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CONTROL OF END-TIDAL HALOTHANE CONCENTRATION

Part A : Anaesthesia Breathing System and Feedback Control of Gas Delivery

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SUMMARY

Conventional anaesthetic breathing systems are not designed to control end-tidal gas concentrations, nor can they be used to measure accurately the uptake of oxygen or of anaesthetic agent. We built and tested a leak-tight closed-loop anaesthetic breathing system with low solubility to volatile anaesthetic agents and with efficient gas mixing. The system included a water-sealed spirometer, a small carbon dioxide absorber, a coaxial tube to the patient, a circulating pump and feedback controllers for system volume and anaesthetic concentration. Feedback control was implemented to adjust and control automatically the end-tidal anaesthetic concentration and the volume of the system with oxygen supplied through a mass flow controller and with halothane supplied by a titrating syringe. Controller gains, as a function of body weight, were found using a nine-compartment tissue uptake model. Stability was maintained with ±50% changes in alveolar ventilation and cardiac output. During subsequent investigations in an animal model, arterial, mixed venous and cerebral venous blood halothane concentrations were measured to show that the feedback-controlled halothane induction was optimized. We conclude that feedback control appears to be clinically applicable for adjusting the end-tidal halothane concentration and system volume to provide a rapid and optimized induction of anaesthesia.

Feedback has been used in anaesthesia to control the concentrations of inhalation anaesthetics, the concentration of oxygen, the volume of ventilation and the volume of the breathing system (Chilcoat, 1973; Coles, Brown and Lampard, 1973; Suppan, 1977; Mapleson et al., 1980; Tatnall, Morris and West, 1981; Morris, Tatnall and Montgomery, 1983; Ross et al., 1983; Schils, Sasse and Rideout, 1983; Westenskow, Jordan and Hayes, 1983a, b). Indeed, when the end-tidal concentrations of the anaesthetic are controlled, induction is shortened, and arterial and brain concentrations achieve greater stability (Chilcoat, 1973; Morris, Tatnall and Montgomery, 1983; Ross et al., 1983; Schils, Sasse and Rideout, 1983; Westenskow, Jordan and Hayes, 1983a, b). Moreover, if the oxygen concentration and the volume of the system are controlled, oxygen consumption ($\dot{V}O_2$) and halothane uptake ($\dot{V}$hal) can be measured (Coles, Brown and Lampard, 1973; Barton and Nunn, 1975; Bushman et al., 1977; Beatty et al., 1982; Ross et al., 1983; Westenskow, Jordan and Hayes, 1983a, b). With feedback control the anaesthetic breathing system becomes easier to use, and the pharmacokinetics of inhalation anaesthesia can be studied, and taught, in detail.

However, conventional anaesthetic breathing systems are not designed to control or measure the uptake of oxygen or halothane: fittings are not leak-tight, fresh gas flowmeters are not precise enough to measure low flows, the volume of the system is difficult to measure and considerable amounts of anaesthetic are absorbed by both rubber and plastic as well as by soda-lime (Lowe, Titel and Hagler, 1971; Morris, 1974; Grodin and Epstein, 1979; Lowe and Ernst, 1981). Thus a new design of breathing system and new sensors are required before a closed-loop technique can be

