Monitoring of O_2 Uptake and CO_2 Elimination During Anesthesia and Surgery

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Peter H. Breen and Abraham Rosenbaum

Introduction

In some areas of medicine, metabolic monitoring and interpretation are advanced. For example, in the critical care medicine unit, pulmonary uptake of oxygen ($\dot{V}_{O_2}$) and elimination of carbon dioxide ($\dot{V}_{CO_2}$) are used to ensure adequate tissue metabolism and drive nutrition therapy. In the exercise physiology environment, $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ are measured during treadmill or bicycle exercise to determine exercise capacity and tolerance and to specifically determine the anaerobic threshold (AT), the point at which metabolic demands require the addition of anaerobic metabolism to aerobic metabolism. In both of these environments, there are mature measurement modalities to determine airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$.

In contrast, there is a dearth of knowledge in the anesthesia community about tissue metabolism, and the relationship between tissue $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ and indirect calorimetry, the estimation of these parameters by measurement of airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$. Metabolic monitoring during anesthesia is mostly confined to two areas: First, the inspired O_2 fraction ($F_{I_{O_2}}$) is monitored to preclude the delivery of a hypoxic gas mixture to the patient. Second, the tidal P_{CO_2} (capnogram) is monitored to ensure a patent airway and to estimate the alveolar P_{CO_2} ($P_{A_{CO_2}}$) by the end-tidal P_{CO_2} ($P_{ET_{CO_2}}$) [1], with little thought to the relationship that $P_{A_{CO_2}}$ is proportional to the ratio of tissue $\dot{V}_{CO_2}$ production and alveolar ventilation ($\dot{V}_A$) [2, 3]. Malignant hyperthermia, with acute and significant increase in production of tissue $\dot{V}_{CO_2}$ is a gross example of how the increased $P_{ET_{CO_2}}$ (given no increase in $\dot{V}_A$) represents the increase in tissue metabolism [1, 2, 4].

We believe that the main reason for the lack of understanding of indirect calorimetry during anesthesia is that the accurate measurement of airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ are challenging in the rebreathing anesthesia ventilation circle circuit. As a consequence, there are few if no measurement devices for indirect calorimetry in the operating room. This is quite remarkable considering the breadth of anesthesia monitoring technologies available to us during anesthesia. The anesthesia machine, ventilator, standard monitors, and advanced monitors (including modalities such as transesophageal echocardiography and cardiac output estimation from arterial pressure waveforms) represent monitoring technologies that cost into the six figures. Yet, we do not routinely monitor the most essential parameter of tissue wellness, which is the maintenance of

P.H. Breen, MD, FRCPC (✉)
Department of Anesthesiology and Perioperative Care, University of California-Irvine Medical Center, The City Drive South, Building 53, Room 227, Orange, CA 92868, USA
e-mail: pbreen@uci.edu

A. Rosenbaum, MD
Department of Anesthesiology and Perioperative Care, University of California, Irvine Medical Center, 101 The City Drive South, Bldg. 53. RM 227, Orange, CA 90868, USA
e-mail: arosenba@uci.edu

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normal aerobic tissue metabolism as evidenced by normal tissue $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$, and the calculated respiratory quotient ($RQ = \dot{V}_{CO_2} / \dot{V}_{O_2}$).

We believe that the anesthesiologist should be interested in the measurement of airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ for three major reasons: First, airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ may quickly and noninvasively detect non-steady-state perturbations that frequently occur during anesthesia and surgery [2]. For example, an abrupt decrease in cardiac output ($\dot{Q}_T$) and venous return causes an acute decrease in $P_{ET_{CO_2}}$ and airway $\dot{V}_{CO_2}$ (and $\dot{V}_{O_2}$). Second, airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ may provide first detection of onset of anaerobic lactic acid metabolism during anesthesia and surgery [5–7]. Third, we believe that there is a relationship between values of tissue $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ and the level of anesthesia depth.

Some of the basic technologies required to measure airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ in the operating room are already available to us, such as the measurement of airway flow ($\dot{V}$) and the measurement of O_2 and CO_2 gas fractions (F_{O_2} and F_{CO_2}) by sidestream sampling. To the extent that we can develop measurement technologies that accurately measure indirect calorimetry during anesthesia and surgery, then these monitors of airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ will be available to all patients undergoing anesthesia, will be inexpensive, will be completely noninvasive, and will pose no risk to the patient (excepting misinterpretation of data).

In this short chapter, we briefly present our approach to the engineering technologies, interpretation, and future potential of the measurement of $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$, and RQ during anesthesia and surgery. The interested reader is referred to the cited references for in-depth analysis and comparison to the literature.

