ELECTROCARDIOGRAPHIC STUDIES DURING THE INHALATION OF
30 PER CENT CARBON DIOXIDE IN MAN

BY
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Carbon dioxide inhalation was first used for the treatment of psychosis by Loevenhart, Lorenz and Waters in 1926, but the results were not encouraging. Meduna (1943), introduced 30 per cent carbon dioxide inhalation as a treatment for psychoneurosis, and claimed good results, particularly in cases of stammering. Since its introduction, this treatment has been used in several thousand cases by Meduna and his associates.

The human electrocardiogram during 30 per cent carbon dioxide inhalation has been studied by McDonald and Simonson (1953), and these authors describe some disturbance of auricular or ventricular activity in 12 of 17 patients investigated. Auricular and ventricular extrasystoles, P wave inversion, alteration in the T wave voltage, together with auricular and supraventricular tachycardia were all found.

In the psychiatric department of this hospital, 30 per cent carbon dioxide inhalation has been studied by McDonald and Simonson (1953), and these authors describe some disturbance of auricular or ventricular activity in 12 of 17 patients investigated. Auricular and ventricular extrasystoles, P wave inversion, alteration in the T wave voltage, together with auricular and supraventricular tachycardia were all found.

In the present paper electrocardiographic studies were carried out in 8 patients (4 males and 4 females) before, during and after 30 per cent carbon dioxide inhalation. The results obtained were not in complete agreement with those of McDonald and Simonson. Evidence of delayed conduction and numerous auricular extrasystoles were observed but no ventricular extrasystoles were seen. Auricular tachycardia, which occurred in 2 subjects on one occasion each, was the only disturbance of rhythm encountered.

METHODS

A mixture of approximately 30 per cent carbon dioxide and 70 per cent oxygen was administered by means of a breathing bag and tightly fitting facepiece from a stock cylinder, via a reducing valve and flowmeter, with the patient lying supine on a couch or trolley. Normally, observations were made during 3 treatments in each of the 8 patients. Additional recordings were made in the 2 subjects in which auricular tachycardia was observed. Treatment was commenced with 10 or 15 respirations of the mixture and the patient's clinical response noted. On subsequent occasions the number of respirations was increased gradually until the number required to produce narcosis was reached (Meduna, 1943). When carbon dioxide inhalation was complete the mask was removed and the patient allowed to breathe room air again. The majority of patients required 35 to 45 respirations of 30 per cent carbon dioxide to produce narcosis, and this was administered in all treatments after the gradual introduction described. Electrocardiographic studies were carried out only after the treatment had been standardized in this manner.

The majority of the electrocardiographic records were taken with an Elmquist portable, though several were made with a standard hospital model Cambridge machine.
A general physical examination was carried out on all patients before treatment, and a nine-lead electrocardiogram (I, II, III, aVF, aVL, aVR, V2, V4, V6) was also recorded at this time. These records were examined to exclude cardiac abnormality and to determine the electrical axis for future reference. As it was only possible to record one lead during treatment and recovery, lead II was chosen as the most suitable. Short runs of leads I, II, and III, were made before the treatment under investigation. Lead II was then recorded throughout the period of inhalation of carbon dioxide and for about 2 minutes of the recovery period, when the inhalation was stopped and the patient breathed room air again.

Arterial Blood Pressure.

Records of systolic and diastolic blood pressures were obtained during carbon dioxide inhalation and recovery. These were at first made using a sphygmomanometer, but subsequently were directly recorded from a needle in the brachial artery by a capacitance manometer. The results obtained by both methods were in complete agreement.

pH Estimations.

The pH of venous blood was determined in a number of patients using a Cambridge pH meter. The blood samples were drawn into nylon syringes which had been rinsed with heparin. The syringes were sealed with caps made from soldered needle hubs, and stored in ice until the pH measurements were made.

Respiratory Records.

These were recorded using two stethographs, one round the chest and one round the abdomen, connected to a single volume recorder from which tracings were obtained on a kymograph.

RESULTS

When 30 per cent carbon dioxide was inhaled, marked respiratory stimulation commenced after about 5 respirations. Increase in depth was more pronounced than increase in rate; in some cases this became extreme, and a gasping type of respiratory pattern occurred. Marked muscular tremor and profuse sweating were commonly present. Salivation was pronounced in many patients.

Cardiac Rate.

There was great variation in the response of the cardiac rate to 30 per cent carbon dioxide inhalation, and no consistent change was found. This is to be expected when it is considered how many factors are involved. Apprehension, the rise in arterial blood pressure, mechanical effects of hyperventilation, stimulation of chemoreceptors, the direct effect of the carbon dioxide on the central nervous system, and the cardiac conducting mechanism, must all exert an influence on the cardiac rate. Table I shows the response to a typical treatment in each patient.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Before CO₂</th>
<th>Cardiac rate per min</th>
<th>PR secs</th>
<th>QT secs</th>
<th>During CO₂</th>
<th>Cardiac rate per min</th>
<th>PR secs</th>
<th>QT secs</th>
<th>After CO₂</th>
<th>Cardiac rate per min</th>
<th>PR secs</th>
<th>QT secs</th>
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<td>0.34</td>
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<td></td>
<td>85</td>
<td>0.14</td>
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</table>
Arterial Blood Pressure.

