Circulatory Dynamics and the Effects of Respiration During Ventricular Asystole in Dogs with Complete Heart Block

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The need for a clearer understanding of the physiological changes accompanying acute ventricular asystole in complete heart block (Stokes-Adams syndrome) is especially important in view of the significant advances made in the therapy of this disorder. In addition, simulating this condition in the laboratory provides a unique approach to the study of cardiorespiratory dynamics and their interrelationships. The difficulty in obtaining a suitable preparation and the acute nature of ventricular asystole probably account for the scarcity of reports in this area.

Erlanger et al. succeeded in producing chronic complete heart block in dogs in 1910. In 1955, Starzl et al. described a surgical approach for severing the atrioventricular (A-V) bundle and studied the cardiovascular changes occurring during acute and chronic heart block. The period of acute ventricular asystole was not studied. Dowling et al. observed the pressure changes in the right ventricle, pulmonary artery, and femoral artery during relatively short periods of asystole in two human subjects.

The present study was undertaken to investigate the following during prolonged ventricular asystole: (1) physiology of independent atrial activity; (2) pressure-flow alterations in the central circulation (heart and lungs); and (3) the influence of respiration on these parameters during periods of spontaneous breathing, intermittent positive pressure breathing, and apnea. The entire study was carried out in the intact anesthetized dog and cardiovascular-respiratory determinations were obtained simultaneously.

Methods

Forty mongrel dogs, weighing 10 to 25 kg., were anesthetized with sodium pentobarbital (30 mg./Kg.). The chest was entered through the fourth right interspace and complete heart block produced by the suture method of Weirich et al. Polyvinyl catheters (O.D., 0.091 in.; I.D., 0.059 inches) of 1.0 ml. volume were placed as follows: (1) through the outflow tract of the right ventricle into the main pulmonary artery (1 cm. distill to the pulmonary valve); (2) through the azygous vein with the tip positioned in the body of the right atrium; (3) directly into the body of the left atrium by an approach dorsal to the junction of the inferior vena cava and the right atrium. The catheters were filled with heparin, closed with metal plugs, and placed subcutaneously. Insulated woven stainless steel wire electrodes were fixed to the right ventricle, pulmonary artery, and femoral artery during relatively short periods of asystole in two human subjects.

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Of the dogs prepared in this manner, 11 demonstrated prolonged periods of ventricular asystole upon cessation of stimulation. These dogs were selected for the present study 4 to 14 days postoperatively. On the day of study the dog was anesthetized with Dial with urethane (Ciba), 55 mg./Kg. intraperitoneally, and given small supplementary doses of intravenous sodium pentobarbital. Dial with urethane was used as an initial anesthetic because of its sustained action and maintenance of a steady level of anesthesia. Respiration was spontaneous and unassisted unless...
TABLE 1
Average Appearance Time in Seconds Utilizing Various Injection and Sampling Sites for Dye-Dilution Studies

<table>
<thead>
<tr>
<th>Injection and Sampling Sites</th>
<th>Control (on pacemaker) (seconds)</th>
<th>Spontaneous respiration (seconds)</th>
<th>Apnea (seconds)</th>
<th>Intermittent positive pressure breathing (seconds)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA to PA</td>
<td>0.2</td>
<td>1.3 ± 0.9</td>
<td>4.8 ± 1.6</td>
<td>4.6 ± 1.5</td>
</tr>
<tr>
<td>PA to LA</td>
<td>2.4</td>
<td>18.1</td>
<td>No appearance</td>
<td>No appearance up to 28 seconds</td>
</tr>
<tr>
<td>LA to PA</td>
<td>11.2</td>
<td>No appearance</td>
<td>No appearance</td>
<td>No appearance</td>
</tr>
<tr>
<td>LA to Ao</td>
<td>0.3</td>
<td>16.1</td>
<td>No appearance</td>
<td>24-35</td>
</tr>
</tbody>
</table>

*RA = right atrium; PA = pulmonary artery; LA = left atrium; Ao = ascending aorta.

