Technical Note

Absorption of Anesthetics by Conductive Rubber in Breathing Circuits

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The amounts of cyclopropane, diethyl ether, halothane and methoxyflurane absorbed by rubber were determined by measuring the rates of infusion of anesthetic liquid or gas required to maintain a constant circuit concentration within a closed breathing system. Rates of absorption were directly proportional to the circuit concentration, the rubber–gas partition coefficients, the areas of exposed rubber, and the square roots of the diffusion coefficients. The observed uptake of each anesthetic was identical to that calculated from diffusion equations. The calculated diffusion coefficients of the above agents in rubber were 14, 1.7, 2.3, and 2.64×10^{-5} cm²/min, respectively. At equipotent anesthetic concentrations, the absolute amounts of anesthetic vapor absorbed by the breathing circuit are nearly the same for all agents. Absorption and elimination of these agents are linear functions of the square root of time and cannot be accelerated by rapid flushing of the circuit. As a consequence, as much as 300 ml of anesthetic vapor may be routinely transferred from one case to a subsequent patient when agents are switched between cases. (Key words: Cyclopropane; Diethyl ether; Methoxyflurane; Halothane; Solubility; Diffusion coefficient; Anesthesia circuits.)

THE DELAYS in the increases in circuit concentrations of anesthetic gases due to anesthetic solubility in rubber have been partially described by Eger and Brandstater.[1] The amount of each agent absorbed by the circuit was directly proportional to the concentration of anesthetic gas and its partition coefficient in rub-

ber. Eger *et al.*[1,2] determined the rubber–gas partition coefficients of halothane (121) and methoxyflurane (739). Titel and Lowe[3] determined the solubilities of eight anesthetics from their retention times on chromatographic columns of conductive rubber. To quantitate further the mechanisms by which anesthetics are absorbed by rubber, we have employed a closed system and measured the amounts of anesthetic required to establish and maintain constant circuit concentrations as a function of time. The circuit uptake of each anesthetic was directly proportional to: 1) the vapor concentration, 2) the rubber–gas partition coefficient, 3) the surface area, 4) the square root of the diffusion coefficient of the agent in rubber, and 5) the square root of time.[4] The observed rates of uptake and cumulative absorption agreed closely with those calculated from a modified form of Fick's law of diffusion.[5,6]

Methods

The anesthetic circuit components investigated, their measured volumes and weights, and calculated internal surface areas are shown in table 1. The areas of the breathing tubes were obtained by pressing strips of aluminum foil to conform to the corrugations of opened sections of tubing (10×10 cm). The actual length of rubber in an 80-cm (32-inch) corrugated tube was 144 cm, and the internal surface area was 1,440 cm². The area (A) of the ventimeter bellows was calculated from the area of the sides and top of the bellows and is given by the following equation:

$$A = \tfrac{1}{2}n\,\pi\,(d_2{}^2 - d_1{}^2) + \tfrac{1}{4}\pi d_2{}^2 \qquad (1)$$

TABLE 1. Volumes, Surface Areas, and Weights of Rubber Breathing Circuit Components

Component	Volume (l)	Area (cm²)	Weight (g)†
Tube 31″ × 4.6″ cir	0.50	1,500	218
Tube 39″ × 4.0″ cir	0.58	1,800	250
Breathing bag	1.00	560	43
Breathing bag	2.00	850	53
Breathing bag	3.00	1,018	70
Breathing bag	4.00	1,316	83
Ventimeter bellows*	1.50	1,500	80

* Air Shields, Inc., Hatboro, Penna.
† Including grommets.

where n is the number of convolutions and d_2 and d_1 are the outer and inner diameters of the bellows, respectively.

