There are a variety of conditions in which the mechanical properties of the lungs may be altered. In 1934, Houssay and Orias noted that cerebral ischemia produced bronchiolar constriction. Moore et al. have shown that there is a direct relationship between pulmonary blood flow and tidal volume. Studies which have related the elastance of the lungs—expressed in terms of the reciprocal of elastance, i.e., compliance—to pulmonary artery flow have yielded somewhat conflicting results. However, it has been demonstrated consistently that pulmonary vascular congestion produced by elevation of the pressure in the left heart, results in a reduction of pulmonary compliance. On the other hand, Lewin et al. have shown that pulmonary compliance also decreases with both systemic and pulmonary hypotension.

There is at present a paucity of studies in which pulmonary mechanical function has been analyzed in terms of pulmonary work during circumstances in which pulmonary and systemic hemodynamic changes are taking place. In the present studies the mechanical properties of the lungs were monitored during periods of ventricular asystole in complete heart block. During this acute episode (simulating Stokes-Adams syndrome) there develops marked pulmonary and systemic hypotension, continued inflow of blood into the pulmonary artery, left atrial pressure elevation, and cerebral ischemia.

How these changes, occurring simultaneously in the intact animal preparation, alter the mechanical behavior of the lungs is the subject of this report. The cardiovascular hemodynamic changes during this period are presented in a separate paper.

**Methods**

Complete heart block was produced in 11 dogs, weighing 10 to 25 Kg., by the method of Weirich et al. At the time of surgery catheters were placed into the right atrium, pulmonary artery, and left atrium. Insulated wire electrodes were fixed to the right ventricle and the ventricular rate was maintained at 84 to 90 per minute by means of a small portable pacemaker. The chest was closed, catheters were placed subeutaneously, and the electrodes to the pacemaker brought to the outside. These methods have been described in detail in a previous report.

Four to 14 days postoperatively the dogs were anesthetized with Dial with urethane, 55 mg./Kg., intraperitoneally and given small supplementary doses of intravenous sodium pentobarbital. The animals were studied in the right lateral decubitus position. Breathing was spontaneous and unassisted.

Right atrial, pulmonary arterial, and left atrial pressures were monitored from the intracardiac catheters. Thoracic aortic pressure was obtained from a catheter introduced through the brachial artery. All pressures were recorded with Statham pressure transducers. The electrocardiogram was obtained during each study.

A cuffed endotracheal tube was inserted, and tidal volume was registered by connecting the endotracheal tube to a 160-L. rigid tank via a double Douglas valve. The added dead space of the endotracheal tube and valve system amounted to 12 ml. The pressure changes produced within the tank during each respiratory cycle were recorded with a Statham pressure transducer. The electrocardiogram was obtained during each study.

This study has been included in a dissertation submitted by Dr. Scarpelli as partial fulfillment for the Ph.D. degree, Department of Physiology and Pharmacology, Duke University School of Medicine, Durham, North Carolina.

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ventilated with room air periodically so that at no time did it contain CO$_2$ concentrations greater than 0.1 per cent.

Intra-esophageal pressure, as an index of intrapleural pressure, was measured from a 15-cm. balloon introduced into the lower segment of the esophagus. Localization of the balloon at this level was accomplished by first passing the balloon into the stomach. While monitoring the pressure excursions, the balloon was pulled back until the distal end was just above the cardiac sphincter. At this point there was a reversal of sign of the pressure change throughout the respiratory cycle. Intra-esophageal pressure was recorded through a Statham pressure transducer which had been calibrated with a water manometer.

Carbon dioxide levels were monitored with a Liston-Becker CO$_2$ analyzer by continuous sampling throughout each respiratory cycle. All data were recorded on a Honeywell Visicorder oscillograph.

**EXPERIMENTAL PROCEDURE**

With the animal in the steady state, viz., regular respiratory rate and rhythm and cardiovascular pressures maintained at a steady level, cardiac stimulation was stopped. There followed a period of ventricular asystole during which spontaneous atrial activity continued. Immediately following the first spontaneous ventricular beat, the animal was returned to the pacemaker and followed until the steady state was re-established. In order to obtain suitably long periods of asystole, ammonium chloride was infused by the method of Guzman et al. Hyperpnea developed following NH$_4$Cl infusion. However, the criteria for the steady state were obtained in each case before any attempt was made to produce asystole. The magnitude of the changes observed during asystole were no different in the acidotic and nonacidotic animals.

