*Annals of Biomedical Engineering*, Vol. 13, pp. 359–372, 1985
Printed in the USA. 

0090-6964/85 $3.00 + .00


# A FEEDBACK CONTROLLER FOR VENTILATORY THERAPY

F.W. Chapman
J.C. Newell
R.J. Roy

Department of Biomedical Engineering
Rensselaer Polytechnic Institute
Troy, New York

*A computerized system that uses feedback of end-tidal $CO_2$ fraction ($F_{ET}CO_2$) to adjust minute volume of a ventilator has been developed and tested. The effectiveness and robustness of the controller were evaluated in five anesthetized dogs. The controller responded to step-changes in the set-point for $F_{ET}CO_2$ by adjusting minute volume so that the $F_{ET}CO_2$ settled to the new set-point in less than 60 sec with less than 20% overshoot. The system exhibited suitable dynamic response to step-changes in set-point with loop gains as large as two times and as small as one-half the optimal value. The breath-to-breath variation in $F_{ET}CO_2$ values during prolonged periods of closed-loop controlled ventilation was smaller than the variation during periods of constant minute volume ventilation in three of five experiments. The controller generally maintained $F_{ET}CO_2$ within $\pm 0.1$ vol% of the set-point. A disturbance to the controlled system was produced by releasing an occlusion of a branch of the pulmonary artery. The controller always responded to this disturbance in a stable manner, returning the $F_{ET}CO_2$ to its desired value within 30 sec. Accurate control of arterial partial pressure of $CO_2$ ($Pa_{CO_2}$) will require modifications enabling the system to determine the relationship between $F_{ET}CO_2$ and $Pa_{CO_2}$.*

***Keywords*** *– End-tidal $CO_2$, Minute ventilation, Alveolar deadspace, Dogs, Closed-loop control.*

## INTRODUCTION

A variety of interventions or changes in condition may alter the arterial carbon dioxide levels in patients maintained on mechanical ventilation in the intensive care environment. Endotracheal suctioning may cause brief periods of hypoventilation or hyperventilation. Metabolic changes may cause slow changes in $\dot{V}_{CO_2}$. Unless minute volume is adjusted, these changes will alter arterial $P_{CO_2}$.

*Acknowledgement*– This study was supported by the National Institute of General Medical Sciences Grant GM 15426 and by Siemens-Elema Ventilator Systems, 1765 Commerce Drive, Elk Grove Village, Illinois 60007.

Address correspondence to F.W. Chapman, Department of Biomedical Engineering, Rensselaer Polytechnic Institute, Troy, NY 12181.

Several investigators have designed, built, and tested controllers to make appropriate changes in minute volume. Ohlson et al. (10) recently reported a digital proportional/integral/derivative (PID) feedback controller of minute volume based on end-tidal $CO_2$ concentration. In tests of this system in anesthetized dogs, the controller maintained the desired arterial $P_{CO_2}$($Pa_{CO_2}$) when $\dot{V}_{CO_2}$ was altered by infusing $NaHCO_3$ but introduced significant error in $Pa_{CO_2}$ in response to interventions that altered alveolar deadspace. Coles et al. (1) used digital proportional/integral (PI) feedback control based on end-tidal $CO_2$ fraction ($F_{ETCO_2}$) to adjust tidal volume while respiratory rate remained fixed. Under steady-state conditions, this system maintained $F_{ETCO_2}$ of anesthetized sheep within close tolerance of its set value. The system was reported to respond quickly to step-changes in set-point and to exhibit a slightly underdamped behavior, but no quantitative descriptions of the dynamic responses of the system were published. East et al. (5) used digital PID feedback control based on $Pa_{CO_2}$ measured by an intraarterial sensor to adjust the combined minute volume of two synchronized ventilators in a differential lung ventilation system. Significant drift encountered in the intraarterial $Pa_{CO_2}$ sensor during tests in dogs led these investigators to suggest that estimation of $Pa_{CO_2}$ based on expired gas or transcutaneous measurements of $Pa_{CO_2}$ might be more useful. Other controllers have been based on feedback of measured $CO_2$ production rate (7–9) and on arterial pH (2). Feedback of $F_{ETCO_2}$ was used in the present system because $F_{ETCO_2}$ may be simply and noninvasively measured at each breath. This allows the system to respond more rapidly than controllers based on $CO_2$ production, and does not require the invasive measurements necessary for feedback of arterial pH.

The purpose of the present study was to implement a computerized, closed-loop controller of ventilation based on $F_{ETCO_2}$ and to examine the behavior of the system over a variety of operating conditions. Disturbances were introduced to demonstrate the controller behavior over a wide range of system gains.

## SYSTEM DESCRIPTION

Computerized feedback control of the minute volume and ventilatory frequency of a Siemens 900C Servo ventilator was implemented with a MINC-11 computer and a Gould Godart capnograph (Fig. 1). Many parameters of the ventilation provided by this ventilator may be modulated by externally supplied analog voltages. A signal from the D/A converter of the MINC computer alters minute volume around the value preset on the front panel of the ventilator to obtain the desired end-tidal $CO_2$ fraction. A second D/A signal adjusts ventilatory frequency to obtain the desired tidal volume.

