Simple contrivance “clamps” end-tidal \( \text{PCO}_2 \) and \( \text{PO}_2 \) despite rapid changes in ventilation

ROBERT B. BANZETT,1,2 RONALD T. GARCIA,1 AND SHAKEEB H. MOOSAVI1

1Physiology Program, Harvard School of Public Health, Boston 02115;
and 2Department of Medicine, Harvard Medical School, West Roxbury Brockton
Veterans Affairs Medical Center, Boston, Massachusetts 02132

Banzett, Robert B., Ronald T. Garcia, and Shakeeb H. Moosavi. Simple contrivance “clamps” end-tidal \( \text{PCO}_2 \) and \( \text{PO}_2 \) constant, even in the case of rapidly changing ventilation. J Appl Physiol 88: 1597–1600, 2000.—The device described in this study uses functionally variable dead space to keep effective alveolar ventilation constant. It is capable of maintaining end-tidal \( \text{PCO}_2 \) and \( \text{PO}_2 \) within ±1 Torr of the set value in the face of increases in breathing above the baseline level. The set level of end-tidal \( \text{PCO}_2 \) or \( \text{PO}_2 \) can be independently varied by altering the concentration in fresh gas flow. The device comprises a tee at the mouthpiece, with one inlet providing a limited supply of fresh gas flow and the other providing reinjected alveolar gas when ventilation exceeds fresh gas flow. Because the device does not depend on measurement and correction of end-tidal or arterial gas levels, the response of the device is essentially instantaneous, avoiding the instability of negative feedback systems having significant delay. This contrivance provides a simple means of holding arterial blood gases constant in the face of spontaneous changes in breathing (above a minimum alveolar ventilation), which is useful in respiratory experiments, as well as in functional brain imaging where blood gas changes can confound interpretation by influencing cerebral blood flow.

hypercapnia; alveolar ventilation; brain imaging; functional magnetic resonance imaging; positron emission tomography

**METHODS**

Overview. The subject expires into a large tube that serves as an alveolar gas reservoir. Inspiratory gas initially comes from a bag reservoir supplied by a high-impedance constant-flow source. As the subject continues inspiration after the fresh gas from the bag has been exhausted, pressure drops in the system, and a spring-loaded valve at the distal end of the alveolar gas reservoir opens. The subject is thus able to breathe in more gas, but its composition is identical to alveolar gas. The minimum alveolar ventilation at which this device will hold constant \( \text{PCO}_2 \) is the alveolar ventilation, which establishes \( \text{PCO}_2 \) with no inspired \( \text{CO}_2 \).

Contrivance design. The contrivance, depicted in Fig. 1, comprises a manifold (T piece) connected to two tubes and a mouthpiece (or tightly sealed mask). One tube, the fresh gas inspiratory limb, provides gas from a 3-liter anesthetic bag via a one-way valve and a 1-m-long by 3.8-cm-ID tube. Fresh gas from a high-impedance flow (e.g., compressed gas tanks) is continuously fed to the anesthetic bag via a flowmeter; the flow through this meter determines the amount of inspired fresh gas or effective alveolar ventilation. The resistance of the line from bag to mouthpiece should be as low as possible. Depending on the requirements of the experiment, the fresh gas can be air, oxygen, or some other oxygen-containing blend to suit the requirements of the experiment (see Varying gas concentration below). In our laboratory, inspired fresh gas is heated and humidified (SCT 3000 Marquest Medical Products), and expiratory tubing is insulated to minimize cooling and condensation.
The other tube connected to the T piece, the expiratory/rebreathing limb, consists of a tube 3.5 m long by 3.8 cm ID that forms a reservoir holding ~4 liters of expired gas. The distal end of this tube terminates in a second T piece. One port of this T piece is attached to a standard one-way valve, allowing expiration (Hans Rudolph model 5710). The other port of the T piece is attached to a rebreathing control valve that allows inspiratory flow when a pressure threshold is exceeded. The rebreathing control valve is typically set to open at 1–2 cmH2O; the minimal setting is determined by the pressure drop during inspiration from the uncollapsed bag, which in turn depends on the resistance of the fresh gas line and the inspiratory flow rate. The threshold valve must be set so that it does not open until the reservoir bag collapses; higher settings will not impair the function of the system but will increase the load faced by the subject.

