CIRCULATORY CHANGES ACCOMPANYING RESPIRATORY ACIDOSIS DURING HALOTHANE (FLUOTHANE) ANAESTHESIA IN MAN*

BY

GERALD W. BLACK†, HARRY W. LINDE, ROBERT D. DRIPPS AND HENRY L. PRICE

From the Department of Anesthesiology, University of Pennsylvania Schools of Medicine, Philadelphia 4, Pennsylvania

The haemodynamic effects of halothane differ considerably from those of the inhalational anaesthetic agents in common use. Data on the response of the circulation of human subjects to halothane is therefore of interest. In the present report the condition of cardiac rhythm, arterial blood pressure and heart rate during halothane anaesthesia at normal levels of alveolar carbon dioxide tension in fifteen subjects is described. No pre-anaesthetic medication was given to these individuals; steady states of anaesthesia were sought and all measurements were made prior to operation. In view of the importance which has been ascribed to hypercarbia in the initiation of cardiac arrhythmias and posthypercarbic hypotension, observations were also made during and after deliberate elevation of the inspired concentration of carbon dioxide. The results in most instances are compared and contrasted with those obtained during cyclopropane anaesthesia.

METHODS

The fifteen subjects studied were patients admitted for minor surgical operations. The ages of these subjects, of whom fourteen were female, ranged from 15 to 49 years. On clinical examination thirteen were found to be in good health, one had symptomless hypertension and one inactive pulmonary tuberculosis. None of the patients was receiving any drug therapy and no pre-anaesthetic medication was given. On arrival in the anaesthetic room each subject was given 15 litres of oxygen per minute by face mask for 5-10 minutes from a Heidbrink anaesthetic machine. A one-way valve (Ruben) was included to make a nonrebreathing system. Halothane was then added from a Fluotec vaporizer and the concentration gradually increased until the induction of anaesthesia was complete, usually in 7-10 minutes. A metal oral airway was inserted in each subject. In most instances the induction of anaesthesia was quiet and satisfactory, although excitement was marked in two subjects and moderate in two others. The high inspired concentration of oxygen—over 95 per cent—the adequate pulmonary ventilation as judged by end-expired $P_{CO_2}$ values and the pink colour of the mucous membranes and nailbeds of the subjects led us to believe that no subject was hypoxic at any time. Respiration was spontaneous and unassisted.

All observations were made before the operation was started. The average time of study was 3 hours, during which time 200-500 ml of 5 per cent glucose in water were given intravenously. The inspired halothane concentration was analyzed by means of a thermal conductivity cell which had been calibrated with weighed amounts of halothane vaporized in oxygen. The percentages of halothane were recorded at 5-minute intervals. Oxygen from the Heidbrink machine was passed through the Fluotec vaporizer and the thermal conductivity cell into a 5-litre bag and then to the patient through the Ruben valve. Thermal conductivity readings were not taken when carbon dioxide was added to the inspired

*This study was supported (in part) by grants from the National Institutes of Health (H-1568-C4) and (H-1884-C3), from the Office of the Surgeon General U.S. Army (DA-49-007-MD-599), and from Ayerst Laboratories, Inc., New York.
†Present address: Department of Anaesthetics, Queen's University, Belfast, Northern Ireland.
gases, for the low conductivity of the latter gas made it difficult to determine the concentration of halothane in the mixture. It is believed that carbon dioxide did not interfere with the functioning of the Fluotec.

The carbon dioxide tension in the expired gases was measured with a Liston-Becker infrared carbon dioxide analyzer using the microcatheter technique of Collier, Affeldt and Farr (1955). The gases were withdrawn by inserting a 20 gauge needle through the rubber face mask and directing it into the lumen of the metal oral airway. It was found that halothane in the concentrations used in this study did not interfere with infrared determination of carbon dioxide. End-expired values of $PCO_2$ were used throughout the studies.

Prior to the induction of anaesthesia the arterial pressure was measured by the auscultatory (Riva-Rocci) method in ten cases, and directly through a needle inserted in the brachial or femoral artery in the remainder. In nine individuals arterial puncture was successful shortly after the induction of anaesthesia, and direct measurements of pressure were therefore possible throughout the remaining period of study in fourteen of the fifteen individuals. In one subject arterial puncture failed, and blood pressure measurements were continued by the auscultatory method. When the direct method was used the pressure pulse was transduced by a strain gauge and the mean arterial pressure calculated by planimetric integration of the pressure curves.