The inhalation of 30 per cent carbon dioxide produced a marked and progressive rise in both systolic and diastolic blood pressure values. When the mask was removed and the patient allowed to breathe room air, the systolic and diastolic blood pressures returned to resting levels again. In several cases the rise in arterial blood pressure was great enough to be considered a potential hazard in the presence of degenerative vascular conditions.

P Wave.

Increased P wave voltage was encountered during treatment and early recovery in the majority of cases, and the wave presented a peaked appearance. Low or inverted P waves were observed in 12 records from 5 patients in association with abnormal complexes. In 3 records the P wave voltage was not increased but the contour changed and it became peaked as in the other cases. Prominent S waves were often seen in conjunction with the increased P waves.

TABLE II
The effect of 30 per cent carbon dioxide inhalation on the pH of venous blood

<table>
<thead>
<tr>
<th>Subject</th>
<th>pH before CO₂</th>
<th>pH during CO₂</th>
<th>pH after CO₂</th>
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<td>7.12</td>
<td>7.38</td>
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<td>7.29 7.16</td>
<td>—</td>
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<td>7.13</td>
<td>7.3</td>
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<tr>
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<td>7.42</td>
<td>7.22 7.12</td>
<td>7.4</td>
</tr>
<tr>
<td>5</td>
<td>7.4</td>
<td>7.24 7.15</td>
<td>7.4</td>
</tr>
</tbody>
</table>

pH Results.

A severe and progressive acidosis was produced during 30 per cent carbon dioxide inhalation (table II). When the carbon dioxide inhalation was stopped the pH values returned very rapidly to normal values again.

ELECTROCARDIOGRAMS

Complexes.

Of 30 electrocardiographic records obtained, 18 showed no abnormal complexes. Three of the patients studied showed no abnormal complexes in any of their recordings. Auricular extrasystoles were present in 12 records obtained from the other 5 patients (fig. 1) and could be identified during treatment or recovery or both. In several, extrasystoles occurred only during recovery when the carbon dioxide treatment was stopped and the patient breathed room air again.

Disturbances of Rhythm.

In 2 patients an abnormal rhythm occurred towards the end of treatment and during the first 45 seconds of the recovery period. This consisted of short runs of auricular tachycardia with scattered auricular extrasystoles (fig. 2). No such abnormal rhythm was observed during the other treatments studied in these patients.

T Wave.

A spiked T wave with a broad base was commonly present during carbon dioxide inhalation and increased T wave voltage was present in all but one of the records. In one of two records which showed the presence of auricular tachycardia the T wave voltage was very low.

ST Segment.

There were isolated instances of ST segment elevation in two treatments on one subject. In one of these records extrasystoles were present. All other records in all patients showed normal ST segments.

PR Interval.

This showed some slight increase in most records during treatment and early recovery (table I). In many cases the interval was difficult to measure due to absence or distortion of the P wave.

QRS.

Some slight increase was present in the QRS interval in all cases during treatment and early recovery.
FIG. 1
Upper tracing shows normal complexes at beginning of 30 per cent CO₂ inhalation. Lower tracing shows presence of auricular extrasystoles occurring towards the end of inhalation.
Paroxysmal auricular tachycardia occurring during 30 per cent CO₂ inhalation. Lower tracing shows one extrasystole. The P and T wave voltage is increased and the PR and QT intervals are prolonged (Lead II).

Fig. 2
There was a marked increase in the QT interval relative to cycle length in all cases during treatment (table I). This was the most definite and consistent finding in the whole series. Figure 3 shows how the inhalation of 30 per cent carbon dioxide is accompanied by a marked increase in the QT interval, which returns to levels, normal for the cycle length, after inhalation ceases. Here the observed QT interval is graphed along with the upper limits of normal for the cycle length, which were obtained from the table by Ashman and Hull (1945). This table derived from observations on several thousand normal subjects can be applied relative to age and sex.

**DISCUSSION**

Inhalation of 30 per cent carbon dioxide produces hyperventilation, severe acidosis and a marked rise in arterial blood pressure. The procedure is unpleasant, and in the conscious untrained subject is associated with a considerable degree of mental stress. Each of these factors is capable of producing changes in the electrocardiogram and it is difficult to decide the relative importance of each.

