ELIMINATION OF CARBON DIOXIDE BY THE LUNG

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The blood level of carbon dioxide, like that of other katabolites, depends upon the balance of production and elimination. By far the greater part is eliminated by the lungs and ventilation therefore controls the arterial tension of CO_2. The clearance of CO_2 differs from that of all other katabolites in that its carrier is gaseous and moreover moves tidally rather than fluvially. On account of the intangible nature of gas and the complexities of tidal flow, the elimination of CO_2 is less readily understood than, for example, that of urea. The significance of oliguria is at once apparent, but hypoventilation is frequently dismissed as "comfortable" breathing.

Although tidal ventilation is common to all the air breathing vertebrates, it has two disadvantages in comparison with the fluvial perfusion of the gills of fishes. Firstly, counter current flow is impossible and therefore the inspired gas cannot be fully utilized. Secondly, a proportion of each breath is wasted in purging the gases lying in the conducting passages. The efficiency of the system is also dependent upon the correct spatial distribution of inspired gas and pulmonary blood flow —as was suggested by John Hunter [1] in the eighteenth century: "As the lungs are to expose the blood to the air, they are so constructed as to answer this purpose exactly with the blood being brought to them, and so disposed in them as to go hand in hand."

In contrast to oxygen uptake, CO_2 elimination is but little affected by an impairment of diffusing capacity, since CO_2 can cross the alveolar-capillary membrane some twenty times more easily than oxygen.[2] Similarly, the total pulmonary blood flow is a factor which can be largely ignored.[3] On one occasion the author diagnosed cardiac arrest by noting a sudden fall in the end-tidal CO_2 concentration, but moderate changes in pulmonary blood flow have negligible effect upon CO_2 elimination.

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There are two further factors affecting the elimination of CO_2 which are of special interest to the anesthetist. Firstly, during anesthesia it is not unusual for a patient to inhale CO_2 of either endogenous or exogenous origin. This must constitute an important barrier to the escape of CO_2 from the body and has undoubtedly contributed to many instances of clinically significant CO_2 retention. The second factor is the large capacity of the body to store CO_2 in the blood and in the tissues. Ventilation is frequently variable from minute to minute during anesthesia and a steady state is probably seldom achieved. Consequently it is common during anesthesia for the rate of CO_2 elimination to differ considerably from the rate of metabolic production of the gas.

Thus it will be seen that the elimination of CO_2 by the lungs during anesthesia is influenced by many factors—some of little importance but others of great clinical significance. The more important factors will be considered separately, with special reference to the circumstances of anesthesia where reliable data exist. In the final section, certain equations are presented for the quantification of CO_2 elimination and for the prediction of the arterial P_{CO_2} from the ventilation.

Ventilation

The most important parameter in CO_2 elimination is the total ventilation of the lungs. The minute volume of respiration is the product of tidal volume and respiratory frequency —gas volumes being measured under the conditions of body temperature and pressure, saturated with water vapor (BTPS). Although there are few reports of reliable measurements of ventilation during anaesthesia, there is no doubt that gross departures from normal are commonplace. To a large extent they depend upon the ability of the anesthetist to detect the changes, to understand their significance and to take the necessary steps towards the restoration of normality.

Spontaneous Respiration. With the exception of nitrous oxide and low concentrations

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TABLE 1

REPORTED VALUES FOR VENTILATION DURING ANESTHESIA WITH SPONTANEOUS RESPIRATION

Source of Data	Anesthetic agents used after induction	Minute volume liters minute	
		Mean	Range
Ridley and Faulconer,[4] 1952	N_2O and ether	9.1	2.0 -15.0
Patrick and Faulconer,[5] 1952	N_2O and ether	9.6	3.0 -16.5
	Thiopental sodium	5.4	0.5 -12.5
*Nunn,[6] 1958	N_2O, meperidine, relaxants	4.16	1.95- 9.10
*Devine *et al.*,[7] 1958	Halothane	5.59	2.47-10.83
*Nunn and Matthews,[8] 1959	Halothane	4.0	1.9 - 7.8

*Minute volume measured at body temperature and pressure saturated with water vapor.

of ether, anesthetic agents almost invariably cause depression of respiration. Chloroform, halothane, cyclopropane, barbiturates and high concentrations of ether may reduce both tidal volume and frequency. Myoneural blocking agents will almost inevitably lower the tidal volume while narcotics may cause slowing of respiration and or diminution of tidal volume. Trichloroethylene and occasionally halothane may cause tachypnea which is usually associated with a fall in tidal volume.

Since the anesthetist is himself the principal variable in the ventilation of the anesthetized patient, it is of limited value to quote figures from any particular center (table 1). The lower limits in particular will be variable and probably the very act of measurement will exclude the worst cases of underventilation.

Artificial Ventilation. When the anesthetist assumes direct control of ventilation, the minute volume may generally be maintained at any level up to about 20 l./minute. It has been the experience of the author that manual compression of the reservoir bag rarely results in underventilation—typical values observed being 9 (range 4–17) l. m. (BTPS).[6] The minute volume is generally more dependent upon the habit of the anesthetist than the needs of the patient.

