THE ROLE OF CARBON DIOXIDE IN ANAESTHESIA*

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DUNCUM in her book "The Development of Inhalation Anaesthesia" (1) states that carbon dioxide was the first gaseous anaesthetic used surgically and mentions that Hickman performed surgical operations on animals under the influence of carbon dioxide as early as 1824. Recently, a large meat-packing organization introduced the novel procedure of using 30 per cent carbon dioxide as an inhalational anaesthetic for hogs, thereby reducing the noise, confusion, labour, and time required in slaughtering operations (2)

Be that as it may, carbon dioxide today plays a very important role in modern anaesthesia. I would like to spend a few moments reviewing with you some of the physiology of carbon dioxide. CO_2 is the most important end-product of tissue metabolism. As such, CO_2 is constantly being produced by the cells, and is carried by the blood to the lungs for excretion. In the blood, CO_2 exists in three forms: (1) as free carbon dioxide, which is dissolved in the water of the blood, (2) as bicarbonate of the plasma, and (3) as carbamino compounds in combination with haemoglobin The amount of free dissolved carbon dioxide determines the tension or partial pressure of the gas. It is the difference in partial pressure of CO_2 which is responsible for CO_2 transport

For example, the CO_2 tension of the body cell is greater than that in the capillary blood, thus CO_2 moves into the blood. Similarly, the partial pressure of CO_2 in mixed venous blood, $P\bar{v}CO_2$ (3) (normally 46 mm Hg) is greater than that in the alveoli of the lungs, $PACO_2$ (normally 40 mm. Hg). Thus CO_2 leaves the blood, enters the alveoli, and is subsequently exhaled The $PACO_2$ is therefore maintained at a constant level and this value is the same as in the arterial blood The partial pressure or tension of CO_2 in the arterial blood is referred to as the $PaCO_2$

It is well known that the pH of the blood is maintained at 7 40 despite the constant production of acid metabolites. This is because of the presence of various buffers in the blood, of which the bicarbonate buffer is the most important, both because of its high concentration and because of its ease of alteration. The body pH is maintained at 7.40, then, because of the constancy of the buffer ratio bicarbonate/carbonic acid which is normally 20/1 In the laboratory, one can use the Henderson-Hasselbalch Equation (4) to calculate $PaCO_2$:

$$pH = 6\,1 + \log \frac{(H\,CO_3'p)}{0.0301\,PaCO_2}.$$

As may be seen, a decrease in this ratio will lead to a decrease in pH. This acidosis may be due either to a decrease in the plasma bicarbonate ion concentration or, on the other hand, to an increase in the $PaCO_2$.

*Presented at the Tenth Annual meeting of the Canadian Anaesthetists' Society, Western Divisions, Regina, Sask , April 21–3, 1955

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If the major change is a decrease in plasma bicarbonate ion concentration, as, for example, in diabetic acidosis, the buffer ratio and, thus the pH, will decrease. This is referred to as *metabolic acidosis.*

When the $PaCO_2$ increases, with the bicarbonate ion concentration remaining about the same, the ratio decreases and so does the pH. This is referred to as *respiratory acidosis.*

In health, therefore, the maintenance of a constant pH depends upon our keeping the $PaCO_2$ at a normal level, which in turn depends upon the adequate elimination of CO_2 by the lungs. This now brings us to a consideration of ventilation.

The tidal volume, or the volume of gas moved in and out of the lungs with each breath, can be divided into two parts. Some of the gas never reaches the alveoli, but remains in the bronchi, trachea, and oropharynx. This gas occupies the dead space volume, so named because as far as respiration is concerned, it is dead or useless—it does not undergo gas exchange The other and important part of the tidal volume is that portion which does reach the alveoli of the lungs and which undergoes gas exchange, that is, the removal of CO_2 and the uptake of oxygen.