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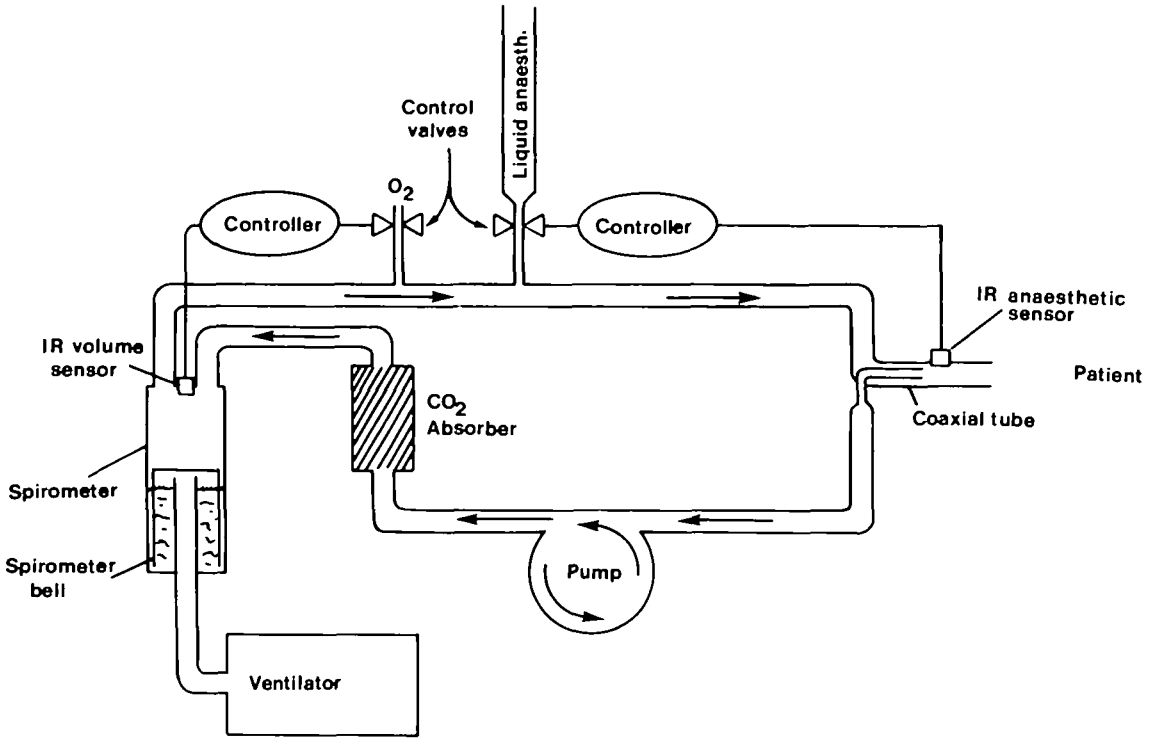

FIG. 1. Block diagram of closed-loop anaesthesia breathing system with feedback control. The infra-red (IR) volume sensor in the spirometer is used to control the oxygen delivery to keep the system volume constant. The infra-red (IR) anaesthetic sensor controls the halothane delivery to keep the end-tidal concentration constant. The patient breathes from the outlet of a coaxial tube within a tube.

used to measure $\dot{V}O_2$, and control the delivery of the anaesthetic.

A leak-tight, closed-loop breathing system has been constructed which ensures low solubility to anaesthetics and efficient gas mixing. Feedback control of the system was tuned using computer simulation. During subsequent animal experiments (see following paper (Zbinden et al., 1986)), arterial, mixed venous and cerebral venous blood-halothane concentrations were measured and showed that feedback control optimized the induction of anaesthesia.

MATERIALS AND METHODS

Figure 1 shows a rebreathing system incorporating a water-sealed spirometer, a carbon dioxide absorber, a coaxial tube, a circulator pump and feedback controllers.

Breathing system

A water-sealed plexi-glass spirometer replaced the traditional thin-walled rubber bellows. A 23-cm column of water between the spirometer and a 2.0-litre polycarbonate bell provided a gas-tight seal. An infra-red sensor (Opto modul ONS 250, Grieshaber AG, Switzerland) mounted in the top of the spirometer measured the position of the bell and a Siemens 900 B Servo Ventilator drove the bell to control ventilation. The carbon dioxide absorber, containing 680 ml of soda-lime, was a 60-cm plexi-glass tube of 3.8 cm i.d.—this small diameter providing an effective seal to the breathing tubes. The expiratory breathing tube (4.5 mm i.d.) lay as a coaxial tube within the inspiratory tube (18 mm i.d.). (Choosing the inner coaxial tube as the expiratory limb did not increase expiratory resistance as the patient could also exhale into the outer tube.) However, this arrangement prevented the pooling of condensed water because it was immediately suctioned off through the expiratory tube and transferred to the carbon dioxide absorber and the bellows.

The circulating pump shown in figure 1 moved gas through the rebreathing system at the rate of 25 litre min^{-1}. The pump (Nalgene Company,

Rochester, N.Y.) replaced functionally the one-way valves of a rebreathing system and insured that, during the expiratory pause, alveolar gas was cleared from the expiratory breathing limb and fresh gas was inspired with the next breath. If the patient exhaled at a rate greater than 25 litre min^{-1}, he exhaled into the inspiratory limb, which was cleared during the subsequent expiratory pause. The pump improved feedback control by decreasing the delay time between the injection of halothane to the system and its detection by the gas analyser.