Over-all Adequacy of Ventilation. Varying opinions have been expressed upon the ventilation required for elimination of CO_2 during anesthesia. Some consider that a higher relative ventilation is required during anesthesia while others maintain that normal ventilation only is required. A need for hyperventilation has often been due to the re-inhalation of CO_2 which was overlooked in the design of the experiment. Other factors are discussed later in this review, but at this stage it is sufficient to say that, in a number of studies, a ventilation normal for the conscious resting subject has been found to result in an approximately normal arterial P_{CO_2} during anesthesia.[6, 9, 10] Such studies have been confined to reasonably fit patients whose tracheas were intubated and in whom re-inhalation of CO_2 was scrupulously avoided. During thoracotomy, the interference with respiratory function is more complicated, and again there are those who believe a higher relative ventilation is required. The evidence for this is unconvincing and the separate aspects of the problem will be discussed.

The extremes of ventilation commonly permitted during anesthesia result in changes of arterial P_{CO_2} which are less marked than might be expected. Thus a ventilation range of 2.5–10.7 l./m. may result in P_{CO_2} changes which are only within the range 22–65 mm. of mercury.[11] During uncomplicated anesthesia, if the re-inhalation of CO_2 is avoided, it is rare for the arterial P_{CO_2} to lie outside the range 17–70 mm. of mercury. The anesthetist may himself verify that these levels can be tolerated by the conscious subject.

Resistance to Breathing. Unpublished studies by Nunn and Ezi-Ashi have shown that a

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threshold pressure resistor (such as a tight relief valve) may cause a reduction in ventilation in proportion to the threshold pressure to be overcome—respiration occasionally being arrested by a threshold pressure drop as low as 12 cm. of water. On the other hand, flow dependent resistors (such as undersized endotracheal tubes) cause relatively little reduction, due to the low peak gas flows occuring during anesthesia with spontaneous respiration. Thus a resistor corresponding to a 25F endotracheal tube (6.0 mm. bore, 15 cm. long) has been found to cause less than 10 per cent reduction of ventilation in an anesthetised adult. There is ample evidence that even in deep anesthesia, respiratory effort can be augmented in the face of obstruction. The initial response occurs within one respiratory cycle and is clearly independent of changes in the blood gases.[12] In due course there follows a further compensation which is probably due to a raised arterial P_{CO_2}. Ventilation may, of course, also be restricted by unsatisfactory posture on the operating table by pneumothorax or by external pressure on the epigastrium or diaphragm.

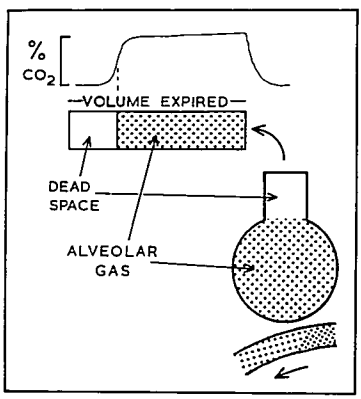

FIG. 1. Diagrammatic representation of the division of expired gas into two components—one from the conducting air passages (anatomical dead space), and the other from the alveoli, in which it has attained equilibrium of P_{CO_2} with the end-pulmonary capillary blood. The plot of CO_2 concentration (at the mouth) against expired volume shows a rise in concentration to the alveolar plateau value after the expiration of a volume equal to that of the anatomical dead space. Thereafter the CO_2 concentration rises gradually in accord with the cyclical changes in CO_2 concentration of the alveolar gas.

Diffusion Respiration. It is well known that, in man, oxygenation may be maintained for long periods in the absence of tidal movement provided that the lungs are in communication with a supply of pure oxygen.[13] For this process diffusion respiration is a misnomer and there is actually a mass movement of oxygen down the trachea. This effectively prevents elimination of CO_2 from the lungs and the arterial P_{CO_2} rises progressively by about 6 mm. of mercury/minute. Tensions in excess of 200 mm. of mercury may easily be obtained and therefore it is probably inadvisable to employ "diffusion" respiration in man for periods of longer than a few minutes.

Anatomical Dead Space

Figure 1 shows the familiar concept of the division of the expired gas into one component from the conducting passages and another from the alveoli. The former contains gas of similar composition to the inspired gas, while the latter contains gas which has reached equilibrium with pulmonary end-capillary blood. As expiration proceeds, the concentration of CO_2 at the mouth rises sharply to the alveolar plateau level after the exhalation of a volume equal to that of the conducting passages. This volume, the anatomical dead space, may be determined by simultaneous measurement of the volume expired and the concentration of a tracer gas at the mouth.[14, 15] Due to mixing at the gas interface, the conducting passages are not *completely* purged of inspired gas until a volume has been exhaled which is equal to approximately double the anatomical dead space. This is termed the kinetic dead space.

Radford [16] has drawn attention to the convenient fact that in normal circumstances the anatomical dead space (ml.) is approximately equal to the weight of the subject (lb.). However, during anesthesia, there are many factors apart from body weight which influence the anatomical dead space.

Posture and Position of the Jaw. It is important to recall that many physiological normal data have been established in the

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sitting or standing position. It is frequently unjustifiable to transfer data from the sitting conscious subject to the supine anesthetised patient and it is quite likely that herein lies the explanation of many of the "abnormal" physiological findings of anesthesia. Fowler [17] recorded the following mean values for the anatomical dead space: sitting, 147 ml.; semi-reclining, 124 ml.; supine, 101 ml.