Pitfalls in the Measurement of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ During Anesthesia

Pulmonary O_2 update is given by

$$\dot{V}_{O_2} = \dot{V}_I \cdot F_{I_{O_2}} - \dot{V}_E \cdot FE_{O_2} \qquad (37.1)$$

where $\dot{V}_I$ and $\dot{V}_E$ are the inspired and expired minute volumes and $F_{I_{O_2}}$ and FE_{O_2} are the inspired and mixed expired O_2 fractions [6, 8, 9]. For $\dot{V}_{O_2}$, separate measurement of both $\dot{V}_I$ and $\dot{V}_E$ leads to substantial error because $\dot{V}_{O_2}$ is a small number calculated as the difference of two large values (inspired $\dot{V}_{O_2}$ and expired $\dot{V}_{O_2}$) [9]. To accurately measure this difference, most airway flowmeters lack sufficient precision and zero stability, and the extra volume in expired gas, due to increased warmth and added humidity compared to inspired gas, must be measured [9]. To address these problems in the critical care and exercise physiology arenas, the Haldane transformation is utilized, which invokes the conservation of the inert gas nitrogen during steady state ($\dot{V}_I \cdot F_{I_{N_2}} = \dot{V}_E \cdot FE_{N_2}$). By solving for $\dot{V}I$ and substitution into Eq. 37.1,

$$\dot{V}_{O_2} = \dot{V}_E \left(F_{I_{O_2}} \cdot FE_{N_2} / F_{I_{N_2}} - FE_{O2} \right). \qquad (37.2)$$

$\dot{V}_{CO_2}$ is derived in a similar fashion [10, 11]. Nitrogen fractions are usually determined by subtraction of F_{O_2} and F_{CO_2} from unity [9], assuming that no other gas species (such as anesthesia gases) are present.

In the critical care medicine unit, $\dot{V}_{O_2}$ is easily determined by an exhaled $\dot{V}$ measurement, a mixed collection of expired gas from the patient (e.g., Datex Deltatrac II Metabolic Monitor; Datex Instrumentarium, Helsinki, Finland [7, 8]) or from the expiratory port of the open circuit non-rebreathing ventilator and by a measurement of $F_{I_{O_2}}$. During anesthesia, the measurement challenges become immense because the mostly rebreathing circle anesthesia circuit returns most of the last exhalation (minus the CO_2 removed by the absorber) to form the next inspiration [6, 12]. Then, there is no way to collect mixed expired gas fractions. Furthermore, gas temperature and humidity are greater in expired than inspired gas and can change significantly during the course of ventilation during anesthesia [13]. Errors in humidity and temperature can significantly affect the determination of inspired and expired volumes and thus cause errors in the measurement of $\dot{V}_{O_2}$ [9].

Our Approach to Measure $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ During Anesthesia

Bymixer-Flow Measurements

The key challenge is how to measure mixed expired gas concentrations in the anesthesia circle circuit.

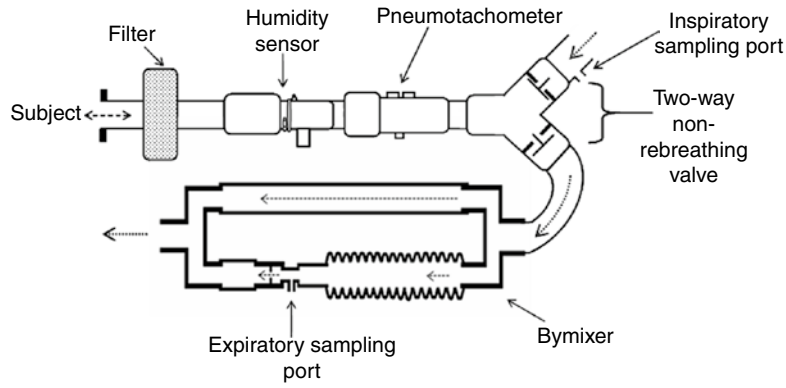

Fig. 37.1 Bymixer used in the specially designed indirect calorimetry apparatus to measure airway O_2 uptake ($\dot{V}_{O_2}$) and CO_2 elimination ($\dot{V}_{CO_2}$) in spontaneously breathing awake patients. The patient breathed through the filter (to prevent contamination), the fast response temperature and humidity sensor (for STPD correction), the pneumotachometer cuvette (to measure gas flow), and the non-rebreathing valve. This valve connected the inspiratory arm inlet and the expiratory arm outlet (incorporating the bymixer). The non-rebreathing valve is depicted during the expiratory phase (Reprinted with permission from Rosenbaum and Breen [14])

To this end, we have invented and developed an implementation of the bymixer (US Patent #7,793,659) [6–8, 14–16], an in-line flow-averaging hydraulic gas mixer (Fig. 37.1). The bymixer diverts a constant proportion of the main flow (upper channel) through an adjustable mixing chamber (bottom channel) which then returns to the main flow. Then, gas sampled from the mixing chamber provides flow-averaged mixed gas fractions. Changes in the size of the mixing chamber and of the resistor (that controls the proportion of bypass flow) determine the response time of the bymixer. The resistor is located immediately downstream (to the left) of the expiratory sampling port (see Fig. 37.1). The bymixer can be easily interpolated into the expiration limb of the anesthesia circle circuit (Fig. 37.2) [6]. We have demonstrated that inspired gas concentrations can vary significantly during inspiration in the circle circuit. Accordingly, we also interpose a bymixer in the inspiratory limb of the anesthesia circle circuit. The bymixers, coupled with an accurate flow sensor at the airway opening or on the expiration limb of the circle circuit, generate accurate bymixer-flow measurements of airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$. We have also developed a spontaneous ventilation apparatus [7] that incorporates the bymixer-flow apparatus, appropriate for measurement of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ in awake breathing patients (see Fig. 37.1).

