**Effect of Carbon Dioxide Excess on Contractile Force of Heart, In Situ**

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DURING an investigation of the effects of various anesthetic drugs on the contractile force of the dog's heart, it became apparent that hypoxia or carbon dioxide excess encountered during anesthesia would produce disturbing changes in the response to the anesthetic drugs. In order to evaluate the magnitude of these changes, a number of dogs were subjected to varying degrees of hypoxia and of CO₂ excess. The purpose of this paper is to report the effects of high concentrations of CO₂ upon the contractile force of the dog's heart measured directly in the presence of an intact circulation.

**METHOD**

As previously described (I) the contractile force of a segment of the right ventricle was measured in open-chest dog preparations by the use of a modified Cushny lever (fig. 1) recording through strain gauge equipment.

ECG recordings were made with an EPL Cardiotron and blood pressure was recorded on a smoked-drum kymograph with the mercury manometer technique. Bilateral cervical vagotomy was performed on all animals.

Each animal was anesthetized with a combination of pentobarbital 15 mg/kg, and barbital 200 mg/kg, i.v., and respired 16 to 20 times/min. by manual compression of a breathing bag connected to an endotracheal tube. After a period of stabilized recordings, carbon dioxide-oxygen mixtures of 5:95 per cent; 10:90 per cent; 25:75 per cent; and 50:50 per cent concentrations were administered by a nonre-breathing technique from a previously calibrated Foregger anesthesia machine and 5-liter reservoir bag. The average intervals of exposure to the CO₂-O₂ mixtures were: 5 per cent CO₂-9 minutes, 10 per cent CO₂-13 minutes, 25 per cent CO₂-12 minutes and 50 per cent CO₂-4 minutes. All results were recorded as the maximum stabilized response to that specific CO₂-O₂ mixture. A total of 36 experiments were performed in 19 animal preparations.

**RESULTS**

The response of the heart to the respired CO₂—O₂ mixtures followed a generally consistent pattern. Figure 2 demonstrates typical responses obtained during the administration of 10 per cent and 25 per cent CO₂.

The data obtained from all open-chest preparations are summarized in table 1. Electrocardiographic tracings demonstrated no cardiac arrhythmias during the experiments. Significant changes were confined to slowing of the rate, to slurring of the S-T segment, and to elevation of the T-wave amplitude. The incidence and
severity of these changes increased as the concentration of carbon dioxide increased in the mixture of the respired gases.

**Discussion**

Many effects of hypercapnia on the heart are known. Slowing of the rate (2), depression of the conduction tissues without partial or complete heart block (3), dilation of the ventricles, and decrease in systolic excursion (4) have been observed clinically and experimentally after exposure to high concentrations of CO₂. Wiggers (5) found no evidence from study of aortic and left ventricular pressure curves that hypercapnia affected the amplitude, gradient, duration of systole or pulse pressure of the dog's heart after exposure to an alveolar pCO₂ of 15 to 60 mm. Hg. Ketcham, King and Hooker (6) and Patterson (7) observed a diminished amplitude of ventricular contraction with concentrations of CO₂ higher than those usually considered to be compatible with life.

The modified Cushny myocardiograph technique has been employed to assay the myocardial effects of various drugs (8, 9). It records the extent of systolic excursion, indicates relative changes in diastolic size (within limits) and determines the isometric systolic tension (IST) or contractile force of a representative segment of right ventricular musculature. The IST readings are easily converted into grams of contractile force by a simple calibration procedure.

Two technical difficulties arose during the course of the experiments and were related to extreme dilation of the heart. Firstly, the maximum diastolic length of the recording muscle segment, under the influence of the highest concentrations of
CO₂, exceeded the initial arbitrary setting of the movable myocardiograph lever in some of the earlier experiments. This prevented measurement of the more extreme decrements in IST. The problem was solved by recording data throughout the entire experiment with two or three graded settings of the myocardiograph lever, and later selecting the series of readings which were taken with a diastolic length immediately greater than the maximum diastolic length encountered during the later phases of the experiment.

Secondly, as dilation of the heart occurred, the spatial relationships of the heart to the thoracic cage and the points of attachment to the myocardiograph were altered to such an extent that the kymographic record of diastolic size became of only qualitative, and not quantitative, value. The recording muscle segment merely bulged upward between the recording arms after a maximum recording capacity of approximately 4 per cent ventricular dilation was reached during the administration of 5 per cent CO₂. Visual inspection of the heart at various intervals throughout each experiment revealed that dilation occurred beyond this limit. In spite of an attempt to increase the capacity of the recording system by moderately suspending the heart during the initial portion of each experiment, this capacity was not significantly changed.

Concentrations of carbon dioxide as low as 5 per cent in the inspired gases produced a decrease in myocardial contractile force (IST) as determined by this technique. The amplitude of systolic excursion diminished. With increasing concentrations of carbon dioxide, each of these features steadily progressed until the

![Fig. 2. KYMOCARPH RECORDING (above) and oscillograph recording (below) obtained with modified Cushny heart levers in open-chest dog preparations. Upper tracing in kymograph recording indicates excursion of Cushny levers. Downward excursion represents systole. Dotted lines serve as reference points for distance between points of attachment of myocardiograph levers on the heart. Encircled arabic numerals correspond to the force in grams transmitted to the levers when they are blocked at a point slightly greater than the usual diastolic position. Lower tracing in kymograph recording made by mercury manometer recording carotid arterial pressure. Roman numerals in both illustrations indicate corresponding sections of oscillograph recordings.