The control of respiration is both chemical and nervous. The chemical control is the $PaCO_2$, which acts directly on the respiratory centre in the medulla. If the $PaCO_2$ of a normal patient rises, the respiratory centre is stimulated This results in an increase in ventilation and greater CO_2 elimination. The $PaCO_2$ is thus returned to its normal value of 40 mm. Hg. Hypoxaemia, or a low partial pressure of oxygen (PaO_2), is also a stimulus for increased ventilation, but it brings about its effect by a different route—by acting on the chemoreceptors of the carotid and aortic bodies and then reflexly influencing the respiratory centre. However, in cases of asphyxia, in which the PaO_2 is decreased and the $PaCO_2$ is increased, the hypoxaemic stimulus plays an insignificant role in the resultant increased ventilation. It is the elevated $PaCO_2$ which stimulates ventilation. A $PaCO_2$ rise of 5 mm. Hg. will result in increased ventilation. However, the PaO_2 would have to decrease by about 60 mm. Hg. from a normal value of 100 mm. Hg to about 40 mm. Hg. before hypoxaemia would stimulate ventilation. This would correspond to breathing 12 per cent instead of 21 per cent oxygen, or breathing air at an altitude of 13,000 feet.

Thus, we breathe primarily to get rid of carbon dioxide. We must maintain an adequate alveolar ventilation to keep our $PaCO_2$ and pH at normal levels. A decreased alveolar ventilation, from whatever cause, will result in an elevated $PaCO_2$—hypercapnia, and a decrease in pH—respiratory acidosis.

From the respiratory point of view, the aim of the anaesthetist should be to maintain normal respiration. This implies normal gas exchange, both for oxygen and carbon dioxide, and can only be accomplished by adequate alveolar ventilation.

Let us now consider the state of the respiratory gases in the alveoli of the lungs a few minutes after a patient has been breathing a high concentration of oxygen The nitrogen in the lungs will be washed out and the alveolar oxygen tension (P_AO_2) will rise from 100 mm. Hg. to about 600 mm. Hg On the basis of a

functional residual volume of 2500 cc., some 1800 cc. of oxygen could be absorbed before the P_AO_2 would fall to its previous level of 100 mm. Hg.—if no additional ventilation took place. Thus the oxygen needs in such a patient could be supplied for at least ten minutes or longer—in the absence of any additional ventilation.

However, within a few seconds the alveolar CO_2 tension would become equal to that of the mixed venous blood and accumulation of the CO_2 would begin in the blood and tissues. This example stresses the importance of an adequate alveolar ventilation.

Let us now consider a patient who has a dead space of 150 cc., tidal volume of 600 cc., and a respiratory frequency of 14/minute. His alveolar ventilation per breath is 600—150 or 450 cc. and his alveolar ventilation per minute is 450×14, or 6300 cc. An anaesthetic mask is now applied which has a dead space of 150 cc. His minute alveolar ventilation will be $(600—150—150) \times 14$, or 4200 cc., if frequency and tidal volume remain the same. Therefore, with the same minute volume of expired air ($600 \times 14 = 8400$ cc.) the addition of the anaesthetic mask has reduced his alveolar ventilation by 30 per cent.

The tidal volume usually increases to compensate for this added dead space in an attempt to maintain a constant alveolar ventilation. In this patient the tidal volume would have to be 750 cc. (an increase of 25 per cent) to maintain the same alveolar ventilation, if respiratory frequency were unchanged.

Anaesthetic agents are known depressants of central nervous system function. The respiratory centre is also depressed, and this is important for two reasons. In the first place, these agents will decrease ventilation with a resultant rise in $PaCO_2$ and respiratory acidosis. Secondly, the sensitivity of the respiratory centre will be lowered, so that the elevated $PaCO_2$ loses its effectiveness as a stimulus to increase the ventilation.

It has been well documented that a small decrease in minute ventilation volume occurs in modern anaesthesia, and the resultant decrease in alveolar ventilation will cause the $PaCO_2$ of the blood, and thus of the body cells, to become elevated when respiration is unassisted The $PaCO_2$ may rise to narcotic levels and values of 100 mm Hg and over have been recorded.

Buckley (5) studied 31 non-thoracic cases during cyclopropane anaesthesia. In 15 cases in which respiration was unassisted, the average $PaCO_2$ at the end of anaesthesia was 85 mm. Hg. (equivalent to 12.3 per cent CO_2), more than twice the normal value and with a range of 55 to 150 mm. Hg. (8–20 per cent). In 16 cases in which respiration was assisted, the rise in $PaCO_2$ was much less, the average highest $PaCO_2$ being 47 mm. Hg. (6 8 per cent).

In one series of pneumonectomies (6) with the patient in the lateral position and performed with respiration unassisted, the $PaCO_2$ rose from 35 to 98 mm. Hg. When a similar operation was done in the prone position, using an Overholt table, the $PaCO_2$ rose to only 47 mm. Hg. Other investigators have shown the value of assisted, controlled or artificial respiration and have been able to keep the $PaCO_2$ from rising during a pneumonectomy.