DYE-DILUTION STUDIES

Utilizing various injection and sampling sites, 157 periods of asystole were studied; 82 during spontaneous respiration, 40 during apnea, and 45 with intermittent positive pressure breathing. Average control appearance times during stimulation were: RA to PA, 0.2 second; PA to LA, 2.4 seconds; LA to Ao, 0.3 second; LA to PA, 11.2 seconds.* During each experiment, ventricular asystole was produced after a constant withdrawal was obtained from the sampling site. Injection occurred 1 to 2 seconds after the onset of asystole.

*RA = right atrium; PA = pulmonary artery; LA = left atrium; Ao = ascending aorta.
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asytole* (dicrotic notch of the last aortic pulse). Duration of injection was 0.2 to 0.4 second.

Right Atrium to Pulmonary Artery

The average appearance time during spontaneous respiration was 1.3 seconds, during apnea 4.8 seconds, and with intermittent positive pressure breathing 4.6 seconds. The short appearance time during spontaneous breathing was significantly different from the appearance times during apnea and pressure breathing (P < 0.01). Right atrial output could be estimated from two curves in one dog during spontaneous breathing. Flow into the pulmonary artery during asystole was 121 ml. and 139 ml./min.; control cardiac output in this dog was 1.5 L./min.

Pulmonary Artery to Left Atrium

During spontaneous respiration, the average appearance time was 18.1 seconds. During apnea and pressure breathing, dye did not appear in the left atrium during periods of asystole up to 28 seconds. Following forced respiration studies in two dogs, the effect of succinylcholine disappeared and the animal resumed spontaneous breathing. The left atrial appearance times then reverted to the original values.

Left Atrium to Pulmonary Artery

In no instance did dye appear at the sampling site in the pulmonary artery after injection into the left atrium during any of the three respiratory conditions.

Left Atrium to Ascending Aorta

Appearance times varied from 10.0 to 25.0 seconds during spontaneous respiration. The dye appeared in the ascending aorta coincident with, or within one second after, the appearance of fluctuations of the aortic pressure tracing which were simultaneous with atrial systole. Appearance of dye never preceded the appearance of these pressure waves. With positive pressure respiration there was generally no dye or atrial pulse appearance in the aorta; in three dogs dye appeared in 24 to 35 seconds. If spontaneous respiration was resumed (four dogs), appearance times returned to the range previously noted for spontaneous breathing. Dye did not appear in the aorta during apnea for periods of asystole lasting up to 30 seconds. In only one instance did atrial pulse waves appear in the aorta during apnea (see "Pressure Relationships" below).

Left Ventri cle to Left Atrium

These studies were done to evaluate the competency of the mitral valve during ventricular asystole with independent atrial activity. The aortic catheter was passed to the left ventricle and very slow injections (3- to 4-seconds duration) were required to prevent premature beats. The appearance time from the beginning of injection was 1.6 to 2.8 seconds. Dye studies during ventricular stimulation showed either no or minute dye deflec-
SPONTANEOUS RESPIRATION

0 5 10 15 SECONDS OF VENTRICULAR ASYSTOLE

FIGURE 2

Characteristic record of pressure events during the first 12 seconds of ventricular asystole during spontaneous respiration (A) and apnea (B). Intra-esophageal (I-E) zero pressure represents the control end-expiratory baseline. All pressures are recorded in mm Hg.

PRESSURE RELATIONSHIPS

An analysis of the pressure relationships of the various compartments of the central circulation and aorta was made to account for the patterns of flow that were present during ventricular asystole.

One hundred and fifty-five periods of asystole were studied, including 100 during spontaneous breathing, 25 during apnea, and 30 during intermittent positive pressure respiration. Pressures in the right atrium (RA), pulmonary artery (PA), left atrium (LA), and ascending aorta (Ao) were monitored simultaneously. Attempts to monitor ventricular pressures were discontinued since the catheter occasionally produced premature beats. Figure 2 is a typical record during spontaneous breathing and apnea. Because of changing instantaneous pressure gradients, a detailed analysis of pressures was made at each of the following phases of the aural cycle: (1) peak systole (a wave); (2) early diastole (0.04 to 0.08 second after end of systole); and (3) end-diastole. All pressures are reported as corrected or net pressures. Averages of all determinations are listed in tables 2 and 3. Instantaneous pressure relationships are shown in figures 3, 4, and 5.