The electrocardiogram (leads I and II) was recorded using needle electrodes. In five cases the needles were inserted while the subject was awake, and in others not until after induction of anaesthesia. The tracings were interpreted according to standard methods (Bellet, 1953).

The arterial blood pressure, the electrocardiogram and the concentration of carbon dioxide were continuously recorded on a Grass polygraph. A paper speed of 150 mm/min was used, with records being taken at 1500 mm/min at intervals of several minutes and during periods of special interest.

The inspired concentrations of halothane ranged from 0.4 to 2.5 per cent. The Fluotec setting was often 3 per cent, but thermal conductivity readings indicated a value consistently lower by 0.3–0.5 per cent. A steady concentration of anaesthetic was administered for at least 20 minutes in every instance in an effort to achieve stable states of anaesthesia.

Varying degrees of hypercarbia were then produced by adding carbon dioxide from a high pressure cylinder. The $PCO_2$ was elevated slowly until ventricular arrhythmias were produced, was maintained at this level for varying periods up to 25 minutes, and was then reduced.

It was planned to study the effect of two or more steady levels of anaesthesia in each subject. When $PCO_2$ was deliberately elevated during low inspired halothane concentrations (0.4–1 per cent) coughing and gagging on the airway made studies unsatisfactory. For this reason, in most subjects hypercarbia was first studied during higher concentrations of halothane. A return was then made to a normal $PCO_2$. A stable state of anaesthesia at a lower concentration of halothane was sought and hypercarbia again produced. The "arrhythmia threshold" was found to be reproducible in the same subject when carbon dioxide inhalation was repeated under similar conditions, but the haemodynamic changes were not. For these reasons all data relevant to arrhythmia production will be included in this report, but only the haemodynamic measurements obtained during the first period of stable anaesthesia and the first episode of hypercarbia will be presented.

The aim in each study was to determine whether cardiac arrhythmias occurred during elevation of $PCO_2$ and, if so, at what level of end-expired $PCO_2$. In some subjects the reproducibility of a "critical arrhythmia level" was studied. In others the influence of different concentrations of halothane and different rates of rise of $PCO_2$ upon the "arrhythmia threshold" was examined.

Standard statistical methods were used to determine the significance of differences between experimental observations (Moroney, 1956). A difference was considered significant when the $p$ value was less than 0.05.

**RESULTS**

**Cardiac Arrhythmias.**

**Normocarbia.** When the end-expired $PCO_2$ lay within the normal range, cardiac rhythm was also normal, with minor exceptions. Depression of the
P wave without increase in the P–R interval was present at some time during anaesthesia in three subjects. In two other individuals slight depression of the S–T segment occurred briefly in one, and S–T elevation in the other.

The concentrations of halothane inspired ranged between 0.4 and 2.5 vols. per cent. When the respirations were unassisted, the end-expired Pco₂ was greater the higher the anaesthetic concentration (p < 0.01). The Pco₂ averaged 42 mm Hg (S.D. = 6) during periods when constant concentrations of halothane in oxygen were being inhaled.

In one subject soft tissue obstruction in the respiratory tract developed following the induction of anaesthesia, resulting in hypercarbia (Pco₂ approximately 60 mm Hg) and a burst of ventricular premature contractions which disappeared with restoration of a patent airway. Another individual gagged repeatedly on an oral airway during light anaesthesia and this was followed by a similar arrhythmia which also vanished when the respirations became regular.

Hypercarbia. Inhalation of carbon dioxide produced abnormalities of cardiac rhythm consisting of atrioventricular nodal rhythm, ventricular extrasystoles and multifocal ventricular tachycardia, in each of fifteen subjects, and in 36 of 38 trials. The ventricular arrhythmias appeared at a characteristic and reproducible Pco₂ “threshold” in each subject at similar concentrations of halothane and rates of rise of Pco₂. This is shown in table I. There was no consistent relation between the concentration of halothane respired and the Pco₂ threshold (fig. 1). The effect of changing the halothane concentration was studied in more detail in seven cases (who served as their own controls). Three were found to show a lesser susceptibility to arrhythmia production when halothane concentration was low than when it was high. The opposite was the case in the four others.