Breath-by-Breath Measurement of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$

An alternate approach to determine mixed expired and inspired gas fractions is to accurately measure flow with respect to time at the airway opening while simultaneously measuring the F_{O_2} and F_{CO_2} of the gas flow. Using CO_2 as an example, at every time interval, dt (usually 5–10 ms), $\dot{V}(t)\ F_{CO_2}(t)\mathrm{d}t$ is the small volume of CO_2 that has entered or exited the airway. The integration of this term over one breath will yield the overall V_{CO_2} per breath [10, 12, 17, 18]. Since the gas fractions are measured by sidestream sampling at the airway opening through a long tube to a measurement bench (with inherent transport and response delays [1, 4, 17–19]), the temporal synchronization of the flow and gas fraction signals is mandatory and challenging [17], especially for $\dot{V}_{CO_2}$. Furthermore, gas volumes must be corrected to standard temperature and pressure dry (STPD) by the values measured by the fast response airway humidity and temperature sensor [9, 11] (see next paragraph). To date, breath-by-breath devices, such as the Datex-Ohmeda M-COVX Airway Module (GE Healthcare, Madison, WI), may have inaccuracy [6, 20] and are not commonly used in the anesthesia environment.

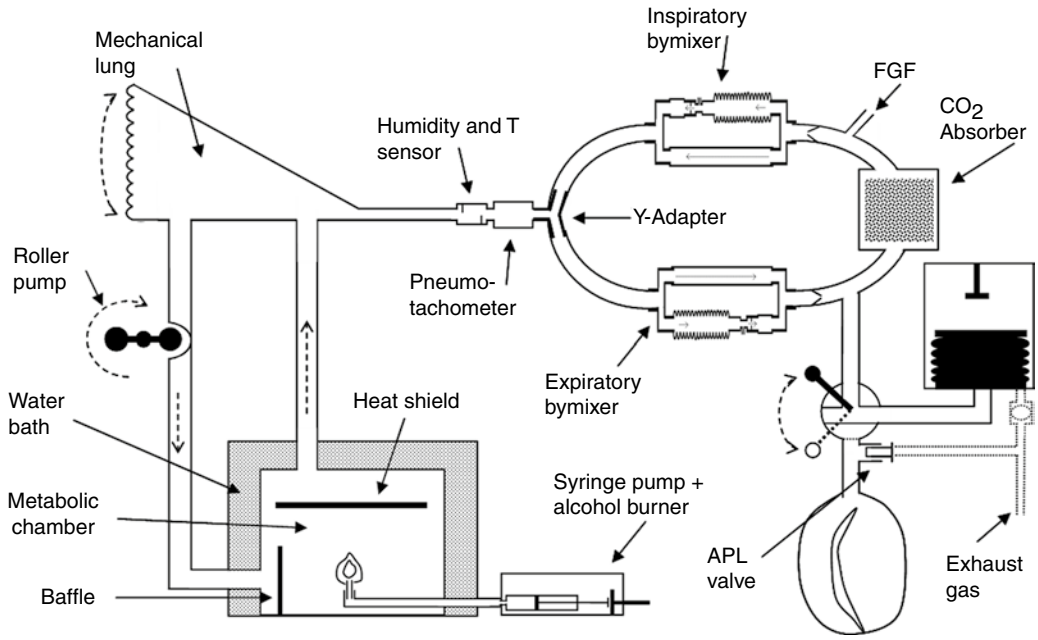

Fig. 37.2 Validation of the bymixer-flow measurement in the anesthesia semi-closed circle circuit by the metabolic lung simulator. Bymixers (in-line mixing chambers) were placed on both the inspiratory and expiratory limbs. *T* temperature, *FGF* fresh gas flow, *APL* adjustable pressure limiting (With kind permission from Springer Science + Business Media: Rosenbaum et al. [6])

Correction for Humidity and Temperature

To address the different and changing values of inspired and expired humidity and temperature (*T*) [13], we have invented and developed a fast response airway sensor of humidity and *T* (US Patent #6,014,890) (Fig. 37.3) [5, 21]. A dry thermocouple (label B) rapidly measures changes in gas *T* (dry *T*). A wet thermocouple (label A) measures humidity by the psychrometry principle, whereby evaporation of water cools the wet thermocouple below the dry *T*. The addition of the airway humidity and *T* sensor significantly improves the bymixer-flow (Haldane principle) measurements of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ [5–8]. For breath-by-breath measurements or when $\dot{V}_I$ and $\dot{V}_E$ are each measured in the bymixer-flow method, then determinations of inspired and expired *T* and humidity are mandatory; otherwise humidity and *T* errors in the measurement of the large inspired and expired volumes become amplified in their difference (small volume of V_{O_2} per breath) [4, 9, 11, 17].

Validation of the Bymixer-Flow Measurement of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$

To validate the bymixer-flow measurements of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$, we developed a metabolic lung simulator (MLS) (see Fig. 37.2) [22]. A mechanical lung is connected by a circular circuit to a metabolic chamber. A precision infusion pump meters pure ethanol into the metabolic combustion chamber to generate precise and variable values of reference $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$. Two roller pumps circulate gas between the mechanical lung and the metabolic chamber. The ventilation circuit (incorporating the inspired and expired limb bymixers, the airway flow sensor, and the fast response humidity and *T* sensor) is attached to the mechanical lung [6–9]. Figure 37.2 depicts the circle anesthesia circuit attached to the MLS [6]. Accordingly, the MLS provides calibrated and adjustable values of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ over a wide range of ventilatory parameters.