The position of the head and jaw will also exert an effect upon the volume of the conducting air passages. Protrusion of the jaw into the "sniffing" position—used extensively during anesthesia without endotracheal intubation—increases the anatomical dead space by some 35 ml.[18] Conversely, if the jaw is allowed to fall back until the posterior third of the tongue touches the posterior pharyngeal wall, the anatomical dead space is reduced by about the same amount. Thus the freedom of the airway is in inverse ratio to the volume of the conducting air passages and it is not without danger to hold forward the jaw of a patient with extreme underventilation. Separating the teeth can increase the dead space by 50–100 ml.[15]

Tracheostomy and Endotracheal Intubation. Approximately half the volume of the anatomical dead space lies above a point 6 cm. above the carina—the level commonly reached by an endo-tracheal or tracheostomy tube.[18] Tracheal intubation therefore results in a considerable reduction of dead space and it is not unusual for a patient with respiratory insufficiency to improve dramatically after tracheostomy without resorting to artificial ventilation. Furthermore it should be noted that an endotracheal or tracheostomy tube may be linked to an anesthetic gas circuit with a total apparatus dead space of no more than 25 ml., whereas a face mask may contribute 50–100 ml. of apparatus dead space.[19] Thus the exclusion of the upper airway may reduce the combined anatomical and apparatus dead space by as much as 150 ml.

Artificial Ventilation. The air passages have a distensibility which is little different from that of the alveoli.[20] A high end-inspiratory pressure will therefore tend to enlarge the anatomical dead space. However this effect is small and, during anesthesia, measurements have failed to detect a significant increase during artificial ventilation by intermittent positive pressure when compared with spontaneous respiration.[11, 21] On the other hand, quite large increases in anatomical dead space have been reported during spontaneous respiration at continuous positive pressure.[22]

Drugs and Hypoxia. Severinghaus and Stupfel [23] found a considerable increase in the anatomical dead space following the administration of 0.5 mg of atropine in man. They also found an increase following the administration of hexamethonium and trimetaphan in dogs, while histamine caused a small reduction. Hypoxia resulted in a decrease in the anatomical dead space [21]—an effect which is attributed to bronchoconstriction.

Tidal Volume. At low flow rates, under conditions of laminar flow, gases advance down tubes with a cone front. A tracer gas may therefore appear at the distal end of a tube before all the gas previously lying in it is washed out. During tidal ventilation this means that the effective anatomical dead space is reduced at low flow rates. The reduction in anatomical dead space at low tidal volumes was predicted in 1915 by Rohrer [24] and demonstrated in man by Briscoe, Forster and Comroe in 1954.[25] This effect is of the greatest importance during anesthesia when the tidal volume may be little larger than the total volume of the conducting air passages. During extreme hypoventilation cardiac pulsations may further reduce the effective anatomical dead space, by mixing the alveolar and dead space gas at the end of inspiration.[26] This effect is masked by normal tidal ventilation, but during gross underventilation of an anesthetized patient, it is possible to detect changes in the CO_2 concentration of the gas lying near the carina which are in phase with the heart beat. On occasions, the author has found that, at the commencement of expiration, the gas in the region of the carina has a P_{CO_2} almost as high as that of the end-tidal gas. This implies that the effective anatomical dead space has been reduced practically to zero. In the patient whose trachea is intubated, the reduction in anatomical dead space may be detected when the tidal volume is less than 350 ml.[11] Below this figure the mean anatomical dead space approximates to 0.18 times the tidal volume.

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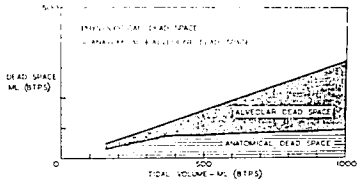

FIG. 2. Values for anatomical and alveolar dead spaces found in healthy, anesthetized intubated subjects.[11] There is no significant difference in this respect between spontaneous respiration and artificial ventilation. Somewhat higher values are found for the alveolar dead space during thoracic surgery.[26]

At higher tidal volumes the increase in anatomical dead space with tidal volume is dependent upon the end-inspiratory lung volume and is of the order of 40 ml. l. tidal volume.[20] The results obtained in anesthetized man by Nunn and Hill [11] are shown in figure 2.

DISTRIBUTION

It is now necessary to consider the gas exhaled after the conducting passages have been purged. Figure 1 suggests that this gas is of uniform composition and in equilibrium with arterial blood. However, during anesthesia this is not true. As in emphysema, an appreciable part of the inspired gas passes to alveoli which are relatively or totally unperfused. Furthermore, it may happen that part of the pulmonary blood flow may pass through alveoli which are relatively or totally unventilated. The effects of these two phenomena on CO_2 elimination are quite different and may best be considered separately.

Ventilation of Underperfused Parts of the Lungs. On the left of figure 3 (after Comroe [27]), is seen an 'ideal' alveolus which is correctly ventilated and perfused. The P_{CO_2} of the gas within this alveolus is identical to that of end-pulmonary capillary blood. In the middle of the figure is seen an alveolus which is ventilated but deprived of its blood supply. It therefore contains gas with only a low P_{CO_2}. (The CO_2 in it is inhaled from the conducting passages having been exhaled by the 'ideal' alveolus during the previous respiratory cycle.) It is at once apparent that the unperfused alveolus cannot directly influence the composition of the arterial blood to which it makes no contribution. Nevertheless, respiratory function is impaired by the wasted ventilation of the unperfused alveolus which constitutes respiratory dead space no less than do the conducting air passages. In the upper left hand corner of figure 3 is seen a compartmented sample of expired gas. This consists of three components—first gas from the anatomical dead space, then gas from the 'ideal' alveolus and the unperfused alveolus. The latter components are exhaled more or less simultaneously and will be completely mixed by the time they have reached the mouth. Severinghaus and Stupfel [28] have termed the component from the unperfused alveoli the *Alveolar dead space* which, together with the *anatomical dead space*, comprises the total effective dead space—now generally termed the *physiological dead space.*