The capnograph continuously samples gas from a tap in the airway proximal to the endotracheal tube and produces an analog voltage proportional to the $CO_2$ fraction of this gas. This is 12 bit A/D converted with a resolu-

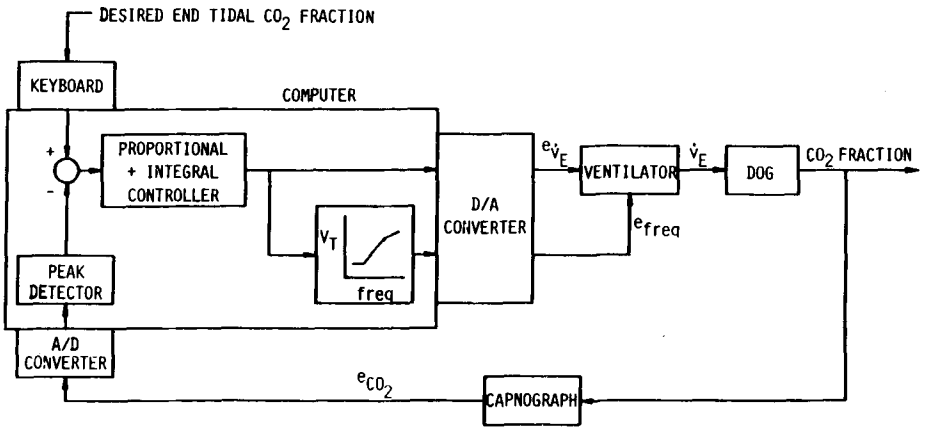


**FIGURE 1. Block diagram of the ventilator control system.**

tion of 0.005 vol% $CO_2$. Peaks in the resulting digital signal are detected by the program and scaled to determine the end-tidal $CO_2$ fraction of each breath. Every 10 sec the controller output $Y(k)$ is calculated using the previous output $Y(k-1)$, the current error $E(k)$, and the previous error $E(k-1)$ according to the digital equivalent of the conventional PI control law (3):

$$Y(k) = Y(k-1) + \alpha K_I T E(k) + \alpha K_P [E(k) - E(k-1)] \tag{1}$$

$$E(k) = -[(F\text{ET}_{CO_2} \text{ of most recent breath}) - (F\text{ET}_{CO_2} \text{ set-point})] \tag{2}$$

where the negative sign outside the brackets in Eq. 2 is necessary for negative feedback because $\alpha$ in Eq. 1 is negative.

The sample period ($T$) of 10 sec was chosen to be long enough to allow at least one breath to occur between controller updates yet short enough to allow reasonable controller response times. Gain constants $K_I$ and $K_P$ were estimated analytically and tuned during preliminary animal experiments as discussed below. $Y(k)$ is used to calculate the minute volume setting for the ventilator. The frequency setting is calculated from this minute volume according to the frequency-tidal volume relationship discussed below. Finally, voltages are D/A converted to update the ventilator settings for minute volume and respiratory frequency.

Proportional and integral gains, $K_P$ and $K_I$, were estimated analytically using a continuous time model of the system (Fig. 2). The incremental model of the dog had the transfer function

$$F\text{ET}_{CO_2}/\dot{V}_E = K_H/(1 + \tau s) \ . \tag{3}$$

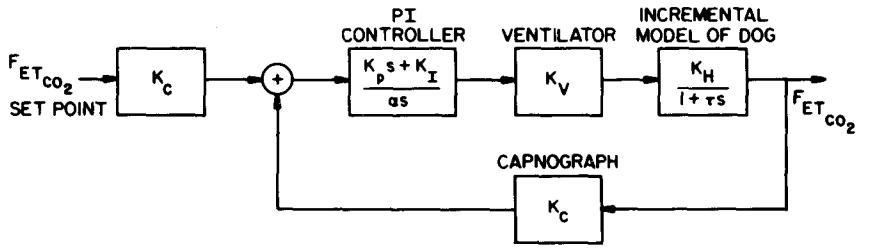


**FIGURE 2. Continuous time model of the control system.**

The change in end-tidal $CO_2$ fraction per unit change in minute volume, $K_H$, was found to be $-0.52$ [vol% $CO_2$/l/min]. The time constant $\tau$ was 0.6 min for $CO_2$ accumulation and 0.25 min for $CO_2$ washout. These values were determined by calculating the time constants for the first 20 sec of the $F$ET$CO_2$ response to stepwise changes in minute volume from 7 to 3 l/min and from 3 to 7 l/min during preliminary experiments in dogs weighing approximately 20 kg.

The controller gains that would produce a maximum overshoot of 10% and a damping ratio of 0.7 were determined using a procedure described by Dorf (4). These gains are given by

$$\alpha K_P = 1.9 \tag{4}$$

$$\alpha K_I = 4.3/\tau \tag{5}$$

where $\alpha \triangleq K_V K_C K_H$. *Since* $\tau$ has a different value for $CO_2$ accumulation than for $CO_2$ washout, the dynamics of the system are different for changes requiring $CO_2$ accumulation than for changes requiring $CO_2$ washout if a single value of $K_I$ is chosen.