Spontaneous Respiration

Respiratory rate increased 35 per cent during ventricular asystole, the increase beginning consistently after the first 10 seconds. There was a gradual increase in tidal volume with the most marked increase also occurring after 10 seconds. End-expiratory intra-esophageal (I-E) pressure increased from 0 to 1.33 cm H2O after 20 seconds of asystole. Generally, there was a fall in tidal volume and I-E
TABLE 2

Net and Mean Pressures, Atrial Rate, and Respiratory Changes during Ventricular Asystole

<table>
<thead>
<tr>
<th>Time after onset of ventricular asystole</th>
<th>Control (on pacemaker)</th>
<th>Spontaneous respiration 5 seconds</th>
<th>Spontaneous respiration 20 seconds</th>
<th>Apnea 5 seconds</th>
<th>Apnea 20 seconds</th>
<th>Positive pressure respiration 5 seconds</th>
<th>Positive pressure respiration 20 seconds</th>
</tr>
</thead>
<tbody>
<tr>
<td>T. Ao pressure (mm. Hg)</td>
<td>110/68</td>
<td>42</td>
<td>15</td>
<td>32</td>
<td>15</td>
<td>24</td>
<td>15</td>
</tr>
<tr>
<td>RA pressure (mm. Hg)</td>
<td>91</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td>8/0</td>
<td>7.3/2.7</td>
<td>10/5.7</td>
<td>4.9/0.6</td>
<td>7.4/2.5</td>
<td>4.7/1.3</td>
<td>7.5/2.0</td>
</tr>
<tr>
<td>PA pressure (mm. Hg)</td>
<td>27/5</td>
<td>6.5/3.0</td>
<td>10/6.1</td>
<td>4.3/0.8</td>
<td>7.2/3.6</td>
<td>4.5/1.6</td>
<td>7.4/2.2</td>
</tr>
<tr>
<td>mean</td>
<td>14</td>
<td>5.0</td>
<td>7.9</td>
<td>2.6</td>
<td>3.8</td>
<td>2.6</td>
<td>3.3</td>
</tr>
<tr>
<td>LA pressure (mm. Hg)</td>
<td>8/0</td>
<td>8.3/2.2</td>
<td>14.6/3.3</td>
<td>5.2/1.7</td>
<td>9.7/0.5</td>
<td>5.5/0</td>
<td>8.4/0.6</td>
</tr>
<tr>
<td>mean</td>
<td>4</td>
<td>4.8</td>
<td>8.4</td>
<td>2.4</td>
<td>3.2</td>
<td>2.8</td>
<td>3.8</td>
</tr>
<tr>
<td>Atrial rate/min.</td>
<td>80</td>
<td>75</td>
<td>82</td>
<td>78</td>
<td>92</td>
<td>80</td>
<td>88</td>
</tr>
<tr>
<td>Respiration rate/min.</td>
<td>40</td>
<td>40</td>
<td>54</td>
<td>20 to 30</td>
<td>20 to 30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tidal volume (ml.)</td>
<td>122.4</td>
<td>124.5</td>
<td>151.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-expiratory I-E pressure (from control baseline) (cm. H$_2$O)</td>
<td>0</td>
<td>+0.67</td>
<td>+1.33</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values represent the average result of each parameter listed.

I. Net (corrected) instantaneous atrial systolic/early-diastolic pressures at 5 and 20 seconds of ventricular asystole with mean pressures (determined planimetrically).

II. Atrial rate and respiratory changes.

Aortic pressure fell rapidly at first and then more gradually (fig. 2A). When the pressure reached 11.5 to 24.4 mm. Hg (average 15.5 mm. Hg) fluctuations in the tracing were seen simultaneously with atrial systole. These waves appeared 9.2 to 28 seconds after the onset of asystole.

