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On-line expiratory CO_2 monitoring

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Summary

The single breath test for carbon dioxide (SBT-CO_2) is the plot of expired FCO_2 or CO_2% against expired volume. It can be monitored during anaesthesia and in the intensive care unit with modest additions to generally available equipment. This paper describes some aspects of a computer program for presenting SBT-CO_2 during controlled ventilation, in particular, the corrections to the primary data necessary for scientific accuracy. Examples are given of how the use of SBT-CO_2 has increased our understanding of factors which influence the arterial-endtidal PCO_2 difference ($PaCO_2$-P_E, CO_2). $PaCO_2$-P_E, CO_2 is, in a given individual, usually dependent on tidal volume and frequency. Changes in lung volume and manoeuvres such as opening the pleura also affect gas exchange. Monitoring CO_2 elimination gives a measure of metabolic rate if ventilation and pulmonary perfusion are maintained. This facilitates ventilatory therapy in situations where CO_2 production is greatly increased, e.g. sepsis and tetanus. On the other hand, if metabolism and ventilation are unchanged, a reduction in CO_2 elimination implies reduced pulmonary perfusion. This can be seen during increased right-left shunting, such as in surgery in patients with congenital heart disease.

Introduction

Monitoring expired CO_2 has for many years been recognised as an adjunct to ventilatory support. It has usually taken the form of measurement of the peak expired or endtidal CO_2 concentration, it being generally assumed that these two terms were synonymous. However, many have experienced the availability of endtidal CO_2 (P_E, CO_2 or F_E, CO_2) as a mixed blessing, the reason being its uncertain relationship to arterial PCO_2, ($PaCO_2$), which is the major measure of ventilatory adequacy. Our understanding of this uncertain relationship has been improved by studying the single breath test for carbon dioxide (SBT-CO_2) and its relationship to $PaCO_2$ (1, 2). Fig. 1 shows a schematic single breath test, i.e. FCO_2 or CO_2% plotted against expired volume. Gas leaving the airway is initially CO_2-free (phase I): later there is a sharp upswing (phase II) as alveolar gas reaches the airway opening. Phase III represents alveolar gas. The slope of phase III is a measure of the spread of ventilation/perfusion ratios within the lung, and is therefore related to the alveolar deadspace (2). Increased phase III slope is seen in bronchitis, emphysema and asthma. However, pulmonary em-

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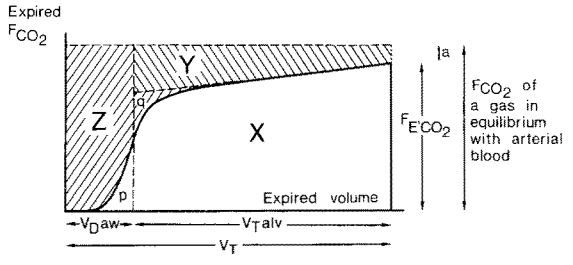

Fig. 1. CO_2 single breath test, i.e. expired FCO_2 versus expired volume, showing deadspace compartments. Areas p and q refer to the 'equal areas' method of Aitken and Clarke-Kennedy (8), by which $V_D$aw can be defined. The upper horizontal line represents the CO_2 content of a gas in equilibrium with arterial blood. Area X represents the volume of CO_2 in the breath; areas Y and Z are defects in CO_2 elimination caused by the alveolar and airway deadspaces respectively. The physiological deadspace fraction $V_D$phys/V_T is given by (Y + Z)/(X + Y + Z). The alveolar deadspace fraction, $V_D$alv/$V_T$alv, is given by Y/(X + Y). (a) is the arterial-endtidal CO_2 difference. (From Fletcher, 1980 (7); Fletcher *et al.*, 1981, (1)).

bolism and reduced pulmonary perfusion of any cause give an increased alveolar deadspace with a flat phase III.

Since the area under the curve represents the volume of CO_2 in the breath, monitoring SBT-CO_2 yields also minute CO_2 elimination, $\dot{V}CO_2$. Depending on the circumstances, $\dot{V}CO_2$ can be an index of metabolism, ventilation, or perfusion. One purpose of this paper is to demonstrate the advantages to be gained from using SBT-CO_2 as opposed to merely recording expired or endtidal PCO_2.