Each component was arranged in a closed system which included a circulating pump and accessory metal tubing (fig. 1). The gas phase within the circuit was recirculated at 30 l/min as measured by a Wright respirometer. The volume of each system was determined from the time constants of exponential wash-in curves obtained at known rates of inflow of 2 per cent propane (C_t), which is not significantly absorbed by rubber or Baralyme.[7]

The circuit concentration of propane or an-esthetic (C_t) was determined automatically every 6 to 10 seconds by transferring a 10-μl (0.01 ml) gas sample to the carrier gas stream of a flame ionization detector.[7] The detector and/or recorder sensitivity was adjusted to give a full-scale recorder response (100 divisions) to the delivered gas (C_i). Under these conditions, the exponential wash-in curves were recorded directly as percentages of concentration delivered. The volume of the system was calculated from the equation:

$$C_t = C_i (1 - e^{-kt}) \qquad (2)$$

where k equals inflow divided by circuit volume. Identical volumes were calculated for each system using the first and second time constants (i.e., when kt equalled 1 and 2).

The absorption rate of an anesthetic gas was determined by initially injecting (as a slug from a glass syringe using a calibrated Harvard infusion pump) the required amount of gas or liquid necessary to raise the known circuit volume to 0.5 or 1.0 per cent concentration. Subsequently, the rate of infusion was reduced continuously to maintain the desired steady-state concentration (±0.02 per cent). The rates of infusion and the total amounts of an-esthetic injected (expressed as ml vapor at
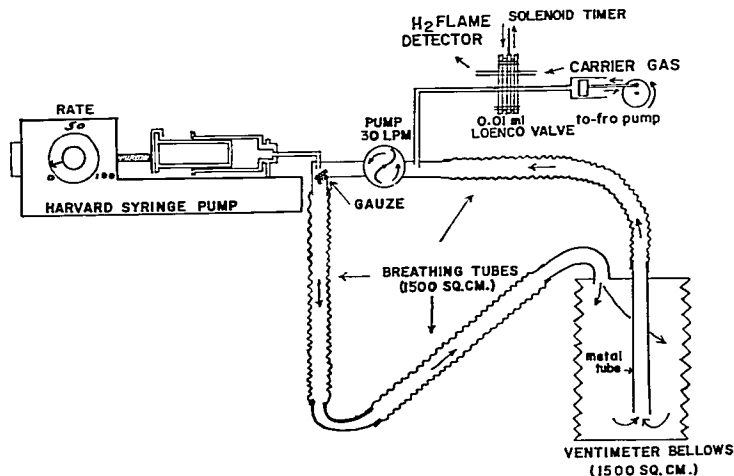

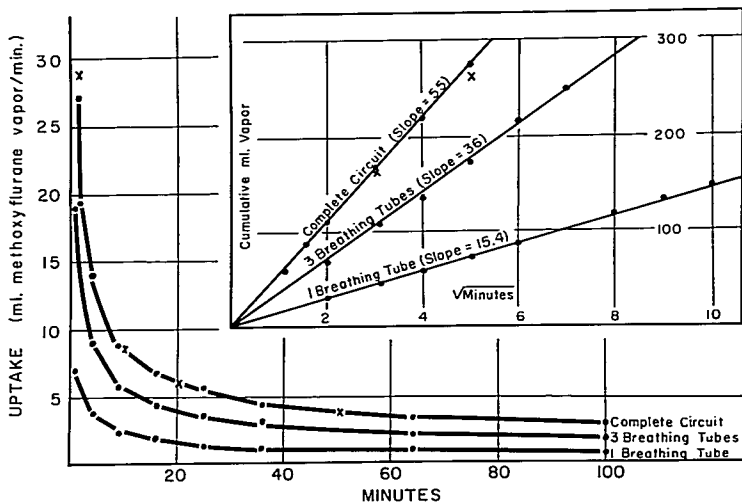FIG. 1. Schematic drawing of the experimental system.

Fig. 2. Uptakes of 0.5 per cent methoxyflurane by various anesthetic circuit components as a function of time. X—X—X = uptake (ml vapor/min/0.5 per cent methoxyflurane/4,300 cm²) calculated from the data of Eger and Brandstater.[1] ●–●–● = observed values. Solid line shows uptake calculated from equation 5. *Inset:* cumulative methoxyflurane uptake as a function of the square root of time. Solid line indicates uptake calculated from equation 4.

room temperature) were recorded at frequent intervals.

