CARBON DIOXIDE HOMEOSTASIS DURING ANESTHESIA.
III. VENTILATION AND CARBON DIOXIDE ELIMINATION

James O. Elam, M.D., and Elwyn S. Brown, M.D.

In conscious healthy man physiologic adjustments normally maintain the alveolar carbon dioxide concentration within a narrow range of tensions. The rate of elimination of carbon dioxide is regulated to equal production of carbon dioxide so that, although instantaneous equality may not be achieved, the average rates of production and elimination over a period of time will be equal.

In the patient anesthetized with a closed breathing circuit, carbon dioxide homeostasis is also dependent upon the efficiency of carbon dioxide removal in the circuit and the effects of the anesthetic agent. Complete removal of carbon dioxide in the closed system has generally been assumed in the absence of clinical evidence of carbon dioxide stimulation. The amount of rebreathing, however, which produces signs of carbon dioxide excess in anesthetized man has not been determined.

A preliminary series of clinical measurements consisted of monitoring the ventilation and respired carbon dioxide concentrations of patients during the routine conduct of anesthesia. Elevations of the alveolar carbon dioxide tension to 48 to 55 mm. of mercury were frequently observed, particularly in procedures exceeding one hour. Respiratory acidosis consistently occurred during prolonged anesthesia with ether by the closed circle filter unless the patient's ventilation was vigorously assisted. Elevated alveolar values of carbon dioxide concentration were rarely encountered when the semiclosed circle system with nitrous oxide-oxygen (5 LPM total flow) was employed with Demerol® supplementation.

The expected onset of carbon dioxide accumulation attending inadequate alveolar ventilation was associated with plane 3 or 4 ether anesthesia, with intravenous administration of barbiturates, with cyclopropane, and with muscle relaxants. An excessive volume of assisted ventilation was required, however, to reverse respiratory acidosis when the closed circle filter was employed. Inordinately large alveolar ventilation values required to maintain normal arterial carbon dioxide tension have previously been reported (1) by Gabbard and associates.

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A rise in alveolar carbon dioxide tension indicates a failure in the homeostatic mechanisms regulating carbon dioxide tension. In the present study, methods previously described (2) were employed to follow changes in ventilation and carbon dioxide elimination during anesthesia. In addition, ventilatory response to increase in inspired carbon dioxide concentration was studied during anesthesia.

METHODS

Continuous records of carbon dioxide concentration in the respired air and respiratory flow rate were obtained throughout the course of anesthesia. In some instances studies were begun before premedication and continued until recovery.

To determine ventilatory response to inspired carbon dioxide, the absorber was partially bypassed stepwise or the partial rebreathing system was employed at various flow rates. The total inspired carbon dioxide, total expired carbon dioxide, net carbon dioxide output, and average expired alveolar carbon dioxide concentration were calculated and the adequacy of the homeostatic mechanisms judged on the basis of maintenance of normal alveolar carbon dioxide concentration.

RESULTS

Inspired Carbon Dioxide Concentration. Elevations of the inspired carbon dioxide concentration were frequently observed when the patient's ventilation increased. A parallel increase in alveolar carbon dioxide concentration accompanied the progressive increase in the inspired carbon dioxide concentration. This carbon dioxide accumulation persisted in spite of vigorously assisted ventilation. In fact, increased ventilation produced a further rise in the inspired carbon dioxide concentration.

Transient elevations of the inspired carbon dioxide concentration to 3.0 per cent were correlated with irregular respiration such as intermittent sighing, coughing and hyperpnea. Several explanations for these deficiencies in carbon dioxide removal in the circle system were considered. Incomplete carbon dioxide absorption by the soda lime was suspected but in many instances the elevated inspired carbon dioxide concentrations persisted after the soda lime was changed. Therefore, the competence of the breathing valves, the external dead space of the circuit, and the possible aerodynamic sources of carbon dioxide rebreathing were also suspect.

Carbon Dioxide Production. During periods when alveolar carbon dioxide concentration remains constant, the carbon dioxide elimination may be assumed to equal the carbon dioxide production. Widely variable rates of carbon dioxide production were obtained with different agents and with the anesthetic planes of a given agent (table 1).

