Relation of Valvular Lesions and of Exercise to Auricular Pressure, Work Tolerance, and to Development of Chronic, Congestive Failure in Dogs

A. C. BARGER, B. B. ROE and G. S. RICHARDSON

From the Department of Physiology, Harvard Medical School, Boston, Massachusetts

The pathogenesis of congestive failure is still uncertain. In 1910 Bolton and Starling (1) wrote that the analysis of the factors involved in the production of the disease was rendered difficult by the impossibility of accurately reproducing these states in animals. Since that time numerous methods have been tried to precipitate congestive failure in dogs. The attempts have met with limited success despite severe injury to the myocardium by coronary ligation (2), injection of silver nitrate (3), implantation of radon seeds (4), or burning of the myocardium (5). Single valvular lesions rarely led to congestive failure (6, 7). The cardiac reserve is apparently so great that nearly lethal injury to the heart must be produced before clear evidence of congestive failure appears in the resting dog.

Landis et al. (8) have suggested the importance of exercise in the pathogenesis of congestive failure, and have shown in acute experiments on dogs that minor decreases in cardiac competence, which are not apparent at rest, may lead to elevation of central venous pressure during exercise. They have postulated that these transient elevations of venous pressure during muscular activity may play an important role in the development of the signs and symptoms of congestive failure.

Our purpose was 1) to study the effects of valvular lesions and of exercise on auricular pressure and work tolerance of unanesthetized dogs, and 2) to attempt to determine which lesions could produce chronic, congestive failure in the dog.

The valvular lesions, limited to the right side of the heart, were: a) insufficiency of the pulmonary valve, b) stenosis of the pulmonary artery, c) the combination of pulmonary stenosis and pulmonary insufficiency, d) insufficiency of the tricuspid valve and e) combined tricuspid insufficiency and pulmonary stenosis.

Pulmonary insufficiency had little effect on auricular pressure or work tolerance over a period of months. Pulmonary stenosis, or pulmonary stenosis plus pulmonary insufficiency, which elevated resting auricular pressure little or none at all, did lead to a significant rise of central venous pressure during exercise. Exercise tolerance was normal (one exception). Tricuspid insufficiency elevated resting auricular pressure moderately. Exercise further increased central venous pressure, but work capacity was normal. The combined insufficiency of the tricuspid valve and pulmonary stenosis led to a syndrome similar to right-sided congestive failure as seen in man.

Received for publication November 9, 1951.

1 The expenses of this investigation were defrayed in part by a grant from the Life Insurance Medical Research Fund and from the Higgins Trust through Harvard University.

2 Fellow of the National Research Council.

384
METHODS

Mongrel dogs, weighing from 19 to 25 kg., were trained to lie quietly during operative procedures done under local anesthesia, and to run on the treadmill. Then, before a standard control experiment was performed on the treadmill, a radiopaque catheter was passed into the right auricle through a metal cannula inserted into a jugular vein. The location of the tip of the catheter, found fluoroscopically with the dog standing, and marked on the thorax, was used for zero refer-

Fig. 1. Sample control experiment on the treadmill. Effects of graded exercise on mean right auricular pressure, heart rate, respiratory rate and rectal temperature in a representative experiment.

ence. *Mean* right auricular pressures were measured with an adjustable manometer attached to the side of the cage. Five per cent glucose with heparin was used instead of saline in order to eliminate the possible effects of salt load. Results were recorded as millimeters of water.

Heart rate was recorded with a cardiotachometer, and respiratory rate with a pneumograph connected to an ink-writing oscillograph. To assess the animals' work tolerance the fasted dogs were exercised for successive 10-minute periods (bottom fig. 1) at increasing speed and grade until exhausted, as evidenced by their inability to maintain the pace. This end point of work tolerance is arbitrary but, by using
graded exercise rather than a single work rate, it was found to be quite reproducible in a given animal.

Following one or more control experiments on the treadmill the first operative lesion was produced. After operation the dogs were allowed a 3-week period of recovery before a postoperative experiment was performed. After this initial postoperative run, the dogs were given nearly daily bouts of exhausting exercise for several months, and at least one more standard treadmill experiment performed before the second operation, if one was contemplated.