Computer recording and presentation of SBT-CO_2

Recording SBT-CO_2 calls for accurate and rapidly responding transducers for expiratory gas flow, $\dot{V}_E$, and for expired CO_2 (F_ECO_2). This is particularly important when studying controlled ventilation in which both $\dot{V}_E$ and the rate of change of F_ECO_2 can be increased. CO_2 must be measured in-line and not via a sampling line. Fortunately the Siemens-Elema Servo ventilator and the CO_2 Analyzer 930 (3) go some way towards providing these conditions. This paper and others (4, 5) describe how we have used the system for scientific measurements. In this system, FCO_2 is measured in-line by an infrared cell between the Y-piece and the patient connector. This makes it possible for the transducer to take a new zero reading during each inspiration, improving stability. By chopping the signal at 180 Hz, even greater accuracy and stability is achieved (3).

Our earliest studies (2) were performed by recording F_ECO_2 and $\dot{V}_E$ on tape, and later playing back the signals to a computer. The latter integrated $\dot{V}_E$ to give V_E, to which the instantaneous values for F_ECO_2 were related, giving SBT-CO_2. The computer also multiplied instantaneous values for $\dot{V}_E$ and FCO_2, and integrated the product to yield expired CO_2 volume. The corrections necessary for scientific accuracy (6) were made after production of SBT-CO_2. As studies proceeded it became evident that it would be advantageous to both present SBT-CO_2 and to perform the necessary corrections on-line, making SBT-CO_2 a clinical, bedside tool.

Corrections necessary for scientific accuracy

1. Rebreathing

There are no one-way valves at the Y-piece and therefore rebreathing may occur. During expiration, expired gas fills the expiratory tubing and the part of the inspiratory tubing nearest the Y-piece. During inspiration this gas in the inspiratory limb is rebreathed, together with part of that in the expiratory limb. Using a radioactive isotope, the rebreathed volume was estimated to be 24 ml with adult tubings (6). With paediatric tubings and Y-piece, it is about 3 ml (5). The effects of rebreathing on measured CO_2 production are almost certainly tidal volume dependent, and should be greatest when V_T is small. Rebreathing may be affected by other aspects of ventilatory pattern. In the first program for producing SBT-CO_2 on-line (4), a value for rebreathed volume could be chosen for the presentation of each breath. However, in the program developed for the 900 I ventilator (Innotek AB, Lund, Sweden), CO_2 concentration is followed during early inspiration, until it reaches zero. The area under this 'inspiratory CO_2' curve is the volume of rebreathed CO_2 (assuming that the

primary signals are synchronised) and thus this value can be subtracted from the expired CO_2 volume.

2. Effects of other gases

The Siemens-Elema CO_2 Analyzer is affected by the presence of both N_2O and O_2 in the carrier gas, although neither gas produces a response in the absence of CO_2. The % error in CO_2 measurement to compared to air as carrier gas was given by:

$$-5.8 + 0.223 \times (\%\ N_2O \text{ in } O_2) \qquad (7)$$

It is therefore important to calibrate the CO_2 analyser with test gases in which the carrier gas composition is suitable. An alternative approach would be to incorporate an algorithm to correct on-line for differences between calibration and measurement gas composition.

3. Alinearity of CO_2 analysis

Although CO_2 analysis with air as carrier gas is linear, this is not so with N_2O and O_2. If the analyser is correctly calibrated at 4% CO_2, F_ECO_2 will be overestimated at values under 4% and underestimated above 4% in an equal parts N_2O/O_2 mixture (6). It is therefore important to use a calibration gas with a CO_2 content in the clinical range. It would of course be possible to include a correction for the alinearity in an on-line program.