Demerol-scopolamine reduced the carbon dioxide production con-
siderably below the patient's basal rate. For example, patient S. D., before premedication, had a carbon dioxide production of 210 cc. per minute, alveolar carbon dioxide tension of 43.5 mm. of mercury and rate of 18.5 per minute. After administration of 100 mg. of Demerol and 0.4 mg. of scopolamine intravenously, the carbon dioxide output

was reduced to 50 cc. per minute, the alveolar carbon dioxide tension increased to 58.5 and the rate decreased to 2.6 per minute. Hence, some accumulation of carbon dioxide had occurred. Subsequent values, however, indicated reversal of this accumulation: carbon dioxide output 75 cc. per minute, alveolar carbon dioxide tension 56 mm. of mercury and rate 3.3 per minute. Therefore carbon dioxide production with maximal depression was approximately 60 cc. per minute.
A low basal carbon dioxide production rate of 123 cc. per minute in patient M. B. was associated with emaciation. The alveolar carbon dioxide tension was 39 mm. of mercury and the rate was 17.2 per minute before premedication. Following intravenous administration of 10 mg. of morphine and 0.4 mg. of atropine, only slight depression appeared within fifteen to thirty minutes. Additional intravenous medication of 100 mg. of Demerol and 0.4 mg. of scopolamine depressed the carbon dioxide production to 85 cc. per minute, the alveolar carbon dioxide tension increased to 41 mm. of mercury and the rate was further reduced to 5 per minute. With maximal depression, accumulation of carbon dioxide did not occur.

Following nitrous oxide-Demerol anesthesia, a large muscular patient, S. G., had a carbon dioxide production of 270 cc. per minute, alveolar carbon dioxide tension of 42.7 mm. of mercury and a rate of 8.5 per minute. Accumulation of carbon dioxide did not occur.

Ether anesthesia was associated with elevated carbon dioxide production rates. In patients M. B. and R. F., the depression of carbon dioxide production following premedication was reversed during plane 2 to values exceeding the initial basal rates: carbon dioxide, 235 cc. per minute for M. B. and 365 cc. per minute for R. F. Three other patients who were given ether, L. O., C. S. and O. S., were studied in the immediate postoperative period. Carbon dioxide productions of 480 cc. per minute, 380 cc. per minute and 390 cc. per minute, respectively, were obtained.

During Pentothal-nitrous oxide anesthesia, carbon dioxide production rates approximated the basal values. Patient P. S., after a total intravenous dose of 1 Gm. of Pentothal, had a carbon dioxide production of 240 cc. per minute, alveolar carbon dioxide tension of 45 mm. of mercury and rate of 24 per minute. An additional 0.5 Gm. of Pentothal depressed the carbon dioxide output to 175 cc. per minute. The alveolar carbon dioxide tension of 47 mm. of mercury indicated initial accumulation of carbon dioxide.

Alveolar Ventilation. Widely variable alveolar ventilation values were found which are related to the carbon dioxide production (table 1). During ether anesthesia which was not complicated by rebreathing, alveolar ventilation for patients M. B. and R. F. ranged from 3.06 to 5.5 liters per minute. Some of these values may reflect a superimposed depression by the premedication. Patients L. O., C. S. and O. S., who were studied several hours after premedication, showed alveolar ventilation of 6.0 to 8.0 liters per minute during planes 2 and 3 of ether anesthesia. These values of alveolar ventilation reflect the demand imposed by the production of carbon dioxide.

The minimal requirements for alveolar ventilation which attend the depression following Demerol-scopolamine are striking. Normal alveolar values of carbon dioxide tension were maintained by M. B. and S. G., with alveolar ventilations of 1.7 and 4.7 LPM. In patient S. D.,
an alveolar ventilation of 0.63 LPM was associated with accumulation of carbon dioxide which was promptly reversed by an alveolar ventilation of only 1.0 LPM. The depression of respiration following Demerol-scopolamine involves a marked reduction in the respiratory rate which is usually compensated by an increase in tidal volume. The resulting alveolar ventilation suffices to maintain carbon dioxide homeostasis at respiratory rates as low as 3.3 per minute. Such reduced ventilation is sufficient because of the concurrent decrease in carbon dioxide production.

![Diagram showing carbon dioxide and flow records](image)

**Fig. 1.** Records of carbon dioxide and flow showing ventilatory response to carbon dioxide rebreathing during ether anesthesia.

Pentothal produced alveolar ventilations of approximately basal values unless an overdose was given.

**Efficiency of Ventilation.** The tachypneic respiration produced by ether in surgical planes results in an excessive ventilation of the dead space to produce the required alveolar ventilation. The dead space ratio (dead space divided by tidal volume) of R. F. in plane 2 was 0.46 to 0.49. In plane 3 the dead space ratio increased to 0.55. The dead space ratio of patient M. B. in plane 3 was 0.51. Thus, only half the minute ventilation was effective as alveolar ventilation.