The low-resistance one-way valves used for the inspiratory and expiratory line had an opening pressure <0.1 cmH2O (Hans Rudolph model 5710). The rebreathing control valve (prototype positive end-expiratory pressure valve, Emerson, Cambridge, MA), which controlled the amount of reinspired alveolar gas, had an adjustable threshold (0 to −7.5 cmH2O). Figure 2 shows the flow vs. pressure curves for various opening settings on this valve. The pressure-flow characteristics were determined by employing a flow source (Lewyt vacuum cleaner model 59) connected to the breathing device at the mouthpiece. Pressure was sampled at the mouth end of the valve, referred to atmospheric pressure.

Operation of the system. Before the subject is connected to the mouthpiece, a normal resting PETCO2 is measured with a fine nasal cannula while the subject sits quietly (5). It is our experience that subjects almost invariably increase ventilation behaviorally when breathing via a mouthpiece or mask. Thus to achieve normal resting PETCO2, it is necessary to impose some rebreathing, even in the baseline state. After the subject is connected to the mouthpiece, the flow of fresh gas into the anesthetic bag is adjusted such that during baseline there is a small amount of alveolar gas reinspired from the expiratory limb. This should be confirmed both by visual verification that the bag fully collapses and by inspection of the tidal PCO2 or PO2 trace to confirm slight reinspiration of alveolar gas. Because baseline ventilation in the mouthpiece requires some reexpiration to achieve resting PETCO2, the system can maintain constant alveolar concentrations in the face of small decreases in ventilation, as well as large increases in ventilation.

Varying gas concentration. For some experiments, it is desirable to vary alveolar gas concentration. This is easily accomplished by altering the content of the fresh gas supply. We find it convenient to use a gas blender to supply fresh gas (e.g., Siemens model 965). For instance, in an experiment requiring constant normoxia and variable PETCO2, one could blend from a gas cylinder containing 21% O2-balance N2 and a tank containing 15% CO2-21% O2-balance N2. The most rapid rise in PETCO2 is accomplished by giving a few breaths of high inspired PCO2 (PICO2) and then gradually reducing the in-

![Fig. 1. Schematic of contrivance. See text for detailed description. Pneumotachometers (P-Tach A and B) are not essential to the function of the system. Tube that forms the reservoir for expired gas is truncated. Solid arrowheads, steady flow; open arrowheads, cyclic flow; arrows with solid lines, inspiratory flow; arrows with dashed lines, expiration.](http://jap.physiology.org/)

![Fig. 2. Pressure-flow characteristic of the rebreathing control valve.](http://jap.physiology.org/)
10 breaths/min. volume was constant at 2 liters and frequency decreased from 20 to 22 to 24 cmH2O. Note that V˙RB increases with increasing ventilation, whether due to frequency or tidal volume change.

Panels a, b, and c: tidal volume was constant at 1 liter and frequency increased from 10 to 15 to 20 breaths/min, respectively. Panels c and d: frequency was constant at 20 breaths/min and tidal volume changed from 1 to 2 liters. Panels d and e: tidal volume was constant at 2 liters and frequency decreased from 20 to 10 breaths/min. Panels c and e: same ventilation (20 l/min) achieved with very different tidal volume-frequency combinations. Data span the range from 10 to 40 l/min. Inspiratory pressure peaks range from –2 to –4 cmH2O. Note that V˙RB increases with increasing ventilation, due to frequency or tidal volume change.

Fig. 3 shows pertinent pressures, flows, and tidal gases during a range of conditions of VT and f voluntarily achieved by one subject. In steady-state conditions, the system was capable of maintaining PETCO2 within ±2 Torr of baseline in the worst case of five subjects tested, and ±1 Torr was the typical performance. We also examined performance when the system was challenged by two- to fivefold rapid transitions between levels of ventilation. We used as a measure of performance the variability of PETCO2 during the 20 breaths surrounding transitions. The worst case showed a standard deviation of 1 Torr, and the best, 0.2 Torr. Median standard deviation of 25 transitions was 0.5 Torr. Typical transitions are shown in Fig. 4. Our measurements show improved precision of PETCO2 regulation over those of Sommer et al. (6), but we do not know whether operation of their system could be further improved.