The average end-expired Pco₂ level at which ventricular arrhythmias first appeared was 92 mm Hg (range 60–140 mm Hg). Subjects who developed multifocal ventricular tachycardia did so at a significantly (p < 0.05) lower level (76 ± 16 (S.D.) mm Hg).

In a similar study during cyclopropane anaesthesia Lurie and associates (1958) showed that the "arrhythmia threshold" was over-estimated in proportion to the rate of Pco₂ rise. A similar observation was made in the present study. For this reason only the results obtained when Pco₂ was elevated at less than 5 mm Hg/min have been included in the present report.

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Per cent halothane</th>
<th>Rate of Pco₂ increase (mm Hg/min)</th>
<th>Pco₂ arrhythmia threshold (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.9</td>
<td>2</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>1.8</td>
<td>4</td>
<td>68</td>
</tr>
<tr>
<td>5</td>
<td>1.8</td>
<td>3</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>1.8</td>
<td>4</td>
<td>80</td>
</tr>
<tr>
<td>9</td>
<td>1.1</td>
<td>4</td>
<td>116</td>
</tr>
<tr>
<td></td>
<td>1.1</td>
<td>4</td>
<td>120</td>
</tr>
<tr>
<td>13</td>
<td>2.0</td>
<td>3</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>2.0</td>
<td>2</td>
<td>82</td>
</tr>
<tr>
<td>14</td>
<td>1.0</td>
<td>5</td>
<td>117</td>
</tr>
<tr>
<td></td>
<td>1.0</td>
<td>5</td>
<td>120</td>
</tr>
</tbody>
</table>
Ventricular extrasystoles were always preceded by normal sinus rhythm except for the minor changes in P wave and S–T segment already mentioned. Multifocal ventricular tachycardia developed in six instances in five subjects. In each case it was preceded by ventricular premature beats. The type of arrhythmia readily changed in a given subject without apparent reason although one type predominated during each period of hypercarbia. Elevating the \( \text{PCO}_2 \) 10–20 mm Hg above the arrhythmia "threshold" was without effect either upon the frequency of ventricular extrasystoles or the number of ectopic foci.

Atrioventricular nodal rhythm occurred on eight occasions in five subjects during hypercarbia. In three instances it was associated with retrograde conduction, and in one with a "wandering pacemaker". Nodal rhythm appeared, if it occurred at all, with the onset of ventricular extrasystoles. In three subjects it persisted after their disappearance.

Reduction of elevated \( \text{PCO}_2 \). Arrhythmias were permitted to continue for from 3 to 25 minutes before they were terminated by reducing the \( \text{PCO}_2 \). As \( \text{PCO}_2 \) declined the number of ventricular foci, and the frequency of ventricular extrasystoles progressively diminished. In one subject the return to normal rhythm was dramatic (fig. 2). The \( \text{PCO}_2 \) at which ventricular arrhythmias disappeared was 72 mm Hg (S.D. = 16). Sinus rhythm was re-established in 80 per cent of cases when \( \text{PCO}_2 \) had reached 60 mm Hg. An increase in the severity of the arrhythmia during the correction of hypercarbia was not observed. The rate of decrease of \( \text{PCO}_2 \) ranged from 5 to 25 mm Hg/min.

Heart Rate and Arterial Blood Pressure.

These data are summarized in table II.

Normal \( \text{PCO}_2 \). Before induction of anaesthesia the heart rate in the fifteen subjects averaged 78 beats per minute, and the arterial pressure 91 mm Hg.
Table II

| Subject | No. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | Average |
|---------|-----|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|-------|
| Age     |     | 30| 16| 42| 33| 23| 36| 17| 32| 49| 35| 22| 39| 33| 15| 45| 80| 62| 72| 60| 66| 104| 74| 47| 129| 45| 72| 100| 67| 67| 57| 47| 47| 36| 47| 36| 57| 63| 63| 56| 56| 56| 36| 36| 57| 67| 67| 57| 47| 47| 36| 57| 67| 67| 57| 47| 47| 36 |