**Hyperventilation.**

True hyperventilation in air is accompanied by a low PCO₂ and alkalosis, and so is not directly comparable to the circumstances of the present investigation. Since inhalation of 30 per cent carbon dioxide causes marked hyperpnoea the mechanical effects of the greatly increased respiratory movements must be considered, for these can cause alterations in intrathoracic pressures, displacement of the electrical axis of the heart, and may initiate reflexes from stretch receptors in the chest. Reflexes during deep breathing have been shown to cause extrasystoles. Ventricular and auricular extrasystoles as well as auricular flutter and fibrillation have been repeatedly described (Stokes, 1910; Smith and Moody, 1923; Burak and Scherf, 1933). Evans (1951) investigated the effect of deep inbreathing in 200 healthy adults and describes the frequent occurrence of extrasystoles and, in one case, of paroxysmal tachycardia. However, unless carbon dioxide elimination is prevented, hypocapnia must be considered as a possible factor in the production of electrocardiographic changes occurring with deep breathing. It is difficult therefore to decide the importance to be attached to the mechanical effects of hyperventilation in the production of electrocardiographic changes in the present series.

**Acidosis.**

The acidosis produced by the inhalation of 30 per cent carbon dioxide is severe and progressive and low pH values were commonly encountered (table II). Gibbs and Gibbs, quoted by Meduna (1950), have shown changes in arterial blood pH from a level of 7.37 to 6.96 after 20 to 35 breaths of 30 per cent carbon dioxide, with an almost immediate return to normal after carbon dioxide inhalation ceases.

Prolongation of the QT interval, a consistent finding in the present investigation, commonly accompanies altered blood calcium or potassium levels (Bellet and Steiger, 1950). Potassium intoxication, which is associated with acidosis, produces alterations in the electrocardiogram similar to those found in the present series of cases. There is an increase in the T wave voltage and the wave shows a peaked, tent-like character, the PR and QT intervals are increased and the QRS complex is also prolonged (Bland, 1956). Ectopic arrhythmias too, have been reported in patients with hyperkalaemia (Somerville, 1951). Respiratory acidosis was studied in the dog during diffusion respiration and with carbon dioxide inhalation, and increase in T wave voltage, QRS voltage and prolongation of the PR interval with slowing of the heart rate noted (Brown and Millar, 1952; Whitehead et al., 1949; Parry, 1949). Using 30 per cent carbon dioxide inhalation in dogs, Brown and Millar (1952) found occasional ventricular extrasystoles and increased T wave voltage during inhalation, but found that ventricular arrhythmias, frequently leading to death, occurred on changing from carbon dioxide back to atmospheric air. In the present series, auricular extrasystoles, and, in one patient, bouts of auricular tachycardia occurred after carbon dioxide inhalation ceased, no abnormal rhythms or complexes being present during the inhalation. It is considered (Brown and Millar, 1952) that the sudden shift in pH back to normal is responsible for this. It would appear that changes in the T wave and PR, QRS, and QT intervals encountered in these cases could be ex-
FIG. 3
Prolongation of the QT interval produced by 30 per cent CO₂ inhalation.

- •• Measured QT interval.
- - - Upper limits of normal QT for cycle length.
- o o Cardiac rate.
plained on the basis of ionic changes occurring during the severe acidosis.

**Hypertension.**

The presence of extrasystoles in patients with hypertension is described by many authors (Peel, 1928; Koppang, 1924; Flaxman, 1940). Hegglin and Halzman (1937) described the appearance of extrasystoles during hypertensive crises in patients with phaeochromocytoma, but it is considered (Scherf and Schott, 1953) that it is not the hypertension of itself, but the circulating pressor amines adrenaline and noradrenaline which are responsible for their production. Dunér (1955) has found that hypercapnia causes an increased release of adrenaline and noradrenaline. Moe et al. (1949) found that a sudden increase in peripheral resistance due to vasoconstriction is badly tolerated by heart muscle and can bring on ventricular tachycardia or even fibrillation. Intense vasoconstriction in muscle vessels occurs during 30 per cent carbon dioxide inhalation (McArdle, Roddie, Shepherd and Whelan, 1957). Undoubtedly the rise in arterial blood pressure produced by the inhalation of 30 per cent carbon dioxide, which is at times extreme and associated with vasoconstriction in the limbs, is a likely factor in the production of the extrasystoles seen in these cases.

**Mental Stress.**

Alterations in the P wave are commonly of emotional origin (Burch and Winsor, 1950), and apprehension or fear could produce the increase in P wave voltage encountered. However, inverted or absent P waves imply that the wave of excitation follows an abnormal pathway through the auricles as in auricular or nodal premature contractions (Burch and Winsor, 1950). Anxiety and fear can produce extrasystoles (Katz, Winton and Megibow, 1947). Fleisch (1933) recorded extrasystoles in two-thirds of subjects investigated during an examination, and Millar and McLean (1941) describe four instances of extrasystoles occurring during severe inner conflicts. It is of importance, also, that nervous factors can increase the incidence of extrasystoles produced by other causes, e.g. hypertension (Scherf and Schott, 1953). Though the rise in arterial blood pressure and hyperventilation together with fear or anxiety on the part of the patient could conceivably produce extrasystoles and alterations in the P wave, the changes in the T wave and intervals suggest a state of ionic imbalance within the myocardium resulting from the severe acidosis. It appears likely, however, that the tolerance of well-oxygenated cardiac muscle to this is considerable, since no serious disturbances of rhythm were encountered in the whole series.