Inadequate alveolar ventilation during anaesthesia may be due to several factors. Impaired function of the respiratory centre by preoperative and anaesthetic drugs and the effect of position have been mentioned. Other factors which

must be considered are: the use of relaxants, the presence or absence of pulmonary collapse, obesity, operations on the open chest, the Trendelenburg and prone positions, and the use of kidney or gall bladder rests. Most of these factors are important in thoracic operations, while others play an important role in non-thoracic cases.

What are the deleterious effects of hypercapnia during anaesthesia? If the $PaCO_2$ is allowed to rise during anaesthesia, there may be a considerable delay in the patient's return to consciousness. Similarly, it may take a few hours before the respiratory acidosis is relieved, and the $PaCO_2$ returns to normal. Brown and co-workers (7) at Minnesota described severe electrocardiographic changes in dogs after release from high CO_2 tensions. Eleven of these fifteen animals developed ventricular fibrillation.

Assisted respirations, therefore, are frequently necessary during anaesthesia to maintain an adequate alveolar ventilation so that the $PaCO_2$ does not rise and so that respiratory acidosis does not occur.

This reminds me of a quotation I heard a Professor of Anaesthesia once make. He said, "Look on acidosis like sin; be against it."

I would now like to say a few words about the syndrome of CO_2 narcosis, a condition which we are recognizing more and more in the patient with severe respiratory insufficiency. Ventilation tracings of a normal individual and of a patient with chronic pulmonary emphysema are shown in Figures 1 and 2.

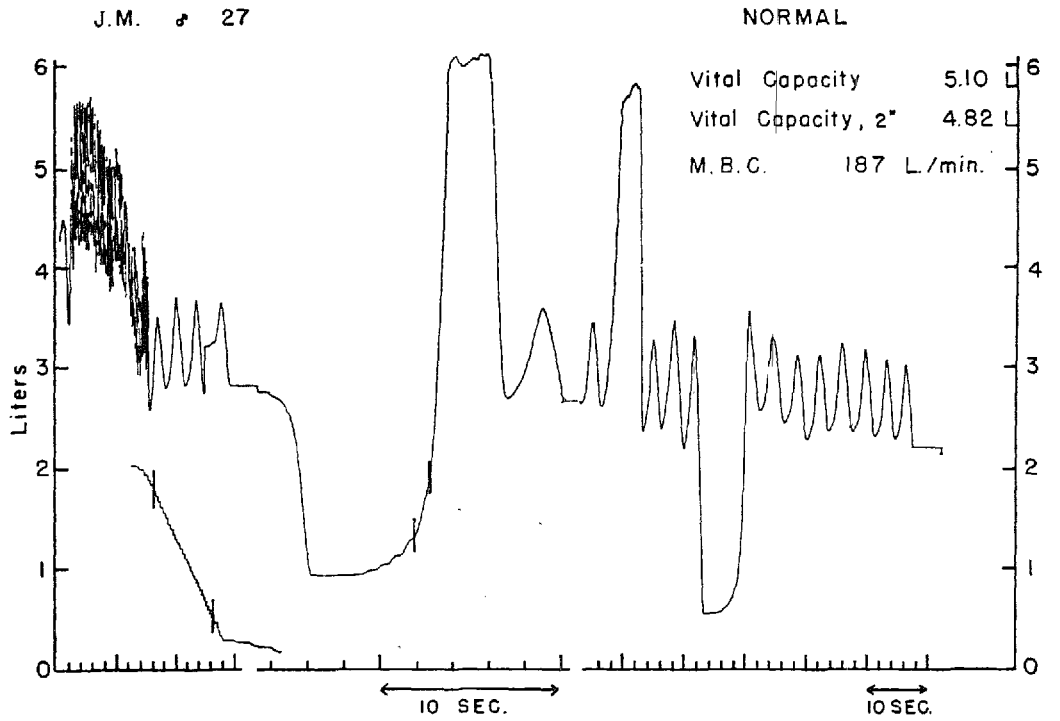

FIG. 1—*Normal Ventilation Tracing.* Tracing was recorded from right to left. The two marks on the vital capacity curve represent the one-second and two-second vital capacities which constitute 82 per cent and 95 per cent of the total. The maximum breathing capacity (M.B.C.) is shown at the extreme left. The lower pen, which is geared to the upper pen in a 25:1 ratio, measures the total volume of air moved during the test.