Results

The rates of uptake of methoxyflurane vapor at 0.5 per cent circuit concentration by the various systems are shown in figure 2. The total cumulative amounts of vapor necessary to maintain this concentration were a linear function of the square root of time (fig. 2, inset). When the rates of infusion of vapor necessary to maintain a steady-state circuit concentration (0.5 per cent) were plotted against the reciprocal of the square root of time, a linear relationship in which the slopes of the lines were half those observed in the inset in figure 2 was found (fig. 3).

The total amounts of 1 per cent cyclopropane, diethyl ether, halothane, and methoxyflurane absorbed by the complete circuit are shown in figure 4. At any given time, the amount of methoxyflurane vapor absorbed at a concentration of 0.5 per cent was approximately half that absorbed at the 1.0 per cent

concentration (*cf.* figs. 2 and 4). The total amount of methoxyflurane absorbed by the individual circuit components was 15 per cent higher than that absorbed by the complete circuit which includes the Baralyme canisters (fig. 5).

The absorption of methoxyflurane by Baralyme was immediate, and increased only slightly on prolonged exposure. The Baralyme in the two disposable canisters weighed 2,400 g, and the volume of granules was 1,200 ml.[9, 10] The canisters absorbed 150 ml of vapor in the first 60 seconds of exposure to 0.5 per cent methoxyflurane, giving a calculated partition coefficient of 25.

Discussion

The diffusion of a vapor or gas into rubber resembles the conduction of heat by a metal. The anesthetic concentration is analogous to temperature, an intensity factor, and the partition coefficient is analogous to specific heat, a capacity factor. According to Fick's law of diffusion,[5, 6] the amount of substance (dn)
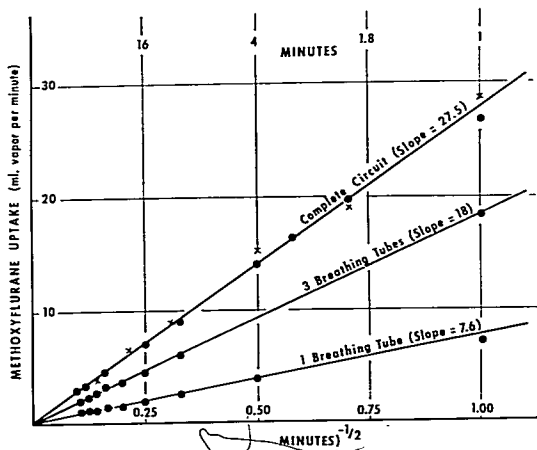
Fig. 3. Rate of circuit uptake (ml vapor/min) of 0.5 per cent methoxyflurane plotted against the reciprocal of the square root of time. X–X–X = uptake (ml vapor/min/0.5 per cent methoxyflurane/4,300 cm^2) calculated from the data of Eger and Brandstater.[1] ●–●–● = observed values. Solid lines are theoretical lines calculated from equation 5; the slopes are half those in figure 2 (inset).

crossing a given area in an infinitesimal time (dt) is proportional to the cross-sectional area (A), the concentration gradient (dc/dx), and, in the case of anesthetics, the rubber–gas partition coefficient (λ):

$$dn = -D\lambda A \ (dc/dx) \ dt \qquad (3)$$

where D is a proportionality constant called the diffusion coefficient. If the concentration of vapor in the gas phase (C_0) is constant, as in this study, the above expression may be integrated to form the following equation[5]:

$$C_t = C_0 \left(1 - 2\sqrt{\pi} \int_0^y e^{-y^2} \, dy\right) \qquad (4)$$

where

$$y = \frac{x}{(2\sqrt{Dt})} .$$

This definite integral may be integrated between the limits zero and time, t, to obtain
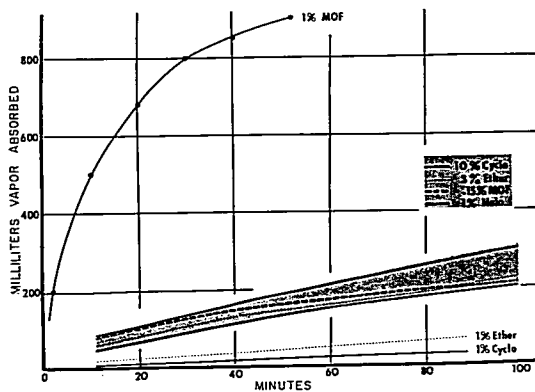

