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A Closed Xenon Anesthesia Delivery System

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XENON was discovered in 1898 and first used as an anesthetic in 1951.[1] It is more potent than nitrous oxide (N_2O) with a minimum alveolar concentration (MAC) of approximately 71%, and its low blood-gas partition coefficient of 0.14 (recently recalculated as 0.115) results in rapid induction and recovery.[2–7] Interest in xenon is high because of medical and environmental concerns about N_2O; however, use may be constrained high cost.[8–10] Fully closed rebreathing circuits are one method of minimizing costs. It is possible to close a conventional circle system, with the anesthesiologist varying the fresh gas flow to match uptake *via* the lungs. However, better control might be achieved by automation of this procedure.[8–11] We describe a closed breathing system that may have advantages *versus* other designs.

Materials and Methods

Breathing System

The breathing system comprised a disposable carbon dioxide absorber–valve unit (King Systems Corp., Noblesville, IN) plus hoses; a mechanical ventilator (Kontron ABT 4000, Milan, Italy) and a bellows system modified by one of the authors (J. D.) to allow oxygen entry into the circle (fig. 1). At equilibrium, oxygen was added automatically at end-inspiration to keep the volume constant, replacing gas uptake from the closed circle. The system volume was approximately 2,170 ml (770 ml circle volume + 900 ml functional residual capacity + 500 ml tidal volume delivered).

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With a xenon–oxygen mixture in the circle, this mechanical arrangement would result in a gradual increase in circle oxygen concentration as uptake of both gases was replaced with oxygen. This tendency was offset by delivery of xenon boluses to the circle *via* a computer-controlled magnetic valve (Airmatic-Allied Inc., Wilmington, OH), to maintain a stable measured oxygen concentration. The computer control algorithm was written using Labview software (National Instruments, Austin, TX) and based on the algorithm of Luttropp *et al*.[8] It was a model-based, forward-feedback loop-control system in which a volume of xenon was delivered to an estimated distribution volume to achieve a target measured oxygen concentration by dilution. The estimated distribution volume comprimised the volumes of the breathing system and lungs plus a volume representing the continuous loss of gas by tissue uptake. Initial xenon overdose to the circle while the algorithm optimized an appropriate distribution volume was prevented by use of a deliberately low 2-l starting value. The computer controlled and recorded xenon bolus volumes by varying the magnetic valve opening time; the flow rate through the valve was constant and known. The condition for xenon delivery was oxygen concentration greater than target value and bellows nearly empty (oxygen about to be added) and previous delivery at 60 s or more (to allow mixing of previous xenon bolus). When running closed, the bellows never filled completely, and, thus, no gas was spilled. Xenon was delivered to the expiratory limb to maximize mixing before it entered the lungs. Leak testing was performed *via* ventilation of a dummy lung. Absence of movement of the oxygen flow indicator confirmed a lack of volume loss. A small leak across the automatic oxygen addition valve mechanism could theoretically be tolerated as any leaked gas would be flushed back by oxygen during the following cycle.

Anesthesia and Surgical Preparation

Experiments were performed in five purebred, large, white male pigs. All complied with the 1986 Animals (Scientific Procedures) Act of the United Kingdom in accordance with the National Institutes of Health guidelines on the use of experimental animals. Anesthesia was induced using a halothane–oxygen–nitrous oxide mixture, and the trachea intubated with use of an uncut 6.5-mm ID cuffed tube (SIMS Portex Ltd., Hythe, UK) without neuromuscular blockade. After right external jugular vein cannulation, anesthesia was maintained with an alphaxalone–alphadolone infusion at 15 $mg \cdot kg^{-1} \cdot h^{-1}$, and mechanical ventilation

