A TIME-PHASED END TIDAL SAMPLER SUITABLE FOR USE
DURING ANAESTHESIA

BY

J. F. NUNN AND A. C. PINCOCK

Departments of Surgery and Medicine, University of Birmingham

It is well known that disturbances of the respiratory acid-base balance may occur during anaesthesia. Severe CO₂ retention will lead to coma and respiratory depression, but in moderate degrees the signs are notoriously inconstant. Previous hypoventilation may be the only reason for suspecting CO₂ retention and unfortunately little help can be afforded by measurement of CO₂ tensions as this presents special difficulties under the conditions of anaesthesia.

The determination of the PCO₂ of arterial blood is complicated by the presence of nitrous oxide, which makes it impossible to use the direct method of Riley et al. (1945). Indirect determination from pH and CO₂ content is possible but the technique requires certain modifications (Orcutt and Waters, 1937) and is inevitably time consuming and laborious. Furthermore, the accuracy is limited by the slope of the CO₂ dissociation curve. It is possible that the method recently described by Astrupp (1956) will be applicable to the conditions of anaesthesia and will provide a means for the rapid and accurate determination of the arterial PCO₂.

Alveolar gas analysis presents an alternative to monitoring the arterial blood. Again nitrous oxide interferes with many methods of gas analysis which may be used for CO₂, but the principal technical difficulty during anaesthesia is sampling. Eastwood and Harbord (1955) have described the collection of alveolar samples from unconscious patients after large passive expirations and Scurr (1956) has used the equilibration method of Plesch (1909) during anaesthesia, thereby obtaining values approximating to the PCO₂ of mixed venous blood.

A more satisfactory technique is the instantaneous analysis of expired gas by the mass spectrometer (Buckley et al., 1952; Woolmer, 1953) or by the rapid infrared gas analyzer (Fowler, 1949; Dubois et al., 1952; Siebecker, 1954; Elam et al., 1955). Not only is it possible to measure the alveolar concentration of CO₂ but, by inspection of the curve, it is possible to establish whether alveolar gas has in fact been sampled. It is unfortunate that rapid gas analysis involves considerable technical difficulties and such methods, while admirably suited to research, have at present little place in the routine care of anaesthetized patients.

It has been established by many workers that normally the PCO₂ of end tidal gas approximates closely to that of alveolar gas and arterial blood (Dubois et al., 1952). With end tidal sampling it is not necessary to use instantaneous methods of gas analysis and the technique is thereby greatly simplified. Terminal end tidal samples may be withdrawn manually by the method of Inkster and Rees (1956), but the automatic "through the valves" devices for end tidal sampling introduced by Henderson and Haggard (1925) and later developed by Rahn, Mohney, Otis and Fenn (1946) are generally unsuitable for use during inhalational anaesthesia. Not only is the instrument dead space too high for the reduced tidal volumes which may be encountered, but in most anaesthetic systems there is some admixture of expired gas with surplus fresh gas supply during the latter part of expiration. Suskind and Rahn (1954) have used a method of this type during intravenous anaesthesia.

Krogh and Lindhard (1914) used the volume of gas expired to actuate collection of samples from various fractions of expired gas. This principle was later used by Loeschke, Opitz and Schoedel (1939) who devised a volume phased
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end tidal sampler to aspirate samples from the trachea after a certain volume had been expired. This method had the advantage of not sampling from short expirations, but it was particularly cumbersome and as the apparatus incorporated a spirometer it could not easily be adapted to artificial ventilation by intermittent positive pressure.

As most measurements of end tidal Pco₂ would be made in a steady state with constant tidal volume and respiratory frequency, the time required for the expiration of a predetermined volume should be reasonably constant. It thus appeared feasible to use a time delay so that sampling could be restricted to that time when alveolar gas occupied the region from which the sample would be collected. Time phasing would retain most of the advantages of volume phasing but would be more convenient in operation and could be made independent of any external breathing apparatus. In particular such a method could be used with most forms of anaesthetic apparatus and with intermittent positive pressure respiration.

The present study was therefore undertaken to determine the feasibility of obtaining alveolar samples with a time phased end tidal sampler. In addition, the colorimetric method of determination of carbon dioxide tension in a gas was investigated as it appeared to be a suitable method for use with the sampler.

