

# *The Solubility of Halothane in Rubber, Soda Lime and Various Plastics*

*Edmond I. Eger, II, M.D., C. Philip Larson, Jr., M.D.,  
John W. Severinghaus, M.D.*

IN the course of an experiment on the rate of change of concentration of halothane in a model anesthetic system, it became apparent that the rate of change lagged far behind that predicted. We believed (as suggested by Galloon<sup>1</sup>) the explanation to be loss of halothane to the substances forming the system, the rubber goods being the most suspect. To confirm this suspicion and in an attempt to find some suitable substitute into and through which halothane would not pass, the following experiments were undertaken.

## **Methods and Results**

### **DETERMINATION OF THE SOLUBILITY OF HALOTHANE IN RUBBER SODA LIME AND VARIOUS PLASTICS**

The solubility of halothane (expressed as the Ostwald partition coefficient) was determined in rubber, polyethylene, polyvinyl, Mylar, Hypalon, Scotch-Pak, and soda lime. The rubber was conductive, corrugated tubing cut into small pieces. Vinyl plastic was in the form of small, thick-walled (1–2 mm.) rings. The other plastics were in the form of small squares, the thicknesses of which were: polyethylene, 1 mil; Mylar, 1 to 10 mils; Scotch-Pak, 2 mils; and Hypalon, about 10 mils. The soda lime was the 4–8 mesh commonly used in anesthesia (hydrated).

The method used to determine partition coefficients has been described in detail,<sup>2</sup> but was altered in two ways in this study. First, all determinations were at room temperature,

and second, the time to reach equilibration was lengthened (48–96 hours). The criterion for stability was lack of appreciable change in the partition coefficient when the time allowed for equilibration was doubled. Rate of loss of halothane from blank flasks containing no test substances was also determined so that this loss with time could be allowed for in the final calculations. A small, but appreciable loss was found, which decreased exponentially with time and amounted to 3.5 per cent in a 24-hour period (fig. 1).

The Ostwald partition coefficients for halothane (at 760 mm. of mercury and  $24 \pm 2^\circ$  C.) were found to be: conductive rubber  $121.2 \pm 11$  (1 standard deviation); polyethylene,  $26.3 \pm 2.3$ ; vinyl plastic, 190; Hypalon, 50; Scotch-Pak, 14; Mylar, less than 1; and soda lime about 1.

### **ILLUSTRATION OF THE EFFECT OF HALOTHANE SOLUBILITY ON THE COURSE OF ANESTHESIA**

*Part A.* A model was prepared, consisting of a 5-liter rubber bag, two lengths of corrugated rubber tubing as are commonly used in circle systems, and a Revel circulator (fig. 2). The total volume of the system with the bag expanded was estimated to be 6–6.5 l. Gases introduced through the tail of the bag were circulated throughout the system by the Revel circulator. Excess gas continuously escaped through a relief valve, which was adjusted so that the bag remained full without appreciable tension. Halothane was vaporized in a Mark II Fluotec with oxygen with a total flow rate of 3 l./minute. Halothane concentration in the escaping gases was analyzed (infrared analyzer) and the results plotted against time. The inflow concentration of halothane

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was monitored at intervals and found to remain constant. The experiment was repeated with nitrous oxide and oxygen. Oxygen or nitrous oxide was flushed through the system until only the pure gas could be detected with an oxygen analyzer (a Pauling meter with a range of 2 per cent inaccuracy). The other gas was then introduced alone at 3 l./minute and the change in oxygen concentration plotted against time. In both the halothane and the nitrous oxide-oxygen experiments concentration changes were plotted as percentage change within the total possible range (= 100 per cent change). A second, somewhat larger, model (8.5 to 9.0 l.) was prepared with polyethylene substituted for rubber, and the above experiments repeated.

Comparative rates of changes in concentration at the point of exit from the first model (rubber parts) for halothane and for nitrous oxide and oxygen are shown in figure 3. The nitrous oxide-oxygen curve rapidly approaches the final concentration while the halothane curve does not approach 100 per cent for 30-60 minutes.

Similar rates of change are plotted for the second model (polyethylene parts) in figure

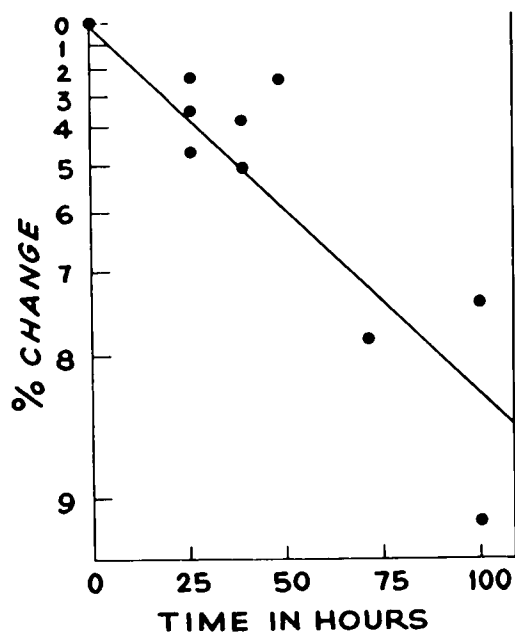


FIG. 1. The rate of loss of halothane from the blank test flasks.

