THE EFFECTS OF CONTROLLED RESPIRATION ON CIRCULATION DURING CYCLOPROPANE ANESTHESIA * † ‡ §

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BECAUSE of the retention of CO_2 during cyclopropane anesthesia, various measures have been advocated to improve ventilation. Intermittent positive pressure breathing ("controlled respiration"), manually performed by the anesthetist, is one of the techniques that is frequently utilized to maintain adequate alveolar ventilation and CO_2 tensions within normal limits. Previous studies of the hemodynamic changes during intermittent positive pressure breathing in non-anesthetized humans have served to indicate changes that may occur during the anesthetized state (1). It has been shown that a mean mask pressure of less than 5 millimeters of mercury does not significantly alter the blood pressure or the cardiac output in normal, conscious human subjects (2). Motley (1) showed that changes in cardiac output were related to increases in mean airway pressure during intermittent positive pressure breathing rather than to the inspiration-expiration time ratio. Other investigators have shown that controlled respiration during surgery associated with blood loss may produce circulatory embarrassment, as evidenced by a lowering of the arterial pressure (3, 4). Still others have reported that the arterial blood pressure was not depressed during cyclopropane anesthesia in the presence of a sustained increase in airway pressure (5). The present investigation was intended to obtain further information concerning the cardio-circulatory effects of low mean airway pressures during controlled respiration in patients anesthetized with cyclopropane.

METHOD

Thirty-four cardiac output and related hemodynamic determinations were obtained on 12 patients prior to operation. These subjects were in good physical condition and had no discernible cardiovascular or pulmonary diseases (average age, 41; range 16–58 years). They

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were brought to a quiet anesthesia room for study ninety minutes after the subcutaneous administration of morphine (5.4 to 8.0 mg.) and scopolamine (0.26 to 0.43 mg.), the dosage varying according to the age, weight and physical status of the patient. They were placed in the supine position with one arm resting above the angle of Louis on a pillow. A 15 gauge needle was inserted in the median basilic vein of the elevated arm for administration of T-1824 (Evans Blue). In 4 of the patients a sterile polyethylene tubing was threaded through the needle and passed into the right heart and pulmonary artery for pressure measurements. A thin-walled 18 gauge needle with stilet was inserted into the brachial artery of the other arm for the collection of blood samples. Electrocardiographic electrodes were appropriately placed and electro-encephalographic electrodes were positioned to record the depth of anesthesia (6). Control observations were made after a steady resting state was maintained for at least 30 minutes. It was considered that a basal resting state was obtained only when the pulse rate was below 84 per minute.

The following hemodynamic changes were evaluated: cardiac output, mean arterial pressure, total peripheral resistance, pulse rate, stroke volume, arterial blood cyclopropane, intrathoracic blood volume, arterial oxygen content and capacity, carbon dioxide content and pH.

The cardiac output was determined by the dye dilution method (7). The injection of T-1824 and collection of samples from the brachial artery were carried out according to the procedures as modified by Etsten and Li (8, 9). Brachial artery, pulmonary artery, central venous and tracheal airway pressures were measured by Statham strain gauges, and continuously recorded on a multi-channel, direct writing oscillograph with a frequency response of 60 cycles per second. The mean pressures were determined by planimetry of the pressure contour. Samples of arterial blood were drawn immediately after the cardiac output determination for analysis of cyclopropane, O_2 content and capacity, CO_2 content and pH. (Cambridge pH meter—research model). The CO_2 tension was calculated from the CO_2 serum content and pH values, using the *nomograms* of Peters and Van Slyke (10). The arterial blood cyclopropane was obtained by the method of Orcutt and Waters (11). The cardiac output was calculated from the dye dilution curve according to the modified method of Hamilton *et al.* (12). The mean circulation time, intrathoracic blood volume and total peripheral resistance were calculated by the conventional formulae (12).