Operations. All operations were performed aseptically under sodium pentobarbital (30 mg/kg.) anesthesia with positive pressure respiration. Insufficiency of the pulmonary valve was produced a) by widening of the pulmonary ring (9), or b) by avulsion of the valve leaflets with a valvulatome introduced through the right ventricular myocardium. The pulmonary artery was stenosed by the method of Hufnagel, Roe and Barger (10). Insufficiency of the tricuspid valve was produced by avulsion of the leaflets with a valvulatome introduced either through the right auricular appendage or through the right ventricular myocardium.

OBSERVATIONS

Effect of Exercise on Normal Dog. The results of a representative control (i.e. preoperative) experiment are charted in figure 1. Following preliminary recording of auricular pressure, heart rate and respiratory rate while the dog was standing quietly on the treadmill, each dog was exercised for consecutive 10-minute periods (see bottom fig. 1) at 2.0 and 3.0 miles per hour on the level, followed by 3.0 miles per hour, first at 5° grade and then at 10°. In order to differentiate more clearly between the results due to progressively increasing intensity of work and those due to its duration, the dogs were returned to the level at 3.0 miles per hour for 10 minutes. The dogs then ran at 4.0 miles on the level, and finally at 10° for successive 10-minute periods at 4.0 miles per hour, 5 etc. until exhausted. After a recovery period of 30 or more minutes the observations were ended. (In a few of the early experiments the exercise started with 1.5 miles per hour on the level.)

In general, heart rate increased as soon as exercise began, and rose stepwise with each work increment to peak levels of 250 to 300 beats per minute. Occasionally, as exhaustion approached, heart rate decreased from the maximum rate, and in a few dogs a definite bradycardia (rates of 30 to 60 beats per minute) was seen, with collapse of the animal.

Respiratory rates varied considerably in any given animal from moment to moment, especially before exercise. During exercise the respiratory pattern tended to be more uniform. The respiratory rate increased with the onset of exercise and continued to rise with each grade of exercise up to 300 to 350 respirations per minute. In contrast to the heart rates, maximum respiratory rates during exercise were observed while the dog was running at 4.0 miles per hour on the level, or 4 miles per hour at 10°. With further increases in the severity of exercise the respiratory rates fell to between 150 and 250 as the breathing became more labored, only to rise rapidly and markedly after exercise to as high as 405. Rectal temperature rose progressively during exercise, reaching 42.0° to 43.5°C. at the usual room temperature of 24 to 28°C.

Mean right auricular pressure (with respect to atmospheric pressure) of normal dogs did not change appreciably during exercise (with rare exceptions) (table 1) even during the gruelling work of running at 6 or 7 miles per hour on a 10° slope.
Table 1. Mean right auricular pressure, heart rate and work tolerance in exercising dogs before and after the production of valvular lesions; autopsy findings