The continuous model in Fig. 2 neglects the discrete time nature and transport delays of the actual system. As a result of these and possibly other shortcomings of the model, when the analytically determined gains were used in preliminary tests in dogs, the overshoot was larger than 10%. The gains were therefore adjusted empirically to reduce overshoot and provide a good compromise between optimized dynamics for $CO_2$ accumulation and optimized dynamics for $CO_2$ washout. This process resulted in controller gains (Table 1) that produced the same overshoot for upward and downward setpoint changes. The empirical values are close to those determined analytically; $K_I$ falls about midway between design values based on $CO_2$ washout and accumulation.

The tidal volume versus frequency curve for the system (Fig. 3) was designed to comply with several constraints. A minimum frequency of eight breaths per minute ensures that at least one breath will occur with each controller update. A minimum tidal volume of 250 ml was necessary to ensure that the

**TABLE 1. Designed and empirically selected values of controller gains.**

| | Design Based on $CO_2$ Washout ($\tau = 0.25$ min) | Design Based on $CO_2$ Accumulation ($\tau = 0.60$ min) | Empirically Selected Values |
|---|---|---|---|
| $\alpha K_P$* | 1.9 | 1.9 | 1.1 |
| $\alpha K_I$ ($sec^{-1}$) | 0.29 | 0.12 | 0.30 |

*$\alpha \triangleq K_V K_C K_H$.

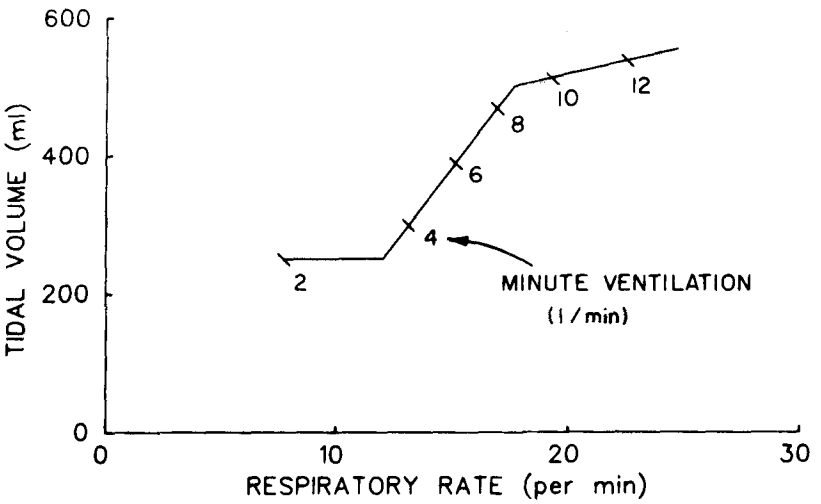


**FIGURE 3. Tidal volume versus respiratory rate relationship, designed for the controller when used with dogs.**

measured end-tidal $CO_2$ fraction was representative of alveolar $CO_2$ fraction. At low minute volumes only respiratory rate was increased to allow more breaths to occur between controller updates. Minute volume is increased above 9 l/min by increasing respiratory rate rapidly to avoid excessive tidal volumes. Minute volume was not allowed to exceed 10 l/min in these experiments.

## METHODS

Five mongrel dogs weighing between 15 and 25 kg were anesthetized with pentobarbital sodium (25 mg/kg i.v.), supplemented by 50- to 100-mg injections as needed throughout the experiment. Heparin sodium was administered intravenously (70 IU/kg) and supplemented with 500-IU injections every 45 min. Dogs were paralyzed with succinylcholine chloride (2 mg/kg i.v.) when necessary to prevent respiratory effort. Isotonic saline was administered

intravenously at approximately 100 ml/h and the dogs were kept warm with a heating pad.

After positioning of an endotracheal tube (10 mm internal diameter), volume-controlled artificial ventilation was begun with a Siemens 900C Servo ventilator controlled in an open-loop mode by the MINC computer. Using a constant inspiratory flow pattern, the ventilator delivered air at 5 l/min with 25% inspiration time, 10% inspiratory pause time, and a respiratory rate of 15 $min^{-1}$. Airway pressure was measured by the ventilator and recorded on a polygraph. Expired gas was exhausted through a chamber containing a small fan. Two computer-controlled solenoid valves switched the capnograph sampling port between this mixing chamber and an airway tap proximal to the endotracheal tube. This allowed measurements of the $CO_2$ content of mixed expired and airway gases, respectively.

A 7F thermodilution balloon catheter (Edwards) advanced from a femoral vein to the pulmonary artery was later used to occlude a branch of the pulmonary artery. A femoral artery was catheterized for pressure measuring and blood sampling. Pulmonary artery and femoral artery pressures were measured with strain gauge transducers and recorded on a polygraph. Blood samples from the femoral artery were analyzed for $Po_2$, $Pco_2$, and pH using standard electrodes (Instrumentation Laboratories Model 113).