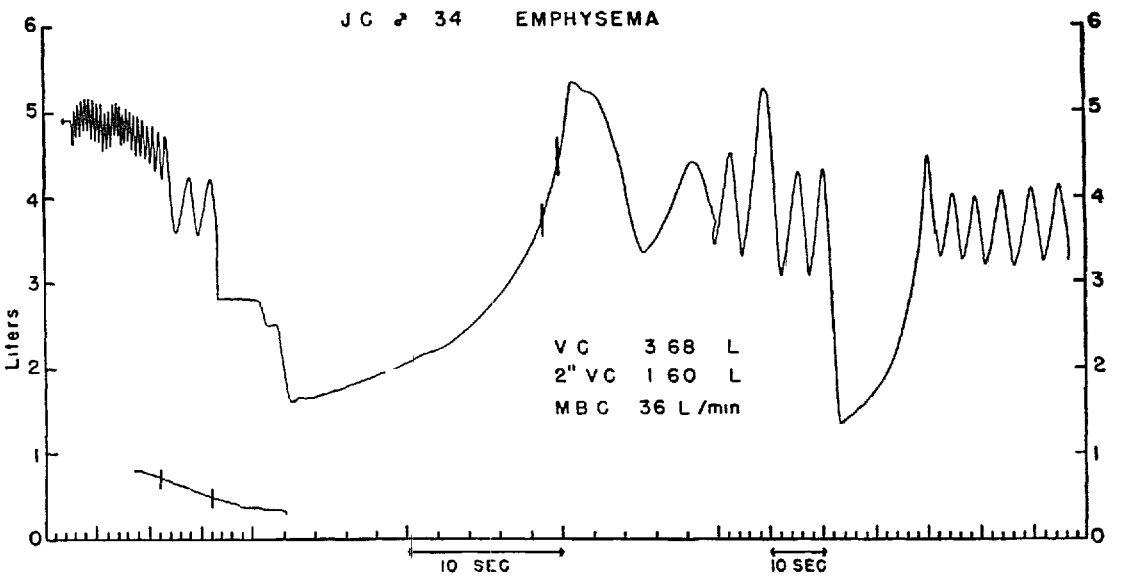

FIG. 2—*Tracing from a case of chronic pulmonary emphysema.* The one-second and two-second vital capacities are 24 per cent and 44 per cent of the total. Compare with Figure 1. The decreased total and one-second vital capacity, and the reduced M.B.C., indicate severe obstructive ventilatory insufficiency.

Patients with chronic pulmonary emphysema, for example, have great difficulty ventilating their lungs. As a result, alveolar ventilation becomes inadequate, the $PaCO_2$ rises and the PaO_2 decreases. The high $PaCO_2$ results in respiratory acidosis, and the low PaO_2 produces arterial oxygen unsaturation and cyanosis. The elevated $PaCO_2$ should act as a respiratory stimulant, but these patients are unable to increase their ventilation because of their increased pulmonary resistance. Finally the respiratory centre becomes completely insensitive to the $PaCO_2$ stimulus. What then controls the ventilation and respiration of these patients? They are now breathing only in response to their oxygen lack. A patient in such a precarious respiratory state may be admitted to the medical ward, possibly with a patch of pneumonia which has taken away a further portion of his functioning lung tissue. The unwary interne, who on examination finds a markedly dyspnoeic, deeply cyanosed patient with râles at both bases, may order morphine for the supposed pulmonary oedema, and oxygen for correction of the cyanosis. He is unfortunately "killing him with kindness" for he is making two mistakes. The morphine will depress the respiration rate, and thus further reduce alveolar ventilation. But more important, he has taken away this man's only stimulus to breathing. The oxygen therapy corrects the hypoxaemia, and alveolar ventilation is further reduced. The $PaCO_2$ soon rises to narcotic levels and the acidosis may cause respiratory arrest and death.

This is the syndrome of CO_2 narcosis. The anaesthetist must be cognizant of the problems of these patients, for he may have to administer an anaesthetic or help in their resuscitation. We have seen that alveolar underventilation and the associated rise in $PaCO_2$ occurs during anaesthesia in patients with normal cardiopulmonary function. The dangers, then, of CO_2 retention and respiratory acidosis are even greater in a patient who has pulmonary disease. The patient

with chest disease may have been given a narcotic before operation, and during operation the gas mixture may have a high tension of oxygen.