**Mean arterial blood pressure (mm Hg)**

| Subject | No. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | Average |
|---------|-----|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|-------|
| Age     |     | 30| 16| 42| 33| 23| 36| 17| 32| 49| 35| 22| 39| 33| 15| 45| 80| 62| 72| 60| 66| 104| 74| 47| 129| 45| 72| 100| 67| 67| 57| 47| 47| 36| 47| 36| 57| 63| 63| 56| 56| 56| 36| 36| 57| 67| 67| 57| 47| 47| 36| 57| 67| 67| 57| 47| 47| 36 |
CIRCULATORY CHANGES DURING HALOTHANE ANAESTHESIA

Hg. Some subjects were apparently apprehensive; tachycardia was the rule in these individuals, although blood pressure was often no greater than when they were visited in the ward on the previous day. The heart rate usually slowed with the induction of anaesthesia, but persistent bradycardia was observed in only nine cases; the others, following transient changes, exhibited either the same or a higher rate than during consciousness. The level of mean arterial blood pressure was reduced by halothane inhalation in all subjects but one, but there was no consistent relationship between the concentration inspired and the degree of hypotension.

Elevated Pco₂. Elevation of the Pco₂ during halothane anaesthesia resulted in an increase in heart rate in all subjects but one prior to the onset of cardiac arrhythmias. An increase in arterial pressure was less frequent, occurring in only nine cases. A reduction in pressure occurred in four, and in one individual (No. 14) the inhalation of carbon dioxide produced hypotension so profound that its administration was terminated.

When ventricular extrasystoles were present, the heart rate was significantly higher than when they were not, and it averaged 96 beats per minute. A rate of 180 beats per minute was attained in each of the two subjects who developed multifocal ventricular tachycardia. The mean arterial pressure was not consistently altered by the development of these arrhythmias. Although the premature beats usually produced effective ventricular contractions, they were sometimes nearly ineffective in producing a pulse (fig. 3).

There was a significant relationship (p < 0.01) between the mean arterial blood pressure just before carbon dioxide inhalation and the Pco₂ “arrhythmia threshold” in that the threshold was higher, the lower the blood pressure (fig. 4). In two subjects in whom blood pressure was low during stable anaesthesia, ventricular arrhythmias could not be produced by carbon dioxide inhalation.

One subject had a mean blood pressure of 45 mm Hg during the stable state of anaesthesia. No ventricular arrhythmias occurred despite inhalation of a concentration of carbon dioxide over 140 mm Hg. The concentration of halothane was then reduced and following a second period of stable anaesthesia when the mean arterial blood pressure was no greater, ventricular tachycardia occurred. This was followed by a fall in pressure and a further rise in heart rate.

FIG. 3
Ineffective pressure pulses produced by ventricular extrasystoles. Compare normal beats.

E.C.G. Lead II

Intra.art. mm Hg
- 150
- 100
- 50
- 0

E.C.G. Lead I

1 —— 3 SEC ———
Arrhythmia threshold (PcO₂) in relation to mean arterial blood pressure (M.A.B.P.).

Arrhythmia threshold (PcO₂) in relation to mean arterial blood pressure (M.A.B.P.).

In this study normal sinus rhythm (or minor variations of it) was always present during halothane inhalation, provided that normal alveolar ventilation was maintained. Bradycardia was common, but the only evidence of pacemaker displacement was a slight change in the shape of the P wave in some cases, indicating a shifting site of impulse formation within the sino-atrial node. Atrioventricular nodal rhythm, ventricular extrasystoles, and other abnormalities of rhythm occurred only when respiratory obstruction or depression was present, or when alveolar carbon dioxide concentration was deliberately elevated by the administration of this gas.

These results contrast with observations made during cyclopropane anaesthesia (Lurie et al., 1958), when ventricular arrhythmias could be produced at normal levels of PcO₂ merely by increasing the concentration of cyclopropane inspired. Possible explanations for this difference between the two agents will be suggested below.