4. Delay in CO_2 analysis

Production series of the Siemens-Elema CO_2 Analyzer 930 have been supplied with two different amplifiers for the CO signal. This has implied different delays in CO_2 analysis. The delay in the $\dot{V}_E$ signal is about 4 ms, and with a powerful amplifier, CO_2 analysis takes a further 8 ms. With the less powerful analyser the difference is about 20 ms (7). This delay affects measurement of both $V_D$aw and CO_2 elimination. Ten patients without lung disease were investigated during IPPV using both amplifiers in turn. Using the less powerful amplifier, $V_D$aw was overestimated by a mean of 11–13 ml, depending on V_T. Tidal CO_2 elimination was underestimated by 1–3% by the less powerful analyser (7).

5. Variations in temperature and water vapour content of expired gas

Expired gas cools as it passes through the endotracheal tube and connector. The water vapour pressure is reduced and F_ECO_2 increases. At the CO_2 cuvette, and again at the expiratory gas flow meter, the gas is heated, but this of course has no further effect of F_ECO_2. It has been estimated that the change in water vapour pressure increases measured F_ECO_2 by 1–2% (6). A suitable BTPS factor for general use is 1.09 (6). To obtain greater accuracy for F_ECO_2 and volume measurements it would be necessary to measure airway temperature during expiration.

6. Compressed gas

During positive pressure ventilation, the volume of compressed gas depends on the end-inspiratory airway pressure and the compliance of the tubings. Most (60–70%) leaves the system at the beginning of expiration before CO_2 is registered at the transducer, and thus gives an artefactual increase in $V_D$aw and V_T (6). Compressed gas which leaves the system after arrival of CO_2 in the transducer produces an increase in measured CO_2 elimination. These errors can be avoided by compensating on-line for compressed gas, which requires that airway pressure be measured continuously. The compressed gas artefact is of moderate consequence in adults if low compliance tubings (e.g. 1 ml/cm H_2O) are used, but in infants the potential error is large.

7. Barometric pressure

An increase of 1% in barometric pressure gives an increase of 1.8% in the CO_2 signal (3). This can be corrected for by calibrating the CO_2 signal at the time of measurement, or by including an on-line correction for ambient pressure.

8. The effect of small tidal volumes

The Siemens-Elema CO_2 Analyzer 930 maintains its stability in use partly because it takes a new zero during each inspiration. However, this feature is based on the assumption that the CO_2 is completely cleared from the cuvette by the inspiratory gas. This is not the case at small tidal volumes. As a

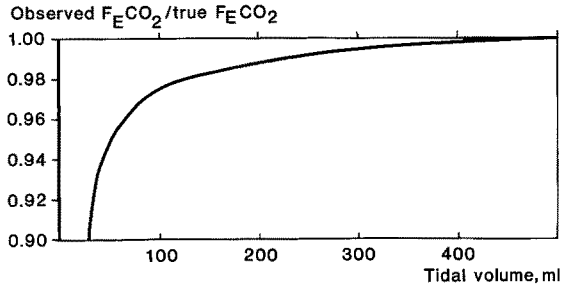

Fig. 2. The tidal-volume dependent error is measured F_ECO_2 (5). At low tidal volumes the CO_2 cuvette is inadequately cleared by the inspiratory gas. As a consequence, CO_2 molecules remain when the CO_2 analyzer takes a new zero, and the following measurement underestimates F_ECO_2.

result there is an underestimate of expired FCO_2 (5). The underestimate is out of proportion to the number of CO_2 molecules remaining in the cuvette because the original CO_2 signal is logarithmic, and is linearised in the CO_2 analyser *after* establishment of new (and at small tidal volumes, incorrect) zero. The relationship between the error and tidal volume is shown in Fig. 2.

Presentation of SBT-CO_2

In order to facilitate recognition of SBT-CO_2 patterns, it is desirable to relate the volume axis to the patient's size. A scale marked as 5, 10 and 15% of predicted total lung capacity (TLCp) is adequate for most routine situations. TLCp can be calculated by the computer from the patient's height, weight and sex. For infants, in whom tidal volumes are large in proportion to lung volume, 25% of TLCp is preferable.

Variables derived from SBT-CO_2

A number of 'non-invasive' variables can be obtained from SBT-CO_2 (Table 1). Only one, V_Daw, requires any calculations in addition to the presentation of SBT-CO_2 (see below). Lung mechanical properties, e.g. peak and pause pressure, compliance, and resistance can also be derived and presented, since both airway flow and pressure are available. Calculation of 'invasive' variables, such as the physiological and alveolar deadspace fractions, can be included in the computer program (4). For these, a value for $PaCO_2$ must be given to the computer.