To ensure that the 2.5-litre system was leak-tight, it was built of thick-walled, 18-mm i.d. p.v.c. tubing. The system was sealed at the patient connection by a rubber stopper and an oxygen flow of 5 ml min^{-1} maintained the system pressure at 60 mm Hg. This small oxygen leak could be ignored when using normal pressures of 20 mm Hg and a 1:1 inspired:expired ratio. There was an additional apparent leak of halothane from the uptake of halothane by the system. To measure this uptake, the system was primed and maintained at 0.87 vol% (1 MAC) for 1 h with the system sealed at the patient connection with a stopper, with normal ventilation and with carbon dioxide added at 100 ml min^{-1}. A 0.10-ml bolus of liquid halothane filled the system to 0.87 vol% and 0.38 ml maintained the concentration for 1 h.

Inspired and end-tidal halothane concentrations were measured with an infra-red sensor (LB-2, Beckman Instruments, Inc., Fullerton, CA). A 500-ml min^{-1} sample taken at the mouthpiece was returned to the breathing system after passing through the heated infra-red sensor head. The analyser was zeroed with room air and calibrated with gas standards (AGA, Pratteln, Switzerland) of 1.00 ± 0.01 and 1.99 ± 0.02 vol% halothane in oxygen.

Oxygen was supplied to the system through a mass flow controller (FC-260, Tylan, Torrence, CA), accurate to ± 0.5% of full scale over a range of 20–1000 ml min^{-1}. The flow controller was calibrated by a timed collection under a rising soap bubble in a 100- or 1000-ml glass cylinder.

Liquid halothane was added to the system in 0.03-µl increments by a titrating syringe (Metrohm). Its effluent was collected over time and weighed for calibration.

Feedback control

Classical proportional–integral (PI) control action (fig. 2) adjusted the oxygen mass flow controller and halothane titrating syringe. The

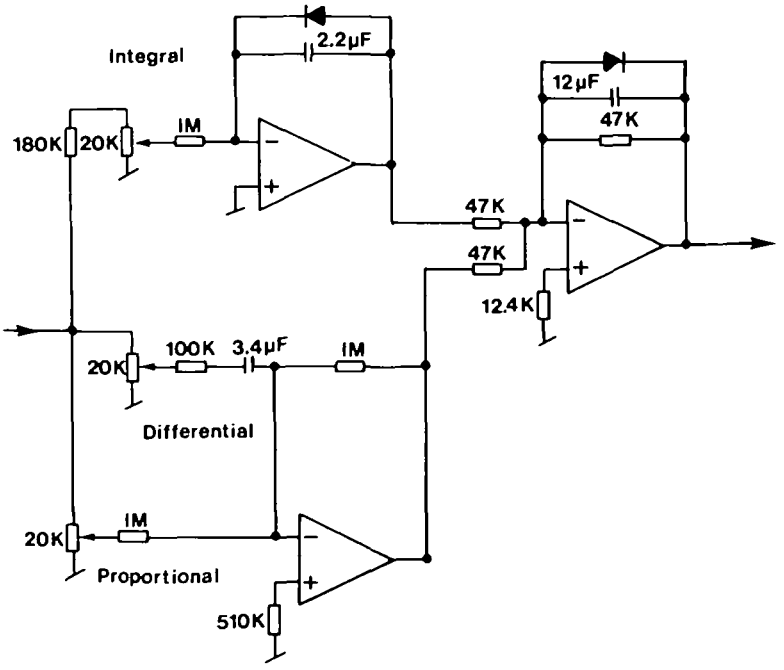

FIG. 2. Analogue control circuit. In our application, the differential gain was set to zero. The integral and proportional 20-K potentiometers were set to give the desired gains.

input to the oxygen controller was the difference between the averaged signal from the IR volume sensor and a preset value corresponding with the midpoint of the spirometer. The output of the controller drove the oxygen flow controller. This control action kept the spirometer bell in its midposition by the addition of oxygen.

