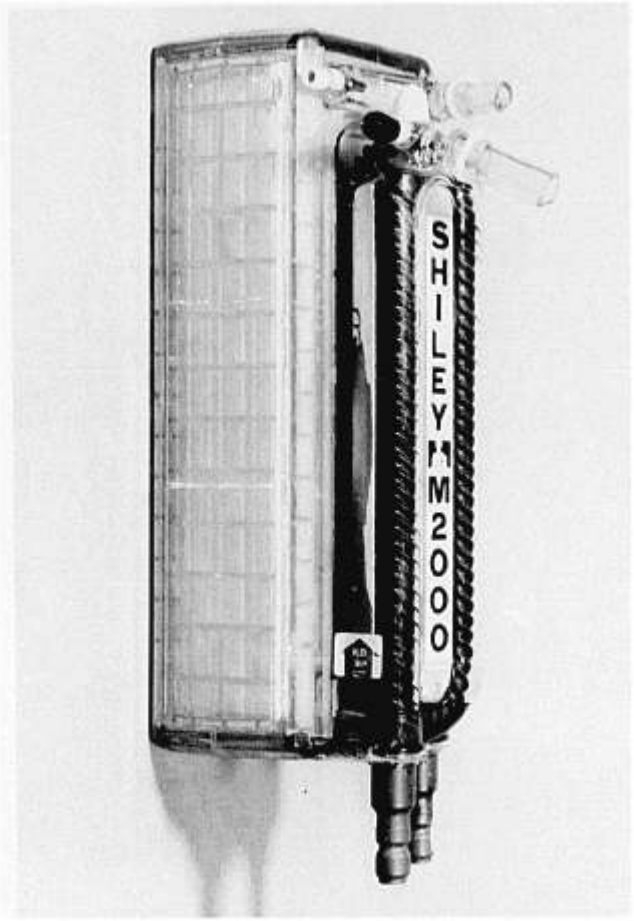

FIG. 1. Arterial outlet port, top, is partially severed from the oxygenator body. A crack extends vertically from the arterial outlet port left of the manufacturer's nameplate to the water inlet and outlet ports at the base.

Total CPB time was 72 min. The patient did not require inotropic support post-bypass. Postoperatively, the patient was hemodynamically stable and neurologically intact.

After this incident, we discovered that enflurane and halothane also crack the polycarbonate housing of Maxima Hollow Fiber, Scimed II, and Shiley M-2000 oxygenators. Arterial filters and cardiotomy reservoirs generally have polycarbonate components as well.

This accident graphically illustrates the fact that ethers, hydrocarbons, and esters act as solvents on plastics.[1] In our institution, the vaporizer was moved away from polycarbonate components. Warning labels should be given serious consideration.

This surgical procedure and anesthetic was performed at Temple University Hospital in 1986. This letter has not been presented at any meeting.

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The Value for Organ-related Clearance of Atracurium: An Over-calculation

To the Editor:—I was a little surprised to read the recent publication by Fisher *et al.*[1] which concluded that more than half of a dose of atracurium was cleared from the body by organ-related clearance. Atracurium, as a molecule, is cleared from the body mainly by destruction of the parent molecule within its distribution volume. The logic for the conclusions in the abovementioned paper I find a little confusing.

Clearance is determined by multiplying the rate constant for elimination by the volume in which that clearance occurs. The authors have derived non-organ clearance by multiplying the rate constant of atracurium obtained *in vitro* by its steady-state distribution volume (V_{ss}), giving a mean clearance of only 40% of the total clearance. For total clearance, I assume they divided the dose by the area—under the curve for the plasma decay, as this agrees with all previous data published. The authors produce an *in vitro* half-life of 31 min, longer than previously published results of 21 min[2] and 25 min.[3] The distribution volume (V_{ss}) reported is very surprising, as steady state did not occur in their experiments, and elimination from both compartments means that the microkinetic parameters K_{12}, K_{21}, and K_{20} are impossible to derive from their model. Their value for distribution volume for

elimination (mean 87.4 ml kg^{-1}) is only 50% of the previously recorded values (mean 157 ml kg^{-1}).[4,5] If either the previously recorded elimination rate constants *in vitro* or the distribution volumes are used, values for non-organ clearance are around 25%.

This value is more in keeping with expected values, as up to 10% of a dose of atracurium has been obtained unchanged in the urine of patients[6] and, having a molecular weight of around 1000 and being ioinized, hepatic clearance of possibly 15% would occur.

Finally, I must mention that the two-compartment model for atracurium with elimination from both compartments was first described by Ward *et al.*[7]

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In reply:—Dr. Ward challenges our conclusion[1] that more than one-half of the clearance of atracurium results from organ-based elimination. He bases his argument on the discrepancy between the *in vitro* half-lives obtained in our study (32 min) and those obtained by Hughes and Chapple[2] (25 min) and Stiller *et al.*[3] (21 min). Unfortunately, Hughes and Chapple provide no details of their experimental design other than their use of plasma (compared with our use of whole blood), so we are unable to explain the differences between their results and ours. Stiller *et al.* added atracurium to plasma maintained at 37° C and determined the concentration of atracurium during a 3-h sampling period; they do not state whether plasma *p*H was measured repeatedly during the study. When we attempted to replicate their experiment, we found that the *p*H of the plasma increased during the sampling period, as a result of a decrease in the concentration of carbon dioxide. This increase in *p*H would be expected to increase the rate of Hofmann elimination, thereby decreasing the *in vitro* half-life of atracurium to a value consistent with the shorter half-life obtained by Stiller *et al.* To simulate physiologic conditions and to prevent problems related to the instability of *p*H, we believed that it was important to maintain a constant *p*H throughout our study. Therefore, we kept the blood in a sealed vessel equilibrated with 5% CO_2 and documented that *p*H did not vary during the study period. Thus, we believe that the shorter *in vitro* half-life obtained by Stiller *et al.* resulted from the instability of *p*H in their study.

Ward is surprised that our value for V_{ss} (87.4 ml/kg) (which he incorrectly terms distribution volume for elimination) is smaller than the values for V_{area} (V_β) obtained in other studies. These terms describe different pharmacokinetic volumes and are not interchangeable. In addition, whenever the organ(s) of elmination are located within the central compartment (as we assumed in our pharmacokinetic model), V_{ss} will be less than V_{area}. In fact, we[4] reported that V_{area} for atracurium was 182 ± 12 ml/kg, a value similar to that reported by Ward *et al.*

Finally, Dr. Ward did describe a two-compartment model for atracurium. However, there are marked differences between his model and ours. Dr. Ward's model cannot be used to determine V_{ss} (or, for that matter, to fractionate clearance into its organ and non-organ components); additional problems with his model have been identified by Hull.[5] In contrast, our model, because it utilizes the *in vitro* rate constant for atracurium elimination, permits determination of these additional pharmacokinetic parameters.

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