Estimation of airway deadspace

The airway deadspace, V_Daw, is the gas volume from the airway opening to the mean position of the alveolar/fresh gas interface, immediately prior to expiration (1). Several methods are available for estimating V_Daw.

1. The 'equal areas' method of Aitken and Clarke-Kennedy (8) and Fowler (9).
2. Langley's method (10).

Both the above methods are difficult to apply in the presence of a sloping phase III.

3. The point of inflexion, i.e. maximum slope, of phase II.
4. The method of Wolff and Brunner, which estimates V_Daw as the mean of a distribution function (11).

At the time of writing, method 4 appears to be the most useful.

Table 1. 'Non-invasive' variables presented by the computer

Airway deadspace, V_Daw, measured by the computer as the point of inflexion in the CO_2 tracing. This is a simpler method than the equal areas method (fig. 1) but gives similar results.
Tidal volume V_T (not including ventilation of the apparatus deadspace V_Dapp)
Total tidal volume, i.e. V_T plus compressed gas volume, but not V_Dapp
Ventilatory frequency, f (bpm)
Expired minute volume, V_E, i.e. $V_T \times f$
End-tidal FCO_2, F_E, O_2, defined as mean FCO_2 of the last 10% of phase III
Tidal elimination of CO_2, V_TCO_2, calculated from the area under SBT-CO_2, minus rebreathed CO_2 volume.
V_DBohr, the deadspace obtained by substituting F_E,CO_2 for alveolar CO_2 in Bohr's equation (22)

Uses of on-line CO_2 monitoring

CO_2 monitoring gives information about ventilation and perfusion of the lung, and CO_2 production in the tissues.

CO_2 production

CO_2 production in the tissues is dependent upon metabolic rate. Increased production is commonly seen in intensive care patients with sepsis and other causes of increased catabolism. It is possible to observe three-fold increases in $\dot{V}_{CO_2}$ during severe sepsis, and doubled values of $\dot{V}_{CO_2}$ during tetanus convulsions. Measuring $\dot{V}_{CO_2}$ facilitates maintainance of adequate ventilation in these cases. CO_2 production is greatly increased in malignant hyperthermia (12, 13). CO_2 production in anaesthetised patients is markedly dependent upon body temperature. After extra-corporeal circulation with hypothermia, $\dot{V}_{CO_2}$ can be doubled by shivering unless body temperature is returned to normal by active warming (14).

CO_2 elimination

CO_2 elimination is dependent upon both lung perfusion and ventilation. If tissue CO_2 production is unchanged, CO_2 elimination can be used to monitor ventilation ($\dot{V}$) and perfusion ($\dot{Q}$). It is thus of help in determining optimal ventilator settings and assessing the effect of ventilator therapy, for instance, in the adult respiratory distress syndrome. When making major changes in ventilator setting, e.g. from volume controlled to pressure controlled ventilation, and/or when changing the inspiratory/expiratory ratio, measurement of CO_2 elimination provides a guarantee of adequate alveolar ventilation. In severe lung disease, small changes, e.g. from 50 to 55% in inspiratory time, can sometimes be elegantly demonstrated to produce large effects on $\dot{V}CO_2$ and hence alveolar ventilation.

If alveolar ventilation and tissue CO_2 production are unchanged, CO_2 elimination becomes a measure of perfusion. A few examples suffice. Congenital heart lesions associated with pulmonary hypoperfusion can be palliated by *aortopulmonary* or *subclavio-pulmonary anastomosis*. The effect of these anastomoses can be quantified intraoperatively by the increase in V_TCO_2. *Ventricular septal defects* are associated with pulmonary hyperperfusion, which can be palliated by reducing pulmonary artery blood flow by banding. Here too the circulatory effects of the palliation can be quantified. Fig. 3 shows the reduction in CO_2 elimination as the surgeon overtightens the pulmonary band, and then releases it after being informed by the anaesthetist. Similar experiences have been reported by others (15).