The ventilation of unperfused alveoli causes certain well defined effects. Firstly, for a given minute volume, the alveolar ventilation will be reduced. Theye and Fowler [29] have, in fact, ligated the pulmonary artery of an anesthetized dog and demonstrated the marked rise in arterial P_{CO_2}. For homeostasis of the arterial P_{CO_2} it is therefore necessary to increase the minute volume if there is ap-

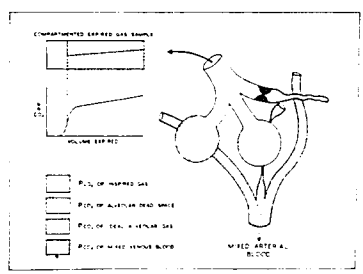

FIG. 3. Diagrammatic representation (after Comroe [27]) of three alveoli which are, from left to right: correctly ventilated and perfused ('ideal'), ventilated but not perfused (dead space effect), and perfused but not ventilated (shunt effect). The intensity of the shading indicates the P_{CO_2} as shown in the key. The physiological dead space is the sum of the volume of the conducting passages (anatomical dead space) and the ventilation of the unperfused alveoli (alveolar dead space). The alveolar plateau of CO_2 concentration slopes rather more steeply than the normal (fig. 1) because the overventilated alveoli tend to empty first.

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preciable ventilation of unperfused alveoli. Secondly, during expiration, the 'ideal' alveolar gas in an expired gas sample will be diluted with gas from the alveolar dead space. Therefore the P_{CO_2} of the end-tidal gas will be lower than that of the 'ideal' alveolar gas. Under these circumstances, it is quite impossible to obtain a sample consisting of pure 'ideal' alveolar gas although its P_{CO_2} may be derived indirectly from that of the arterial blood to which it closely approximates.[30] Thus, it is possible to demonstrate a significant arterial to end-tidal P_{CO_2} difference when there is ventilation of unperfused alveoli. Normally the difference is too small to detect with the analytical methods at our disposal. The existence of an arterial to end-tidal P_{CO_2} difference is of importance for two reasons. Firstly, it is the simplest method of detecting the presence of an alveolar dead space. Secondly, a correction is required if we wish to deduce the arterial P_{CO_2} from analysis of the end-tidal gas with either an infrared analyzer or an end-tidal sampler used in conjunction with a slow method of analysis.[31]

The measurement of the alveolar dead space requires the simultaneous determination of the anatomical and physiological dead space. Subtraction will then indicate the alveolar dead space if present. Reference has already been made to a suitable method for the determination of the anatomical dead space.[14, 15] The physiological dead space, according to the definition used in this review, is measured by the solution of Bohr's equation using the P_{CO_2} of the arterial blood as suggested by Enghoff [32] in 1938.

It is well known that there is a large alveolar dead space in emphysema [33] and it will clearly be present in regional obstruction of the pulmonary circulation—as by air emboli.[28] In anesthetized man, however, the first suggestion of maldistribution was the demonstration of a significant arterial to end-tidal P_{CO_2} difference by Severinghaus, Stupfel and Bradley.[34] This was confirmed by Ramwell [35] and by Nunn and Hill,[11] who also measured the alveolar dead space simultaneously and showed that there was a significant positive correlation with the arterial to end-tidal P_{CO_2} difference.

All workers seem agreed that in a healthy anesthetised man, the mean arterial to end-tidal P_{CO_2} difference is of the order of 5 (S.D. 2.5) mm. of mercury. It is not apparently influenced by the tidal volume or the arterial P_{CO_2}, and it does not depend on whether respiration is spontaneous or artificial. It is, however, slightly higher during thoracotomy [36] when there are various additional causes of maldistribution. It would appear that the arterial P_{CO_2} may be derived from the end-tidal P_{CO_2} with sufficient accuracy for most clinical purposes in patients with normal distribution. However, if the patient has emphysema, there might be a very large arterial to end-tidal P_{CO_2} difference which could be unsuspected. Herein lies the greatest disadvantage of monitoring P_{CO_2} by means of the end-tidal sample.

Values for the alveolar dead space in anesthetised man have been reported by Nunn and Hill [11] and are represented in figure 2. The values accord well with those found in anesthetized dogs.[21] The physiological dead space was found to be a function of tidal volume and for nonthoracic operations the mean value was 0.32 times the tidal volume for the healthy patient whose trachea was intubated. This is convenient since it follows that the alveolar ventilation is a constant fraction (0.68) of the minute volume. The alveolar ventilation may therefore be derived from the minute volume without attempting to compute a value for the anatomical dead space. The physiological dead space is influenced by whether respiration is spontaneous or artificial only in so far as it is dependent upon tidal volume. A slightly larger physiological dead space is found during thoracotomy [36] and there is some evidence that it increases with the duration of anesthesia.[37] It will, of course, be larger in old age and with emphysema.[33] Cooper [38] has found that the physiological dead space may occupy as much as two thirds of the tidal volume during anesthesia.

In the absence of such conditions as pulmonary embolism the cause of the alveolar dead space in anesthetized man is obscure. It is unlikely that it is due to a spread of the normal spatial scatter of ventilation-perfusion ratios, since it is not invariably associated with increased venous admixture.[10] It is possible

that it is due to the ventilation of parts of the lung which are deprived of their blood supply. Posture alone may render the uppermost parts of the lung avascular and it is almost certainly true that the perfusion of the lingula and right middle lobe is minimal during anesthesia in the supine position. However, it may well be that subtle regional disturbances of pulmonary vasomotor control are responsible for the defect in distribution.