Sets of data, obtained at times specified below, consisted of measurements of $F\text{ET}co_2$, $F\bar{\text{E}}co_2$, $\dot{V}co_2$, $Pao_2$, and arterial pH.

The phasic capnograph signal for airway $CO_2$ fraction was A/D converted at approximately 200 Hz and passed through a software peak detector to determine $F\text{ET}co_2$ for each breath. A keyboard-initiated sequence for measuring mixed expired $CO_2$ fraction ($F\bar{\text{E}}co_2$) switched the capnograph sampling port to the mixing chamber for expired gas and began A/D conversion at 2.5 Hz of the capnograph signal. $F\bar{\text{E}}co_2$ was calculated by averaging over each of three 10-sec intervals. This sequence was initiated only after holding minute ventilation constant for at least 5 min. Agreement of $F\bar{\text{E}}co_2$ calculated for the three intervals was checked to verify the steady state of the system. The rate of carbon dioxide production ($\dot{V}co_2$) was calculated by multiplying average $F\bar{\text{E}}co_2$ by minute volume. The phasic capnograph signal and the D/A voltage controlling minute volume were recorded on the polygraph.

### *Determination of Sensitivity Parameter*

Minute volume was changed to 5.3 l/min and a data set was taken after 8 min. Minute volume was then changed to 4.5 l/min and another data set was taken 8 min later. The patient sensitivity parameter $K_H$ was calculated from these data sets according to

$$K_H = \Delta F\text{ET}co_2 / \Delta \dot{V}_L \tag{6}$$

using these steady-state data.

### *Prolonged Open- and Closed-Loop Ventilation*

Next, the loop was closed with the $F\text{ET}_{CO_2}$ set for 5 vol%. Recording of time and $F\text{ET}_{CO_2}$ of each breath began when $F\text{ET}_{CO_2}$ reached $5.0 \pm 0.1$ vol% and continued for the next hour. After 30 to 40 min, the loop was opened and the ventilator continued delivering the same minute volume for 20 to 30 min. Intravenous injections of pentobarbital, heparin, and, in several cases, succinylcholine were the only interventions made during this segment of the experiment.

### *Stepwise Changes of Set-Point with Different Loop Gains*

The loop was then closed with a set-point of 5.5 vol% and the designed loop gain. When the $F\text{ET}_{CO_2}$ settled to $5.5 \pm 0.05$ vol%, the set-point was changed to 4.5 vol%. When $F\text{ET}_{CO_2}$ had settled to $4.5 \pm 0.5$ vol%, the set-point was returned to 5.5 vol%. This sequence was then repeated after changing both $K_I$ and $K_P$ to 0.2, 0.5, 2, or 5 times their starting values. The order of these changes was chosen randomly and all were used in each experiment. The time and $F\text{ET}_{CO_2}$ of each breath were recorded on disk during these sequences and were later used to quantitatively describe the effect of gain on the dynamic response of the system.

### *Changes in $F\text{ET}_{CO_2}$ Induced by Occlusion of a Branch of the Pulmonary Artery*

Next, minute volume was set to 5.5 l/min during open-loop ventilation. A data set was taken when $F\text{ET}_{CO_2}$ changed by no more than 0.05% during 1 min. Using the pulmonary arterial pressure waveform as a guide, the thermodilution catheter was withdrawn to a position just distal to the pulmonary valve. The balloon was inflated with 1.5 ml of air and the magnitude of the resulting drop in $F\text{ET}_{CO_2}$ was used to verify that the balloon was in a large branch of the pulmonary artery (A to B in Fig. 4). When the $F\text{ET}_{CO_2}$ changed by no more than 0.05 vol% in a minute, a data set was taken. In this way, the magnitude of the response of the open-loop system to occlusion of that branch of the pulmonary artery was measured. The loop was closed to maintain that $F\text{ET}_{CO_2}$. One to two minutes later, the balloon was quickly deflated to produce a disturbance in the controlled system (C in Fig. 4). The resulting changes in minute volume and the $F\text{ET}_{CO_2}$ and time of each breath were recorded in a data file on the computer disk for analysis. Another data set was taken when $F\text{ET}_{CO_2}$ and minute volume had settled, 7 to 8 min after balloon deflation. Details of this sequence are apparent in polygraph charts from a typical run (Fig. 4).

After obtaining the data set, open-loop ventilation was resumed with a minute volume of 5.5 l/min. Sensitivity ($K_H$) was again determined by following the procedure previously described in which data sets were taken for ventilation with 5.5 and with 4.5 l/min.