Throughout this article the term "dead space" refers to anatomical dead space. This has recently been defined by Harris (1956) as that part of the respiratory tract which is filled with inspired gas at the end of inspiration and with alveolar gas at the end of expiration.

**METHOD**

The sampling mechanism is operated by the differential pressure which develops, during expiration, across the slight resistance afforded by the mouthpiece or the endotracheal tube connec-

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**Fig. 1**

Circuit of the time phased end tidal sampler and CO₂ analyzer.
tion. This pressure is independent of the actual tracheal pressure changes during respiration and is thus unaffected by the manner of the breathing—whether spontaneous or artificial with a positive pressure during inspiration. The differential pressure across a normal endotracheal tube connection containing a concentric sampling tube (2.5 mm o.d.) is of the order of 3 mm water during quiet breathing with a peak flow rate of 18 litres/min. This has been found to be sufficient to operate contacts by means of a differential tambour (fig. 1).

When the contacts are closed at the start of expiration a magnetically operated valve puts the sampling pump in communication with the analyzer through which gases will be drawn. Simultaneously a potential is applied to a relay through a variable resistance-condenser network so that the pause before the relay is closed is controlled by the resistance. When the relay eventually closes two sets of contacts are closed; one starts the sampling pump while the other discharges the condenser. At the end of expiration the differential pressure switch is opened and the magnetically operated valve brings the sampling to an abrupt end. By reversal of the pressure leads it is possible to sample during inspiration.

The CO\textsubscript{2} analyzer is similar in principle to that described by Brinkman and Lamberts (1952), in which the gas is brought into contact with a buffered solution of an indicator. A solution of 0.005 per cent bromthymol blue with 0.05 per cent sodium bicarbonate is used and this changes colour from blue to yellow according to the tension of CO\textsubscript{2} to which it is exposed. Equilibration takes place in a cuvette with a sintered glass bottom, below which the gas is introduced from a side tube. By this means the gas stream is broken up into fine bubbles, thereby accelerating the attainment of equilibrium.

The light transmission of the solution, using a yellow filter, is measured by a barrier-layer-type photo cell and a galvanometer. The side tube is not in the optical pathway and sampling may be interrupted for reading. Frothing in the cuvette causes dye to be absorbed on to the foam and a much higher rate of gas flow is possible if the inside of the cuvette is treated with a silicone antifoaming agent. Approximately 1 ml of gas is sampled each breath.

The polythene sampling tube has an internal diameter of 1.5 mm and is passed down the airway to a point as near the carina as possible. During inspiration a small quantity of the indicator descends through the sintered glass plate displacing gas backwards along the sampling tube. It is felt that this may prevent diffusion of inhaled gases into the open end of the sampling tube, which has been a source of error in the past (Bracken—personal communication).

**ASSESSMENT OF THE METHOD**

The phasing of the end tidal sampler was studied by simultaneous recording of ventilation and the aspiration of samples. Respiration was simulated with a reciprocating pump and recorded on a spirometer, while the sampling tube was connected to a tambour, the movements of which signalled the duration of sampling (fig. 2).

The speed of response of the CO\textsubscript{2} analyzer was studied by drawing alternately air and a mixture of 10.5 per cent CO\textsubscript{2} in air through the analyzer. The galvanometer deflection was noted every 15 seconds until equilibrium had been obtained. The phasing of the sampling was intermittent and similar to that which would be used during normal respiration.

The CO\textsubscript{2} analyzer was calibrated against a number of cylinders containing CO\textsubscript{2} mixtures up to 10 per cent, the composition of which had been determined by the micro method of Scholander (1947). Duplicate analyses were required to agree within 0.03 per cent. With zero galvanometer deflection when no light fell upon the cell, the deflection was noted when these mixtures were drawn through the cuvette under constant conditions of light intensity and photo-cell sensitivity. The barometric pressure and the temperature of the cuvette were noted.