**Mean PA-LA pressure relationships.** Mean pulmonary arterial pressure fell below RA pressure within 2 to 3 seconds, after which there was a gradual rise in both, with the mean RA pressure maintained slightly above PA. Mean PA pressure fell below LA within 2 to 3 seconds, and after this mean PA-LA pressure gradients varied. From 3 to 12 seconds after the onset of ventricular asystole, there was either no gradient or a slight gradient favoring either PA or LA. However, after 12 to 14 seconds, the mean LA pressure gradually became greater than PA (average 0.6 mm. Hg). At the same time, there was a gradual increase in the end-expiratory intraesophageal (I-E) pressure. After 20 to 30 seconds of asystole, end-expiratory I-E pressure began to fall. The mean LA pressure then fell to a greater extent than PA and usually became less than PA before stimulation was resumed.

**Instantaneous PA-LA pressure relationships during atrial systole.** During the first 3-5 seconds, there were small and indefinite waves in the RA, PA, and LA tracings, but thereafter these became quite prominent. After 5 seconds, the LA systolic pressure was consistently greater during both inspiration and expiration (fig. 3). The average IA-PA systolic gradient during inspiration was 0.9 mm. Hg at 5 seconds of asystole and 3.1 mm. Hg at 20 seconds. During expiration, the gradients were 2.4 and 4.9 mm. Hg at 5 and 20 seconds, respectively. The increase in LA-PA systolic gradient during exhalation is statistically significant (table 3).

**Instantaneous PA-LA pressure relationships during early atrial diastole.** During early diastole, PA pressure was consistently higher than LA in both inspiration and expiration (fig. 3). During inspiration, the average gradient was 2.0 mm. Hg at 5 seconds and 3.4 mm. Hg at 20 seconds, while the gradient during expiration was 1.1 and 1.3 mm. Hg, respectively. The fall in this
TABLE 3

**PA-LA Instantaneous Pressure Gradients for Three Phases of the Atrial Cycle**

<table>
<thead>
<tr>
<th>Time after onset of ventricular asystole</th>
<th>Spontaneous respiration</th>
<th>Apnea</th>
<th>Positive pressure respiration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5 seconds</td>
<td>20 seconds</td>
<td>5 seconds</td>
</tr>
<tr>
<td>I. PA-LA instantaneous pressure gradients (mm. Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. a wave</td>
<td>Inspiration</td>
<td>Expiration</td>
<td>Inspiration</td>
</tr>
<tr>
<td></td>
<td>0.9 LA &gt; PA 2.4 LA &gt; PA</td>
<td>3.1 LA &gt; PA 4.9 LA &gt; PA</td>
<td>0.9 LA &gt; PA 2.5 LA &gt; PA</td>
</tr>
<tr>
<td>2. Early diastole</td>
<td>2.0 PA &gt; LA 1.1 PA &gt; LA</td>
<td>3.4 PA &gt; LA 1.3 PA &gt; LA</td>
<td>1.1 PA &gt; LA 2.5 PA &gt; LA</td>
</tr>
<tr>
<td>3. End diastole</td>
<td>1.9 LA &gt; PA 1.0 LA &gt; PA</td>
<td>2.8 PA &gt; LA 1.3 LA &gt; PA</td>
<td>t</td>
</tr>
<tr>
<td>II. Average of PA-LA instantaneous pressure gradients throughout asystole (mm. Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. a wave</td>
<td>Inspiration</td>
<td>Expiration</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.46 ± 0.75 LA &gt; PA</td>
<td>4.48 ± 1.0 LA &gt; PA — Average 1.02 (P &lt; 0.01) increase with expiration.</td>
<td></td>
</tr>
<tr>
<td>2. Early diastole</td>
<td>2.69 ± 1.7 PA &gt; LA</td>
<td>0.88 ± 0.4 PA &gt; LA — Average 1.81 (P &lt; 0.01) decrease during expiration.</td>
<td></td>
</tr>
<tr>
<td>3. End diastole</td>
<td>PA &gt; LA</td>
<td>LA &gt; PA — Inspiration-expiration reversal of gradients.</td>
<td></td>
</tr>
</tbody>
</table>

*(1) Peak of the a wave (systole); (2) 0.04 to 0.08 second after onset of diastole (early-diastole); (3) end-diastole. I. Average PA-LA instantaneous pressure gradients at 5 and 20 seconds of ventricular asystole. II. Average of gradients determined throughout asystole in inspiration and expiration.