In contrast, the bradypneic respiration produced by Demerol-scopolamine in surgical planes results in an economy of the minute
ventilation because of the marked increase in tidal volume. Previous to the administration of ether, patient M. B., with maximum effect of premedication, had a dead space ratio of 0.35. Patient S. G. had a dead space ratio of 0.33 following Demerol-scopolamine.

With the shallow rapid respiration attending Pentothal anesthesia, the minute ventilation is relatively inefficient. Patient P. S. had a dead space ratio of 0.71 during Pentothal anesthesia.

The external dead space for the values cited here approximated that of an anatomical anesthesia mask and Y-attachment.

**Ventilatory Response to Inspired Carbon Dioxide.** Figure 1 illustrates the two channel records of respired carbon dioxide and flow which were obtained during anesthesia. In this patient during plane 1 ether anesthesia, alveolar carbon dioxide tension varied between 28 and 32 mm. of mercury. The steady state value in plane 3 indicated a normal alveolar carbon dioxide tension of 40 mm. of mercury. During inspiratory flow the carbon dioxide record indicates negligible concentrations at the end of inspiration. At the point designated “A,” the absorber was partially cut out so that a fraction of expired air was bypassed to the breathing bag. Note the gradual increase in the inspired carbon dioxide concentration to 0.7 per cent (5 mm. of mercury) and the concomitant elevation of alveolar carbon dioxide tension to 44 mm. of mercury. A continued rise in inspired carbon dioxide concentration to 4.6 per cent was attended by an increased ventilation evident in the flow record. With this degree of rebreathing, alveolar ventilation was tripled, resulting from an increase in tidal volume and in respiratory rate. The ventilatory response did not prevent carbon dioxide accumulation, however, since the alveolar carbon dioxide tension increased to 47 mm. of mercury. Termination of rebreathing by detaching the circle system at the Y-attachment was promptly followed by a return of the inspired carbon dioxide concentration to that of ambient air and a prompt decline in alveolar carbon dioxide tension to 37 mm. of mercury (at “B,” fig. 1). Hyperventilation continued to reduce the patient’s alveolar carbon dioxide tension to 34.5 mm. of mercury.

Carbon dioxide accumulation may be represented as the departure from a constant alveolar carbon dioxide concentration, and the degree of ventilatory deficiency in carbon dioxide elimination as the additional alveolar ventilation required to prevent an elevation of alveolar carbon dioxide tension (fig. 2). The ventilatory responses produced by increase in inspired carbon dioxide during ether, Demerol and Pentothal anesthesia are graphically represented in figure 3. Accumulation of carbon dioxide occurs when the alveolar ventilation fails to compensate completely for the increasing concentration of carbon dioxide in inspired air.

During plane 1 ether anesthesia, carbon dioxide homeostasis is well maintained (fig. 3). In patients L. O. and C. S., alveolar ventila-
Fig. 2. Adequacy of ventilatory response to inspired carbon dioxide.

Dotted and dashed lines represent an adequate ventilatory response to inspired carbon dioxide concentration. An inadequate response is indicated when the alveolar ventilation accompanying a given inspired carbon dioxide concentration falls to the left of the dashed line. The concomitant rise in alveolar carbon dioxide concentration indicates the degree of carbon dioxide accumulation. The normal response curve for a given patient is calculated from the modified alveolar equation utilizing the carbon dioxide production rate and alveolar carbon dioxide concentration of the control period.

tion increased in response to carbon dioxide concentrations of 2.2 and 4.2 per cent sufficiently to prevent significant accumulation of carbon dioxide. During planes 2 and 3 ether anesthesia, patients E. F. and O. S. were unable to increase alveolar ventilation sufficiently and a

Fig. 3. Ventilatory response during anesthesia to inspired carbon dioxide concentrations.

The data given in table 2 are plotted according to the relationships shown in figure 2. A striking ventilatory deficiency during plane 3 ether anesthesia is exhibited by patient O. S.
progressive carbon dioxide accumulation is indicated by the increasing values of alveolar carbon dioxide tension.

During Demerol-scopolamine-nitrous oxide anesthesia, adequate ventilatory response was manifested by S. G. for inspired carbon dioxide concentrations of 0.8 to 2.4 per cent. When nitrous oxide is administered with the semiclosed circle absorption system, elevations in inspired carbon dioxide are minimized. Moreover, the low carbon dioxide output attending Demerol depression places less demand upon both the alveolar ventilation and the absorber.