The simplified discussion based on figure 3 should not be taken to imply that in fact certain alveoli are totally unperfused. It is more likely that there are regions of relative underperfusion, but they can still be quantified as though alveoli were sharply divided into those perfused and those unperfused.

Perfusion of Underventilated Part of the Lungs. On the right of figure 3 is shown an alveolus which is perfused but not ventilated. This allows venous blood to enter the pulmonary veins and so constitutes a shunt or venous admixture which results in an alveolar to arterial P_{O_2} difference. This effect may be present during anesthesia if there is airway occlusion due to bronchial obstruction by secretions, misplaced endotracheal tubes or kinking of the bronchi during thoracotomy. It is also possible that alveoli may be relatively underventilated. A raised alveolar to arterial P_{O_2} difference has been found in some but not all of two series of anesthetized patients whose lungs were ventilated artificially.[10, 29]

Although venous admixture, causes a marked reduction in the arterial P_{O_2}, this is largely due to the low slope of the upper reaches of the oxyhemoglobin dissociation curve. The effect on the arterial P_{CO_2} is much less marked. The normal arterio-venous P_{CO_2} difference is only 6 mm of mercury and therefore a venous admixture as much as 50 per cent of the cardiac output would raise the arterial P_{CO_2} by only 3 mm. of mercury—a difference which would not be easy to detect with existing methods for the determination of arterial P_{CO_2}. Theye and Fowler [29] have obstructed one bronchus of an anesthetized dog and found only negligible increase in P_{CO_2} of the arterial blood—total ventilation being maintained at the same level. However, this may in part be due to reflex reduction in perfusion of the non-ventilated lung.

It would thus appear that for practical purpose we can dismiss regional underventilation from a consideration of the factors affecting the elimination of CO_2 from the lungs. This is not to say that it is unimportant, since it interferes considerably with the oxygenation of the arterial blood and may well proceed to frank atelectasis. It should be noticed in passing that the failure of regional underventilation to cause a significant increase in the arterial P_{CO_2} is the basis of the indirect determination of the 'ideal' alveolar P_{CO_2} by analysis of the arterial blood. This concept, formulated by Riley and associates has been the foundation of much recent investigation of pulmonary function.

Inhaled Carbon Dioxide

With a fixed alveolar ventilation, the presence of CO_2 in the mixed inspired gas will increase the alveolar P_{CO_2} additively above the tension it would have reached if the inspired gas were free from CO_2. Thus if ventilation is held constant at a level which will result in an arterial P_{CO_2} of 40 mm. of mercury when the inhaled gas is free from CO_2, then the inhalation of a gas with P_{CO_2} 10 mm. of mercury will raise the arterial tension to 50 mm. of mercury. If the P_{CO_2} of the inspired gas is higher than that of the mixed venous blood then there will be a net CO_2 uptake rather than the usual output. The inhalation of 10 per cent CO_2 results in a CO_2 uptake which continues for several minutes until the mixed venous P_{CO_2} is higher than that of the inspired gas.

During anesthesia, CO_2 of either endogenous or exogenous origin may be inhaled. This may be intentional or, on the other hand, may be quite unsuspected by the anesthetist. At the outset we may discount the significance of the origin of the CO_2 except that if it is endogenous, then the rate of increase of the arterial P_{CO_2} will be unlikely to exceed 6 mm. of mercury per minute even with total rebreathing. The inhalation of exogenous CO_2 can cause a very rapid increase in the arterial P_{CO_2}. The inhalation of 30 per cent CO_2 (Meduna [40]) is associated with a rise of arterial P_{CO_2} of the order of 140 mm Hg in less than one minute.

The effect of the inhalation of CO_2 upon

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the elimination of the gas depends to a large extent upon the respiratory response. During artificial ventilation, no response is usually possible. The conscious subject breathing spontaneously responds vigorously up to high concentrations of CO_2 (20 per cent) in the inhaled gas. However, during anesthesia with spontaneous respiration the response is diminished but still present.[41]

The inhalation or re-inhalation of CO_2 during anesthesia is deliberately employed for many different reasons. The stimulation of respiration will accelerate the uptake or elimination of volatile agents. Intermittent stimulation with CO_2 is valuable to offset the tendency towards atelectasis due to prolonged quiet breathing without change of posture. Inhalation of CO_2 will generally elevate the blood pressure although this may usually be achieved by more satisfactory methods. A novel indication for CO_2 inhalation has arisen from the introduction of deep hypothermia with body temperatures of less than 20 C.[42] At these low temperatures, the CO_2 production practically ceases and gross CO_2 depletion results from the gentle pulmonary ventilation required to prevent atelectasis. If the lungs are ventilated with 5 per cent CO_2 in oxygen, the arterial P_{CO_2} will be maintained slightly above 35 mm. of mercury. It should perhaps be stressed that there is as yet no general agreement on whether the arterial *p*H, P_{CO_2} or plasma $[HCO_3^-]$ should be maintained constant during hypothermia. It is inevitable that one or more parameters must deviate considerably from the normal.

Hypothermia *per se* would appear to offer no barrier to the elimination of CO_2. Unpublished observations by the author revealed normal values for the physiological dead space at 29 C. It was therefore not surprising that moderate overventilation was found to result in considerable reduction of the arterial P_{CO_2}. Minute volumes of 8.50 and 12.40 l./m. (BTPS) resulted in arterial P_{CO_2} of 14.3 and 9.6 mm. of mercury respectively (corrected for patients' body temperature).