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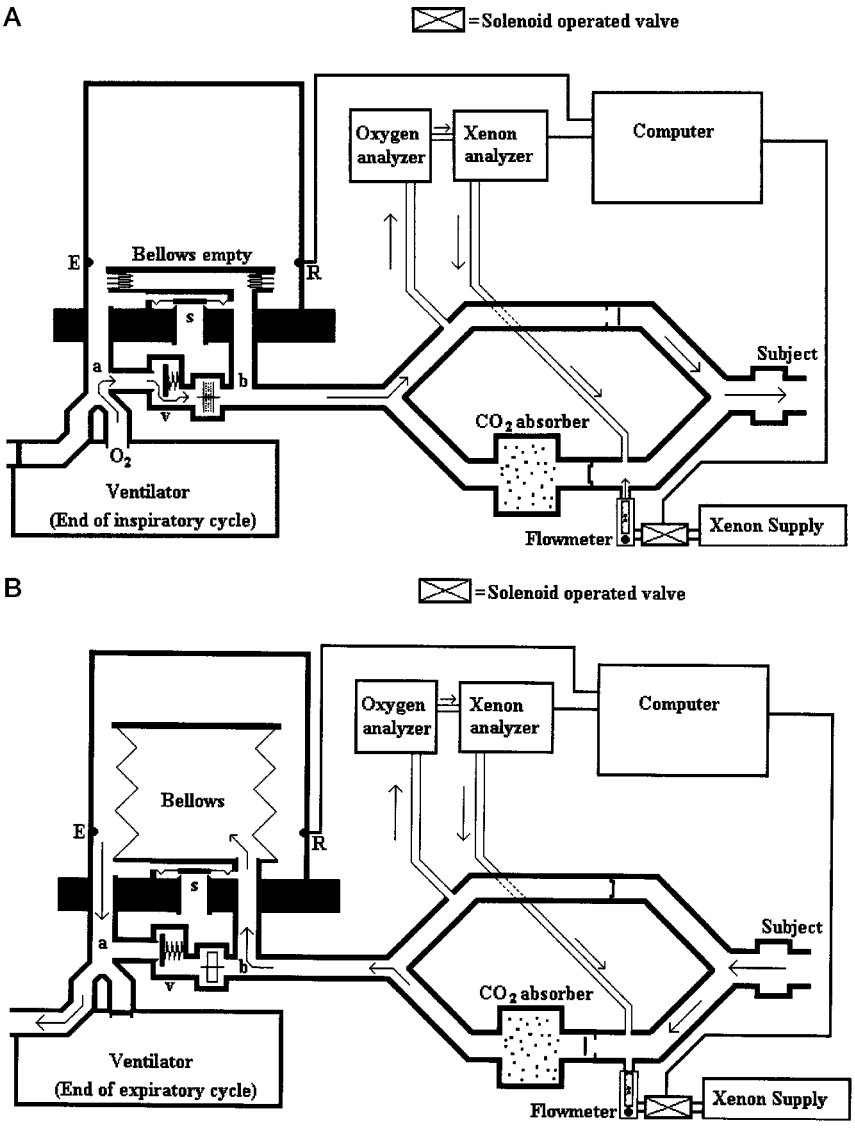

Fig. 1. (*A*) Breathing system at end-inspiration. The bellows deflate and the lungs inflate as oxygen is driven into the "bottle" by the ventilator. Because of net uptake of gas *via* the lungs, the bellows will be empty before the end of each inspiratory cycle of the ventilator. Once the bellows are empty, the pressure at (a) exceeds the pressure at (b) and oxygen moves from (a) to (b) into the circle through a lightly sprung one-way valve (v), while a rotating vane indicator makes this visible to the operator. The motive power for this is supplied by the ventilator. An infrared beam running from emitter (E) to receiver (R) informs the computer of the volume status of the bellows. (*B*) Breathing system at end-expiration. Recoil of the lungs and chest propels gas through the expiratory limb of the circle. An absorbent removes carbon dioxide. The valve (v) is closed and the bellows fills. At end-expiration, the volume in the bellows will be less than the tidal volume set on the ventilator, *i.e.* set tidal volume minus the volume of gas consumed in the previous cycle. A spill valve (s) is incorporated if an operator wishes to use gas ± volatile from an external source for conventional operation or to flush the circle; then the bellows will fill completely in expiration, with excess gas spilling in the normal way.

continued with use of a 30% oxygen–70% nitrogen mixture.

Measurements

The volume of each xenon bolus (V_1) stored in the computer database was given by the equation

xenon flow through valve (l/s)

$\times$ duration of valve opening (s)

Summation of all values of V_1 gives the total xenon volume used at ambient temperature and pressure as estimated by the computer (V_c). Weighing of the xenon cylinder before and after each experiment allowed a more accurate calculation of the total volume used (V_w). Small errors in the values of V_1 as a result of the opening and closing times of the magnetic valve could be reduced by multiplying each by a correction factor defined as V_w/V_c.

A Servomex 570A paramagnetic oxygen analyzer (Servomex Ltd., Crowborough, Sussex, UK) was used to measure the circle oxygen concentration and data was recorded and continuously fed to the control algorithm. Xenon concentration was simultaneously measured using a calibrated Minison ultrasonic analyzer (Thomas Swan and Co., Ltd., Cambridge, UK). The sample gas was dried *via* passage through a 10-ml container of silica gel desiccant beads upstream of the analyzers, to reduce xenon measurement error, and returned to the circle otherwise unchanged.