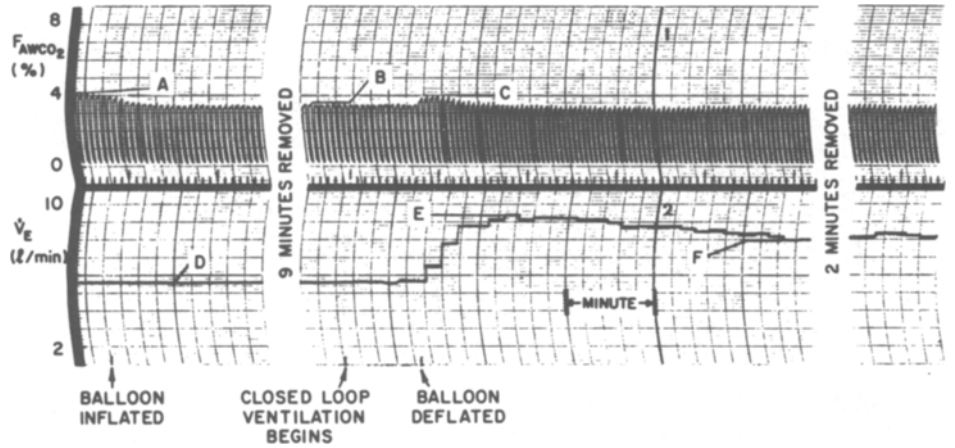


**FIGURE 4. Strip charts from one experiment showing airway carbon dioxide fraction ($FAWCO_2$) and minute volume ($\dot{V}_E$) as a branch of the pulmonary artery is occluded (balloon inflated) during open-loop ventilation and then released during closed-loop control. Capital letters identify experiment steps for Table 4.**

## RESULTS

The change in end-tidal $CO_2$ fraction per unit change in minute volume ($K_H$) determined once at the beginning and once at the end of each experiment had a mean value over five experiments of $-0.5 \pm 0.10$ (vol% $CO_2$/l/min)].

### *Variation of End-Tidal $CO_2$ Fraction During Prolonged Open- and Closed-Loop Ventilation*

End-tidal $CO_2$ fraction varied less during closed-loop than during open-loop ventilation in three of five experiments (Table 2). In all five experiments, closed-loop ventilation resulted in mean $FETCO_2$ of 5.00 vol%. The mean values of minute volume delivered to accomplish this varied from 3.8 to 5.3 l/min (Table 2). Figure 5 contrasts histograms of $FETCO_2$ values during periods of open-loop (unshaded) and closed-loop ventilation (shaded) in a typical experiment.

### *Step-Changes in $CO_2$ Set-Point*

Upward and downward changes in $FETCO_2$ set-point resulted in different $FETCO_2$ responses. After a set-point change from 5.5 to 4.5 vol%, the controller adjusted minute volume, causing the $FETCO_2$ to drop below 4.5 vol% before settling to that value. For the correct loop gain, the ratio of the size of this overshoot to the size of the set-point change was $16 \pm 2.1\%$ ($n = 5$). The time required for the $FETCO_2$ to change from 10 to 90% of the desired change, called the 10 to 90 rise time ($T_{10\text{-}90}$), was $14 \pm 4$ sec ($n = 5$). The

**TABLE 2. Means and standard deviations of breath-by-breath end-tidal carbon dioxide fractions and minute volumes during periods of open-loop and closed-loop controlled ventilation.**

| | Open-Loop Ventilation: | | | | Closed-Loop Ventilation: | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $F_{ET}CO_2$ (vol%) | | | $\dot{V}_E$ (l/min) | $F_{ET}CO_2$ (vol%) | | | $\dot{V}_E$ (l/min) | | |
| Experiment | $\bar{x}$ | SD | $n$ | $\bar{x}$ | $\bar{x}$ | SD | $n$ | $\bar{x}$ | SD | $n$ |
| 2 | 4.90 | 0.064 | 592 | 4.87 | 5.00 | 0.037 | 895 | 5.14 | 0.25 | 376 |
| 3 | 5.00 | 0.25 | 489 | 4.55 | 5.00 | 0.033 | 431 | 4.59 | 0.30 | 270 |
| 4 | 4.91 | 0.062 | 711 | 4.18 | 5.00 | 0.043 | 924 | 3.92 | 0.18 | 410 |
| 5 | 4.88 | 0.042 | 311 | 5.16 | 5.00 | 0.052 | 833 | 5.25 | 0.26 | 322 |
| 6 | 5.34 | 0.259 | 417 | 3.58 | 5.00 | 0.078 | 815 | 3.77 | 0.33 | 398 |

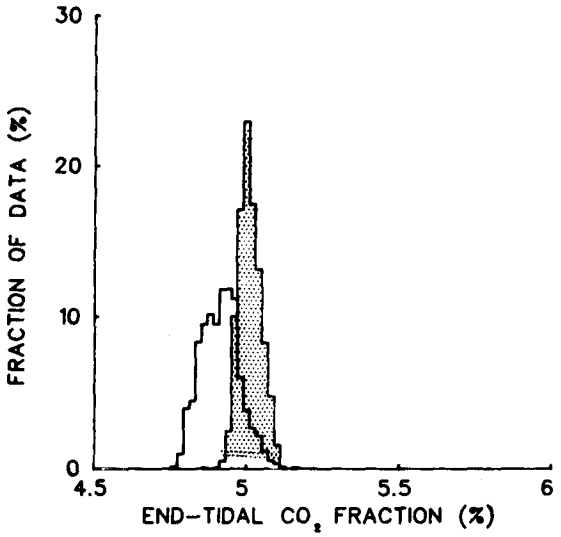


**FIGURE 5. Histograms of the breath-by-breath end-tidal carbon dioxide fraction during half-hour periods of open-loop (unshaded) and closed-loop (shaded) ventilation in a typical experiment.**

$F_{ET}CO_2$ response to set-point changes from 4.5 to 5.5 vol% was characterized by rise times 3 times longer but with the same overshoot as the response to the change from 5.5 to 4.5 vol%.