Fig. 4 shows a reduction in CO_2 elimination due to an increasing right-to-left shunt in a child with Fallot's tetralogy. At the time of the recording the surgeon was in the process of ligating a patent ductus arteriosus. The manipulation led to an increasing pulmonary resistance, either caused by narrowing of the pulmonary outflow tract or by raised pulmonary artery resistance. This led to increased R-L shunting through the VSD, causing hypoxia, acidosis and reduced CO_2 elimination. Cardio-pulmonary bypass was rapidly instituted.

The patient illustrated in Fig. 5 shows how lung function can change during the course of an operation. Manipulation of a carcinoid tumour caused a sudden large increase in alveolar deadspace, presumably by the release of vasoactive substances affecting lung perfusion. The anaesthetist noticed this first as a large and inexplicable fall in P_E, CO_2 and $\dot{V}_{CO_2}$. Later in the course of the operation, a more normal alveolar deadspace was recorded, and the $PaCO_2$-P_E,CO_2 difference returned to a normal value. To the author's knowledge, low CO_2 output has on several occasions given warning of cardiac arrest or arrhythmia when an ECG was either unavailable or unhelpful. Although 'unexpected' values for CO_2 elimination *can* be the result of apparatus dysfunction, it the author's opinion that derangements of CO_2 elimination should be regarded as warnings of serious disturbances in pulmonary blood flow, until this possibility has been eliminated.

The shape of SBT-CO_2

Studying the shape of SBT-CO_2 gives information about the nature of gas exchange derangements

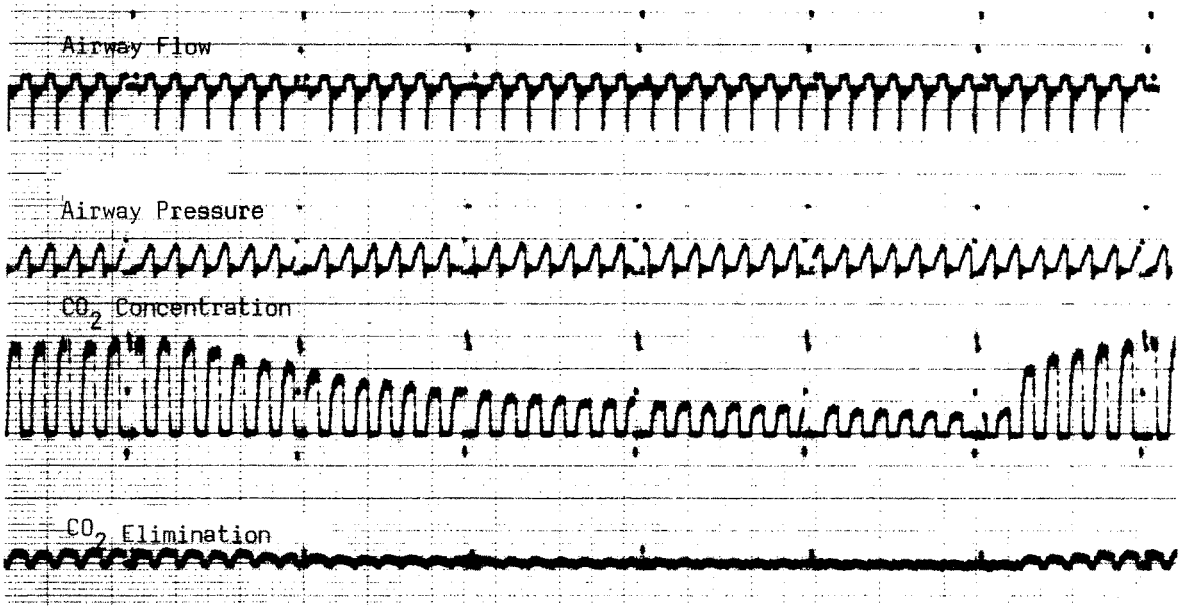

Fig. 3. Tracings obtained during operation on a child with a VSD. and coarctation of the aorta. After repair of the coarctation, the surgeon tightens a band round the pulmonary artery. As a result, expired CO_2 concentration and CO_2 elimination (lower tracings) are reduced. The anaesthetist then warns of reduced perfusion, the surgeon releases the band and CO_2 elimination resumes. The upper two tracings show that ventilation remained unchanged.