The oxygen controller was tuned by trial and error while changing the system volume by 1-litre steps. With a proportional gain of 2.5 min^{-1} and integral gain of 0.15 min^{-2}, the bell reached its midposition in 1.2 min. The proportional gain (min^{-1}) equalled the oxygen flow (ml min^{-1}) into the system divided by the difference between the averaged system volume and a preset volume (ml). The integral gain (min^{-2}) equalled the oxygen flow (ml min^{-1}) into the system divided by the integral over the time of the difference between the averaged system volume and preset volume ($\int$ ml dt = ml min). Integral gain units were, therefore, ml min^{-1} ml^{-1} min^{-1} or min^{-2}. The oxygen flow controller's maximum of 1 litre min^{-1} was the main factor which limited the response time.

The halothane controller also used the PI circuit in figure 2. Its input was the difference between the target end-tidal halothane concentration and the measured end-tidal concentration taken from the Beckman LB-2 peak detector. A voltage-controlled oscillator converted the PI controller output to discrete pulses to drive the titrating syringe which then delivered 0.03 ml at each pulse. This control action maintained the end-tidal halothane concentration at the target value. For the animal study, the gains were initially set at proportional = 0.4 ml min^{-1} $vol\%^{-1}$ and integral = zero. When the animal study was completed, the uptake model variables were modified to fit the data and the model used to improve the tuning of the halothane PI controller. Integral gain was added to eliminate the offset error which appeared in the animal study.

Tuning of the halothane controller

We used the uptake model of Zwart, Smith and Beneken (1972), described in the appendix, to tune the halothane controller. Our anaesthesia breathing system (fig. 3) was modelled with two compartments: a 2.5-litre physical volume and a 6.02-litre virtual volume which simulated uptake by the components of the system, including the soda-lime. Gas transfer between the two compartments was augmented by the circulating pump. This simple model gave a match between simulated and

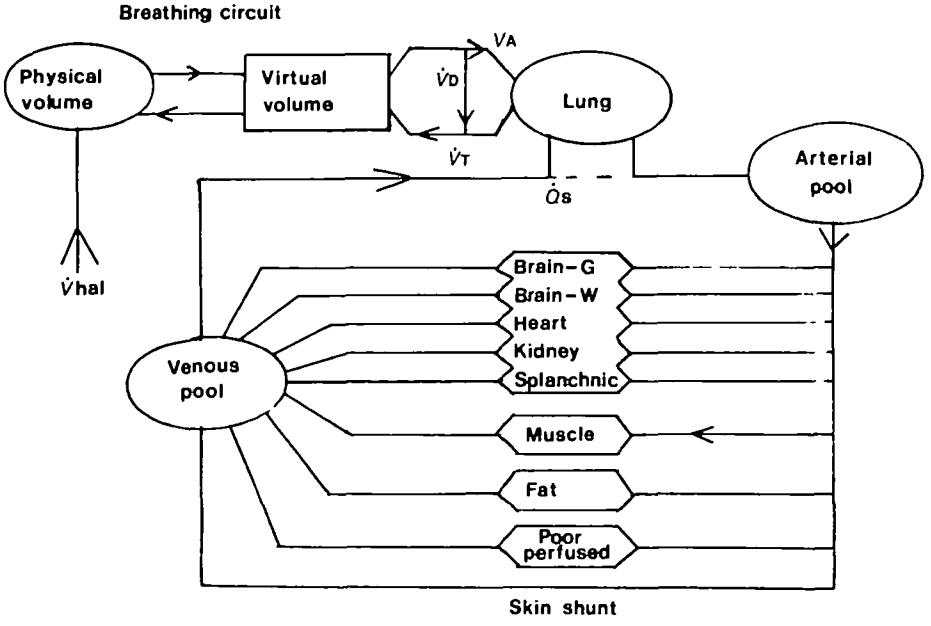

FIG. 3. Block diagram of Zwart's anaesthetic uptake and circulation model. The model has halothane-dependent blood flow to nine tissue compartments, halothane dependent $\dot{Q}t$, and fixed arterial–venous shunt. We added the component for our breathing system and an end-tidal halothane calculation.