Comparisons were made between the P\textsubscript{Co\textsubscript{2}} of end tidal samples measured by the analyzer and the P\textsubscript{Co\textsubscript{2}} of Haldane-Priestley (1905) end inspiratory alveolar samples which were analyzed by the method of Scholander. The alveolar samples were collected after the subject had reached a steady respiratory state as shown by the end tidal P\textsubscript{Co\textsubscript{2}}.
The observations were repeated on the same subject at various tidal volumes which were obtained by varying the respiratory frequency while keeping the alveolar ventilation and Pco₂ at values not far removed from normal. Breathing was in time with a metronome and the tidal volumes were calculated from the minute volume which was measured with a dry gas meter. Simultaneous measurements of the alveolar and end tidal Pco₂ were plotted against the tidal volume.

The dead space of the subject was determined from Bohr's formula, using the concentration of CO₂ in the alveolar gas and the mean concentration in the expired gas which was collected in a Tissot spirometer for the measurement of the tidal volume.

RESULTS

With a constant tidal volume and respiratory frequency, it was possible to delay the commencement of sampling to any part of the expiratory phase (fig. 2). With maximum delay the sample was terminal and should correspond with the method of Rahn et al. (1946). With an intermediate delay it should be possible to sample mixed alveolar gas and obtain results similar to Loeschke et al. (1939). The persistence of sampling after the apparent cessation of expiration was inherent in the apparatus but did not exceed 0.25 seconds. Similar results were obtained during inspiratory sampling with the leads reversed.

The CO₂ analyzer showed 95 per cent response after 45–75 seconds and appeared to be little
influenced by the rate of aspiration of the sample (fig. 3).

The galvanometer deflections obtained during calibration with different tensions of CO₂ are shown in figure 4. Cuvette temperatures fell into three groups. It will be seen that while the effect of temperature was negligible with low tensions of CO₂, it was significant throughout most of the range of alveolar CO₂ tensions. In figure 5 the galvanometer deflections are expressed as a percentage of the deflection obtained with a gas of PCO₂ 36.0 mm Hg at the same temperature. The shaded areas include all the 54 points obtained during calibration between 21 and 28°C and suggest that with two fixed points—no light falling on the cell and the deflection at PCO₂ 36.0 mm Hg—the calibration curve is reasonably constant at the various temperatures. The maximum error from the mean is ±0.5 mm Hg up to PCO₂ 50 mm Hg and ±3 mm Hg at PCO₂ 70 mm Hg.

The comparison with alveolar samples (fig. 6) shows that, in the present study, above a tidal volume of 300 ml (b.p.t.s.) the difference between the PCO₂ of Haldane-Priestley end inspiratory alveolar samples and end tidal samples analyzed by the colorimetric method did not exceed 2 mm Hg, which is within the combined error of the two methods. The mean alveolar PCO₂ exceeded the mean end tidal PCO₂ by 0.4 mm Hg (standard deviation 1.3 mm Hg). Below a tidal volume of 300 ml progressively
Simultaneous determinations of alveolar and end tidal Pco₂ at various tidal volumes. The dead space of the subject was 150 ml.

Larger divergencies occurred until at 200 ml the difference was of the order of 15 mm Hg.

The dead space in the sitting position was found to be 150 ml. This is in accord with a body weight of 143 lb (65 kg) as shown by Radford (1955).

**DISCUSSION**

The results indicate that, with a constant tidal volume and respiratory frequency, it is possible to use time phasing to delay sampling until a reasonably constant volume has been expired. Due to the inertia of the apparatus sampling continues approximately 0.25 seconds after the apparent end of expiration, but it is unlikely that inspiration will commence within this period.

During anaesthesia and intermittent positive pressure ventilation (for which this apparatus was particularly designed) the respiration is generally slow and there is also a postexpiratory pause. In addition, the dead space distal to the sampling point at the carina will normally contain alveolar gas which will pass the sampling point a second time during early inspiration.

The sensitivity of the pressure switch may be increased under certain conditions by allowing one side of the tambour to communicate with the atmosphere and actuating the mechanism with either a positive or negative airway pressure.

The colorimetric method of CO₂ analysis has the advantages of simplicity and lack of interference by other gas—particularly nitrous oxide. The response time is, however, slow and breath-to-breath changes in Pco₂ cannot be detected.

Rather will the method indicate the mean end tidal Pco₂ over the previous minute, which is generally adequate during clinical use.