After the control observations during the resting state were made, oxygen was administered for ten minutes, followed by the administration of cyclopropane by means of the to-and-fro absorption technique. Endotracheal intubation was performed using either a No. 35 or No. 38 Magill tube with inflatable cuff. The patient was maintained at a moderate depth of anesthesia as indicated by EEG level III and the

blood cyclopropane concentration of 8–15 mg. per cent. Repeated observations were made during the phase of spontaneous respiration and during the phase of controlled respiration.

The term "controlled respiration" implies intermittent positive pressure breathing obtained by manual compression of the anesthetic bag during inspiration, followed by a rapid release of the bag pressure for the expiratory phase. The expiratory time averaged twice that of inspiration, and the mean tracheal pressure ranged from + 1.5 to + 6 cm. of water. The airway pressure contour was similar to the type III curve described by Cournand *et al.* (13).

Continuous and simultaneous tracings of the brachial artery pressure, tracheal airway pressures, ECG and EEG were recorded throughout the entire procedure. Cardiac output and other related hemodynamic studies were made only when the cardiac rate and rhythm were regular.

RESULTS

Cardiac Index.—The mean cardiac index during the resting state was 3.53 L./min./m² (S.D. ± 0.66); 3.34 (S.D. ± 0.70) during spontaneous respiration with cyclopropane anesthesia; and 2.53 (S.D. ± 0.39) during controlled respiration. Of the 12 patients, 4 had cardiac output values during controlled respiration that were not significantly different from those during spontaneous respiration. These values were within the limit of error of the method (9). Eight patients were below the 12 per cent level, and the range of decrease was from − 16

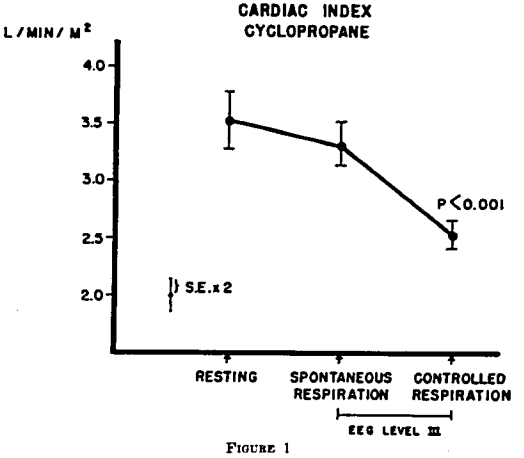

FIGURE 1

to − 52 per cent. The average reduction of the cardiac index during controlled respiration was 22.4 per cent as compared with the average value during spontaneous respiration ($P < 0.001$). (fig. 1.)

Pulse Rate.—The mean value of the pulse rate during the resting state was 69 ± 10 per minute. It decreased to 63 ± 10 per minute during spontaneous respiration and was 60 ± 9 per minute during controlled respiration. The pulse rate was not significantly changed during both types of respiration at the cyclopropane EEG level III ($P > 0.05$).

Stroke Volume.—The mean value of the stroke volume during the resting state was 84 ± 12 cc.; during cyclopropane anesthesia with spontaneous respiration it was 88 ± 19, and with controlled respiration it was 68 ± 13. The decrease of the stroke volume during controlled respiration occurred in 11 of the 12 subjects. The average fall in stroke volume was 20.6 per cent ($P < 0.001$). (fig. 2.)

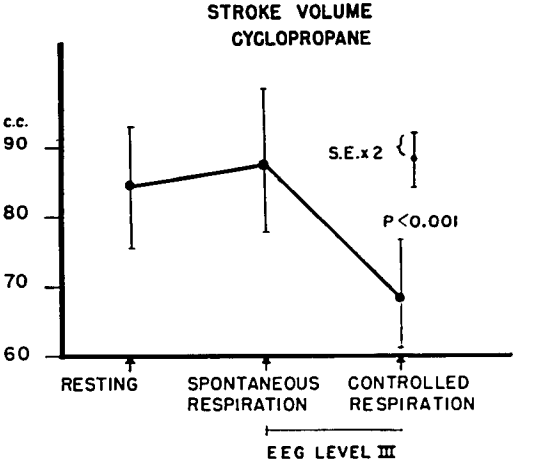

FIGURE 2

Mean Arterial Blood Pressure.—The average value of mean arterial blood pressure was 94 ± 17 mm. of mercury during the resting state; during spontaneous respiration it was 102 ± 16 mm. of mercury, and during controlled respiration it was 93 ± 16 mm. of mercury. The mean arterial blood pressure during controlled respiration was significantly ($P < 0.02$) lower than that during spontaneous respiration with cyclopropane but not significantly changed from the values obtained during the resting state ($P > 0.05$). (fig. 3.)

