, it suggests that under the rules established by the investigators at the outset of the study, and subsequently validated by referees, they were unable to demonstrate a difference in the tested treatments. Clearly, Helman et al. were plagued with the common problem of a sample size insufficient to deal with a small “effect size” (i.e., the strength of the treatment on the measured outcome). Another example of the Beezlebab of the clinical trial is, namely, does absence of evidence constitute evidence of absence?

What really disturbs me about Helman et al.’s paper is where it leaves us. First, the authors conclude that there was no significant

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difference between the treatments. Then, through the use of the mathematically spurious process of “relative risk” calculation, they deduce that desflurane is associated with 2.3 times the incidence of pre bypass ischemia than sufentanil (17% vs. 7%).

These kinds of clinical studies have little practical moment to the ultimate consumer of them, the practitioner. Investigations that purport to test hypotheses with treatments involving insufficient subjects predictably, as in the present case, arrive at ambiguous conclusions. Rather than focusing on type 1 versus type II errors, I believe that the larger problem is one of investigators trying to do too much with too little. The investigation spanned a period of from August 1990 to April 1991—what, I ask, was the hurry? Investigators should ask themselves, if sufficient time, money, personnel, or energy are not available for the task at hand, perhaps the task should not be undertaken. Careful attention to these issues may help avoid ambiguous and confusing messages communicated to readers such as myself who depend heavily upon scientific publications for rational practice decisions.

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Reference


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