Fig. 4. Comparison of the cumulative uptakes of cyclopropane, diethyl ether, halothane, and methoxyflurane by rubber in a complete anesthetic circuit. The shaded area illustrates the nearly equivalent cumulative absorptions at equipotent anesthetic concentrations.

FIG. 5. Comparison of the cumulative methoxyflurane uptake by individual circuit components with the complete anesthetic circuit (including Baralyme) at 0.5 per cent concentration. Note the high initial absorption of methoxyflurane by Baralyme—150 ml.
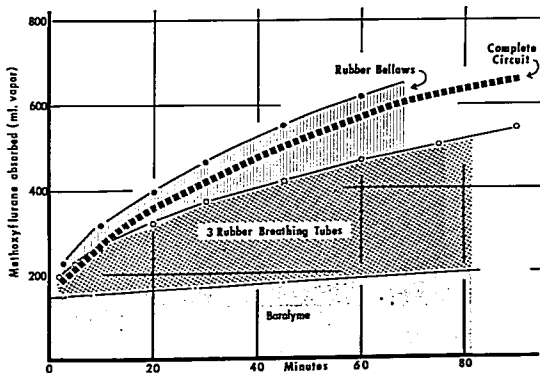
the quantity of anesthetic ($Q_{0,t}$) which crosses the surface plane ($x = $ zero) in time t and is equal to:

$$Q_{0,t} = C_0 A \lambda \, (D/\pi)^{\frac{1}{2}} \, t^{\frac{1}{2}} \quad (5)$$

where C_0 is the circuit concentration in atmospheres, A is the surface area in cm^2, λ is the rubber–gas partition coefficient, and D is the diffusion coefficient in cm^2/minute. The rate of anesthetic uptake per minute is obtained by differentiating equation 5:

$$dQ_{0,t}/dt = 0.5 C_0 A \lambda \, (D/\pi)^{\frac{1}{2}}/t^{\frac{1}{2}} \quad (6)$$

Plots of $Q_{0,t}$ vs. $\sqrt{t}$ and $dQ_{0,t}/dt$ vs. $\sqrt{1/t}$ are straight lines with slopes equal to $C_0 A \lambda (D/\pi)^{\frac{1}{2}}$ and $0.5 \ C_0 A \lambda (D/\pi)^{\frac{1}{2}}$, respectively (cf. slopes of lines in fig. 2 inset and fig. 3).

The internal surface area of a single breathing tube 39 inches long is approximately 1,800 cm^2 (table 1). Using a mean circuit concentration of 0.5 per cent (0.005 atm) and a methoxyflurane rubber–gas partition coefficient of 630,[3] the diffusion coefficient (D) for methoxyflurane in rubber is approximately 2.64×10^{-5} cm^2/min. The corresponding diffusion coefficients for cyclopropane, diethyl ether, and halothane are 14.0, 1.7, and 2.3×10^{-5} cm^2/min, respectively. The diffusion coefficients of methoxyflurane and halothane are nearly inversely proportional to the square roots of their respective molecular weights of 165 and 197. In figure 2 the single breathing tube was 39 inches long (1,800 cm^2), while the three breathing tubes in series were each 30 inches

long (1,500 cm$^2 \times 3$). The surface area of the single breathing tube was 40 per cent of the surface area of the three breathing tubes in series. Similarly, the observed rate of uptake of the single tube was 42 per cent of that in the three-tube system. The total surface area of the complete circuit consisting of three breathing tubes (4,500 cm^2) and the ventimeter bellows (1,500 cm^2) was 6,000 cm^2. The uptake of the complete circuit (55 ml vapor/$\sqrt{t}$) was 1.17 times greater than that predicted from the uptake per unit area of the breathing tubes, and suggests some loss of anesthetic through the thin-walled bellows.