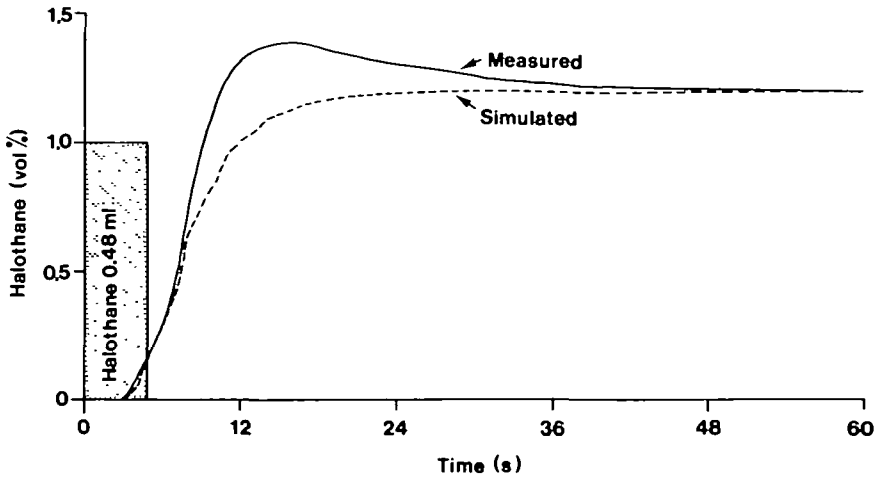

FIG. 4. Measured and simulated halothane concentration following the delivery of 0.48 ml of liquid halothane to the system. Halothane was given by titrating syringe. Concentration was measured by the anaesthetic sensor at the patient connection. This curve was produced with soda-lime in the absorber, a pump rate of 25 litre min^{-1} and carbon dioxide 100 ml min^{-1} added to simulate the animal's carbon dioxide production.

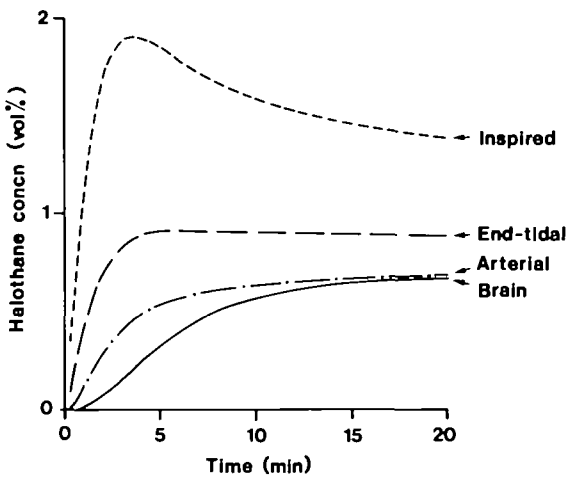

FIG. 5. Simulated response of the optimally tuned PI controller showing inspired, end-tidal, arterial and brain grey tissue concentrations. The model used a 20% arterial–venous shunt and 30% alveolar deadspace.

measured concentrations after delivering a bolus of halothane (0.48 ml) to the system (fig. 4). The match was adequate for the purpose of tuning the feedback controller.

The model was implemented in Fortran 77 on a DEC 11/44 computer using a discrete time model with a 1-s time increment. Transport delays were introduced as appropriate: 2 s for the infusion of halothane, 3 s for the system inspiratory limb and a further 3 s for the expiratory limb.

We used the model to tune the end-tidal halothane PI controller (fig. 2). During closed-loop simulation of induction, the proportional gain was increased to increase the rate of increase in the end-tidal concentration, but the inspired halothane concentration was kept to a maximum of 3.0 vol%. At this limit, end-tidal overshoot did not occur. The integral gain was gradually increased until the difference between the target and measured end-tidal concentration was zero, which occurred 20 min after induction. However, as the integral gain was increased, the proportional gain was decreased to prevent the maximum concentration from exceeding 3.0 vol%. For body weights (wt) from 5 to 100 kg, the desired response was achieved using the gains:

$$P = [0.015\,(wt) + 0.29]\ ml\ min^{-1}\ vol\%^{-1}$$

$$I = 0.006e^{0.057(wt)}\ ml\ min^{-2}\ vol\%^{-1}$$

As the weight changed, the tidal volumes, blood volumes, $\dot{Q}t$ (cardiac output), $\dot{V}_A$ (alveolar ventilation) and FRC (functional residual capacity) were scaled linearly according to weight. The simulated response for a 35-kg patient is shown in figure 5.