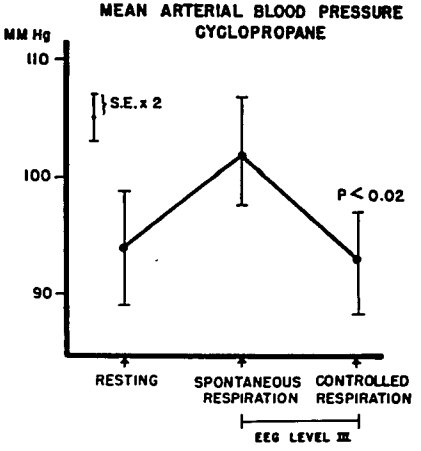

FIGURE 3

Total Peripheral Resistance.—The mean total peripheral resistance during controlled respiration was increased in 10 of the 12 cases as compared with the values during spontaneous respiration. The average value of the mean calculated total peripheral resistance during the resting state was 1411 dynes-sec.-cm.$^{-5}$ ± 420. During cyclopropane anesthesia with spontaneous respiration it was 1548 ± 350, and during controlled respiration was 1856 ± 340. (fig. 4.)

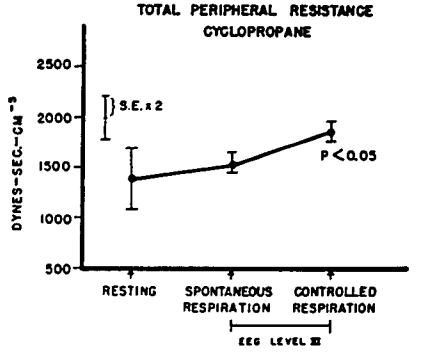

FIGURE 4

Intrathoracic Blood Volume Index.—The intrathoracic blood volume index during the resting state was 1.13 L./m². During cyclopropane anesthesia with spontaneous respiration it was 1.03 L./m² ± 0.32, and during controlled respiration it was 0.90 L./m² ± 0.24. These values were not significantly changed ($P > 0.5$).

Tracheal Airway Pressure.—The range of mean tracheal pressure during controlled respiration was from + 1.5 to + 6.0 cm. H_2O. The average value of airway pressure of the group during controlled respiration was + 3.1 cm. H_2O.

Arterial CO_2 Tension.—The average of the mean pCO_2 during the resting state was 44 mm. of mercury ± 3.0. During spontaneous respiration of the cyclopropane anesthesia it was 57 mm. of mercury ± 3.8, and during controlled respiration it was 40 mm. of mercury ± 3.7. The CO_2 tension was significantly higher during spontaneous respiration than during controlled respiration ($P < 0.001$). (fig. 5.)

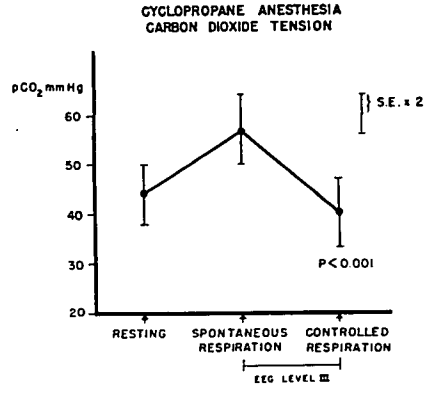

FIGURE 5

Mean Circulation Time.—The mean circulation time was 19 seconds during the resting state, 18 seconds during spontaneous respiration, and 22 seconds during controlled respiration under cyclopropane anesthesia.