†Variable with reversal of gradients. See text.
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A-wave, o-Early Diastole, d-Late Diastole

PA-LA gradient during exhalation is statistically significant (P<0.01).

Instantaneous PA-LA pressure relationships during late atrial diastole. During inspiration, end-diastolic pressure was higher in PA than LA (1.9 mm. Hg gradient at 5 seconds and 2.8 mm. Hg at 20 seconds). During expiration, LA pressure was higher: 1.0 mm. Hg at 5 seconds and 1.3 mm. Hg at 20 seconds (table 3).

Apnea

With the onset of ventricular asystole, the Ao pressure fell rapidly at first and then more gradually (fig. 2B). Aortic pressure remained above LA systolic pressure levels even with asystoles of 25-seconds duration, and there was no transmission of the atrial pulse wave in the aortic pressure tracing during apnea, with one exception. In this instance, after 33 seconds of asystole, atrial pulse waves appeared in the Ao when the pressure had fallen to 10 mm. Hg.

Pulmonary arterial pressure fell below RA within 3 seconds, and thereafter both showed a gradual rise with the mean RA pressure remaining higher than PA. Within 2 seconds, PA pressure fell to the range of pressures seen in the LA, and after this the PA-LA instantaneous pressure relationships varied with the phase of the atrial cycle (fig. 4). The amplitude of the a waves in the RA, PA, and LA increased progressively during ventricular asystole. Throughout ventricular asystole, atrial systolic pressure was greater in the LA than PA, averaging 0.9 mm. Hg greater after 5 seconds and 2.5 mm. Hg after 20 seconds (table 3). During early diastole, the pressure gradient reversed, and the PA pressure was higher than LA. At 5 seconds, the average gradient was 1.1 mm. Hg, increasing to 2.5 mm. Hg at 20 seconds. The direction of the end-diastolic pressure gradients varied and were the smallest gradients noted. During the first 10 seconds, end-diastolic pressures were usually higher in the LA and from 10 to 20 seconds the gradient, when present, consistently narrowed. RA-LA instantaneous pressure gradients showed the same relationships as did PA-LA. The early diastolic fall was always greater in the LA than in PA or RA.

Although there was variation in instantaneous pressure gradients, the mean pressure was consistently higher in PA than LA throughout asystole (table 2).

Atrial rate varied from 50 to 110 per...
minute and showed an average increase of 20 per cent above preasystole levels. This increase generally occurred after 10 seconds of asystole. The I-E pressure increased gradually from −1.23 to −0.69 cm H₂O, never reaching atmospheric pressure.

**Intermittent Positive Pressure Respiration**

A tidal volume of 200 to 340 ml., at a rate of 20 to 30 per minute, was employed. The I-E pressure ranged from −0.1 to +2.5 mm Hg with each respiratory cycle.

The aortic pressure fall was similar to that observed during apnea; however, after 23 to 28 seconds of asystole, the Ao pressure fell to LA systolic levels (11 to 13 mm Hg) and atrial pulses were recorded in the Ao.

PA pressure fell below RA initially and after 3 seconds both showed a gradual rise. Within 1 to 2 seconds, the PA pressure fell to the level of the IA, and after 4 seconds the PA-LA pressure relations varied with the phase of the atrial cycle (fig. 5). LA systolic pressure averaged 1.6 mm Hg greater than PA throughout asystole. This gradient did not increase as seen during apnea. However, the amplitude of RA, PA and LA waves increased during asystole. In early diastole the PA pressure averaged 1.6 mm Hg greater than LA. There was no change in this gradient with prolonged asystole. After 5 seconds, end-diastolic pressure averaged 1.3 mm Hg greater in LA than PA, and there was no narrowing of this gradient during asystole. The RA-LA instantaneous pressure relationships paralleled PA-LA. The LA early diastolic fall in pressure was greater than PA and RA, as noted during apnea.

In 80 per cent of the periods of asystole studied, mean LA pressure averaged 0.9 mm Hg greater than PA; in the remaining, PA mean pressure was slightly greater (average 0.2 mm Hg). This reversal of mean pressure gradients could not be correlated with duration of asystole, pre-existing pressure levels, phase of respiration, atrial rate, or absolute LA and PA pressures. Mean PA and LA pressures increased 0.7 and 1.0 mm Hg, respectively, during asystole from 5 to 20 seconds (table 2).