There are many reports of respiratory measurement during anesthesia in which a high arterial P_{CO_2} is associated with hyperventilation. Most of these studies give little information as to the gas circuit employed and assuming that the various measurements are reasonably accurate, one is driven to the conclusion that unsuspected re-inhalation of CO_2 was taking place. Indeed the only other possible explanation is that large areas of the lung were inexplicably deprived of their blood flow.

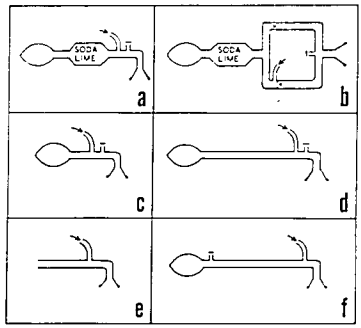

FIG. 4. Gas circuits commonly used in Great Britain which may result in rebreathing of CO_2. All can be unsatisfactory during spontaneus respiration but circuit *f* is less so during artificial ventilation.

The elimination of CO_2 from anesthetic circuit is discussed at length elsewhere in this symposium. However, the practice in the United States and Great Britain differs considerably, and figure 4 shows those circuits in current use in Great Britain which commonly permit the re-inhalation of CO_2. Circuits *a* and *b* both pass the expired gas twice over soda lime: this must inevitably introduce an apparatus dead space for CO_2 in the connections to the canister on the side of the patient. Furthermore this dead space will increase as the proximal soda lime becomes exhausted. Evans [43] in 1938 was perhaps the first to draw attention to the disadvantage of passing the gases to-and-fro over the soda lime, and since that date many authors have confirmed his findings. It should, however, be mentioned that these objections are applicable only under conditions of low fresh gas flow. With a high flow (7 l./m.) circuit *b* in particular is perfectly satisfactory and the performance is little impaired by omitting to charge the canister. Circuits *c*, *d*, *e* and *f* have been considered by Mapleson [44] who

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suggested that, to prevent rebreathing, all required a gas flow in excess of the patient's minute volume. Practical studies [15, 16] have confirmed Mapleson's reasoning. Recently, however, attention has been drawn to the fact that these considerations only apply during spontaneous respiration, and, in fact, circuit *f* is satisfactory during artificial ventilation (D. Waters, personal communication).

Figure 5 shows three gas circuits which are effective in preventing rebreathing. Circuit *a* (The Magill attachment) is extensively used in Great Britain and there is little doubt that rebreathing is prevented during spontaneous respiration when the fresh gas flow rate is at least as great as the minute volume.[44, 45, 46] Furthermore, Mapleson has shown that should rebreathing occur the alveolar ventilation will equal the fresh gas flow rate.[47] Circuit *b* ensures that the inhaled gas will be a mixture of fresh gas and expired gas which has traversed the length of the canister. There is abundant evidence that the inhaled CO_2 concentration should be effectively zero. Finally circuit *c* must preclude any possibility of rebreathing provided that the valves are competent.

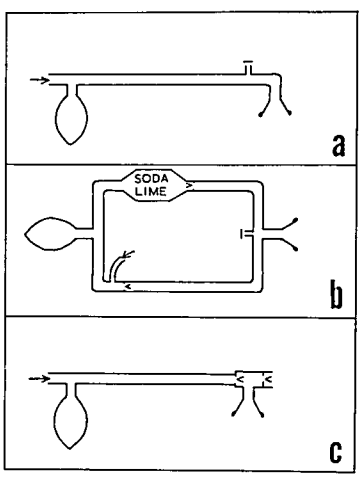

FIG. 5. Gas circuits commonly used in Great Britain which will normally prevent the rebreathing of CO_2. Circuit *a* is not satisfactory during artificial ventilation.[56]

It should be stressed that, in the quantification of the effect of rebreathing, it is the mean inspired CO_2 concentration which is important rather than the minimum—the value indicated by the dip of the tracing of a rapid CO_2 analyzer sampling at the mouth. The mean CO_2 concentration of the inhaled gas is difficult to determine and in fact requires the simultaneous recording of inspired volume and instantaneous CO_2 concentration with subsequent determination of the mean with respect to volume (the mean being represented by the height of a rectangle of length corresponding to the tidal volume and whose area is equal to that under the curve of CO_2 concentration plotted against inspired volume).

Before leaving the subject of inhaled CO_2 concentration it is of interest to consider the retention of CO_2 which is a common feature of anesthesia with cyclopropane without assisted respiration. There would appear to be three factors which all contribute to the same end. Firstly, cyclopropane may cause respiratory depression which is disproportionate to the depth of anesthesia; this is especially true if a preanesthetic narcotic has been given. Secondly, it is frequently administered with an inhaled oxygen concentration of over 80 per cent. Under these conditions, cyanosis develops only in the presence of the most extreme underventilation and therefore there is no visual warning of moderate underventilation. Finally, cyclopropane is frequently administered in the gas circuits *a* and *b* shown in figure 4, with minimal flows of the fresh gas mixture. Under such conditions the mean inspired CO_2 concentration is generally in excess of 2 per cent.