**CALCULATIONS**

End-tidal CO$_2$ measurements were made directly from the tracings obtained. Pulmonary compliance (C) was calculated as the ratio of the tidal volume to the change in intra-esophageal pressure between instants of zero air flow at the tidal volume extremes. In the range of tidal volumes observed in these experiments, intra-esophageal pressure very closely parallels intrapleural pressure. Total pulmonary airway resistance (R) was calculated by the method of Cook et al. Pressure-volume respiratory loops were constructed by dividing the inspiratory and expiratory phase of each respiratory cycle into five equal time intervals and measuring the pressure and volume at each interval. Pulmonary work was calculated planimetrically from these loops by the method of Otis et al. Changes in the functional residual capacity (FRC) of the lungs were estimated by measuring the changes from the end-expiratory lung position during the steady state, as recorded in the tidal volume tracings.

Eighty periods of asystole were produced, from which thirty periods were selected at random for detailed analysis as described. The data reported for each parameter studied represent average values.

**Results**

The cardiovascular and pulmonary measurements obtained simultaneously during ventricular asystole are presented in table 1. An example of a typical recording is shown in figure 1.

**CARDIOVASCULAR**

These findings have been analyzed and discussed in detail previously. The changes which are pertinent to the present report are summarized as follows. Aortic pressure fell rapidly at first and continued to fall, at a slower rate, throughout the period of ventricular asystole. Pulmonary arterial pressure fell markedly at the onset of asystole and then showed a slight steady rise throughout.
TABLE 1

Average Values of Observations Made During the Control Period and Ten and Twenty Seconds After the Onset of Ventricular Asystole

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>10 seconds</th>
<th>20 seconds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic pressure (mm. Hg)</td>
<td>110/68</td>
<td>8.0</td>
<td>7.9</td>
</tr>
<tr>
<td>mean</td>
<td>91</td>
<td>5.5</td>
<td>4.1</td>
</tr>
<tr>
<td>Left atrial pressure (mm. Hg)</td>
<td>5/0</td>
<td>8.0/3.5</td>
<td>10.0/5.7</td>
</tr>
<tr>
<td>mean</td>
<td>2</td>
<td>6.0</td>
<td>8.1</td>
</tr>
<tr>
<td>Right atrial pressure (mm. Hg)</td>
<td>27/5</td>
<td>7.5/4.0</td>
<td>10.0/6.1</td>
</tr>
<tr>
<td>Pulmonary artery pressure (mm. Hg)</td>
<td>27/5</td>
<td>7.5/4.0</td>
<td>10.0/6.1</td>
</tr>
<tr>
<td>mean</td>
<td>14</td>
<td>6.0</td>
<td>7.9</td>
</tr>
<tr>
<td>Ventricular rate (per min.)</td>
<td>84-90</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Atrial rate (per min.)</td>
<td>75</td>
<td>75</td>
<td>82</td>
</tr>
<tr>
<td>Respiratory rate (per min.)</td>
<td>40</td>
<td>39 (extrapolated)</td>
<td>54 (extrapolated)</td>
</tr>
<tr>
<td>Tidal volume (ml.)</td>
<td>122.4</td>
<td>128.1</td>
<td>151.3</td>
</tr>
<tr>
<td>End-tidal pCO₂ (mm. Hg)</td>
<td>39.1</td>
<td>21.1</td>
<td>9.5</td>
</tr>
<tr>
<td>FRC (AmL from control baseline)</td>
<td>0</td>
<td>21.9</td>
<td>30.2</td>
</tr>
<tr>
<td>Respiratory work (Gm.-cm.)</td>
<td>82.9</td>
<td>115.3</td>
<td>75.2</td>
</tr>
<tr>
<td>Inspiratory viscous</td>
<td>472.0</td>
<td>533.1</td>
<td>814.8</td>
</tr>
<tr>
<td>Inspiratory elastic</td>
<td>128.7</td>
<td>107.5</td>
<td>246.3</td>
</tr>
<tr>
<td>Expiratory viscous</td>
<td>554.9</td>
<td>648.4</td>
<td>890.0</td>
</tr>
<tr>
<td>Work/breath</td>
<td>4.5</td>
<td>5.1</td>
<td>5.9</td>
</tr>
<tr>
<td>Work/ml. tidal volume</td>
<td>23,196</td>
<td>25,576</td>
<td>48,600</td>
</tr>
<tr>
<td>Work/min.</td>
<td>16.0</td>
<td>15.3</td>
<td>14.0</td>
</tr>
<tr>
<td>Pulmonary compliance (ml./cm H₂O)</td>
<td>16.0</td>
<td>15.3</td>
<td>14.0</td>
</tr>
<tr>
<td>Pulmonary airway resistance</td>
<td>4.15</td>
<td>4.99</td>
<td>5.19</td>
</tr>
</tbody>
</table>

Although the magnitude of the changes may have varied slightly, they were qualitatively the same in each instance.