We also note that PETCO2 can be raised to a new steady-state level within a few breaths by using high levels of inspired CO2, but the return to baseline can be slow, if one simply returns inspired CO2 to zero, because alveolar ventilation is limited by design. If it is desired to lower PETCO2 more rapidly, it is possible to temporarily increase the flow of fresh gas (after noting the flow to which to return).

Fig. 4. Typical examples of rapid changes (Δ) in ventilation. Each breath is represented by 1 data point. Top: change from 12 to 70 l/min, accomplished by increasing tidal volume (VT) from 0.5 to 3 liters at constant respiratory frequency (f). Bottom: change from 26 to 16 l/min accomplished by decreasing f from 30 to 19 breaths/min at constant VT. Notice that end-tidal PCO2 is essentially unchanged throughout these transitions.
adopts a breathing pattern of very small VT with high f, the subject reduces real alveolar ventilation below minimum alveolar ventilation. This may occur if the subject reduces minute ventilation, or if the subject adopts a breathing pattern of very small VT with high f, so that much of the fresh gas penetrates no further than the anatomic dead space. Whereas this pattern of breathing is unphysiological in humans, it implies that the device will not work in animals that pant (although the problem should be ameliorated by the effects of high-f mixing). Furthermore, these devices do not automatically adapt to changes in metabolic CO₂ production.

Subjects did detect a slight added resistance to breathing, as would be predicted from psychophysical data. Many subjects could detect the change in pressure as the bag collapsed and the rebreathing control valve opened. We were able to keep inspiratory pressure drops below a level objectionable to most subjects. This required careful attention to the minimization of impedance in the fresh gas limb so that the rebreathing control valve threshold could be set to typically 1 cmH₂O. If necessary for a particular experiment, the impedance of both limbs of the device could be reduced further.

Troubleshooting common problems. This system has been in use in our laboratory for 2 yr. We encountered several problems while setting up and learning to use this device. Most problems result in a fall in PETCO₂ at high ventilation. Possible causes are as follows: 1) VT in large subjects may exceed the volume of the expired gas reservoir; this is easily remedied by extending the length of the reservoir tube. 2) Inward leaks (especially when a face mask is used) compromise operation by allowing added fresh gas into the system. 3) The threshold valve may open prematurely because of a) valve malfunction or b) excessive resistance in the fresh gas line, which causes the pressure drop to exceed threshold before the bag collapses. This malfunction can be detected by setting fresh air flow just above minute ventilation (so the bag does not fully collapse) and observing whether PₐCO₂ remains zero throughout inspiration. 4) There is excessive fresh gas flow at baseline.

Another common problem is excessive pressure drop or pressure fluctuation during inspiration (usually brought to our attention by the subject). Possible causes are as follows: 1) sticky valves; 2) high resistance of inspiratory limb requiring a high opening pressure setting for rebreathing control valve; and 3) excessive mass of rebreathing control valve flapper can create a resonant system interacting with the inerterance or compliance of the gas in the alveolar reservoir. We first tried rebreathing control valves with weight thresholds and found them unsuitable for this reason.

Conclusion. The contrivance presented here is simple to implement, provides somewhat more precise regulation of end-tidal gases than previous designs, and conveniently allows one end-tidal gas to be independently varied.

We thank our subjects for their time and cooperation and George Emerson of J. H. Emerson Company for designing and constructing a prototype valve to meet our specifications.

This study was supported by National Heart, Lung, and Blood Institute Grant HL 46690.

Address for reprint requests and other correspondence: R. B. Banzett, Physiology Program, Dept. of Environmental Health, Harvard School of Public Health, 665 Huntington Ave., Boston, MA 02115–6021.

Received 27 December 1999; accepted in final form 3 January 2000.

REFERENCES