The Steady State

Carbon dioxide differs from oxygen in that large stores of it exist in the body. Therefore, changes in tension are accompanied by the transfer of large quantities of CO_2 into or out of the body—a process which inevitably takes time. Following a step change of ventilation the new level of P_{CO_2} is attained eight times as slowly as for P_{O_2}, half change taking place in about four minutes.[48] During re-equilibra-

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tion at a new P_{CO_2}, the CO_2 output may differ markedly from the rate of metabolic production. In equilibrium, the arterial P_{CO_2} is determined by CO_2 production, alveolar ventilation and inhaled CO_2 concentration. But at all times, whether in equilibrium or not, the arterial P_{CO_2} is determined by CO_2 *output*, alveolar ventilation and inhaled CO_2 concentration.

Figure 6 indicates the time course of changes in arterial P_{CO_2} and CO_2 output following step changes in alveolar ventilation. It will be apparent that the system is closely analogous to a simple integrating circuit—the arterial P_{CO_2} being represented by the charge on the capacitor and (CO_2 output–CO_2 production) by the current flowing through the resistor. In figure 6 it is assumed that the slope of the whole body dissociation curve is 100 ml. CO_2/mm. of mercury P_{CO_2} and that the changes are exponential with a half change time of four minutes.[48]

During artificial ventilation with a mechanical ventilator, it is possible to achieve a reasonably steady respiratory state. However, during spontaneous respiration or manual artificial ventilation, there is usually a continual passage of CO_2 into and out of the body stores—clearly shown by the wide variation in values for CO_2 output recorded by Elam and Brown.[49] Since the arterial P_{CO_2} is governed by output rather than by metabolic production, the unsteady state is a serious handicap to predictions of arterial P_{CO_2} from ventilation and probable metabolic rate.

Quantification *

By a rearrangement of the Bohr equation, the CO_2 output may be expressed as follows:

$$\dot{V}_{CO_2} = (F_{ACO_2} - F\bar{i}_{CO_2})(\dot{V} - f.V_D). \quad (1)$$

Provided that: All gas volumes are measured under the same conditions of temperature and pressure,† and corresponding definitions apply

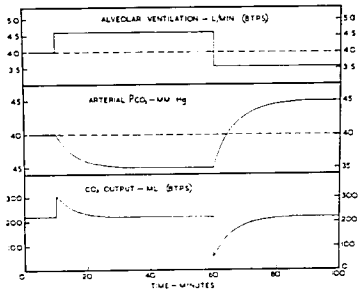

Fig. 6. Time course of changes in arterial P_{CO_2} and CO_2 output, following the step changes in alveolar ventilation shown at the top. It is assumed that the slope of the whole-body CO_2 dissociation curve is 100 ml./mm. of mercury and that the function attains half value in four minutes.[48]

to "alveolar" and "dead space." It is, however, generally more useful to arrange the equation with the alveolar CO_2 concentration on the left hand side thus:

$$F_{ACO_2} = \frac{\dot{V}_{CO_2}}{\dot{V} - f.V_D} + F\bar{i}_{CO_2}. \quad (2)$$

If by "alveolar" is meant 'ideal' alveolar, then the corresponding dead space is the physiological dead space according to its definition in this paper, and $P_{ACO_2} = Pa_{CO_2}$. Therefore:

$$Pa_{CO_2} = (P_B - P_{HOH})\left(\frac{\dot{V}_{CO_2}}{\dot{V} - f.V_D} + F\bar{i}_{CO_2}\right). \quad (3)$$

That is to say that the arterial P_{CO_2} is determined solely by the dry barometric pressure (P_B–P_{HOH}), the CO_2 output ($\dot{V}_{CO_2}$), the alveolar ventilation ($\dot{V}$–f.V_D) and the mean CO_2 concentration of the inhaled gas ($F\bar{i}_{CO_2}$). If it is accepted that the alveolar ventilation is a constant fraction (1–X) of the minute volume, then the equation can be further simplified thus:

$$Pa_{CO_2} = (P_B - P_{HOH})\left(\frac{\dot{V}_{CO_2}}{X.\dot{V}} + F\bar{i}_{CO_2}\right). \quad (4)$$

Prediction of the Arterial P_{CO_2} from Ventilation

Direct determination of the arterial or even the end-tidal P_{CO_2} will probably always be

* In this section symbols are in accord with the recommendations of the committee for standardisation of definitions and symbols in respiratory physiology headed by Pappenheimer (1950).[50]

† Although it is customary to express $\dot{V}_{CO_2}$ under standard conditions of temperature and pressure dry, it is more convenient for the present purpose to convert the volume to body temperature and pressure saturated.

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more difficult than measurement of the ventilation. It is, therefore, tempting simply to measure the ventilation and predict the arterial P_{CO_2}. Perhaps the converse is of greater value —to predict the ventilation required to maintain a normal P_{CO_2}.

The success of prediction depends upon ascribing values to the various terms on the right hand side of equations 3 or 4. Generally, P_B, and P_{H_2O} present no problem. Also, under the circumstances in which a prediction is made, F_{CO_2} will generally be zero. The problem therefore devolves on ascribing values for CO_2 output and alveolar ventilation.