Respiratory rate did not change during the first 10 seconds of asystole. At approximately 10 to 12 seconds after the onset there was an abrupt acceleration of the respiratory rate to 35 per cent above the control value. Tidal volume progressively increased, with the most marked increase occurring after 10 seconds. Functional residual capacity decreased steadily throughout the period of asystole. The largest, single decrease occurred during the first 5 seconds (16.4 ml.), with an additional decrease of 4 to 5 ml. during each succeeding 5-second interval. At the end of 20 seconds the FRC had decreased by 30.2 ml.

PULMONARY

The changes to be presented were seen consistently in each of the 80 periods of asystole.
value. Total pulmonary airway resistance increased with the onset of asystole and exceeded the control value by 25 per cent at 20 seconds.

The pressure-volume loops from which the pulmonary work data (table 1) were obtained are presented in figure 2. Total work per breath—this is actually inspiratory work, since the work of expiration in all cases is passive—increased steadily throughout asystole and at 20 seconds represented a 60.4 per cent increase over the control value. The increase in respiratory elastic work closely paralleled the increase in total work, while inspiratory viscous work increased moderately at first and, at 20 seconds, fell to levels similar to those obtained in the control period. Expiratory viscous work also increased, and at 20 seconds it was 91.4 per cent greater than the expiratory viscous work recorded during the control period. Total work per minute was calculated at 10 and 20 seconds of asystole. The marked increase at 20 seconds (117 per cent) is related primarily to the increased respiratory rate.

Respiratory rate, tidal volume, PRC, C, R, and respiratory work each returned to control values within 30 to 60 seconds after ventricular stimulation was re-established. In several experiments in which the period of asystole exceeded 20 seconds, the tidal volume progressively decreased, the PRC approached the control level, and respiratory activity became less vigorous.

The end-tidal CO₂ fell consistently and steadily throughout asystole from the average control value of 39.1 mm Hg. In a few cases in which CO₂ determinations were made during periods of asystole lasting longer than 20 seconds, the end-tidal CO₂ continued to fall, reaching levels of 3 to 5 mm Hg. Comparably low alveolar CO₂ levels (0.5 per cent or less) were observed by Severinghaus et al. in the ipsilateral lung following temporary unilateral pulmonary artery occlusion. End-tidal CO₂ returned to control levels within 30 seconds after stimulation. In those cases where one or more spontaneous ventricular beats preceded the re-establishment of artificial stimulation, end-tidal CO₂ increased following each beat and fell again with each respiratory cycle occurring between beats.

**Discussion**

The increase in respiratory rate, which was consistently noted about 10 to 12 seconds after the onset of ventricular asystole, likely represents a reflex response to local tissue hypoxia. During the period of ventricular asystole systemic circulation is at a virtual standstill; no blood reaches the aorta from the left atrium until approximately 16 seconds after the onset of asystole, aortic pressure is at a minimal level, and the return of blood to the right heart essentially represents drainage from the systemic venous and capillary reservoirs through the driving force of right atrial and respiratory activity. Since it is generally accepted that reduction of the hemoglobin saturation to a critical level of 90 per cent is required to augment the chemoreceptor...
drive to respiratory activity, the time rate of development of the increased respiratory rate provides a fair indication of the rate at which hemoglobin desaturation occurs at the tissue level when circulation is stagnant. The systemic CO\(_2\) accumulation which occurs during this time may also be an important factor in augmenting tidal volume and respiratory rate.

The immediate and continued fall of functional residual capacity (FRC) may be due to several cardiovascular changes which tend to compromise pulmonary air capacity by increasing the volume of the central circulation. These include the continued venous return to the right heart and the cardiac dilatation which is seen consistently during ventricular asystole. Further, there is flow established from right atrium into pulmonary artery (121 to 139 ml./min.) within 3 seconds of asystole, while flow into the aorta occurs later (average 16 seconds), resulting in more blood entering than leaving the central circulation during the major portion of the period of asystole. By extrapolation the rate of FRC fall during this period is 90.6 ml./min. Another factor which may contribute to the fall in FRC is the increased tidal volume per se. The small decrease in pulmonary compliance* may be related to the development of some degree of pulmonary vascular congestion. The factors indicating the presence of pulmonary vascular congestion include the greater flow into than out of the central circulation, the small, but progressive increase in left atrial pressure, the immediate and continued lowering of the FRC, and the reduced flow rate through the pulmonary vasculature. The average fall of compliance at 20 seconds was 12.5 per cent. This lies within the range of compliance decrease reported by Cook et al. (average fall of 18 per cent ± 11 per cent), who produced congestion acutely by occluding the aorta. In their experiments, however, the decreased compliance and pulmonary vascular congestion were associated with a concomitant rise of left atrial pressure amounting to 28 cm. H\(_2\)O. Borst et al. also found a high correlation between elevated left atrial and pulmonary venous pressures and decreased compliance. They suggested that the effect might be due either to capillary and/or venous distention or to increased filtration through the capillary walls. Our investigations favor the former interpretation, since pulmonary vascular congestion was produced in the absence of a markedly elevated atrial or venous pressure. Lewin et al. have noted a decrease in compliance in association with systemic and/or pulmonary hypotension. No mechanism has been defined. The general hypotension seen in our experiments may be another factor contributing to the decreased compliance.