In the oscillograph recording, small horizontal lines correspond to 2.7 gm. force; curved vertical lines correspond to 1-sec. time intervals.](image)
heart was permanently injured with 5 minutes exposure to 50 per cent CO₂. Petechial epicardial hemorrhages appeared and the heart rapidly dilated and weakened.

Four additional, acute, dog experiments were performed using a strain gauge arch of fixed length (9) instead of the modified Cushny levers to determine contractile force. These results were similar to those obtained by the modified Cushny levers for the various concentrations of CO₂.

Several incidental actions of carbon dioxide upon the medulla, the peripheral blood vessels and the heart were irregularly noted throughout the course of these experiments. A brief, initial, slight rise in blood pressure was occasionally encountered whenever concentrations below 10 per cent were respired. The heart rate slowed as a result of direct depression of the S.A. node and the conduction tissue of the heart. Terminal muscular fasciculations and increased muscular tonus were observed and attributed to alterations of the normal muscular metabolism.

A characteristic, transient, cardiovascular 'rebound' frequently followed the withdrawal of high concentrations of carbon dioxide. The contractile force response suggested an epinephrine-like action, yet this has been obtained in the isolated heart, and was not accompanied by a typical pressor reaction in our experiments. Brown and Miller (10) have recently investigated this phenomenon and reported a high incidence of ventricular fibrillation under such circumstances; they do not suggest a definite explanation for the increased myocardial irritability.

Although the striking effect of hypercapnia was a pronounced decrease in the force of myocardial contractions, a gradual return of the IST to control level occurred in several experiments wherein concentrations of 5, 10 and 25 per cent CO₂ were employed for 15 to 30 minutes, thus distinguishing the depressant action of CO₂ from that of the common cardiac depressant drugs. Some inherent recovery mechanism of the cardiac muscle or of the blood supply to the heart is evidently responsible for the return of contractility. Barbour and Seevers (11) have previously observed the development of tolerance to CO₂ in rats.

A progressive shift of the venous blood pH with increasing concentrations of inhaled CO₂ has been measured in dogs under generally similar conditions by Spencer et al. (12). Forty per cent CO₂ produced a pH of 6.8 and the buffer systems of the blood prevented significantly greater changes with 50 per cent CO₂. Similar studies have been reported in the isolated dog's heart (13), in the rat (14) and in man (15). Direct infusions of acid solutions which decreased the pH to 6.25 were shown by Gertler, Hoff and Humm (16) to severely impair myocardial contractility, but these effects did not become conspicuous until near the terminal stages.

These experimental results have clinical significance. Anesthesiologists have become more concerned with the implications of carbon dioxide excess and recognize

<table>
<thead>
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<th>FUNCTION OBSERVED</th>
<th>CO₂ CONCENTRATION</th>
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<tr>
<td></td>
<td>5%</td>
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<tr>
<td>Contractile force (I.S.T.)</td>
<td>-13</td>
</tr>
<tr>
<td>Systolic excursion</td>
<td>12</td>
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<tr>
<td>Heart rate</td>
<td>-7</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>-14</td>
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<td>Av. time CO₂ administered, min.</td>
<td>9</td>
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that its elimination is of equal importance to adequate oxygenation of the patient. Clinical studies have related cardiovascular changes during and following cyclopropane anesthesia to hypercapnia (17). Asphyxia has become a recognized etiological factor in cardiac arrest and in anesthetic convulsions. Seegers (18) stressed the narcotic potency of carbon dioxide when permitted to accumulate during anesthesia, and Eastman et al. (19) report that CO₂ often is useless when employed during resuscitation, since the medulla is usually depressed by anoxia to such an extent that it is incapable of responding to CO₂ stimulation.

Cardiopulmonary function tests have been devised and employed to evaluate the condition of patients with chronic pulmonary disease and congenital heart disease. The degree of pulmonary disability, in some instances, has been related partially to the increased pCO₂ observed (20). Further study will undoubtedly attribute a substantial portion of the impaired cardiac reserve of these patients to the persistently elevated blood levels of carbon dioxide.

**SUMMARY**

In 36 acute experiments, a modified Cushny myocardiograph was employed to measure the effect of carbon dioxide mixtures on the contractile force of a representative segment of the right ventricle. Heart contractile force decreased and the amplitude of systolic excursion decreased. Pronounced cardiac dilation occurred. The extent and rapidity of these changes were roughly proportional to the concentration of carbon dioxide in the respired gases. Carbon dioxide differed from the common and typical cardiac depressants in that the heart sometimes regained its original contractile force during continuous administration of the gas, and again, when the carbon dioxide was withdrawn, a characteristic and marked 'rebound' effect sometimes appeared.

**REFERENCES**