The ventilatory response to carbon dioxide during Pentothal anesthesia tends to vary with the schedule of dosage so that steady states are not readily obtained. Inadequate ventilatory response to an inspired carbon dioxide concentration of 2.5 per cent was elicited in patient P. S. after administration of 1.5 Gm. of Pentothal in divided doses. At the time the inspired carbon dioxide concentration was increased to 4.95 per cent the patient apparently had regained normal ventilatory response to carbon dioxide.

**DISCUSSION**

For normal conscious subjects breathing ambient air, the alveolar ventilation is predictable during a steady basal state from the carbon dioxide production and the alveolar or arterial carbon dioxide concentration by means of the alveolar equation:

\[
\left( \text{Alveolar ventilation} \right) = \frac{\text{CO}_2 \text{ production}}{\text{Alveolar CO}_2 \text{ concentration}}.
\]

During inhalation anesthesia the presence of significant concentrations of carbon dioxide in the inspired air complicates the alveolar equation:

\[
\left( \text{Alveolar ventilation} \right) = \frac{\text{CO}_2 \text{ production}}{\left( \text{Alveolar CO}_2 \text{ concentration} \right) - \left( \text{Inspired CO}_2 \text{ concentration} \right)}.
\]

It is apparent that the alveolar ventilation required to effect carbon dioxide homeostasis must increase when there is rebreathing of carbon dioxide.

For the range of carbon dioxide production rates encountered in these studies, the alveolar ventilation required when inspired carbon dioxide concentration ranges between 1 and 5 per cent has been calculated (table 2). It may be noted that an alveolar ventilation of 35.7 LPM would be required for a carbon dioxide production of 500 cc. per minute with an inspired carbon dioxide concentration of 4 per cent. Carbon dioxide production rates of this order were observed during ether anesthesia in the present series when the closed filter was used. Gabbard and associates have reported alveolar ventilation values of
10 to 27 LPM during maintenance of normal arterial carbon dioxide tension in patients with ether-oxygen closed system anesthesia for abdominal procedures (1). Although inspired carbon dioxide concentration was not measured in their study, the difficulty of maintaining normal arterial carbon dioxide concentration was attributed to inadequate ventilation. Since the studies of Gubbard et al. involved the use of closed circle filters which were found to exhibit both valve leak and inadequate absorption, their results appear to be considerably influenced by rebreathing.

The significance of carbon dioxide rebreathing in the development of respiratory acidosis has not been implicated in the reports of Beecher et al. (3, 4), Gibbon et al. (5), Miller et al. (6–8) and Stead et al. (9).

### TABLE 2
**Alveolar Ventilation Required to Maintain Normal Alveolar Carbon Dioxide Tension When Carbon Dioxide Production Rates and Inspired Carbon Dioxide Concentrations Are Varyed**

<table>
<thead>
<tr>
<th>CO₂ Production Rate (cc./min.)</th>
<th>(Inspired CO₂ Concentration)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0%</td>
</tr>
<tr>
<td>100</td>
<td>1.85</td>
</tr>
<tr>
<td>200</td>
<td>3.71</td>
</tr>
<tr>
<td>300</td>
<td>5.57</td>
</tr>
<tr>
<td>400</td>
<td>7.42</td>
</tr>
<tr>
<td>500</td>
<td>9.27</td>
</tr>
</tbody>
</table>

The studies of ventilatory response to inspired carbon dioxide indicate that ether, Demerol and Pentothal anesthesia may be attained without serious impairment of the patient’s regulation of alveolar ventilation. The need for abdominal relaxation, however, often dictates planes of anesthesia or paralysis which are attended by ventilatory deficiency. The ventilation requirements may then easily be met by artificial ventilation unless the circle filter fails to absorb the expired carbon dioxide. The inordinately large values of assisted or controlled ventilation, which are required when inspired carbon dioxide increases, are inefficient (table 2).

The interrelated mechanisms governing the transfer of carbon dioxide from the patient’s tissues to the absorber of the gas machine are schematically indicated in figure 4. Carbon dioxide is produced at various rates in the tissues as modified by the effect and dosage of the anesthetic agent. Carbon dioxide is eliminated in the closed system entirely by chemical reaction with soda lime in the absorber. To
maintain carbon dioxide homeostasis, the quantity of carbon dioxide produced must equal that eliminated.