**Anaesthesia and Carbon Dioxide accumulation.**

Cardiac irregularities under anaesthesia have been reported by many authors. The work of McDowall (1938), Meek (1940), Robbins (1945) and Johnstone (1950), suggest the importance of carbon dioxide accumulation as a factor. That carbon dioxide accumulation is common during general anaesthesia is undoubtedly true. Many factors such as the respiratory depressant action of anaesthetic agents (Dripps and Dumke, 1943), the increased use of muscle relaxants (Churchill-Davidson, 1958), the inefficiency of artificial ventilation (Gordon et al., 1951), and the increase in respiratory deadspace (Severinghaus and Stupfel, 1955; Pask, 1958), are responsible. Since most of these factors favour the production of hypoxia, it seems likely that disturbances of cardiac rhythm which occur will be aggravated by this, for severe hypoxia can itself produce a condition resembling fibrillation in the mammalian heart (Schwartz, 1949). Autonomic imbalance due to the anaesthetic agent used may produce cardiac irregularities, when a reflex is initiated by traction on a viscus (Wakefield, 1947; Maher et al., 1934) or from irritation of the glottis (Burstein et al., 1950). It is possible, therefore, that carbon dioxide accumulation under anaesthesia could be productive of more serious disturbances than were encountered in the present series, in which the acidosis, though very severe, was of short duration and uncomplicated by hypoxia or other factors.

**SUMMARY**

Electrocardiographic studies were made in 8 patients before, during, and after inhalation of 30 per cent carbon dioxide in oxygen for periods from 1 to 2 minutes. The inhalation caused hypertension and hyperpnoea and a marked fall in the pH of venous blood.

In spite of the severity of the respiratory acidosis, auricular extrasystoles were the only abnormal complexes seen, and were observed in 12
records from 5 of the 8 patients. No serious disturbances of rhythm were encountered. Periods of paroxysmal tachycardia were observed in 2 patients on one occasion each.

Increase in the PR, QRS and QT intervals suggested delayed conduction within the myocardium, and was considered to be a direct effect of the acidosis.

It is considered that the absence of hypoxia and other complicating factors distinguish the dangers of inhaling carbon dioxide in oxygen from carbon dioxide accumulation occurring during anaesthesia. Provided that patients free from cardiovascular disease are selected, carbon dioxide in oxygen can be administered as a therapeutic procedure without serious disturbance to cardiac function.

ACKNOWLEDGMENTS

I wish to thank Dr. P. P. O’Malley, psychiatrist, for the cases used in this study, and Dr. J. P. Donaghy for his assistance with the electrocardiographic interpretation. I am also indebted to Dr. I. C. Roddie, Queen’s University, Belfast, for his help and advice.

REFERENCES


ELECTROCARDIOGRAMS DURING INHALATION OF CARBON DIOXIDE


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NEWS FROM THE FACULTY OF ANAESTHETISTS OF THE ROYAL COLLEGE OF SURGEONS

**Honorary Fellowship in the Faculty of Anaesthetists.** The Council of the College, acting on the recommendation of the Board of Faculty, has elected the following to the Honorary Fellowship in the Faculty:

- Harold Randall Griffiths
- Ashley Skeffington Daly

**Fellowship in the Faculty by Election.** The Council of the College, acting on the recommendation of the Board of Faculty, has elected the following to the Fellowship in the Faculty:

- Robert Henry Palmer Fitzpatrick
- Alexandre Goldblat
- Torsten Gordh
- Geoffrey Arthur Haydock
- Eric Nilsson

**Joseph Clover Lecture.** Dr. J. A. Lee, F.F.A.R.C.S., has been appointed to give the Joseph Clover Lecture in March 1960, in place of Dr. H. J. Brennan, who has resigned for reasons of health.

**Nuffield Prize.** Dr. Sylvia Lock Seung Hui, M.B., B.S., of the University of Hong Kong, has been awarded the Nuffield Prize, having obtained the highest marks in the Primary Examination for the F.F.A.R.C.S. held in December 1958.

**Adviser in Postgraduate Studies.** Dr. W. D. Wylie, F.F.A.R.C.S., has been appointed Faculty Adviser in Postgraduate Studies. He will be pleased to advise, and arrange instruction for, any postgraduates studying anaesthetics in this country.