These step response characteristics were not seriously degraded by increasing or decreasing loop gain by as much a factor of two. For values of $K_I$ and $K_P$ between 0.5 and 2 times their nominal values, overshoot was less than $23 \pm 6.5\%$ and $T_{10\text{-}90}$ was less than $58 \pm 12$ sec in the five animals tested. Decreasing these gains below one-half their nominal value made the response more sluggish; increasing these gains by a factor of five produced growing oscillations in several cases.

### *Release of Occlusion of a Branch of the Pulmonary Artery*

Inflation of the balloon in the pulmonary artery caused the $Paco_2$ to rise and the $FETco_2$ to decrease, elevating the alveolar deadspace to tidal volume ratio by 0.2 ± 0.03 (Table 3). Figure 4 shows polygraph charts from one run of this test. Table 4 summarizes seven responses in four dogs by presenting the mean and standard deviation of the minute volume and $FETco_2$ values indicated by the capital letters in Fig. 4.

During the first minute following release of the occlusion, the $FETco_2$ began increasing but was then returned to the set-point as the controller made appropriate adjustments in minute ventilation. This transient increase in $FETco_2$ ranged from 55 to 90% of the change in $FETco_2$ produced by inflating the balloon during open-loop ventilation. The system responded in a stable manner to release of the occlusion in all experimental trials.

## DISCUSSION

Proportional plus integral control of ventilation can quickly correct changes in end-tidal $CO_2$ brought about by hyperventilation or hypoventilation. The controller changed minute volume appropriately and returned the $FETco_2$

**TABLE 3. Summary of arterial and end-tidal $Pco_2$ values during seven runs of occlusion and release of a branch of the pulmonary artery.**

| | Before | During | After |
|---|---|---|---|
| $Paco_2$ (mm Hg) | 34.9 ± 5.3 | 37.6 ± 6.7 | 28.6 ± 4.3 |
| $PETco_2$ (mm Hg) | 31.2 ± 1.8 | 25.9 ± 1.4 | 25.9 ± 1.5 |
| Change in ($Paco_2 - PETco_2$) (mm Hg)* | 0 ± 0 | 8.0 ± 2.8 | −1.0 ± 1.7 |
| $V_{D_{AL}}/V_T$ (%)† | 9 ± 1 | 29 ± 12 | 8 ± 13 |

*The arterial to end-tidal $CO_2$ gradient before occlusion has been subtracted from each arterial to end-tidal gradient.

†$V_{D_{AL}}/V_T = 1 - PETco_2/Paco_2$.

**TABLE 4. Summary of seven responses to occlusion of a branch of the pulmonary artery and release of the occlusion during closed-loop controlled ventilation. The capital letters A–F refer to steps in the experiment, identified in Fig. 4.**

| | Step in Experiment | | |
|---|---|---|---|
| | A | B | C |
| $FETco_2$ (vol%) | 4.38 ± 0.25 | 3.62 ± 0.20 | 4.19 ± 0.24 |
| | D | E | F |
| Minute volume (l/min) | 5.5 | 9.4 ± 0.6 | 7.5 ± 0.5 |

to within 0.1 vol% $CO_2$ of its desired value in less than 1 min after the set-point was changed or an occlusion of a major branch of the pulmonary artery was released. The rapidity with which the controller returned $F\mathrm{ET}\mathrm{CO}_2$ to its set-point after either of these interventions suggests that such a controller would speed the return to suitable $CO_2$ levels in apneic patients following interventions such as endotracheal suctioning.

Closed-loop control of ventilation can prevent the drift of $F\mathrm{ET}\mathrm{CO}_2$ that accompanies changes in carbon dioxide production rate in otherwise apneic patients. The $Pa\mathrm{CO}_2$ of patients with head injuries is often maintained below normal as a means of reducing cerebral blood flow, thus reducing intracranial pressure (ICP). There may be risks involved with further unintended decreases in $Pa\mathrm{CO}_2$ below this low level. Since the departures of $F\mathrm{ET}\mathrm{CO}_2$ from its set-point are small, infrequent, and of short duration, closed-loop control of ventilation may allow physicians greater confidence in the use of more aggressive hyperventilatory therapy to combat increases in ICP.