Figure 37.4 demonstrates the excellent correlation of bymixer-flow measurements of airway $\dot{V}_{O_2}$

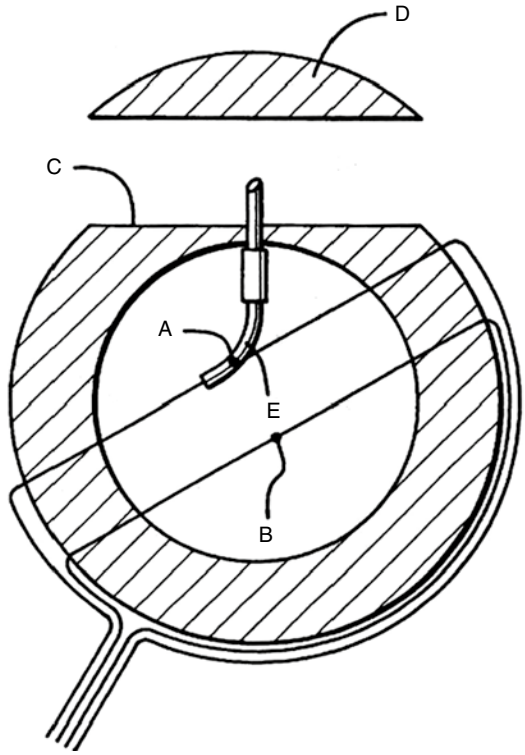

Fig. 37.3 Axial cross-section view of the humidity sensor (US Patent #6,014,890). Two tiny thermometers (copper-constantin thermocouples) (*A*, *B*) were mounted across the lumen of the common airway adapter (*C*). A water reservoir (*D*) supplied a continuous flow of water through dialysate tubing (*E*) to maintain a water envelope around thermocouple A to measure wet temperature (*T*). The other dry thermocouple (B) measured the gas *T*. With a decrease of the relative humidity (RH) of gas flowing through the airway adapter, evaporation from the wet thermocouple decreased wet *T* below dry *T* (psychrometry principle) (Reprinted from Breen [21])

and $\dot{V}_{CO_2}$ compared with the stoichiometric values with an anesthesia circle circuit (see Fig. 37.2) [6]. Limits of agreement analysis generated percent errors (mean ± 1.96 SD) of 2.5 ± 9.8 % for $\dot{V}_{O_2}$ and −1.2 ± 7.2 % for $\dot{V}_{CO_2}$. Using the MLS, we found similar excellent validation of bymixer-flow measurements of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ during ventilation with the open non-rebreathing ventilation circuit [5, 8] and during ventilation with the spontaneous breathing apparatus for awake patients (see Fig. 37.1) [7]. There is no gold standard reference measurement of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ for patients under anesthesia ventilated with the anesthesia circle circuit. Accordingly, the rigorous validation of the bymixer-flow system measurements of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ against the MLS was mandatory. The MLS also encompasses basic features of mammalian gas kinetics ("central lung connected by $\dot{Q}_T$ and venous return to peripheral metabolism") [22], which allows the bench testing of non-steady-state perturbations (e.g., abrupt decrease in roller pump "$\dot{Q}_T$").

Clinical Rationale to Measure $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ During Anesthesia

We believe that there are at least three main areas of clinical interest for the measurements of airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ during anesthesia and surgery.

Non-Steady-State Gas Kinetics During Anesthesia

There are many acute perturbations during anesthesia and surgery that cause immediate changes in airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$. For example, during an experimental abrupt decrease in cardiac output ($\dot{Q}_T$) (Fig. 37.5) [3, 23], the airway $\dot{V}_{CO_2}$ and $P_{ET_{CO_2}}$ decrease because the decrease in venous return reduces CO_2 delivery from the peripheral tissues to the lung. The lung functions as a mixing chamber in which $P_{A_{CO_2}}$ decreases because CO_2 delivery from tissues to lung decreases while the level of minute ventilation remains constant. At the same time, the simultaneous reduction in pulmonary perfusion pressure (due to reduction in $\dot{Q}_T$) increases the amount of high alveolar ventilation-to-perfusion ($\dot{V}_A / \dot{Q}$) lung units [1, 4]. The exhalation from high $\dot{V}_A / \dot{Q}$ lung units contains less CO_2 which dilutes $P_{ET_{CO_2}}$ below $P_{A_{CO_2}}$ [23–25]. The respective oxygen variables behave in an analogous fashion [2, 11, 26]. If the reduction in $\dot{Q}_T$ is sustained, the recovery of airway $\dot{V}_{O_2}$ is faster than the recovery of $\dot{V}_{CO_2}$, because the peripheral stores of CO_2 in the body are much greater than the stores of O_2.