Stability of end-tidal control was maintained

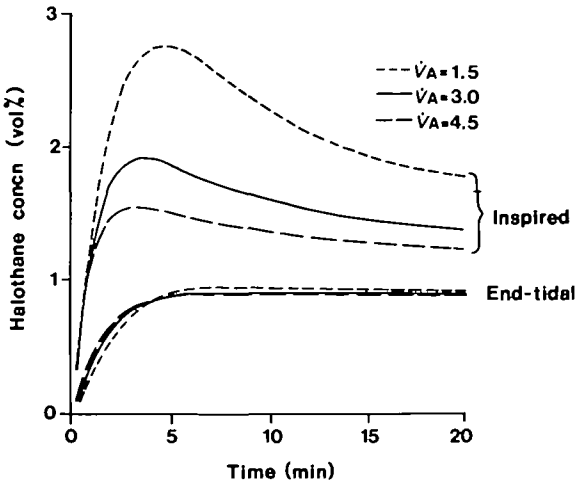

FIG. 6. Simulated response with $\dot{V}A = 1.5$ litre min^{-1}, 3.0 litre min^{-1} and 4.5 litre min^{-1}. The upper three curves are the inspired concentration, the bottom three are the end-tidal.

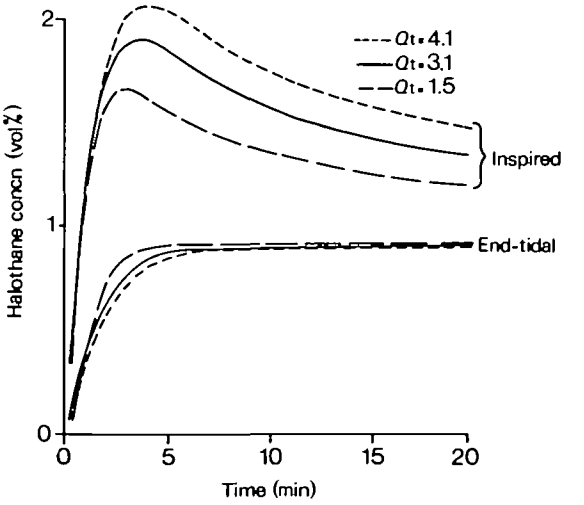

FIG. 7. Simulated response with initial $\dot{Q}t$ of 4.1 litre min^{-1}, 3.1 litre min^{-1} and 1.5 litre min^{-1}.

despite significant changes in $\dot{V}A$ and $\dot{Q}t$. Using the PI gains for a 35-kg patient, $\dot{V}A$ was increased and decreased by 50% with the results shown in figure 6. Changing $\dot{Q}t$ by $\pm 50\%$ (fig. 7) had little influence on end-tidal concentration.

DISCUSSION

The response time of our end-tidal halothane controller was less than the 10–15 min reported for other controllers using the closed-loop system (Ross et al., 1983; Westenskow, Jordan and Hayes, 1983a, b), but more than the 1–2 min reported for non-rebreathing system controllers (Mapleson et al., 1980; Tatnall, Morris and West, 1981; Morris, Tatnall and Montgomery, 1983). More rapid responses could be achieved using our controller in a non-rebreathing system where gas concentrations, can be changed on a breath-to-breath basis, but the advantages of the closed-loop system (humidification, economy, ecology and monitoring $\dot{V}O_2$ and $\dot{V}$hal) seemed more important than a decrease in response time. Our closed-loop controller achieved a more rapid response than other closed-loop controllers as a result of rapid mixing, small system volume and a well-tuned controller.

A leak-tight breathing system should be ideal for monitoring $\dot{V}O_2$ if errors from nitrogen accumulation, changes in FRC, and leaks are avoided (Nunn and Pouliot, 1962; Owen-Thomas et al., 1971; Nisbet et al., 1973; Barton and Nunn, 1975). Our breathing system was constructed to overcome the leaks found in most commercial systems, the water-sealed spirometer which replaced the normal rubber bellows in the ventilator being the most significant improvement. Our feedback controller and precision mass flow controllers kept volume constant and recorded the inflow of fresh oxygen with a 1% accuracy, thereby obtaining an accurate measurement of $\dot{V}O_2$.

The average system volume was kept constant, but if the system is used during spontaneous breathing it may be better to keep the end-expiration system volume constant. With spontaneous breathing, the tidal volume will change from breath to breath, causing the average system volume to fluctuate. A device which measured the system volume at end-expiration would be more stable, as FRC is more constant than average lung volume.