<table>
<thead>
<tr>
<th>DOG NO.</th>
<th>EXPTL. CONDITION</th>
<th>MEAN RT. AUR. PRESS., MM. WATER</th>
<th>HEART RATE/ MIN.</th>
<th>WORK TOL. ANHED</th>
<th>EXTENT OF LESION (AUTOPSY)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Standing</td>
<td>At max. work rate</td>
<td>Standing Max. rate</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>Control</td>
<td>+5</td>
<td>+25</td>
<td>110</td>
<td>228 Norm.</td>
</tr>
<tr>
<td>I</td>
<td>PI (1)</td>
<td>+5</td>
<td>110</td>
<td>85</td>
<td>240 Norm.</td>
</tr>
<tr>
<td>I</td>
<td>PI (2)</td>
<td>+10</td>
<td>-10</td>
<td>70</td>
<td>240 Norm.</td>
</tr>
<tr>
<td>2</td>
<td>Control</td>
<td>+20</td>
<td>+115</td>
<td>75</td>
<td>315 Norm.</td>
</tr>
<tr>
<td>2</td>
<td>PI</td>
<td>+30</td>
<td>+110</td>
<td>112</td>
<td>305 Norm.</td>
</tr>
<tr>
<td>3</td>
<td>Control</td>
<td>+20</td>
<td>0</td>
<td>104</td>
<td>210 Norm.</td>
</tr>
<tr>
<td>3</td>
<td>PI (1)</td>
<td>0</td>
<td>+10</td>
<td>117</td>
<td>231 ?</td>
</tr>
<tr>
<td>3</td>
<td>PI (2)</td>
<td>-35</td>
<td>+10</td>
<td>123</td>
<td>207 ?</td>
</tr>
<tr>
<td>4</td>
<td>Control</td>
<td>-5</td>
<td>-25</td>
<td>94</td>
<td>219 Norm.</td>
</tr>
<tr>
<td>4</td>
<td>PS (1)</td>
<td>0</td>
<td>+10</td>
<td>64</td>
<td>246 Norm.</td>
</tr>
<tr>
<td>4</td>
<td>PS (2)</td>
<td>+75</td>
<td>+70</td>
<td>63</td>
<td>198 Norm.</td>
</tr>
<tr>
<td>4</td>
<td>PS (3)</td>
<td>+35</td>
<td>+90</td>
<td>113</td>
<td>235 Norm.</td>
</tr>
<tr>
<td>4</td>
<td>PS &amp; PI (1)</td>
<td>+50</td>
<td>+140</td>
<td>102</td>
<td>249 Norm.</td>
</tr>
<tr>
<td>4</td>
<td>PS &amp; PI (2)</td>
<td>+45</td>
<td>+100</td>
<td>87</td>
<td>240 Norm.</td>
</tr>
<tr>
<td>5</td>
<td>Control</td>
<td>+75</td>
<td>-30</td>
<td>96</td>
<td>278 Norm.</td>
</tr>
<tr>
<td>5</td>
<td>PS (1)</td>
<td>-25</td>
<td>+30</td>
<td>114</td>
<td>297 Norm.</td>
</tr>
<tr>
<td>5</td>
<td>PS (2)</td>
<td>20</td>
<td>-10</td>
<td>102</td>
<td>264 Norm.</td>
</tr>
<tr>
<td>5</td>
<td>PS &amp; PI (1)</td>
<td>+25</td>
<td>+85</td>
<td>105</td>
<td>229 Norm.</td>
</tr>
<tr>
<td>5</td>
<td>PS &amp; PI (2)</td>
<td>+25</td>
<td>+50</td>
<td>114</td>
<td>234 Norm.</td>
</tr>
<tr>
<td>6</td>
<td>PS (1)</td>
<td>+90</td>
<td>+335</td>
<td>111</td>
<td>261 -4</td>
</tr>
<tr>
<td>6</td>
<td>PS (2)</td>
<td>+105</td>
<td>+400</td>
<td>117</td>
<td>261 0</td>
</tr>
<tr>
<td>6</td>
<td>PS (3)</td>
<td>+105</td>
<td>+335</td>
<td>114</td>
<td>261 0</td>
</tr>
<tr>
<td>7</td>
<td>Control</td>
<td>+15</td>
<td>+10</td>
<td>125</td>
<td>204 Norm.</td>
</tr>
<tr>
<td>8</td>
<td>Control</td>
<td>0</td>
<td>-60</td>
<td>82</td>
<td>219 Norm.</td>
</tr>
<tr>
<td>8</td>
<td>TI (1)</td>
<td>+110</td>
<td>+190</td>
<td>116</td>
<td>285 Norm.</td>
</tr>
<tr>
<td>8</td>
<td>TI (2)</td>
<td>+135</td>
<td>+175</td>
<td>96</td>
<td>240 Norm.</td>
</tr>
<tr>
<td>9</td>
<td>Control</td>
<td>0</td>
<td>0</td>
<td>85</td>
<td>219 Norm.</td>
</tr>
<tr>
<td>9</td>
<td>TI (1)</td>
<td>+130</td>
<td>+235</td>
<td>162</td>
<td>258 Norm.</td>
</tr>
<tr>
<td>9</td>
<td>TI (2)</td>
<td>+125</td>
<td>+300</td>
<td>188</td>
<td>195 -4</td>
</tr>
</tbody>
</table>