Experimental Protocol

A standardized 30-min nitrogen washout maneuver was performed using a Mapleson D system and a mechanical ventilator with a fresh gas flow of 10 l/min, set at 14 breaths/min, and a tidal volume varied to maintain a constant partial pressure of arterial carbon dioxide ($Paco_2$). The closed breathing system, which was primed

Table 1. Xenon Expenditure

O_2 concentration (%) in circle	100, decreasing to 30	30	30	30	30	30
Time interval (min)	0–15	15–30	30–60	60–90	90–120	120–240
Median Xe expenditure over time interval (l)	4.1	0.8	1.5	0.9	1.0	4.0
Range	3.0–4.4	0.5–1.5	1.2–1.6	0.7–1.3	0.7–1.1	—
Median Xe expenditure over time interval (ml/kg)	121	24	41	28	28	121
Range	94–133	13–47	35–48	18–39	21–33	—

Xe = xenon; O_2 = oxygen.

with oxygen, then was connected. The oxygen concentration was reduced to 80, 60, 40, and then 30%, with two cycles of the algorithm permitted at each of these steps for the algorithm to optimize the estimated xenon distribution volume (1 min/cycle). The final 30% oxygen target remained unaltered for the remainder of the experiment, which lasted 2 h in all five animals but was extended to a total of 4 h in one animal. Nitrogen concentration was measured intermittently using a mass spectrometer (model SX200; VG Quadropoles Ltd., Middlewich, Chesire, UK). Values are expressed as the median and range.

Results

The weight of the pigs was 33 kg (range, 32–39 kg). The median volume of xenon used for the 2-h administration periods (at 22°C and atmospheric pressure) was 7.9 l (range, 7.4–9.1 l). In the 4-h administration, for a 33-kg pig, this volume was 13.1 l (table 1). More than half the xenon necessary for 2 h administration was used in the first 30 min.

An example of the performance of the system during a 2-h period is shown graphically in figure 2.

By the 90- to 120-min measurement interval, the median xenon volume necessary decreased to 1 l every 30 min, and in the pig that received xenon for 4 h, xenon expenditure continued at a similar rate.

Each time a new lower target oxygen concentration was set, the xenon concentration increased in a stepwise fashion, stabilizing within three cycles of the algorithm and within 5 min. The median nitrogen concentration in the breathing system after 2 h was 9.4% (range, 9–11.6%) and was 14.5% after 4 h.

Discussion

The system functioned as intended. We performed a computer simulation using the NARKUP 4.11 program (Drs. D. C. White and G. G. Lockwood, Northwick Park Hospital, Harrow, UK), which uses a xenon blood-gas partition coefficient of 0.14. The simulated xenon expenditure for our system was 4.9 l after 2 h.[12] The observed median xenon expenditure of 7.9 l after 2 h is good compared to the "ideal" value and is similar to the 7.6 l observed by Luttropp *et al.*, who used a functionally closed exchanger system in pigs of similar weight.[8] In engineering terms, our breathing system should be closed, with zero gas loss; however this is difficult to achieve in practice. Our dynamic leak test relied on a rotating vane to show leaks. These have inertia and friction; therefore, a slight leak might be missed. A static leak test also would have been advisable. Xenon diffuses well through certain materials, for example, silicone rubber. Luttropp *et al*. Showed a loss of 1.5 l *via* silicone hoses over 2 h in similar experiments.[8] In the current study, the hoses, the gas sampling, and the return lines were made of polyethylene, through which xenon dif-