Pulmonary Artery Pressure.—In 4 experiments where the pulmonary arterial pressures were recorded during cyclopropane anesthesia, it was found that the systolic, mean and pulse pressures in the main pulmonary artery were consistently elevated during all levels of cyclopropane anesthesia. The mean pulmonary artery pressures increased from 4 to 10 mm. of mercury, with an average increase of 7.5 mm. of

TABLE 1

PULMONARY ARTERY PRESSURES

mm. Hg

Pt. No.	Resting State			Cyclopropane EEG Level III					
				Spontaneous Respiration			Controlled Respiration		
	Syst.	Dias.	Mean	Syst.	Dias.	Mean	Syst.	Dias.	Mean
4	25	13	19	36	21	28	32	9	17
5	17	5	10	26	7	14	18	6	10
6	25	10	15	32	11	22			
7	23	9	15	34	15	25	23	7	14

mercury. In 3 of the patients controlled respirations lowered the pulmonary artery pressures (table 1).

DISCUSSION

This study was undertaken in an effort to evaluate the cardiocirculatory changes during manually performed intermittent positive pressure breathing in patients anesthetized with cyclopropane to an Electro-encephalographic level III. Observations made during controlled respiration are compared with those made during spontaneous respiration at the same level of anesthesia. The technique of controlled respiration was based on the Cournand type III curve with a short inspiratory period, a longer expiratory period, and the expiratory mean mask pressure as nearly atmospheric as possible in order not to influence the circulation adversely. This method is the most common one used to maintain adequate ventilation in clinical anesthesia (14).

In those subjects where the cardiac output was reduced during controlled respiration there were other significant changes: the stroke volume decreased, the total peripheral resistance increased and the pCO_2 returned to the normal level. There were no significant changes in pulse rate, mean arterial blood pressure, intrathoracic blood volume and oxygen saturation. It is apparent that controlled respiration can depress the cardiac output during cyclopropane anesthesia without affecting the mean arterial blood pressure or pulse rate. These changes are of great significance when one considers that they may take place in the presence of a low mean airway pressure and an elevated central venous pressure which occurs during cyclopropane anesthesia.

It has been stated that the increase in central venous pressure during cyclopropane anesthesia minimized the effect of the increased airway pressure in impeding the venous return to the heart (5). At this time, it is difficult to determine precisely the responsible mechanisms. One must consider, however, some of the factors that may in part be responsible for the change in cardiac output.

In a previous report it was shown that the change in cardiac output during cyclopropane anesthesia varies according to the level of narcosis (15). In a light level (blood cyclopropane 5–10 mg. per cent) the average value of the cardiac output was reduced 22 per cent, and during the deeper levels the cardiac index returned toward the normal level. It was considered that the increase in pCO_2 during the deeper planes of anesthesia was partly responsible for the elevation of the cardiac output values. It appears reasonable to assume that the lowering of pCO_2 during controlled respiration reveals the true cyclopropane effect on the cardiac output.

A lowering of oxygen consumption may occur because muscles of respiration are at rest during controlled respiration. Crafoord states that oxygen consumption is decreased during intermittent positive pressure breathing (16). If this is the case, the decreased demand for oxygen by the tissues may be considered as a factor affecting the feed-back mechanism which regulates the cardiac output.

The decrease in stroke volume as measured by the dye dilution method represents a decrease in blood flow from the left ventricle. Therefore, it is possible that the technique of controlled respiration also impairs the flow of blood from the lungs to the heart, even during cyclopropane anesthesia. Taylor (17) demonstrated by opening the thoracic cage in dogs that the cardiac output fell during positive pressure breathing. He concluded that the increase in pulmonary vascular resistance impaired the blood flow to the left side of the heart.

It was found that the mean pulmonary artery pressure increases during cyclopropane anesthesia with spontaneous respirations and returns to the normal levels during controlled respiration (18). There was a partial positive correlation between the carbon dioxide tension and the pulmonary artery pressure. Our findings of the effect of controlled respiration are in agreement with Werkö's observation (2) that the mean pulmonary artery pressure decreases during intermittent positive pressure breathing. The probable reasons for the lowering of the pulmonary artery pressure during cyclopropane anesthesia are: [1] improved ventilation, resulting in a lowered pCO_2, and [2] induced bronchiolar dilatation by increasing the airway pressure, possibly overcoming the bronchoconstriction "effect" of cyclopropane. Rodbard has shown that bronchoconstriction can cause an increase in pulmonary artery pressure (19).