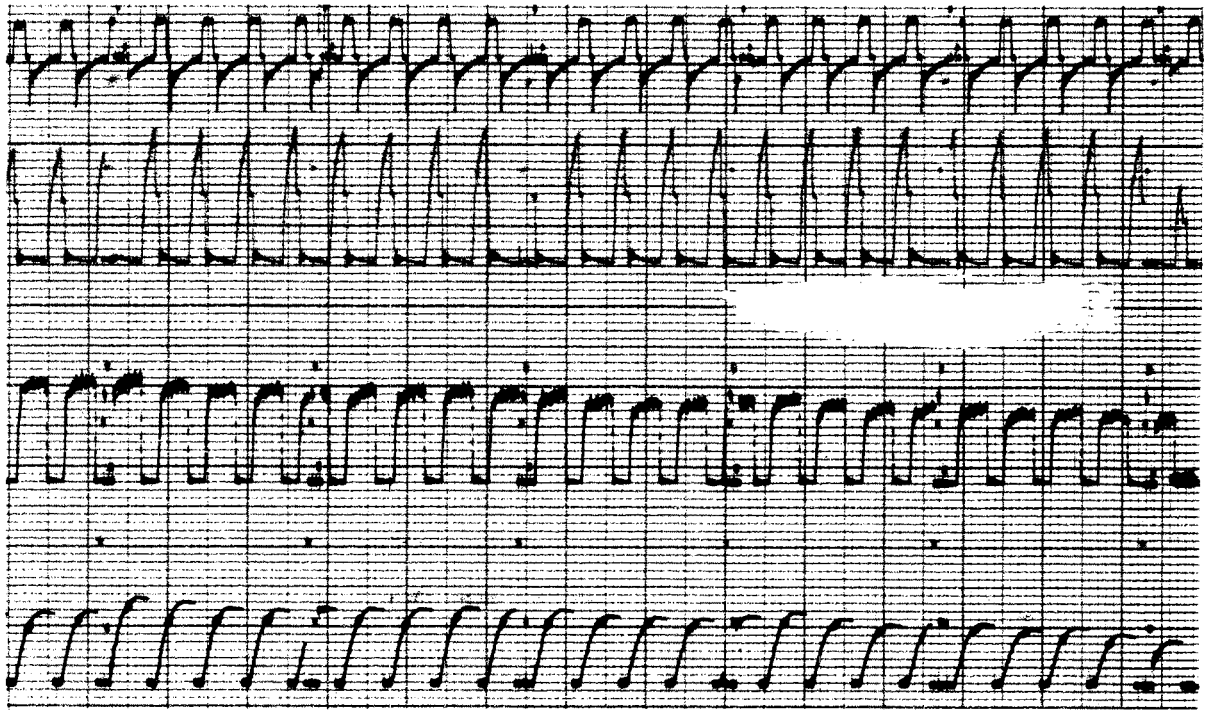

Fig. 4. Tracings (as in Fig. 3), obtained during operation on a child with Fallot's tetrology and patent ductus arteriosus. Before instituting cardiopulmonary bypass, the surgeon attempts to ligate the patent ductus. This causes an increase in R-L shunting and thus a reduction in pulmonary perfusion. Though ventilation is maintained, CO_2 elimination and F_ECO_2 are reduced. Cardiopulmonary bypass was rapidly instituted.