The control system was fast and stable when loop gain was between 0.5 and 2.0 times its nominal value. Controller gains were initially chosen using an estimated value of the sensitivity parameter $K_H$ of $-0.52$ [vol% $CO_2$/(l/min)]. The loop gain deviated from its nominal value if the true value of $K_H$ deviated from its estimated value. Thus, when $K_H$ was within a factor of 1/2 to 2 of its estimated value, the system was found to be stable and to have a good dynamic response. The sensitivity parameter depends on the $CO_2$ production rate and alveolar minute ventilation ($\dot{V}_A$) as follows:

Since $$\dot{V}\mathrm{CO}_2 = \dot{V}_A F\mathrm{ACO}_2 \cong \dot{V}_A F\mathrm{ET}\mathrm{CO}_2 \tag{7}$$

and $$\dot{V}_E = \dot{V}_A + \dot{V}_D \tag{8}$$

it follows that

$$K_H = \frac{\partial F\mathrm{ET}\mathrm{CO}_2}{\partial \dot{V}_E} \cong \frac{\partial(\dot{V}\mathrm{CO}_2/\dot{V}_A)}{\partial \dot{V}_E} \cong \frac{\dot{V}\mathrm{CO}_2}{\dot{V}_A^2} \tag{9}$$

Equation 9 indicates that $K_H$ is not constant over $\dot{V}_E$. Assuming a constant airway deadspace of 50 ml and a constant $\dot{V}\mathrm{CO}_2$, we find that $K_H$ given by Eq. 9 is one-third as large when $\dot{V}_E$ is 8 l/min as it is when $\dot{V}_E$ is 5 l/min. It is 3 times as large at 3 l/min as it is at 5 l/min. Thus, the steady-state relationship between $F\mathrm{ET}\mathrm{CO}_2$ and $\dot{V}_E$ is not linear. These numbers, however, are based on the assumption that $\dot{V}\mathrm{CO}_2$ is constant. During transient responses this is not the case. An increase in $\dot{V}_E$ washes $CO_2$ out, thus transiently increasing the $CO_2$ elimination rate even if metabolic production is constant. The increase in $\dot{V}\mathrm{CO}_2$ in the numerator of Eq. 9 counteracts the increase in $\dot{V}_A$ in the denominator. It is this effect that gives the controller suitable dynamics around its operating point, even though the steady-state relationship between $F\mathrm{ET}\mathrm{CO}_2$ and $\dot{V}_E$ is quite nonlinear. Carbon dioxide elimination

must, nevertheless, remain within a factor of 2 of its expected value during use of the controller to assure suitable dynamics around this operating point. This analysis also indicates that it may be necessary to reestimate $K_H$ and to adjust the controller gains if a markedly different operating point is desired.

Some of the variation in the alveolar deadspace/tidal volume ratio ($V_{D_{AL}}/V_T$) (Table 3) between experiments can be attributed to inaccuracy in calibrating the capnograph and the blood gas analyzer. Nevertheless, measured changes in the alveolar deadspace/tidal volume ratio caused by balloon inflation and deflation were not strongly affected by this factor. The increase in $V_{D_{AL}}/V_T$ indicates that the distribution of ventilation with respect to perfusion was significantly altered by occluding the pulmonary artery branch. The response of the closed-loop system to a disturbance of such a magnitude demonstrates the stability of that system.

The system presented here controls $F\text{ET}_{CO_2}$ rather than $Pa_{CO_2}$. To adequately control $Pa_{CO_2}$ in this manner, it is necessary to determine the relationship between $Pa_{CO_2}$ and $F\text{ET}_{CO_2}$ and to identify circumstances under which this relationship may change. Whitesell et al. (13) found that the mean difference between temperature-corrected $Pa_{CO_2}$ and peak expired $P_{CO_2}$ of anesthetized patients without lung disease was less than 1 mm Hg. Although patients with lung disease had larger arterial-to-peak expired $P_{CO_2}$ gradients, the gradient tended to be constant in each patient. Osborn (11) also found that the arterial to end-tidal $P_{CO_2}$ gradient was relatively constant in a study of 25 patients maintained on ventilators following open heart surgery. Osborn indicated that one or two arterial $P_{CO_2}$ measurements a day would be sufficient to determine the size of the gradient and to verify that estimates of $Pa_{CO_2}$ based on end-tidal $P_{CO_2}$ were accurate. Changes in lung mechanics or in perfusion may alter the relationship between arterial and end-tidal $P_{CO_2}$. Nevertheless, the $F\text{ET}_{CO_2}$ controller can be used to control $Pa_{CO_2}$ at desired levels, provided that the set-points are corrected for changes in the arterial/end-tidal $P_{CO_2}$ ratio. The $P\text{ET}_{CO_2}/Pa_{CO_2}$ ratio is related to alveolar deadspace according to this expression derived from the alveolar deadspace equation:

$$\frac{P\text{ET}_{CO_2}}{Pa_{CO_2}} = 1 - \frac{V_{D_{AL}}}{V_T} \tag{10}$$

When no changes in the alveolar deadspace/tidal volume ratio occur, the $Pa_{CO_2}$ can be accurately controlled to desired levels by measuring the $Pa_{CO_2}/P\text{ET}_{CO_2}$ ratio once and selecting the $F\text{ET}_{CO_2}$ set-point accordingly. When alveolar deadspace changes, the factor relating $P\text{ET}_{CO_2}$ and $Pa_{CO_2}$ also changes and the $F\text{ET}_{CO_2}$ controller will control for incorrect $Pa_{CO_2}$ levels until the correction factor is updated. Thus, the duration of any errors in $Pa_{CO_2}$ is limited to the length of time between arterial blood samples. Transcutaneous $P_{CO_2}$ measurements can also be used to determine $Pa_{CO_2}$ trends