The accuracy of the $\dot{V}$hal measurement is not known. The flow of halothane to the closed-loop equals $\dot{V}$hal of the patient only after correction is made for $\dot{V}$hal of the system. Our system used metal and p.v.c. components and a small soda-lime absorber to reduce system uptake, but approximately 0.48 ml of liquid halothane was taken up by the system during the first 1 h at 1 MAC. System uptake cannot be compensated for easily, as it will change when the patient's $\dot{V}CO_2$ alters the temperature and humidity of the soda-lime (Lowe,

Titel and Hagler, 1971) and, therefore, its uptake of halothane. As soda-lime accounts for more than one-half of the total uptake by the system, and its uptake depends on its state of hydration, $\dot{V}$hal can be measured accurately only after this variability is accounted for.

Before the system can be used clinically, two improvements are needed. The present circulation pump could generate dangerous airway pressures if the breathing hose became kinked, and carbon dioxide rebreathing could occur if the pump stopped. The circulating pump should be replaced with a fail-safe, pressure-limited pump. Air entrainment could result from a system leak and feedback control systems may fail. Therefore, secondary monitoring is required for oxygen concentration, system volume and halothane concentration. Feedback control does, however, seem clinically applicable, the adjustments of end-tidal halothane concentration providing a rapid and optimal induction of anaesthesia.

APPENDIX

The uptake model of Zwart, Smith and Beneken (1972) contains nine tissue compartments (fig. 3). The partial pressure in each compartment is described by:

$$P(t) = P(o) + \frac{1}{\lambda_b V_b + \lambda_t V_t} \int_0^t \{\lambda_b q_b(t)[P_i(t) - P(t)]\}\, dt$$

where λ = solubility coefficient for blood (b) and tissue (t)
P = agent partial pressure in tissue compartment (t), or in blood entering the compartment (i) or in blood leaving the compartment (o)
$q_b(t)$ = blood flow as a function of vascular conductance and arterial halothane concentration, and
V = compartment tissue volume (t) or blood volume (b).

The agent partial pressure in the lungs is given by:

$$P(t) = P(o) + \frac{1}{\lambda_b V_b + \lambda_t V_t + V_a} \times \int_0^t \{\lambda_b q_b(t)[P_{vl}(t) - P(t)] + q_v(t)[P_{il}(t) - P(t)]\}\, dt$$

where V_a = functional residual capacity + 0.5 tidal volume
P_{vl} = agent partial pressure in venous blood
P_{il} = agent partial pressure in inspired air, and
$q_v(t)$ = ventilation of the lung corrected for deadspace.

The arterial and mixed venous compartments are:

$$P(t) = P(o) + \frac{1}{\lambda_b V_b + \lambda_t V_t} \int_0^t \{\lambda_b[\Sigma q(t) P_i(t) - \dot{Q} P(t)]\}\, dt$$

where $\dot{Q}$ = cardiac output, and
$\Sigma q(t) P_i(t)$ = summation over all flows entering the compartment.

Halothane concentration in the physical compartment of the anaesthesia breathing system is:

$$P_c(t) = P_c(o) + \frac{1}{a} \int_0^t \{[P_B u(t) - c(P_c(t) - P_i(t))]\}\, dt$$

where $u(t)$ = halothane added (litre min^{-1} pure vapour as ideal gas),
$P_c(o)$ = halothane partial pressure initially in the system
a = 2.5-litre physical system volume (fig. 3)
c = 25-litre min^{-1} circulating pump speed (fig. 1), and
P_B = barometric pressure.

The concentration in the virtual compartment of breathing system is:

$$P_i(t) = P_i(o) + \frac{1}{b} \int_0^t \{[c(P_c(t) - P_i(t))] - q_v(t)[P_i(t) - P_A(t)]\}\, dt$$

where P_A = alveolar halothane partial pressure, and
b = 6.02-litre virtual system volume (figure 3—uptake by the breathing system and soda-lime).

To the model we added a calculation for the end-tidal halothane partial pressure (P'hal). The end-tidal gas is a mixture of alveolar gas and alveolar deadspace (V_D) gas. Theoretically the deadspace gas has the same halothane concentration as the inspired gas (P_i) because it comes from nonperfused regions which empty in parallel with alveolar compartments. The relative contribution of P_i and P_A to the end-tidal gas is assumed to be directly proportional to the alveolar deadspace fraction (V_D/V_A):

$$P'\text{hal} = \frac{V_D}{V_A} P_i + \left(1 - \frac{V_D}{V_A}\right) P_A.$$

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