**Discussion**

Our studies are consistent with and extend the findings of Dowling et al. During spontaneous respiration the aortic pressure fell to 11.5 to 24.4 mm Hg. Aortic pressure was consistently at or below LA systolic pressure levels when the atrial pulse was recorded in the Ao tracing. Only with the appearance of the LA pressure waves did dye appear in the Ao. In these experiments, therefore, the atrial pulse wave, as recorded in the Ao tracing, represents the ejection of blood from the left ventricle into the Ao during atrial systole. Further evidence that these are actually "flow waves" is the delay in appearance or complete absence of atrial waves and dye in the Ao during ventricular asystole with apnea and intermittent positive pressure breathing. In these instances, Ao pressure remains greater than LA systolic pressure for a considerably longer time and the pulse and dye appeared only when LA systolic pressure exceeded Ao pressure. These atrial waves must be distinguished from those reported by Heyman in peripheral arteries in complete heart block when arterial pressure exceeded LA pressure. It is unlikely that such waves represent actual flow, although Ao pressure was not recorded. That we did not observe similar waves is probably due to the relatively low sensitivity of the transducer employed to monitor aortic pressure. It, therefore, appears that two types of atrial waves may be recorded in the arterial system and that the LA to aorta pressure gradient must be considered in determining their significance. A parallel phenomenon was confirmed for the right heart by determination of an approximate RA output into the PA of 121 to 139 ml./min. during ventricular asystole. Due to the low pressure and resistance in the pulmonary vasculature, the appearance of dye is more rapid.

Kilburn and Sieker showed that positive pressure breathing decreased both cardiac output and central blood volume and that negative pressure breathing increased cardiac output, stroke volume, and, to a lesser extent, the central blood volume. In our studies, there-
was a significant delay in the appearance time of dye from RA to PA during positive pressure breathing and apnea as compared to spontaneous breathing. The lower net pressure in the RA, PA, and LA during apnea and pressure breathing is best accounted for by a lower central blood volume due to decreased venous return. The mean pressure levels recorded after 20 seconds of asystole during positive pressure breathing and apnea are similar to those noted in Bell's study of ventricular fibrillation with artificial respiration.

The LA pressure tracing is of interest (fig. 2B). During ventricular asystole the LA systolic pressure is greater than that in the RA. This is due to the higher resistance against which blood is ejected from the LA. The rapid rise in pressure during early diastole indicates rapid filling of the left atrium during ventricular asystole. Filling of the LA during diastole represents inflow from the pulmonary veins and regurgitation from the left ventricle. The possible contribution of bronchial flow was suggested by the work of Bell who found that the heart and lungs behave as a common chamber during prolonged ventricular fibrillation. He observed a rapid appearance (6 to 8 seconds) of I^131 in the left atrium via bronchial circulation following injection into the aorta. In our studies, five injections of dye into the thoracic aorta were made 1 to 2 seconds after the onset of asystole. In no instance did dye appear in the LA (asystole 20 to 30 seconds). This suggests that due to the rapid fall in aortic pressure bronchial flow is very small, if present, during ventricular asystole.

Dye-appearance studies indicate that there is flow from LV to LA during ventricular asystole. Hawthorne has postulated that there is mitral regurgitation due to fluctuations of the ventricular circumference and base to apex length during ventricular asystole in complete heart block. This retrograde flow occurs in the presence of the LV to LA diastolic pressure gradient reported by Sarnoff et al.

The consistent PA to LA pressure gradient seen during early diastole reflects the difference in the volume/capacity ratio within the two systems, viz., relatively high pulmonary and low LA volumes.

Respiratory variations produced reversal of the PA-LA pressure gradients only in the late diastolic phase of the auricular cycle. At this time, flow from PA to LA would be enhanced during inspiration, and no flow would occur during expiration.