Deficient removal of carbon dioxide in the external breathing circuit obviously increases the concentration of inspired carbon dioxide. Unless the volume of respired gas passing through the absorber is increased so that the rate of removal remains equal to the rate of production of carbon dioxide, respiratory acidosis occurs. With existing equipment, the only means of increasing the circulation of gas through the absorber is by increasing the ventilation. Therefore, as inspired carbon dioxide concentration increases, accumulation of carbon dioxide is inevitable unless the patient is able to increase alveolar ventilation or unless artificial ventilation is provided. Increased ven-

\[
\text{CO}_2^- \text{ PRODUCED} \quad \text{CO}_2^- \text{ ACCUM.} \quad \text{CO}_2^- \text{ EXPIRED} \quad \text{INCOMPLETE ABSORPTION VALVE LEAK} \quad \text{CO}_2^- \text{ INSPIRED}
\]

**Fig. 4.** Factors effecting carbon dioxide elimination during closed system anesthesia.

ventilation becomes progressively ineffective with exhaustion of the absorbent. Even excessive alveolar ventilation cannot prevent carbon dioxide accumulation in the presence of complete rebreathing. Assuming an intact ventilatory response to carbon dioxide during anesthesia, rebreathing imposes an unnecessary expenditure of energy upon the patient.

With carbon dioxide accumulation, the alveolar or arterial carbon dioxide concentrations do not increase in proportion to the amount of carbon dioxide retained because of the buffering capacity for carbon dioxide of the blood and body fluids. Consequently, large amounts of carbon dioxide are retained without marked increase in either the arterial or alveolar carbon dioxide tension. As the buffer systems become saturated with carbon dioxide the hydrogen ion and carbon dioxide concentrations change more rapidly. Obviously, the circulation
constitutes the link between the carbon dioxide produced in the tissues and that eliminated in the lungs. Circulatory shunts in which the venous blood bypasses ventilated lung reduce the efficiency of carbon dioxide transfer from the tissues to the alveolar air. The significance of factors in carbon dioxide homeostasis, such as the release of fixed acids, changes in the buffer systems and alterations in the ventilation-perfusion ratio, cannot be evaluated or interpreted in the presence of an unknown but appreciable degree of carbon dioxide rebreathing.

Conclusions

The maintenance of normal carbon dioxide tension in the anesthetized patient depends upon a balance between production and elimination of carbon dioxide. In the absence of carbon dioxide rebreathing the patient's production of carbon dioxide determines the requirement for alveolar ventilation. The carbon dioxide production of adult anesthetized patients has been found to vary between 60 cc. and 500 cc. per minute, depending primarily upon the anesthetic agent. Alveolar ventilation required to maintain carbon dioxide homeostasis may, therefore, vary between 1.0 and 8.6 LPM. During Demerol-scopolamine anesthesia, normal alveolar carbon dioxide tension may be maintained with an alveolar ventilation as low as 1.0 LPM and a respiratory rate of 3.3 per minute. With plane 3 ether anesthesia, normal alveolar carbon dioxide tension was not maintained with an alveolar ventilation of 4.9 LPM and a respiratory rate of 34 per minute. Carbon dioxide accumulation was consistently found during ether anesthesia at the surgical planes necessary to provide abdominal relaxation.

In the presence of carbon dioxide rebreathing, the requirement for alveolar ventilation is determined not only by the patient's production of carbon dioxide but also by the concentration of inspired carbon dioxide. With the increased rate of carbon dioxide production observed during ether anesthesia, an increase in inspired carbon dioxide concentration imposes an additional burden upon the ventilation. The tachypneic breathing during ether anesthesia is not suited to an efficient response to inspired carbon dioxide. Approximately 1 liter of dead space ventilation is wasted for each liter of alveolar ventilation. With sodium Pentothal\textsuperscript{®}, this inefficiency may be doubled. By contrast, the slow deep breathing during Demerol-scopolamine anesthesia affords an economical response to inspired carbon dioxide. Approximately 0.5 liter of dead space ventilation is expended for each liter of alveolar ventilation.

An adequate ventilatory response to inspired carbon dioxide concentrations below 4.2 per cent was intact in planes 1 and 2 ether anesthesia, in demerol-scopolamine-nitrous oxide anesthesia, and in pentothal-nitrous oxide anesthesia of only moderate depth. The ventilatory response to carbon dioxide in plane 3 ether anesthesia was not sufficient to prevent accumulation of carbon dioxide.
**Summary**

Application of the infrared carbon dioxide analyzer and the pneumotachograph to problems of carbon dioxide homeostasis during anesthesia has demonstrated that a frequent cause of respiratory acidosis is rebreathing of carbon dioxide. Elevation of the inspired carbon dioxide concentration imposes a superfluous demand upon the alveolar ventilation.

The patient’s alveolar carbon dioxide tension may be maintained at a normal value provided rebreathing of carbon dioxide is eliminated and provided the ventilation is assisted when agents are employed that produce weakness or paralysis of the respiratory muscles.

**REFERENCES**