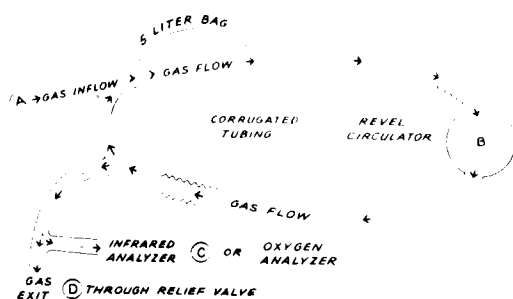


FIG. 2. The first model system used in this study. Gas enters at (A), is drawn by the Revel circulator (B) through the 5-liter bag and length of corrugated tubing, is forced through a second length of tubing and then either exists through the relief valve (C) where the concentration is monitored (D) or is recirculated.

4. Again the nitrous oxide-oxygen curve rapidly approaches its final concentration while the halothane curve falls behind. However, the lag is considerably reduced from that found in the first model.

Included in figures 3 and 4 is the predicted graph\* of the washout of those systems with a 3 l./minute flow (the flow used in the experiment). A volume of 6.25 l. was assumed for the first model and 8.65 l. for the second. The graphs overlay the points obtained with nitrous oxide-oxygen and are evidence of the lack of any effective uptake of nitrous oxide or oxygen.

**Part B.** Halothane at a constant concentration (1.45 per cent) was allowed to flow through the first model for six hours, after which it was flushed with 10 l./minute of pure oxygen for two minutes. Then 500 ml. per minute flow of pure oxygen was introduced into the system and the rate of change of concentration relative to the original saturating concentration plotted, as before, in relation to time (fig. 5). This experiment was repeated using nitrous oxide instead of halothane. Nitrous oxide concentration changes were determined as before with the oxygen analyzer.

Figure 5 illustrates the maintenance of a significant concentration of halothane in the model outflow by the halothane escaping from

\* Per cent change =  $100 (1 - e^{-rt/V_s})$  where  $r$  = inflow rate;  $V_s$  = volume of the system; and  $t$  = time in minutes.

the rubber. Measurable concentrations persist in the outflow for several hours, an effect not observed when nitrous oxide was used.

### Discussion

Little previous work has been done on the solubility of anesthetics in various components of anesthetic systems. Waters and Schmidt<sup>2</sup> suggested that cyclopropane either is soluble in rubber or rapidly diffuses through it. Galloon<sup>1</sup> suggested the same for halothane. The solubility of halothane in rubber may be related to its fat solubility, since they are struc-

turally somewhat similar, both containing numerous consecutive carbon-carbon linkages. If this is true, then all the new halogenated hydrocarbons for use in anesthesia are likely to be highly rubber soluble.

The results of this study have both theoretical and practical implications. For example, any study which attempts to determine uptake of halothane in humans must also account for uptake by components of the experimental system itself. It would appear that the substitution of Mylar for rubber would eliminate this problem, but unfortunately

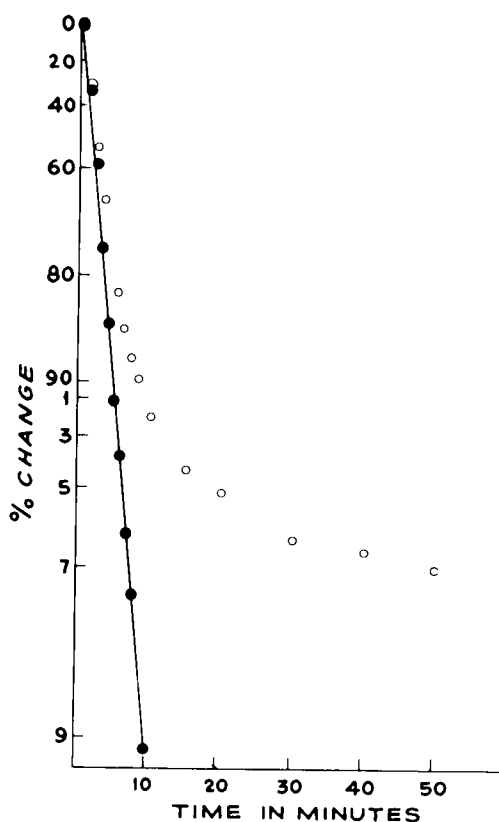


FIG. 3. Results obtained from the first model system (containing rubber) comparing the rate of change of concentration between halothane-oxygen (open circles) and nitrous oxide-oxygen (closed circles). Total volume of the system ( $V_s$ ) taken to be 6.25 l. The inflow ( $r$ ) equaled 3 l./minute. Each graph represents an average of three determinations. The line overlying the points obtained with nitrous oxide-oxygen is the graph of the equation:

$$\text{Per cent change} = 100(1 - e^{-rt/V_s})$$

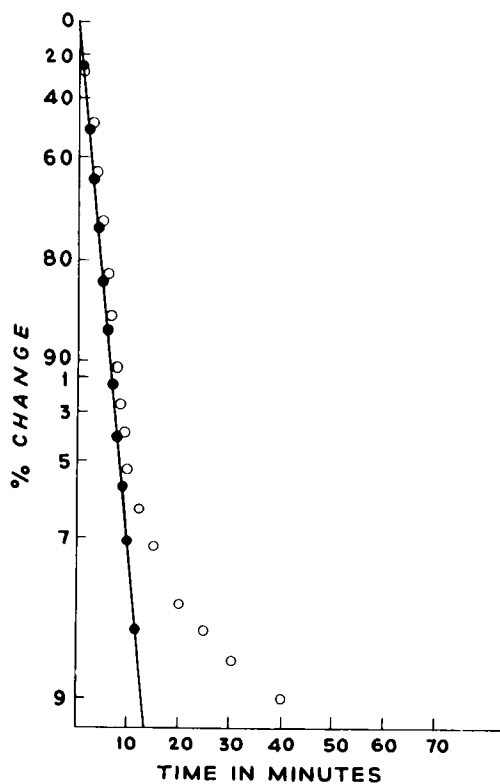
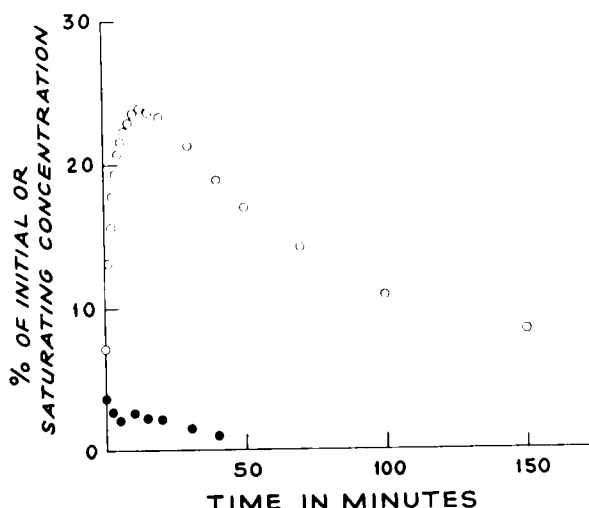


FIG. 4. Results obtained from the second model system (containing polyethylene) comparing the rate of change of concentration between halothane-oxygen (open circles) and nitrous oxide-oxygen (closed circles). Total volume ( $V_s$ ) of the system taken to be 8.65 l. The inflow ( $r$ ) equaled 3 l./minute. Each graph represents an average of two determinations. The line overlying the points obtained with nitrous oxide-oxygen is the graph of the equation:

$$\text{Per cent change} = 100(1 - e^{-rt/V_s})$$

FIG. 5. Illustration of the re-entry of halothane into the model system. The model was saturated with 1.45 per cent halothane for 6 hours. The system was flushed with oxygen at 10 l./minute for two minutes. Flow was then reduced to 0.5 l./minute and change of concentration plotted in relation to time. Similarly the system was saturated with nitrous oxide for 13 hours and flushed with oxygen. As before, the flow was reduced to 0.5 l./minute and the change of concentration plotted in relation to time. Halothane noted as open circles and nitrous oxide as closed circles.



Mylar thus far has been too brittle for this purpose. Polyethylene, since it has a larger partition coefficient for halothane than Mylar, is a less adequate substitute, but does reduce the rate of loss considerably.

Practically, the uptake of halothane by rubber goods has the following implications. First, induction with halothane theoretically may be slowed because of the consequent reduction in halothane concentration presented to the patient. This delay in induction will be exaggerated at low flows, but can be effectively eliminated by utilizing higher flows.<sup>4,5</sup> Second, during halothane anesthesia a considerable amount of halothane may be taken up by the rubber goods. If a subsequent anesthetic is given with the same equipment by a closed system, for example, with a gas such as cyclopropane, halothane will be released from the rubber in quantities which theoretically might significantly add to the cyclopropane anesthesia. The end effect might be an overdose of total anesthetic with what would be a "normal" amount of cyclopropane.

### Summary

The Ostwald partition coefficients for halothane at 760 mm. of mercury and 24° C. have been determined for rubber (121.2), polyethylene (26.3), polyvinyl (190), Hypa-

lone (50), Scotch-Pak (14), Mylar (less than 1), and soda lime (about 1).

Model systems utilizing rubber goods commonly found in an anesthetic circle system have been used to show that (1) the uptake of halothane by rubber may theoretically slow induction and (2) the subsequent release of halothane from rubber may theoretically supplement the effect of subsequent anesthetics in which the same anesthetic equipment is used.

The halothane (Fluothane) for this study was supplied Ayerst Laboratories.

### References

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