We have developed a numerical analysis model of mammalian gas kinetics during

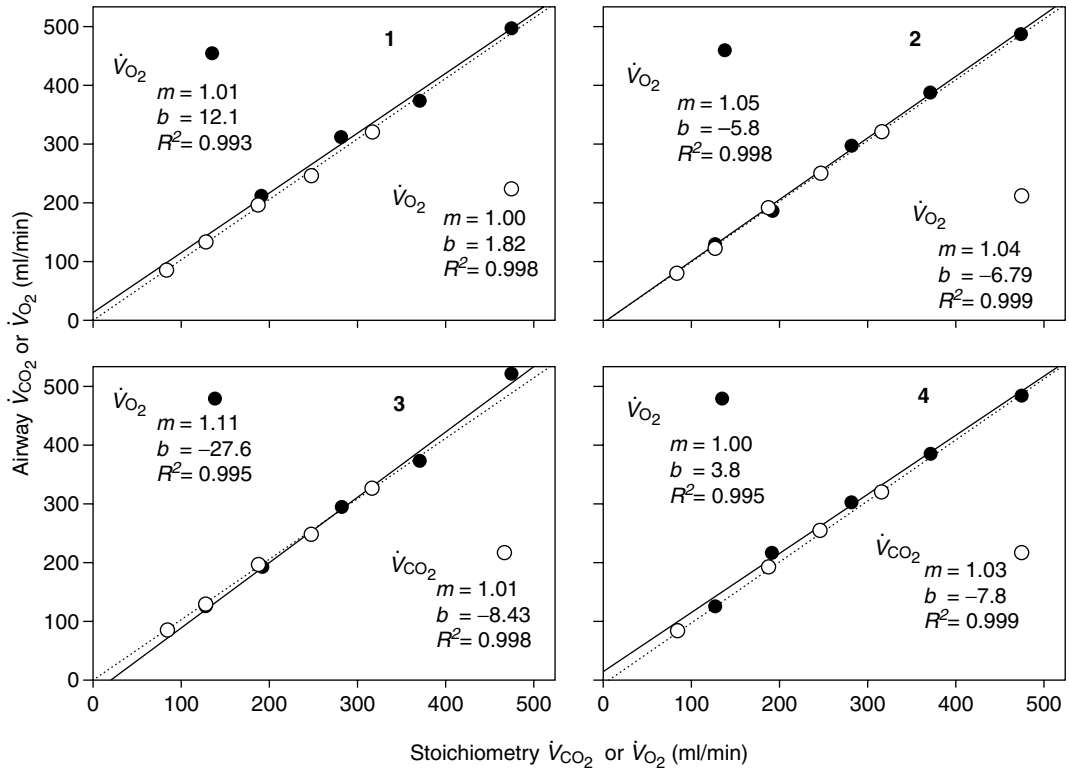

Fig. 37.4 Circle anesthesia circuit. Linear regression of bymixer-flow measurements of CO_2 elimination ($\dot{V}_{CO_2}$, *open circles*, and *dotted lines*) and O_2 uptake ($\dot{V}_{O_2}$, *solid circles*, and *lines*) versus the stoichiometric values generated by metered ethanol combustion in the metabolic lung simulator (MLS). Each panel (1-4) is a separate experiment. *m* slope, *b* Y intercept, and R^2 coefficient of determination (Reprinted with permission from Rosenbaum and Breen [14])

non-steady state [23], which encompasses a five-compartment lung model spanning the clinical range of $\dot{V}_A/\dot{Q}$ abnormalities (pulmonary shunt, low $\dot{V}_A/\dot{Q}$ or venous admixture, normal lung, high $\dot{V}_A/\dot{Q}$, and infinite $\dot{V}_A/\dot{Q}$ or alveolar dead space). The central lung compartment is connected to the peripheral tissue compartment through $\dot{Q}_T$ and venous return. Figure 37.6 displays model data for the effects of abrupt and sustained decrease in $\dot{Q}_T$ similar to the preceding paragraph. This gas kinetics model has been useful to elucidate mechanisms underlying observed data, to test new hypotheses, and to conduct virtual experiments that cannot be studied in patients or are too difficult to control in experimental animals.

The interested reader is referred to other studies that involve acute perturbations that acutely affect airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$, including application of positive end-expiratory pressure (PEEP) [18, 24, 27, 28], onset of pulmonary embolism [29], relief of pulmonary embolism [25], onset of combined carbon monoxide and cyanide poisoning [11, 30, 31], bronchial flap-valve obstruction [26, 32], and leaking inspiration valve in the circle circuit [33]. Better understanding of how airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ change during these acute perturbations should be able to help the clinician with early and non-invasive detection, diagnosis, and management of these conditions. Some non-steady-state principles are already seeping into clinical medicine. For example, the best index of return of spontaneous circulation during cardiopulmonary resuscitation is an increase in $P_{ET_{CO_2}}$ (representing the increase in CO_2 transport from the peripheral tissues to the lung as venous return and $\dot{Q}_T$ increase) [1, 3].