Systolic and early diastolic pressure gradients were also significantly affected by respiratory variations in that inspiration accentuated PA pressure in relation to LA and expiration had the reverse effect. This agrees with the finding of Hamilton et al. that extreme inspiratory effort against an obstructed airway increases the pulmonary arteriovenous pressure gradient. During apnea and positive pressure breathing, the LA-PA systolic and early diastolic gradients were in the same directions seen during spontaneous breathing. However, the end-diastolic gradient during pressure breathing was from LA to PA throughout, the direction seen only in expiration during spontaneous breathing.

Dye appearance from PA to LA during asystole was approximately seven times slower than during ventricular stimulation. Flow during apnea and pressure breathing in asystole was further diminished or entirely absent.

During spontaneous breathing, the mean LA pressure gradually became greater than the mean PA pressure. Despite the gradual development of a LA to PA mean pressure gradient, flow occurred from the pulmonary artery to the left atrium. This is best accounted for by the PA to LA pressure gradient in early diastole and during late diastole with inspiration.

Thompson et al. demonstrated that respiratory movements can produce blood flow in the absence of cardiac contractions. At the conclusion of one of our experiments, NH4Cl was infused rapidly until atrial contractions disappeared, yet the ventricles responded well to stimulation. Cardiac arrest was produced then while spontaneous breathing continued. Following injection into the
right atrium, the dye appeared in the pulmonary artery at 6 seconds despite absence of all cardiac action, and large fluctuations of the dye curve occurred coincident with respiratory movements ("respiratory pump").

Our studies did not show whether flow occurred from LA to PA during asystole despite the development of a LA to PA mean pressure gradient during spontaneous and intermittent positive pressure respiration. However, one dog with surgically induced aortic insufficiency (not included in this series) was studied, and with the onset of asystole the LA pressure rose to 17/11 mm. Hg in 3 seconds. Dye studies during spontaneous respiration in this animal showed LA to PA appearance times of 3 to 4 seconds. Little found evidence for a "valvelike" closure of the pulmonary veins at low pressure levels (less than 5 mm. Hg) in open-chest dogs during apnea. Our studies gave no information concerning this phenomena in the intact dog.

The actual pressure-flow relationships at the pulmonary arteriolar and capillary levels remain to be clarified. Borst et al.,21 using open-chest dogs with continuous positive pressure respiration, found that, at a LA pressure of less than 7 mm. Hg, there was a persistent pressure difference between PA and LA at zero flow. This phenomenon was not present at higher LA pressures and indicated a "critical closing pressure" at this level in their preparation. The existence of a critical closing pressure may account for the failure to detect dye in PA to LA injections during apnea and positive pressure respiration as contrasted to its appearance during spontaneous breathing when the net left atrial pressures were higher.

Summary

Pressure-flow changes during ventricular asystole (but with atrial activity present) were studied in 11 dogs with complete heart block. The influence of respiration on these parameters was evaluated during spontaneous breathing, intermittent positive pressure respiration, and apnea. During spontaneous breathing, the pulmonary artery pressure initially fell below the right atrial pressure following the onset of ventricular asystole. Both pressures then showed a gradual rise which was accompanied by flow of blood into the pulmonary artery (estimated to be 121 to 139 ml./min.). The mean pressure in the left atrium became greater than that in the pulmonary artery, concomitant with a gradual rise in the end-expiratory intrathoracic pressure. Despite this mean pressure change, flow from the pulmonary artery to the left atrium was demonstrated. Analysis of the instantaneous pressures during the atrial cycle showed that flow could occur during early atrial diastole in both phases of respiration and throughout atrial diastole during inspiration. Following each atrial beat, the left atrium received blood from the pulmonary veins and left ventricle (mitral regurgitation). There was a continued fall in the aortic pressure and, when it was exceeded by the left atrial systolic pressure, blood was propelled into the aorta. These pressure-flow changes were affected by positive pressure respiration and apnea. All pressures were significantly lower during these respiratory conditions and flow from the pulmonary artery to left atrium could not be demonstrated. The marked effects of respiration on the circulatory dynamics in animals during ventricular asystole must be considered in the interpretation of the results of studies, particularly in thoracotomized or apneic dogs, whenever there are conditions of low flow or pressure in the central circulation.

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