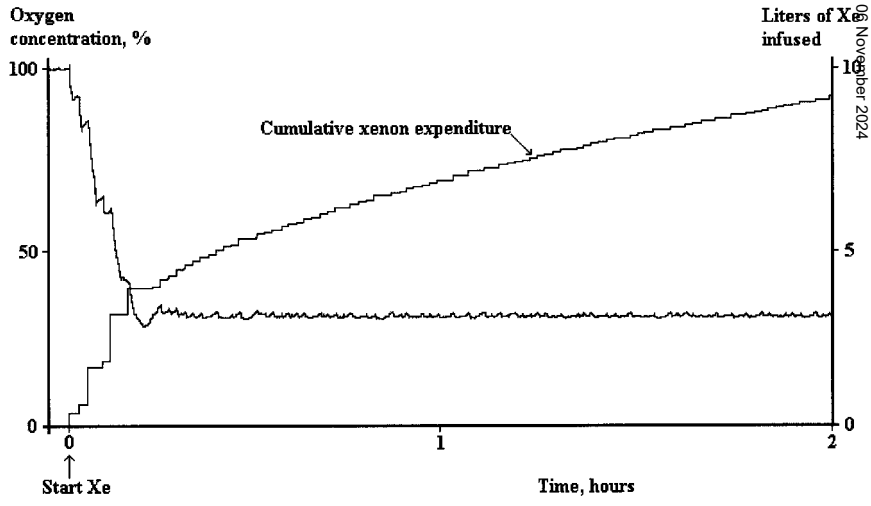

Fig. 2. Example of a 2-h xenon administration period in pig 4. Target oxygen concentration was set to 80, 60, 40, and then 30%. The measured oxygen concentration in the breathing system and the cumulative xenon expenditure are shown.

fuses poorly, and the xenon analyzer contained stainless steel tubing. However, a latex rubber bellows was used because polyethylene was unavailable, endotracheal tubes and cuffs were made of silicone rubber, and the oxygen analyzer internal hoses were made of synthetic rubber. These were potential routes of xenon loss.

With closed systems, accumulation of gases such as nitrogen and methane can dilute the delivered xenon concentration. A denitrogenation period is necessary if 1 MAC of xenon is to be delivered (71%) because flushing the circle to remove nitrogen is extremely expensive. Measured nitrogen concentrations were approximately 10% after 2 h despite denitrogenation; therefore, this problem is clinically relevant. If xenon use were balanced by adjunctive agents, as in conventional anesthetic practice, modest xenon dilution by nitrogen could be tolerated. Suitable adjuncts include opioids and very-low-dose propofol target-controlled infusion. These have been used clinically by other groups (personal verbal communication, Priv. Doz. Dr. Thomas Marx, M.D., Xenon Group, University of Ulm, Germany, September 3, 1999).

In summary, we described a closed anesthesia system that could also be used as part of a conventional anesthesia circle system. We demonstrated that it could successfully and economically deliver a 70% xenon–30% oxygen mixture for up to 4 h in a pig model. With appropriate safety devices, this system could be developed as a practical closed anesthesia system using xenon alone or in conjunction with volatile or intravenous agents.

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References

1. Cullen SC, Gross EG: The anesthetic properties of xenon in animals and human beings with additional observations on krypton. Science 1951; 113:580–2

2. Luttropp HH, Thomasson R, Dahm S, Persson J, Werner O: Clinical experience with minimal-flow xenon anaesthesia. Acta Anaes Scand 1994; 38:121–5

3. Lachmann B, Armbruster S, Schairer W, Landstra, Trouwborst A, Van Daal G-J, Kusuma A, Erdmann W: Safety and efficacy of xenon in routine use as general anaesthetic. Lancet 1990; 335:1413–5

4. Steward A, Allott PR, Cowle AL, Mapleson WW: Solubility coefficients for inhaled anaesthetics for water, oil and biological media. Br J Anaesth 1973; 45:282–93

5. Goto T, Suwa K, Uezono S, Ichinose F, Uchiyama M, Morita S: The blood-gas partition coefficient of xenon may be lower than generally accepted. Br J Anaesth 1998; 80:255–6

6. Nakata Y, Goto T, Morita S: Comparison of inhalation inductions with xenon and sevoflurane. Acta Anesthesiol Scand 1997; 41:1157–61

7. Goto T, Saito H, Shinkai M, Nakata Y, Ichinose F, Morita S: Xenon provides faster emergence from anesthesia than does nitrous oxide–sevoflurane or nitrous oxide–isoflurane. ANESTHESIOLOGY 1997; 86:1273–8

8. Luttropp HH, Rydgren G, Thomasson R, Werner O: A minimal-flow system for xenon anaesthesia. ANESTHESIOLOGY 1991; 75:896–902

9. Bader S, Brand T: Reclaiming volatile and gaseous anaesthetics: Anasthesie-Intensivmed Notfallmed Schmerzther 1997; 32:46–8

10. Saito H, Saito M, Goto T, Morita S: Priming of anesthesia circuit with xenon for closed circuit anesthesia. Artif Organs 1997; 21:70–2

11. Burov NE, Makeev GN, Potanov, VN, Kornienko LIu: Alternative means for reducing the cost of xenon anesthesia. AnestezioII Reanimatol 1997; 4:71–4

12. Lockwood GG, White DC: Effect of ventilation and cardiac output on the uptake of anaesthetic agents from different breathing systems: a theoretical study. Br J Anaesth 1991; 66:519–26