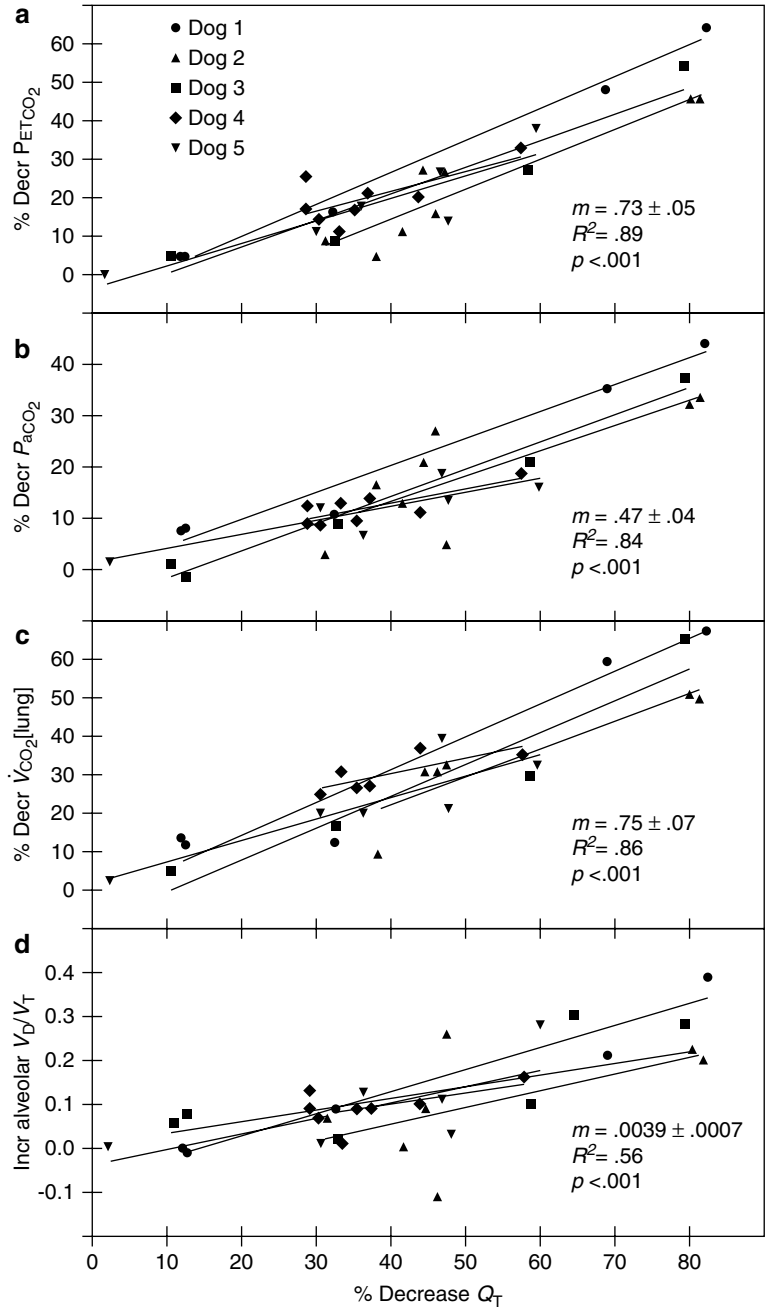

Fig. 37.5 Effects of 32 vena cava balloon inflation sequences in five anesthetized dogs to decrease cardiac output ($\dot{Q}_T$). During each balloon inflation sequence, the *y*-axis variable is correlated against the percent decrease in $\dot{Q}_T$. Panel (**a**) percent decrease in end-tidal P_{CO_2} ($P_{ET_{CO_2}}$). (**b**) Percent decrease in arterial P_{CO_2} (Pa_{CO_2}). (**c**) Percent decrease in pulmonary $\dot{V}_{CO_2}$ ($\dot{V}_{CO_2}[lung]$). (**d**) Arithmetic increase in alveolar dead space/tidal volume ratio (V_d/V_t). The linear regression line for each dog is shown. *m* average (±SD) slope for five dogs, R^2 coefficient of determination (Reprinted with permission from Isserles and Breen [3])

Can Indirect Calorimetry First Detect Onset of Anaerobic Lactic Acidosis?

During exercise physiology testing, as workload increases (treadmill or bicycle ergometer), aerobic metabolism increases and airway $\dot{V}_{CO_2}$ and $\dot{V}_{O_2}$ rise together. Then, the plot of $\dot{V}_{CO_2}$ versus $\dot{V}_{O_2}$ generates a straight line of slope equal to $RQ = \left(\dot{V}_{CO_2} / \dot{V}_{O_2}\right)$ (Fig. 37.7) [34]. At a point on the line called the anaerobic threshold (AT), further exercise demand requires the addition of anaerobic metabolism, which generates more $\dot{V}_{CO_2}$ and the slope of the line and RQ increases [11].

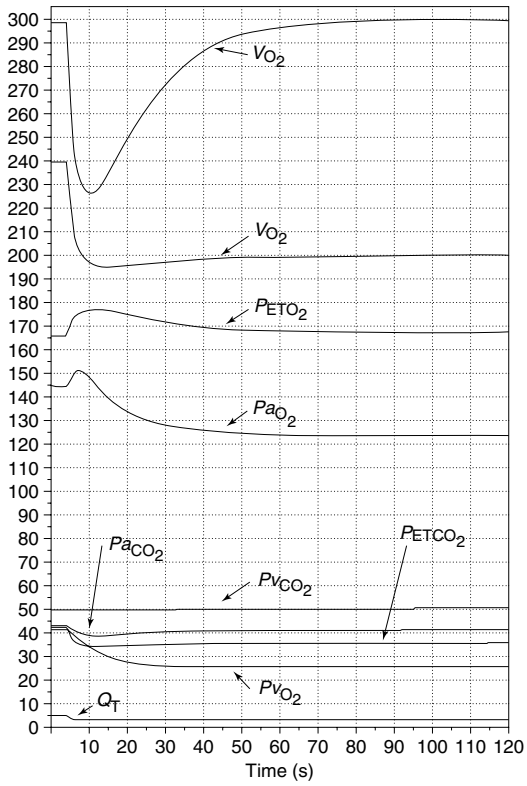

Fig. 37.6 Numerical analysis model of non-steady-state gas kinetics, showing the effects of an abrupt reduction in cardiac output ($\dot{Q}_T$) from 5 to 2.5 L/min. Length of *y*-axis is 120 s. $\dot{V}_{O_2}$, pulmonary O_2 uptake (ml/min); $\dot{V}_{CO_2}$, pulmonary CO_2 elimination (ml/min); $P_{ET_{O_2}}$, end-tidal P_{O_2}; Pa_{O_2}, arterial P_{O_2}; $P_{\bar{v}_{CO_2}}$, mixed venous P_{CO_2}; Pa_{CO_2}, arterial P_{CO_2}; $P_{ET_{CO_2}}$, end-tidal P_{CO_2}; and $P_{\bar{v}_{O_2}}$, mixed venous P_{O_2} (all partial pressures, *P*, are in mmHg) (Reprinted from Breen)