The circuit concentration was monitored just proximal to the infusion site. As a consequence, the mean circuit concentration was initially higher than 0.5 per cent by an amount equal to half the rate of vapor infusion per minute divided by the rate (deciliters/min) at which the gas was recirculated (i.e., [vapor infusion rate ÷ 2] ÷ 300). The error introduced by this factor is less than 2 per cent after six minutes and diminishes rapidly with time.

Comparison of the observed rates of uptake of methoxyflurane in the present investigation with those calculated from the results of Eger and Brandstater [1, 2] indicates that the results are nearly identical (table 2) when allowances are made for variations in surface area and methods. The rates of uptake in the latter study were calculated from the difference between inflow and circuit (pop-off) concentra-

TABLE 2. Rates of Uptake of Methoxyflurane by Anesthetic Circuits in
Closed and Semiclosed Systems

Inflow Rate (l/min)	Delivered Gas		10 Minutes			20 Minutes			50 Minutes		
	Per Cent	ml Vapor/min	Pop-off		Uptake/min/per cent	Pop-off		Uptake/min/per cent	Pop-off		Uptake/min/per cent
			Per Cent	ml Vapor		Per Cent	ml Vapor		Per Cent	ml Vapor	
0 (closed)	1.0	—	0	0	19	0	0	11.0	0	0	5.0
1†	1.9	19	0.74	7.4	15	0.93	7.5	12.3	1.14	11.4	6.7
3†	1.9	57	1.24	37.0	16	1.38	41.4	11.3	1.56	47.0	6.4
8†	1.9	152	1.65	122.0	18	1.73	138.4	7.8	1.77	140.6	6.7

* Area = 6,000 cm².

† Ref. 1, estimated area = 4,300 cm².

tions and expressed as uptake/min/per cent circuit concentration. These authors observed that the circuit concentration was only 85 per cent of the delivered concentration after 17 hours of exposure to 1 l/min of 1.7 per cent methoxyflurane. After a minute of flushing followed by an oxygen flow of 3 l/min, the circuit concentration was only 37 per cent of the delivered concentration, or approximately 44 per cent of the circuit saturation. Since each molecule within the rubber may diffuse in either direction (toward the inner or outer surface), it may be predicted that approximately half of the absorbed agent may be recovered at the inner surface. By our calculations, 3,300 ml of methoxyflurane were absorbed and 1,800 ml re-entered the circuit during the 500-minute washout period (areas under the uptake and washout curves described by these authors). The rates of vapor uptake during the saturation process reported by these investigators were 2.9 and 2.1 ml vapor/min at 6 and 22 hours, respectively. These results are consistent with our data. Using the reported mean circuit concentrations of 1.2 and 1.5 per cent methoxyflurane and a rubber surface area of 4,300 cm², the predicted rates of uptake calculated from equation 5 are 3.1 and 2.05 ml vapor/min, respectively (D[methoxyflurane] = 2.6×10^{-5} cm²/min).

The solubilities of anesthetics in rubber are proportional to their solubilities in lipids of white and grey brain matter.[8] Since anesthetic potency is directly proportional to anesthetic solubility in brain lipids, it follows that the rates and amounts of absorption by rubber are nearly the same for all agents at equipotent anesthetic concentrations (shaded area, fig. 4). This fixed amount of absorption represents larger and larger fractions of the delivered concentrations as the potencies of the agents increase. The effect is to prolong the induction periods of the more potent agents, which have the lowest vapor pressures and require the lowest circuit concentrations.