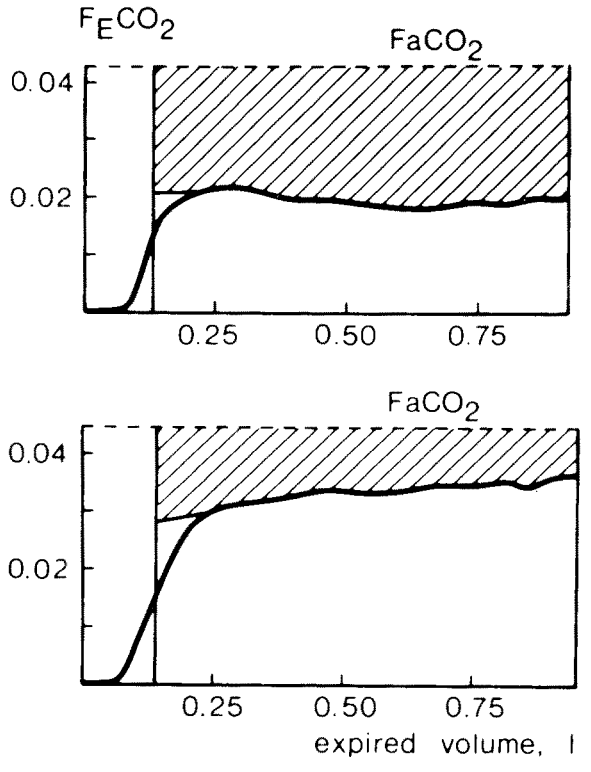

Fig. 5. SBT-CO_2 from a patient with carcinoid tumour. Top: a sudden reduction in CO_2 elimination was seen when the surgeon began to handle the tumour. Bottom: later, when the tumour had been removed, SBT-CO_2 reverted to a more normal appearance with an upwards sloping phase III and a normal arterial-endtidal difference.

e.g. pulmonary embolism, and explains changes in physiological deadspace brought about by e.g. sternotomy (4) and the lateral position (15). It allows analysis of subtle derangements in gas exchange such as the small increase in phase III slope associated with increased pulmonary perfusion (5). When phase III slopes downwards i.e. negative slope, endtidal and peak expired CO_2 are no longer synonymous. For a review of factors influencing the shape of SBT-CO_2, the reader is referred to the author's thesis (7).

Estimation of arterial PCO_2 from endtidal PCO_2

As stated previously, the usefulness of expired CO_2 monitoring has sometimes been doubted, because of uncertainty as to the significance of P_E,CO_2. Endtidal, or peak expired CO_2, gives the PCO_2 of the lung units whose contribution to the expirate arrives last at the airway opening. Whether or not the PCO_2 of this part of the expirate is equal or approximately equal to $PaCO_2$ depends on (a) the magnitude of the alveolar deadspace, and (b) the spread of ventilation/perfusion ratios, expressed as the slope of phase III of SBT-CO_2.

During controlled ventilation in adults, there is usually an increased alveolar deadspace fraction and phase III usually has a slope. The alveolar deadspace is due to several factors: maldistribution of inspired gas *between* lung units, and maldistribution of gas *within* units – both the results of airways disease. In addition, raised airway pressure during controlled ventilation may adversely affect the distribution of perfusion. Both within-units and between-units mismatching may be improved by increasing V_T, at least if frequency is reduced at the same time (2). This increases the ventilation of 'slow' lung units, and the effect on SBT-CO_2 is to give a flatter phase III but a smaller $PaCO_2$-P_E,CO_2. If V_T is great enough, $PaCO_2$-P_E,CO_2 may become zero or negative (2).

Thus for a given individual, $PaCO_2$-P_E,CO_2 is tidal volume and frequency dependent. The most important factors associated with an increased $PaCO_2$-P_E,CO_2 difference are age and airways disease, in particular smoking. The $PaCO_2$-P_E,CO_2 increases significantly with age in smokers but not

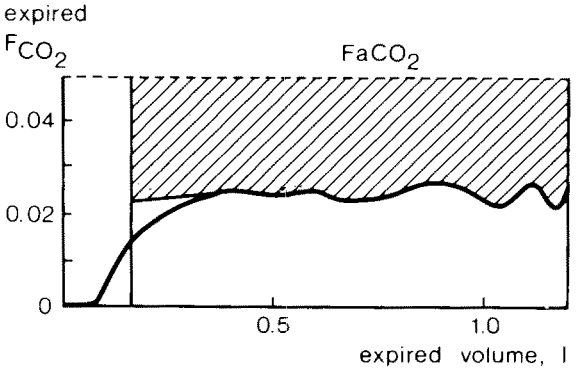

Fig. 6. SBT-CO_2 recorded during controlled ventilation in a patient with pulmonary embolism. Lung perfusion scintigrams showed multiple large defects. The 'cardiogenic oscillations' are caused by the heart expressing gas from lung regions with different FCO_2s.