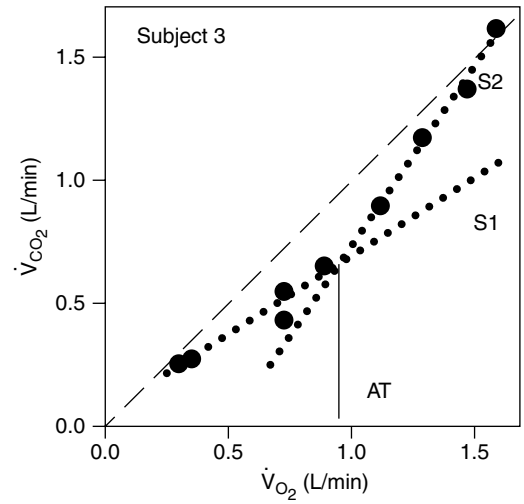

Fig. 37.7 Bymixer-flow measurements (see Fig. 37.1) of pulmonary CO_2 elimination ($\dot{V}_{CO_2}$) plotted against O_2 uptake ($\dot{V}_{O_2}$) in an untrained subject during increasing exercise load. *S1* and *S2* are linear regression lines. The anaerobic threshold (*AT*) is the $\dot{V}_{O_2}$ when the slope of $\dot{V}_{CO_2} / \dot{V}_{O_2}$ increases (Reprinted from Rosenbaum and Breen [35])

Of course, patients under anesthesia and surgery are not exercising. In fact, early data (see below) suggests a reduction in airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ under anesthesia. Thus, when patients under anesthesia and surgery suffer from anaerobic lactic acidosis, there must be regional and/or global hypoperfusion of tissues [35].

In a study modeling regional hypoperfusion of tissues, we measured bymixer-flow $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ in three anesthetized patients before and after release of a leg tourniquet during orthopedic surgery [36]. We hypothesized that tourniquet inflation and leg ischemia would cause regional anaerobic lactic acidosis. Upon tourniquet release, we expected airway $\dot{V}_{CO_2}$ and $\mathrm{RQ}\left(\dot{V}_{CO_2} / \dot{V}_{O_2}\right)$ to increase. Upon tourniquet release, there were abrupt increases in $\dot{V}_{O_2}$ (35±6 %) and $\dot{V}_{CO_2}$ (28±14 %) in all patients. *RQ did not increase* because the increase in $\dot{V}_{O_2}$ was greater than the increase in $\dot{V}_{CO_2}$. After tourniquet release, the increase in airway $\dot{V}_{O_2}$ represented the increased O_2 consumption of the ischemic tissue, enhanced by the shift of the oxyhemoglobin dissociation curve to the right and vasodilatation in the tissues. The recovery (decrease) of $\dot{V}_{O_2}$ towards the pre-tourniquet release value occurred in about 5 min. The recovery of $\dot{V}_{CO_2}$ was much slower because of buffering by blood and the higher tissue storage of CO_2 [29].

Another study examined global hypoperfusion of tissues. Currently, the presence of anaerobic lactic acidosis under surgery is assessed by intermittent arterial blood gas analysis and calculation of the base deficit (BD, difference between the calculated HCO_3 concentration and the normal value of 24 mM/L after the blood P_{CO_2} has been algorithmically tonometered to its normal value of 40 mmHg) [37]. We have conducted preliminary studies in three anesthetized patients undergoing long liver surgeries (about 500 min) [38].