Although the cardiac output may fall during controlled respirations with cyclopropane anesthesia, it must be pointed out that this reduction of blood flow may be due to the effect of the anesthetic agent. Compensatory mechanisms are intact, as evidenced by the increase in total peripheral resistance to maintain adequate perfusion pressure to vital organs. The findings of this study indicate that physiologic levels of arterial blood oxygen and carbon dioxide can be maintained by manual intermittent positive pressure breathing (con-

trolled respirations) and that the measured reduction of the cardiac output is apparently not deleterious to the circulation.

SUMMARY

The hemodynamic changes in human beings during controlled respiration under cyclopropane anesthesia were studied. It was found that the cardiac output may be reduced in the presence of a low mean airway pressure and a normal carbon dioxide tension. The possible mechanisms are discussed.

ACKNOWLEDGMENT

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ANNUAL MEETING OF THE AMERICAN MEDICAL ASSOCIATION

ATLANTIC CITY, NEW JERSEY

The Section on Anesthesiology of the American Medical Association will meet at 9:00 a.m. on June 8, 9 and 10 in the Ambassador Hotel. The following program has been announced:

Wednesday, June 8

Fifty Years of Organized Anesthesia. Albert M. Betcher, Benjamin J. Ciliberti, Paul M. Wood, and Lewis H. Wright.
Controllable Analgesia During Surgery with Continuous Drip Meperidine: Analysis of 1,000 Cases. H. M. Ausherman, W. K. Nowill, and C. R. Stephen.
The Use of Chlorpromazine in the Anesthetic Management of 2,000 Patients. Ellis K. Hultzman.
Steroid Anesthesia: A Report on Its Use in Surgery. Francis J. Murphy, Neri P. Gundagni, and Francis L. DeBon.
The Use of Nisentil-Levallorphan Mixtures for the Supplementation of Nitrous Oxide-Oxygen Anesthesia. Francis F. Foldes, Mark Swerdlow, E. Lipschitz, Gertrude Weber, and Leo A. Pirk.
Management of Adrenocortical Insufficiency During Surgery. Charles L. Burstein, James A. Nicholas, Charles J. Umberger, and Philip D. Wilson.

Thursday, June 9

The Importance of Asphyxia Neonatorium: A Statistical Analysis. Schuyler G. Kohl.
Prevention of Asphyxia Neonatorium by the Obstetrician. Nicholson J. Eastman.
Prevention of Asphyxia Neonatorium by the Anesthesiologist. Meyer Saklad.
The Value of Drugs, Oxygen, and Carbon Dioxide as Stimulants to Respiration in the Apneic Infant. Ralph M. Tovell.
Morphology of the Newborn Infant's Lungs, as Related to Distensibility, Blood Supply, and Gas Exchange. Edith Potter.
Pressures and Volumes Involved in Expansion of the Newborn Infant's Lungs. Richard Day.
The Role of the Laryngologist in Resuscitation of the Newborn. Paul H. Holinger.
Methods of Resuscitating the Newborn Infant. Practical discussion by all participants.

Friday, June 10

The Influences of Anesthesia on Infant Mortality Rate in Cesarean Section. P. C. Lund.
The Twenty-Four Hour Medical Anesthesia Coverage for Obstetric Patients. John J. Bonica.
Anesthesia for Patients Undergoing Operations on the Mitral Valve: Review of Four Years' Experience. Robert T. Patrick.
Chairman's Address: Bellafoline in Clinical Anesthesia. Ralph S. Sappenfield.
A Study of the Mortality Rate in a Series of Cholecystectomies With and Without the Use of a Muscle Relaxant. Paul H. Lorhan and C. C. Chen.
An Evaluation of Antiemetic Drugs and Their Effect on Postoperative Nausea, Vomiting and Retching. Mark R. Knapp and Henry K. Beecher.