Burns and co-workers (1957) reported that ventricular premature contractions occurred when the concentration of halothane was high and that a reduction of vapour strength abolished them. However, these authors found that halothane reduced the minute and, even more, the tidal volume of respiration. This effect was more marked at high concentrations of halothane. It seems inevitable that the alveolar PcO₂ increased when the vapour strength of halothane was elevated, and it is likely that this could have caused cardiac arrhythmias which were incorrectly attributed to halothane per se. Unfortunately, the PcO₂ was not estimated. Much the same thing can be said for the results of Johnstone (1956) and Hudon et al. (1957). This is not to say that hypercarbia is the only cause of cardiac arrhythmia during halothane inhalation; but it is a likely cause until its existence can be eliminated.

pressure was higher (60 mm Hg), elevation of the PcO₂ to 110 mm Hg gave rise to ventricular extrasystoles.

In the other subject the mean arterial blood pressure was 40 mm Hg during stable anaesthesia and the addition of carbon dioxide reduced this to 30 mm Hg at a point when the PcO₂ was 82 mm Hg. In view of the hypotension, the concentration of halothane was reduced. In the period of stable anaesthesia which followed this the mean arterial blood pressure was 60 mm Hg and ventricular premature contractions were subsequently produced by elevating PcO₂ to 117 mm Hg.

Reduction of elevated PcO₂. Following withdrawal of carbon dioxide and the return to normocarbia the minimum arterial blood pressure averaged 69 mm Hg. Minima occurred between 2 and 10 minutes after the return of PcO₂ to normal. A marked decrease in pressure, compared to observations made just before the induction of hypercarbia, was observed in one patient (No. 9), and a moderate reduction occurred in two other cases (Nos. 2 and 3). With these exceptions no patient exhibited a reduction in pressure as great as 10 mm Hg compared with that measured in the period of stable anaesthesia before carbon dioxide inhalation. In two cases the pressure was significantly higher after carbon dioxide inhalation than it had been before. When the minimum blood pressure was observed, the average heart rate was 86 beats per minute, and individual values were almost uniformly higher than before hypercarbia.

DISCUSSION

In this study normal sinus rhythm (or minor variations of it) was always present during halothane inhalation, provided that normal alveolar ventilation was maintained. Bradycardia was common, but the only evidence of pacemaker displacement was a slight change in the shape of the P wave in some cases, indicating a shifting site of impulse formation within the sino-atrial node. Atrioventricular nodal rhythm, ventricular extrasystoles, and other abnormalities of rhythm occurred only when respiratory obstruction or depression was present, or when alveolar carbon dioxide concentration was deliberately elevated by the administration of this gas.

These results contrast with observations made during cyclopropane anaesthesia (Lurie et al., 1958), when ventricular arrhythmias could be produced at normal levels of PcO₂ merely by increasing the concentration of cyclopropane inspired. Possible explanations for this difference between the two agents will be suggested below.

Burns and co-workers (1957) reported that ventricular premature contractions occurred when the concentration of halothane was high and that a reduction of vapour strength abolished them. However, these authors found that halothane reduced the minute and, even more, the tidal volume of respiration. This effect was more marked at high concentrations of halothane. It seems inevitable that the alveolar PcO₂ increased when the vapour strength of halothane was elevated, and it is likely that this could have caused cardiac arrhythmias which were incorrectly attributed to halothane per se. Unfortunately, the PcO₂ was not estimated. Much the same thing can be said for the results of Johnstone (1956) and Hudon et al. (1957). This is not to say that hypercarbia is the only cause of cardiac arrhythmia during halothane inhalation; but it is a likely cause until its existence can be eliminated.
In the present study, elevation of the end-expired PCO₂ initiated cardiac arrhythmias in every subject. This result is in agreement with those of Johnstone (1956) and Stephen et al. (1957) who, however, did not measure the degree of hypercarbia necessary to initiate abnormalities of rhythm. In our subjects the end-expired PCO₂ at which a ventricular arrhythmia appeared ranged from 62 to over 140 mm Hg (average 92 mm Hg). This “threshold” was not influenced by the depth of halothane anaesthesia in any consistent way. The arrhythmias persisted while carbon dioxide concentration remained at the “threshold” level or above, further elevation did not increase their severity, and reduction of the PCO₂ led to their abolition.