The calibration curve is reasonably constant at different temperatures and is almost linear up to a Pco₂ of 55 mm Hg. It is necessary to refer to a standard gas mixture at frequent intervals until thermal equilibrium has been obtained within the cuvette. Thereafter the stability is good and reference every 20 minutes is sufficient.

Small cylinders of 5 per cent CO₂ in oxygen are suitable for use as standards, as not only are they readily available but their Pco₂ lies somewhere near the middle of the range encountered during anaesthesia. The contents may differ considerably from the composition claimed by the manufacturers and it is necessary to analyze the contents of each cylinder which is used for calibration.

It is convenient to prepare a direct reading scale for the galvanometer, and in this may be incorporated a correction for gases which, when sampled, are saturated with water vapour at body temperature.

There is close agreement between end tidal
samples and Haldane-Priestley end inspiratory alveolar samples at normal tidal volumes. However, there is a discrepancy below a tidal volume of 300 ml when the volume expired is insufficient to wash out the dead space. This defect can be reduced by sampling from the carina if an endotracheal tube is in use. Lilly (1946) has referred to the expired volume required to wash out the dead space as the kinetic dead space, and Fowler (1948) found this to be of the order of 325 ml when the anatomical dead space was 156 ml. The present study is in reasonable agreement with these figures and it would appear, in general, that a tidal volume of at least double the anatomical dead space is required for sampling alveolar gas at the end of expiration. When sampling from the carina, a tidal volume of 140 ml should normally be adequate, since the work of Fowler and Blakemore (1951) and Folkow and Pappenheimer (1955) suggests that only one-third of the dead space is below the carina.

End tidal sampling in the presence of a defect of gas mixing was demonstrated in a patient with emphysema who was being ventilated by intermittent positive pressure during an attack of bronchopneumonia. The Pco₂ of the end tidal samples was compared with instantaneous analysis of the expired gas (fig. 7). It will be seen that the normal plateau of CO₂ in the alveolar gas was replaced by a steep gradient and although the end tidal sample represented the mean value on the gradient no expired gas approached the Pco₂ of the arterial blood which was determined simultaneously by the method of Riley et al. (1945). Under these conditions no gas analysis technique can reveal the true state of gaseous acidosis or alkalosis and there is no alternative to the analysis of arterial blood.

The results have shown that under normal conditions time phased end tidal samples had a Pco₂ closely approximating to alveolar gas and therefore to arterial blood. However, there are three factors which must be considered in the light of these results. First, the phasing of a sample must correspond to the alveolar fraction of the expired gas and must not be contaminated with dead space gas. Secondly, it must be known that the tidal volume is sufficient to wash out the dead space up to the point from which the sample is withdrawn. Thirdly, a defect of gas mixing
associated with under perfused areas of the lung may introduce a gradient between the arterial and the end tidal Pco₂. The arterial Pco₂ will usually be higher than the end tidal Pco₂ and this information may be of value.

When there is no reason to suspect that the end tidal tensions differ from the arterial, time phased end tidal sampling offers a simple and convenient method for monitoring changes in Pco₂ and figure 8 is a typical example of the continuous estimations of Pco₂ which are possible. The method has been used extensively with various anaesthetic techniques and also during the recovery phase. It has proved valuable in the treatment of prolonged respiratory failure by cabinet-type respirators and by intermittent positive pressure ventilation. It has also been of use for the determination of the alveolar Pco₂ in normal subjects breathing through mouthpieces and for the investigation of the inspiratory CO₂ concentration in various types of breathing apparatus.

SUMMARY

(1) A method of end tidal sampling is presented, in which alveolar gas is obtained by delaying sampling during the expiratory phase with a variable condenser-resistance network. The CO₂ tension of the samples is determined continuously with a colorimetric analyzer.

(2) In the normal subject the Pco₂ of the samples agrees closely with the Pco₂ of Haldane-Priestley end inspiratory alveolar samples, provided that the tidal volume is sufficient to wash out the dead space.

(3) Practical applications of the technique are outlined.

FOOTNOTE

Further development work for the commercial production of this apparatus is being carried out in conjunction with the medical division of Stanley Cox Ltd.
REFERENCES


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