The most notable contribution in this field has been that of Radford.[16] His familiar nomogram is designed for prediction of correct tidal volume given body weight, sex and respiratory frequency. However, the nomogram was not designed primarily for anesthesia and accordingly there is no correction for the reduction in carbon dioxide output during anesthesia demonstrated in 1851 by John Snow [51] and since confirmed by others.[8, 10, 52, 53, 54] Radford also used constant values for the anatomical dead space whereas it is apparent that, during anesthesia, the physiological dead space should be used since it is by no means constant and may differ widely from the anatomical. Nevertheless, it happens that these factors largely cancel one another and in practice the nomogram shows no serious systematic error when applied to anesthetized patients.[9, 55] In fact, a method of prediction based specifically on data from anesthetized patients has been found no more accurate for prediction of correct ventilation although perhaps more suitable for prediction of arterial P_{CO_2} during the abnormal ventilation which is commonplace during anesthesia.[55] This method is based on prediction of the CO_2 output (presumed to be 14 per cent below basal with a respiratory exchange ratio of 0.82) and interpolation in the appropriate curve on a plot of arterial P_{CO_2} against alveolar ventilation (fig. 7). Additional abscissae are provided for minute volume on the assumption that the alveolar ventilation is 0.7 times the minute volume during extrathoracic surgery,[11] and 0.65 times the minute volume during thoracic surgery.[56] No correction was made for the increase in metabolism and the loss of CO_2 from the pleura which have been reported in anesthetized dogs with an open pneumothorax.[57] Fortunately these effects would appear likely to cancel one another to a large extent, probably resulting in no great change in the CO_2 output by the conventional route.

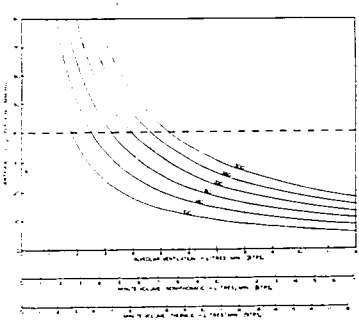

FIG. 7. Relationship between arterial P_{CO_2} and alveolar ventilation for different values of CO_2 output (ml. BTPS). Additional scales along the abscissa show minute volume as explained in the text. (Reproduced by permission of *Anesthesia*.)

The value of predictions during anesthesia is severely limited by certain circumstances which cannot easily be avoided. During spontaneous respiration, the ventilation is usually changing from minute to minute. Therefore the CO_2 output is constantly fluctuating about the rate of metabolic production and, over a short period, may introduce a larger error into the prediction of the arterial P_{CO_2}. Nevertheless prediction of the correct long term ventilation for CO_2 homeostasis is valid. During thoracotomy, the respiratory dead space is subject to wide variations dependent upon the retraction of the expired lung and other activities of the surgical team.[56] Under these circumstances therefore, prediction of the arterial P_{CO_2} or even of the correct ventilation is of limited value. Nevertheless the variations in physiological dead space are not gross and in uncomplicated thoracic surgery prediction of arterial P_{CO_2} from figure 7 has yielded negligible systematic error and a standard deviation of error of under 6 mm. of mercury.[55] Radford's nomogram also shows little systematic error during thoracic surgery but a comparable random error. As a general rule it would ap-

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TABLE 2

TYPICAL VALUES FOR VENTILATION AND ARTERIAL P_{CO_2} WHILE CONSCIOUS AND WHILE ANESTHETIZED. ARTIFICIAL VENTILATION IS MAINTAINED AT THE LEVEL FOUND IN THE CONSCIOUS SUBJECT WHILE SPONTANEOUS RESPIRATION IS AT A LEVEL TYPICAL OF A PATIENT ANESTHESIZED WITH AN AGENT OTHER THAN ETHER

	Conscious and Basal	Anesthetized and Trachea Intubated		
		Artificial ventilation		Spontaneous Respiration
		Extra-Thoracic Surgery	Thoracic Surgery	
CO_2 output, ml./m. (BTPS)	230	195	195	195
Tidal volume, ml. (BTPS)	420	420	420	240
Resp. frequency, BPM	15	15	15	17
Minute volume, ml./m. (BTPS)	6,300	6,300	6,300	4,100
Dead space, ml. (BTPS)				
Anatomical	140	65	65	45
Alveolar	0	75	85	35
Physiological	140	140	150	80
Apparatus	0	30	30	30
Total	140	170	180	110
Alveolar ventilation, ml./m. (BTPS)	4,200	3,750	3,600	2,200
Arterial P_{CO_2}, mm.Hg	39	37	39	63

Barometric pressure is 760 mm.Hg and the patient's body temperature 38 C.

pear that during thoracic surgery normal arterial P_{CO_2} may be maintained by a minute volume close to that of the patient when conscious and resting provided that there is no rebreathing of CO_2 or excessive apparatus dead space. Finally, during automatic artificial ventilation with the chest closed, the results of prediction are satisfactory. Carbon dioxide output, in due course, lies close to the rate of metabolic production and the physiological dead space may be predicted with considerable accuracy.

SUMMARY

To summarize a subject as extensive as CO_2 elimination, it is perhaps best to tabulate typical ventilatory data for a patient—first while conscious, then when anesthetized (table 2). During anesthesia with artificial respiration, ventilation is maintained at the level found while conscious. During anesthesia with spontaneous respiration, ventilation is typical of a patient anesthetized with an agent other than ether.

The value for the arterial P_{CO_2} suggested in table 2 during anesthesia with spontaneous respiration, is rather higher than that found in practice. The discrepancy has a two-fold origin. Firstly, many observations have been made during the first 40 minutes of anesthesia when the CO_2 output is still less than the rate of metabolic production. Secondly, the use of an infrared CO_2 analyzer, sampling continuously from the lower end of an endotracheal tube, will tend to wash out the apparatus dead space during the post-expiratory pause. Under these conditions, one would expect an arterial P_{CO_2} of 55 instead of 63 mm. of mercury.

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