While these findings resemble those previously reported during cyclopropane anaesthesia (Lurie et al., 1958), there are important differences. First, the PCO₂ threshold for the production of arrhythmias during cyclopropane anaesthesia (mean 74, range 44–107 mm Hg) was significantly lower than during halothane anaesthesia. Second, the higher the concentration of cyclopropane inspired, the lower was the alveolar PCO₂ at which arrhythmias occurred. Third, arrhythmias, instead of disappearing when PCO₂ was reduced, sometimes increased in frequency. An exacerbation of arrhythmia typically occurred only when the PCO₂ was reduced at a rapid rate (i.e. over 40 mm Hg/min). Since in the present study the maximum rate of fall was only 25 mm Hg/min this difference may be more apparent than real. Even so, exacerbation occurred occasionally during cyclopropane anaesthesia at rates of reduction as low as 15 mm Hg/min.

An explanation for these differences between halothane and cyclopropane has been sought by us in studies of the sympatho-adrenal responses to anaesthesia and hypercarbia (Price et al., 1959). Many anaesthetics, including halothane and cyclopropane, “sensitize” the myocardium to the actions of the catechol amines. Since one of these actions is the production of arrhythmias, it is evident that disorders of rhythm can result, if the anaesthetic itself or some change associated with its inhalation (e.g. hypercarbia or hypoxia) calls forth sympatho-adrenal activity. This idea is not new, for it resembles Levy’s (1911) views on chloroform. What is new is the existence of methods adequate to estimate the degree of sympathetic response from microchemical analysis of peripheral blood (Price and Price, 1957). Cyclopropane inhalation was found by us to increase the concentration of noradrenaline in plasma when the PCO₂ was normal. Halothane did not do so (Price et al., 1959). Carbon dioxide inhalation during cyclopropane anaesthesia produced a further increase in noradrenaline concentration, and adrenaline also appeared in the plasma in large amounts (Price et al., 1958). During halothane anaesthesia the sympatho-adrenal response to hypercarbia was weak. Reduced reactivity of the sympathetic nervous system during halothane anaesthesia thus may explain the absence of ventricular arrhythmias at normal PCO₂ levels, as well as the relatively high PCO₂ required for their production. The synergism between cyclopropane and carbon dioxide in producing arrhythmias, in contrast, could result from the fact that both substances produce a common effect, namely increased sympathetic nervous discharge.

The high PCO₂ needed to produce arrhythmias during halothane administration may be related also to the arterial hypotension which this anaesthetic commonly produces, for it has been shown that ventricular arrhythmias are more easily produced when blood pressure is high than when it is low (Moe et al., 1948). In addition to acting centrally to produce stimulation of the sympathetic nervous system, carbon dioxide acts peripherally causing vasodilatation and decreased myocardial contractility. When the sympathetic response is reduced, as it may be by halothane, the peripheral effect may predominate, resulting in arterial hypotension. In four of our subjects the blood pressure response to hypercarbia was indeed that of reduction of pressure, and marked increases in pressure rarely occurred. These facts may also help in explaining the high arrhythmia threshold.

The small degree of post-hypercarbic hypotension usually found during halothane anaesthesia is similar to the experience of Lurie and associates (1958) during cyclopropane administration, and also to that of Sechzer et al. (1959), in conscious man. Observations made in this laboratory during the past several years make us believe that when hypotension occurs in surgical patients following the correction of respiratory
acidosis, the degree of blood pressure reduction is related as much to such factors as reduction of anaesthetic concentration, blood loss, and motion, as to Pco₂ reduction.

SUMMARY
The effects of halothane inhalation on arterial blood pressure and cardiac rate and rhythm during normocarbia and hypercarbia were studied in fifteen subjects. The electrocardiogram, end-expired carbon dioxide tension, and brachial arterial pressure were recorded continuously. Hypercarbia was produced by carbon dioxide inhalation. Significant abnormalities of cardiac rhythm did not occur except during airway obstruction or carbon dioxide inhalation. Arterial pressure was consistently, and heart rate inconsistently, reduced. When carbon dioxide was administered, abnormal cardiac rhythms were produced in every case. The average Pco₂ at which these arrhythmias occurred was 92 mm Hg. Hypertension during carbon dioxide inhalation was not marked; it was sometimes absent, and hypotension occasionally occurred. Return of the elevated Pco₂ to normal was associated with hypotension which, however, was pronounced in only three cases.

REFERENCES