The sustained increase in total pulmonary airway resistance during ventricular asystole is most likely a reflection of bronchiolar constriction. Houssay and Orias have demonstrated bronchoconstriction during cerebral ischemia. This has been confirmed by Daly et al. in their studies of selective brain perfusion with hypoxic blood. Severinghaus et al. and Swenson et al. have shown that local airway CO\(_2\) levels may influence bronchiolar tone and that with a fall in airway CO\(_2\) concentration there follows bronchiolar constriction most probably at or distal to the terminal bronchioles. In their experiments constriction was seen when the CO\(_2\) levels reached 1 to 2 per cent and less. Similar levels were attained during the period of ventricular asystole in the present studies. The relative importance of the central and local mechanisms was not clarified by these studies. Indeed, the possibility that local O\(_2\) levels may influence bronchial tone was also suggested (see below).

The experiments of Severinghaus and Swenson indicate that atelectasis develops beyond the constricted airways. However, it is unlikely that this occurred in the present studies. In the first place tidal volume did not decrease, but in fact increased during
ventricular asystole. Secondly, ventilation, compliance, and resistance returned to control levels within one minute after the onset of pacemaker stimulation, whereas control ventilation was re-established after a considerable period (up to one hour) in the former studies.

Analysis of the work done during asystole reveals that there is an increase of total inspiratory work (60.4 per cent greater than the work done during the control period) and that this is an increase of inspiratory elastic work primarily. The increase in elastic work is a function of the increased tidal volume and the decreased compliance. The decreased efficiency with which inspiratory elastic work is done is evidenced by the 31 per cent increase of inspiratory work when this is calculated in terms of work done per milliliter of air moved.

The relatively greatest rise in work performance occurred during expiration. Here the viscous work was 91.4 per cent greater than during the control period and 55 per cent greater per ml. of air moved. Since this calculation expresses the work performed in moving air through the airways of the lungs and to a lesser extent, the work of moving the thoracic structures themselves, one may conclude that the increase in expiratory viscous work is secondary to the increase in pulmonary airway resistance. Salzano and Hall have shown that hypoxic hypoxia (low oxygen levels in both the lung airways and systemically) results in equivalent elevations of both inspiratory and expiratory viscous work. In the present studies, where only expiratory viscous work increased, there was systemic hypoxia without a lowering of lung airway oxygen levels (respiratory rate and depth were increased and end-tidal CO₂ levels fell). This indicates that oxygen levels in the pulmonary airways may have a local regulatory function in the control of bronchiolar tone.

End-tidal CO₂ fell to extremely low levels (3 to 5 mm. Hg) during ventricular asystole. This is an expression of the paucity of pulmonary capillary blood flow. Upon resumption of ventricular stimulation end-tidal CO₂ quickly returned to control levels. No consistent overshoot of the control level was observed. In those instances in which slow, spontaneous ventricular beats ended the period of asystole, the intermittent rise of end-tidal CO₂ following each ventricular systole and fall with each respiratory cycle between beats demonstrates the rapidity and sensitivity with which end-tidal air reflects the condition within the alveoli.

Summary

Eleven mongrel dogs were studied in which complete heart block had been produced surgically. Ventricular rate was maintained by artificial stimulation until the time of study. Each experiment involved abrupt cessation of stimulation and the monitoring of pulmonary mechanical behavior during the ensuing period of ventricular asystole. These studies have shown that all aspects of the mechanical behavior of the lungs are altered during ventricular asystole in complete heart block. The changes which occur during this short interval of time are basically attributable to the systemic, stagnant hypoxia and the central vascular congestion. The pulmonary changes produced include augmentation of the rate and depth of breathing, reduction of the functional residual capacity, decreased pulmonary compliance, and increased pulmonary airway resistance. The result is that both the inspiratory and expiratory work of breathing are increased, while the efficiency of breathing is decreased. All of these alterations occur within the 20-second period of ventricular asystole and are restored to control levels soon after the re-establishment of a normal ventricular rate. The possible mechanisms involved are discussed.

Acknowledgment

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