The amounts of cyclopropane and halothane absorbed at 1 per cent circuit concentrations after 100 minutes were 35 and 205 ml, respectively (fig. 4). Halothane diffuses into rubber 5.9 times faster than cyclopropane. Since diffusion is proportional to the partition coefficient (λ) and inversely proportional to the square root of molecular weight (mol wt), the predicted ratio is 6.3:1.‡ The observed diffusion rate of methoxyflurane was 31 times that of cyclopropane, compared with a predicted ratio of 35:1. The diffusion rate of diethyl ether, however, was about twice the diffusion rate of cyclopropane, in contrast to a predicted value of 4.8. This deviation from ideal behavior of the diffusion of diethyl ether suggests the possibility of hydrogen bonding between rubber and the oxygen molecule of ether. Hydrogen bonding would both increase the apparent ether–rubber partition coefficient and limit diffusion. The reported diffusion coefficient of ether in air is lower than that predicted from the diffusion coefficients of other gases in air.[11]

$$\ddagger \quad \frac{\lambda \text{ halothane}}{\sqrt{\text{mol wt halothane}}} \div \frac{\lambda \text{ Cyclopropane}}{\sqrt{\text{mol wt cyclopropane}}}$$

$$= \frac{120}{\sqrt{197}} \div \frac{9}{\sqrt{42}} = 6.3$$

The present study and those of Eger and Brandstater[1] and Eger et al.[2] are not strictly comparable to actual clinical conditions. With a nonbreathing technique, only the anesthetic loss to the inspiratory breathing tube (single tube, fig. 2) is clinically pertinent. Under these conditions losses to the inspiratory tube are fixed at any given concentration of gas delivered and are relatively independent of the total flow. For example, at a delivered flow rate of 10 l/min of 0.5 per cent methoxyflurane, the rates of anesthetic uptake by rubber (one tube) after one and 16 minutes, were 8 and 2 ml of vapor/min, respectively (figs. 2 and 3). The amounts of delivered vapor (50 ml/min) absorbed were 16 and 4 per cent, respectively. At a flow rate of 5 l/min the absorption by rubber would be nearly the same; however, the percentages of the delivered gas lost to the circuit are doubled (32 and 8 per cent, respectively).

In closed systems the inspiratory and expiratory limbs of the anesthetic circuit are exposed to different concentrations of gas, and the uptake by rubber must be calculated separately for each (equation 4). Under clinical conditions (0.2 per cent mixed expired methoxyflurane) the circuit losses will be much smaller than those reported by Eger et al.[1,2] at 1.7 per cent inspired concentrations.

When a nonrebreathing technique is used during a patient's emergence from anesthesia, the amount of absorbed anesthetic returned to the circuit from the inspiratory tube (1,500 cm²) and inhaled by the patient is only 25 per cent of that reported by Eger et al.[1,2] for the complete circuit (4,300 cm²). This amount represents only 12.5 per cent of the total circuit, or 50 per cent of the inspiratory tube absorption, since only half of the absorbed anesthetic re-enters the circuit. With conventional anesthetic techniques involving little or no rebreathing, the expiratory circuit makes little or no contribution to prolongation of induction or emergence.

In contrast to the absorption process, which simulates diffusion into an infinite system (rubber) at constant concentration, desorption or elimination from rubber represents diffusion from a finite system (rubber) into a infinite system (zero circuit concentration). The elimination may be described by equation 5, where

C_0, the anesthetic concentration in rubber, is an exponentially decreasing function. So long as the flushing rate is adequate to maintain a near-zero circuit concentration, elimination is dependent upon the diffusion coefficient of the agent in rubber and cannot be accelerated by increasing the rate of flushing of the circuit. The time required for elimination of a given amount of anesthetic is considerably longer than its corresponding period of absorption. One consequence of this slower process of elimination is the transfer of a given anesthetic used for one patient to subsequent patients anesthetized with the same equipment. In cases of suspected hypersensitivity to a particular inhalation agent, the entire circuit should be replaced with unexposed tubing and unexposed carbon dioxide absorbent, if exposure to this agent is to be avoided.

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