Another example is the group of patients with kyphoscoliosis. The major ventilatory defect in these patients is the greatly reduced vital capacity. Figure 3 shows the ventilation tracing from such a patient. Preoperative physical examina-

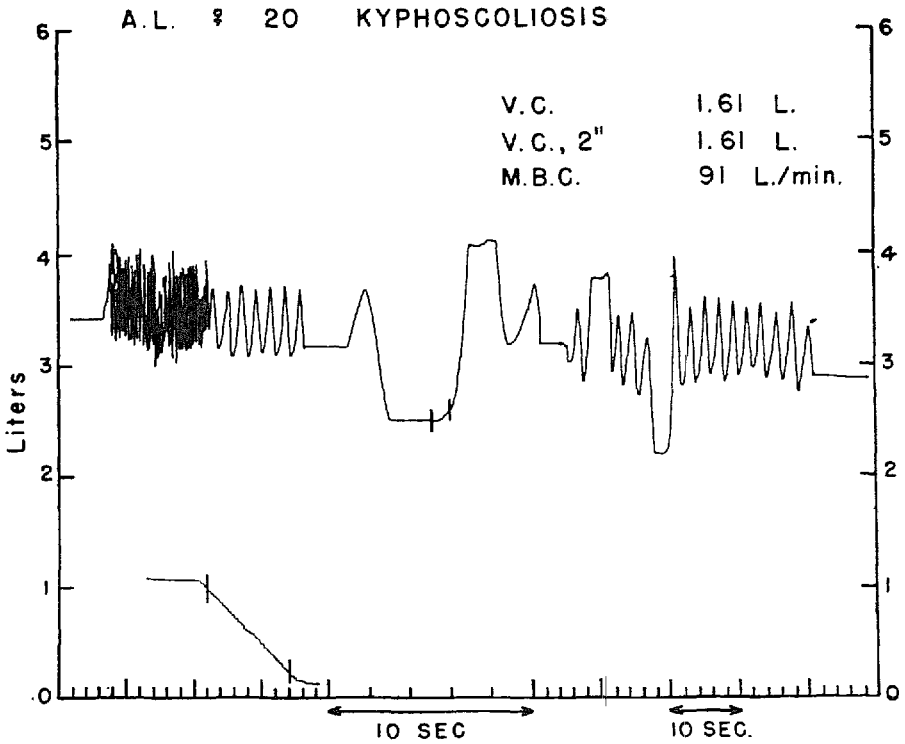

FIG. 3—*Tracing from a case of kyphoscoliosis.* This is an example of restrictive ventilatory insufficiency. The per cent one-second vital capacity and the M.B.C. are normal, but the total vital capacity itself is greatly reduced.

tion may otherwise be normal and they may not complain of any dyspnoea. Since their tidal volume is limited because of the reduced vital capacity, they depend upon an adequate respiratory frequency to maintain alveolar ventilation. If the respiratory rate of a normal individual is reduced, the tidal volume will increase in a compensatory manner. However, these patients with kyphoscoliosis are unable to increase their tidal volume because of their limited chest expansion. Thus, after preoperative morphine, respiratory rate is slowed, tidal volume is fixed, and alveolar underventilation occurs. As a result, $PaCO_2$ rises and again we have the complications of respiratory acidosis, CO_2 narcosis, and possibly death. This may occur on the ward either before or after operation. The same situation may also occur in patients with Marie-Strümpell's arthritis, or in the other types of arthritis in which there is costal fixation and restricted chest expansion.

CO_2 also produces vascular effects. An increased $PaCO_2$ results in a stimulation of the chemoreceptors, which act on the vasomotor centre to produce peripheral vasoconstriction. An elevated $PaCO_2$ also acts locally, producing vasodilation.

The resultant effect of hypercapnia on the level of blood pressure will be a balance between these two actions. Usually, the central effect predominates. Buckley (5), for example, showed that the hypertension encountered during cyclopropane anaesthesia was related to the duration of hypercapnia.