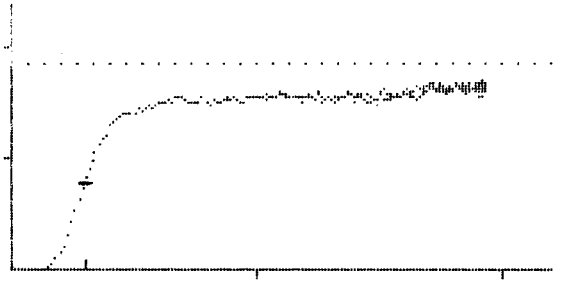

Fig. 7. SBT-CO_2 from child with R-L shunting due to pulmonary stenosis and atrial septal defect. The markings on the the volume axis are 5 and 10% of TLCp; on the vertical axis 2 and 4% CO_2. There is a large (by children's standards) alveolar deadspace fraction and $PaCO_2$-P_E, CO_2 difference.

in non-/or ex-smokers (Fletcher, unpublished material). In smokers the increase was about 0.2 kPa per decade of adult life. In a larger unsegregated material (2), $PaCO_2$-P_E,CO_2 increased by about 0.1 kPa per decade (unpublished observations).

Exceptions to the general rule of frequency and tidal volume dependency can occasionally be seen. Pulmonary embolism (Fig. 6) gives a flat phase III with a large alveolar deadspace fraction, little or not at all improved by increasing V_T. SBT-CO_2 has a similar appearance in children with congenital cardiac disease leading to pulmonary hypoperfusion and right to left shunting (Fig. 7). In neither case does increasing V_T improve the relationship between arterial and alveolar PCO_2.

Variations in $PaCO_2$-P_E,CO_2 during anaesthesia and surgery

As well as the effects of tidal volume and frequency (see above), intraoperative manoeuvres can change $\dot{V}/\dot{Q}$ relationships and hence $PaCO_2$-P_E,CO_2. Hypovolaemia and induced hypotension without volume substitution (17) increases the P_E,CO_2 difference: induced hypotension with maintained blood volume may not have the same effects. Institution of extra-corporeal bypass also increases the $PaCO_2$-P_E,CO_2 difference. Turning to the lateral position increases the $PaCO_2$-P_E,CO_2 difference of the upper lung, especially when the pleura is opened (18). Retraction of the upper lung during thoracotomy in children also increases $PaCO_2$-P_E,CO_2 (16). Large increases in $PaCO_2$-P_E,CO_2 have been seen following repair of atrial septal defects (19). Here the mechanism is thought to be a sudden reduction in pulmonary perfusion and pressure. Increases in $PaCO_2$-P_E,CO_2 and changes in the shape of SBT-CO_2 can be seen during procedures such as systemic-pulmonary anastomosis when blood flow through a pulmonary artery is temporarily reduced by vessel clamping. In theory, successful surgery of this type, intended to increase pulmonary perfusion, should reduce a pathologically increased CO_2 difference. This has not been convincingly observed in the author's own practise, however.

Although data have been presented showing a large variation in $PaCO_2$-P_E,CO_2 during major surgery (20), the experimental protocol did not permit the authors to relate the changes to specific surgical or anaesthetic manipulations. In the author's experience, important events associated with changes in lung volume (21), such as opening and closing the sternum, and the use of extra-corporeal bypass did not have any large or consistent effects on $PaCO_2$-P_E,CO_2 (4).

$PaCO_2$-P_E,CO_2 is thus a dynamic variable with large interindividual, and under certain circumstances, large intra-individual variation. It is the author's practise to establish the $PaCO_2$-P_E,CO_2 relationship early in the course of an anaesthetic, and continue to follow P_E,CO_2 and CO_2 elimination thereafter. Sudden reductions in P_E,CO_2 are regarded as indicating reduced pulmonary perfusion.

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