in adults (12). This suggests that a system which simultaneously monitors transcutaneous and end-tidal $P_{CO_2}$ may be able to detect changes in the end-tidal to arterial $P_{CO_2}$ relationship and indicate the need for a timely blood sample to determine the $P_{ETCO_2}/P_{aCO_2}$ ratio. Alternatively, it may be possible to obtain an improved estimation of $P_{aCO_2}$ using estimates of sequential alveolar deadspace obtained from the single breath test for $CO_2$ in conjunction with the end-tidal $CO_2$ fraction (6).

We have demonstrated a stable, closed-loop controller of ventilation over a range of operating conditions. With the incorporation of a technique to detect changes in alveolar deadspace, it may be possible to accurately control arterial $P_{CO_2}$ in mechanically ventilated subjects.

## REFERENCES


1. Coles, J.R., W.A. Brown, and D.G. Lampard. Computer control of respiration and anaesthesia. *Med. Biol. Eng.* 11:262-267, 1973.
2. Coon, R.L., E.J. Zuperku, and J.P. Kampine. Systemic arterial blood pH servocontrol of mechanical ventilation. *Anesthesiology* 40:201-204, 1978.
3. Deshpande, P.D. and R.H. Ash. *Elements of Computer Process Control.* Research Triangle Park, N.C.: Instrument Society of America, 1981.
4. Dorf, R.C. *Modern Control System.* Reading, Mass.: Addison Wesley Publishing Co., 1981, p. 117.
5. East, T.D., D.R. Westenskow, N.L. Pace, and L.D. Nelson. A microcomputer-based differential lung ventilation system. *IEEE Trans. Biomed. Eng.* BME-29:736-740, 1982.
6. Fletcher, R. and B. Jonson. Deadspace and the single breath test for carbon dioxide during anesthesia and artifical ventilation: Effects of tidal volume and frequency of ventilation. *Br. J. Anaesth.* 56:109-120, 1984.
7. Jordan, W.S. and D.R. Westenskow. Microprocessor control of ventilation using carbon dioxide production (Abstract). *Anesthesiology* 51:S380, 1979.
8. Mitamura, Y., T. Mikami, H. Sugawara, and C. Yoshimoto. An optimally controlled respirator. *IEEE Trans. Biomed. Eng.* BME-18:330-337, 1971.
9. Mitamura, Y., T. Mikami, and K. Yamamoto. A dual control system for assisting respiration. *Med. Biol. Eng.* 13:846-853, 1975.
10. Ohlson, K.B., D.R. Westenskow, and W.S. Jordan. A microprocessor based feedback controller for mechanical ventilation. *Ann. Biomed. Eng.* 10:35-48, 1982.
11. Osborn, J.J. Cardiopulmonary monitoring in the respiratory intensive care unit. *Med. Instrum.* 11:278-282, 1977.
12. Rafferty, T.D. Relationship between transcutaneous and arterial carbon dioxide tension in adult patients anesthetized with nitrous oxide-fentanyl and nitrous oxide-enflurane. *Anesth. Analg.* 60:504-507, 1981.
13. Whitesell, R., C. Asiddao, D. Gollman, and J. Jablonski. Relationship between arterial and peak expired carbon dioxide pressure during anesthesia and factors influencing the difference. *Anesth. Analg.* 60:508-512, 1981.


## NOMENCLATURE

$F_{ACO_2}$ = alveolar carbon dioxide fraction.
$F_{AWCO_2}$ = airway carbon dioxide fraction.
$F_{\bar{E}CO_2}$ = mixed expired carbon dioxide fraction.
$F_{ETCO_2}$ = end-tidal carbon dioxide fraction.
$K_C$ = capnograph gain (V/vol% $CO_2$).
$K_H$ = change in $F_{ETCO_2}$ per unit change in $\dot{V}_E$.

$K_I$ = integral gain of controller.
$K_P$ = proportional gain of controller.
$K_V$ = ventilator gain (l/min/V).
$Pa\text{CO}_2$ = arterial partial pressure of carbon dioxide.
$Pa\text{O}_2$ = arterial partial pressure of oxygen.
$T_{10\text{-}90}$ = 10 to 90% response time.
$\dot{V}_A$ = alveolar ventilation.
$\dot{V}\text{CO}_2$ = carbon dioxide production rate.
$\dot{V}_D$ = ventilation of airway deadspace.
$\dot{V}_E$ = minute volume.
$\alpha$ = $K_V K_C K_H$.
$\tau$ = time constant of response of $F\text{ETCO}_2$ to change in $\dot{V}_E$.
$s$ = Laplace transform variable.