The syndrome of so-called "cyclopropane shock" is well known to anaesthetists. Some experimental observations are pertinent in this respect. In 1927, Goldstein and Dubois (8) showed in normal individuals that during a re-breathing experiment in which the CO_2 elimination was decreased, the blood pressure rose. They also showed that following the cessation of re-breathing, there was a marked fall in blood pressure. In those cases which develop cyclopropane shock, the $PaCO_2$ is markedly elevated at the time the anaesthetic is discontinued. The precipitating factor in producing this syndrome seems to be that as the anaesthesia wears off, excess CO_2 is blown off at a more rapid rate with the result that the buffer mechanisms can no longer cope with the situation, and rapid pH changes occur. This syndrome is seen more frequently when cyclopropane is used, because of the marked respiratory centre depression which cyclopropane produces. However, it may be seen with other types of anaesthesia that are associated with marked hypercapnia and respiratory acidosis

Finally, I would like to say a word about the use of 5 per cent carbon dioxide in oxygen (carbogen) as a resuscitating agent. Individuals who are in need of resuscitation are already in a state of respiratory insufficiency They are already in a state of hypercapnia and respiratory acidosis. The aim of resuscitation, then, is the improvement of alveolar ventilation to ensure an adequate oxygen tension, and also to remove the excess body CO_2. As we have seen, with high tensions of CO_2 the sensitivity of the respiratory centre is lowered so that it can no longer respond to this endogenous CO_2 stimulus How then can exogenous CO_2 (as 5 per cent CO_2 in oxygen) be expected to stimulate respiration? It can only lead to more severe respiratory acidosis. The simultaneous administration and vigorous removal of a therapeutic agent is treatment reduced to absurdity.

In closing, I would like to repeat the admonition. "Look on acidosis like sin, be against it"

Summary

The physiology of CO_2 is briefly reviewed. Inadequate alveolar ventilation does occur during anaesthesia in normal individuals, and this results in CO_2 retention and respiratory acidosis Some of the contributing factors to this undesirable result are discussed, they include the use of preoperative and anaesthetic drugs, and the position of the patient. The syndrome of CO_2 narcosis is discussed. The vascular effects of hypercapnia are reviewed in relation to the syndrome of cyclopropane shock. Five per cent CO_2 in oxygen is not recommended as a resuscitating agent.

Résumé

Le dioxyde de carbone, dissous dans l'eau du sang artériel, détermine la pression partielle du CO_2 Celle-ci est appelée $PaCO_2$. Le rapport de la concentration de l'ion bicarbonate du plasma sur le $PaCO_2$ détermine le pH du sang artériel. Le

contrôle chimique de la respiration étant le $PaCO_2$, on comprend que le volume minime de ventilation alvéolaire (cette partie de la ventilation totale qui subit un échange gazeux), le $PaCO_2$ et le pH du sang artériel, sont intimement liés l'un à l'autre. Si un patient respirant un mélange gazeux riche en oxygène arrêtait de respirer, ses besoins organiques en oxygène seraient satisfaits pour 10 minutes. Cependant, en quelques secondes, cette diminution de la ventilation alvéolaire résulterait en une élévation du $PaCO_2$ et en une acidose respiratoire. Une telle diminution de la ventilation alvéolaire peut se présenter en anesthésie moderne chez des patients à fonction cardio-pulmonaire normale. La position du patient et l'effet des agents préopératoires et anesthésiques sur le centre respiratoire sont parmi les plus importants facteurs susceptibles d'affecter la ventilation durant l'anesthésie.

Le syndrome de narcose au CO_2 se rencontre fréquemment chez les patients souffrant de maladie pulmonaire chronique ou encore qui ont une scoliocyphose. L'anesthésiste doit être au courant des problèmes qui comportent ces patients car il peut être appelé à les anesthésier ou encore à faciliter leur ressuscitation.

Le CO_2 produit aussi des effets vasculaires Buckley a démontré que l'hypertension produite lors d'une anesthésie au cyclopropane était attribuable à la durée de la retention du CO_2. De même, dans les cas qui développent un choc au cyclopropane, le $PaCO_2$ était très élevé quand cet agent fut discontinué.

L'usage de dioxyde de carbone à 5 pour cent dans l'oxygène comme agent ressuscitateur ne doit pas être recommandé parce que les patients qui ont besoin de ressuscitation sont déjà dans un état d'insuffisance respiratoire et un tel traitement peut seulement conduire à une acidose respiratoire plus sévère

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