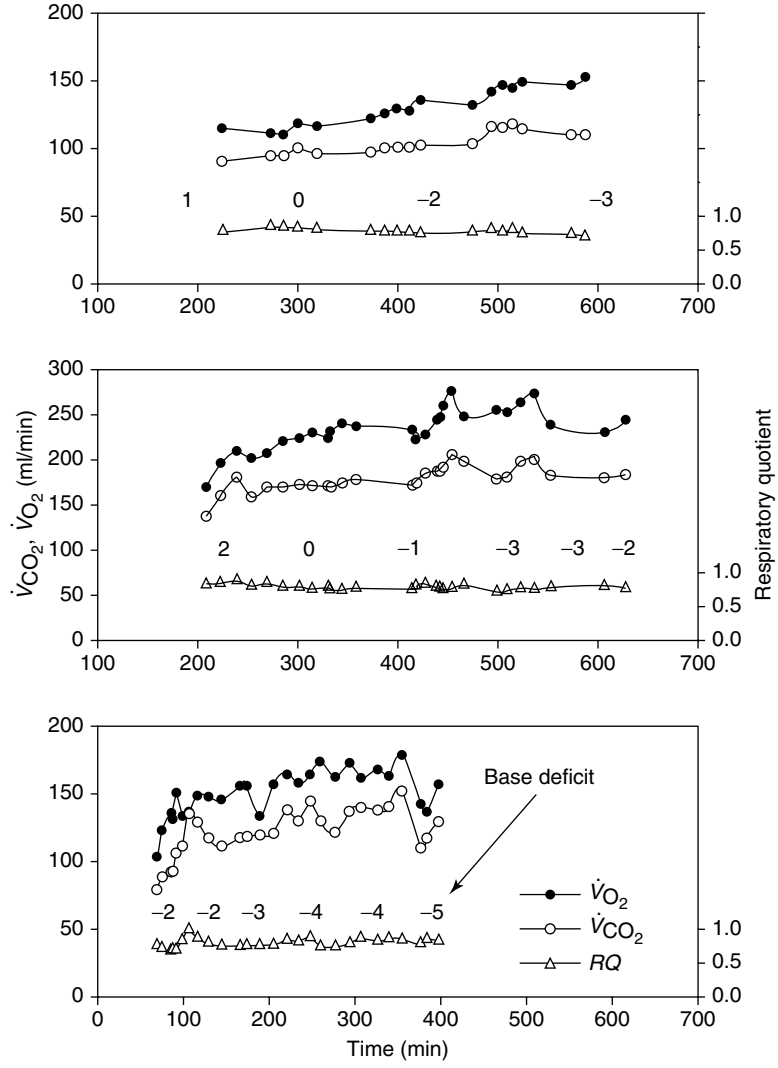

Fig. 37.8 Bymixer-flow measurements of pulmonary O_2 uptake ($\dot{V}_{O_2}$) and CO_2 elimination ($\dot{V}_{CO_2}$) and respiratory quotient ($RQ = \dot{V}_{CO_2} / \dot{V}_{O_2}$) in three anesthetized patients undergoing long liver surgeries. Base deficit (*BD*) is determined from intermittent arterial blood gas analyses (Reprinted from Beroukhim et al. [39])

BD grew more negative by 4–5 mM/L. Normally, the increase in BD suggests hypovolemia, tissue hypoperfusion, and metabolic lactic acidosis, and the primary anesthesia team delivered continuous fluid resuscitation. To our surprise, simultaneous bymixer-flow measurements of airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ did not decrease (and even increased) and the RQ did not increase but remained relatively constant (0.72–0.85) (Fig. 37.8) [38]. These are first data, we believe, strongly suggesting that noninvasive measurements of airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ can quickly and noninvasively confirm euvolemia and normal tissue aerobic metabolism despite the development of significant base deficit and can prevent needless fluid administration (including blood products). Other mechanisms for the measurement of base deficit in these patients must be sought, including the possible development of hyperchloremic metabolic acidosis. Further studies are planned to delineate the relationships between anaerobic lactic acidosis and airway measurements of $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$ and RQ [30, 31], including the possibility, in a preoperative assessment, to estimate perioperative risk by identifying the anaerobic threshold (AT) during exercise [7].

Effect of Anesthesia on Tissue Metabolism, as Measured by Airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$

Using the bymixer-flow measurement system, we have measured $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ before and after induction of anesthesia [39]. Average (±SD) $\dot{V}_{O_2}$ pre- and post-induction were 3.5 ± 0.7 and 2.1 ± 0.5 ml/kg/min, respectively (40.1 % decrease, $p < 0.05$). Average $\dot{V}_{CO_2}$ pre- and post-induction were 3.1 ± 1.0 and 1.8 ± 0.4 ml/kg/min, respectively (40.6 % decrease, $p < 0.05$). Over anesthesia induction, the respiratory exchange ratio (RER = airway $\dot{V}_{CO_2} / \dot{V}_{O_2}$) remained stable (0.87 ± 0.15). These dramatic decreases (about 40 %) in airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ were sustained throughout the post-induction period until surgical incision. The sustained decreases in airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ and the constant RER support a reduction in metabolic rate rather than a decrease in $\dot{Q}_T$. We plan further studies to delineate the relationships among anesthesia depth and tissue metabolism as measured by airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$. Other factors that can affect tissue metabolism must be considered, including the degree of surgical stimulation and the level (if any) of neuromuscular blockade [17].

Conclusion

As detailed in the three numbered sections above, we believe that the bymixer-flow measurements of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ (and the calculated value, $RQ = \dot{V}_{CO_2} / \dot{V}_{O_2}$) may noninvasively and quickly detect non-steady-state perturbations (such as an abrupt decrease in cardiac output) during anesthesia and surgery and may offer a window into the state of metabolism and tissue wellness. We plan to test the hypothesis that indirect calorimetry measurements of airway $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ will help diagnose and drive treatment of these pathophysiology perturbations and improve patient outcome.

For example, one implementation of goal-directed fluid management is to administer fluid volume to maintain the stroke volume variation (SVV, the decrease in stroke volume induced by increased thoracic pressure during mechanical ventilation) less than 13 %. But is this increase in cardiac output what the patient needs? Perhaps the "goals" of goal-directed fluid management should be reconsidered. We hypothesize that a better endpoint may be airway measurements of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ which can estimate the global level of tissue metabolism and can specifically seek an increase in the RQ, which might reflect onset of anaerobic lactic acidosis.

We suggest that the current developments to measure indirect calorimetry during anesthesia may have parallels to the development of pulse oximetry. Development of pulse oximetry has epitomized the maximal extraction of patient information from a noninvasive measurement, which now includes measurements of methemoglobin, carboxyhemoglobin, and hemoglobin, as well as indices of peripheral tissue perfusion. In a similar fashion, we predict that airway measurements of $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ will provide the "missing link" to metabolic monitoring during anesthesia. As researchers and clinicians gain more experience with these indirect calorimetry data, we believe that other clinical physiologic and pathophysiologic relationships will be discovered.

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