A. Pulmonary insufficiency (PI)

B. Pulmonary stenosis (PS) and subsequent pulmonary insufficiency

C. Tricuspid insufficiency (TI) and subsequent PS leading to failure

1 The only unoperated dog to show such a rise.  2 Dog panting.  3 Excited.  4 Degree of decreased work tol. designated by - to - - - -  5 Dog collapsed at 2 mph on the level.
Usually auricular pressure fell slightly as the severity of exercise increased, although occasionally there was no change, or even a slight rise of 25 mm. water (one exception). However, immediately after strenuous exercise auricular pressure dropped sharply (to between \(-50\) and \(-100\) mm. water), a decrease which appears to coincide with the greater negativity of the intrathoracic pressure during panting, and noted by direct measurement in a few dogs.

**Effect of Insufficiency of Pulmonary Valve.** Insufficiency of the pulmonary valve was produced in three dogs. The degree of damage to the valve varied from partial avulsion of one cusp to damage of all three cusps (table 1). All three dogs had grade 1 to 2 systolic murmurs in the pulmonic area. Diastolic murmurs could not be detected aurally, but phonocardiographic records taken on dog 2 revealed a faint, short diastolic murmur.

Pulmonary insufficiency alone had remarkably little effect on mean auricular pressure or work tolerance in two dogs (dogs 1 and 2). Figure 2 is a representative example of a treadmill experiment before and after the production of pulmonary regurgitation. Mean right auricular pressure at rest, during graded exercise and after exercise was essentially the same in the two experiments. Heart rate and respiratory rates were also unchanged postoperatively. There was no detectable reduction in work tolerance even after months of strenuous exercise. The results are summarized in table 1. Dog 3, a much older animal, showed a slight reduction in work tolerance over a period of months but this reduction may have been due to ageing rather than to the valvular lesion.

Figure 3A is an example of the right ventricular (*top*) and pulmonary artery (*bottom*) pressure tracings of one of the dogs with pulmonary insufficiency (*dog 3*). The pressure drop in the pulmonary artery during diastole is more rapid than normal and the diastolic pressure falls to the same level as right ventricular diastolic pressure.

**Effect of Stenosis of Pulmonary Artery.** Pulmonary stenosis was produced in three dogs. The diameter of the pulmonary artery was reduced by 20 to 60 per cent (table 1). Figure 4 summarizes the data on *dog 4*. Following operation auricular pressure was not significantly different from control measurements at rest or during
exercise, and exercise tolerance was unchanged. After 6 weeks of daily, exhausting exercise resting auricular pressure was slightly elevated (35-75 mm. water). However, the dog was able to run for an additional 20 minutes at 6 and 7 miles per hour at 10°, and auricular pressure rose to 90 mm. of water at peak exercise. Figure 3B shows the systolic pressure drop across the pulmonary stenosis, and the normal right auricular pressure tracing in this dog shortly after the first operation. The data on the other dogs with pulmonary stenosis are summarized in Table I.

Whenever pulmonary stenosis greater than 60 to 70 per cent of the diameter of the artery was attempted at one operation the animals died within 1 to 3 days. Not infrequently, when a high degree of stenosis was attempted the heart appeared by inspection at operation to be able to tolerate the load for the first 5 to 10 minutes. Suddenly, however, the heart rate would decrease, dropping from between 150 to 200 beats per minute to between 20 to 40 within a minute or so. This bradycardia would progress to complete asystole, unless the artery clamp was immediately removed.

The heart rate would then gradually rise to previous levels. The operation could then be resumed and completed with a somewhat lesser occlusion of the pulmonary artery.

One dog (dog 6) survived a 60 to 70 per cent occlusion, although he had almost constant runs of extrasystoles for several days after operation. At the first postoperative experiment (3 weeks after operation) his resting auricular pressure was elevated to approximately 100 mm. of water (fig. 5 and Table I). With the onset of exercise mean right auricular pressure rose sharply to 175 mm. of water, and rose markedly with each work increment to a level of 335 mm. of water. For the first two postoperative experiments his endurance appeared to be slightly reduced. However, with further daily graded exercise he was able to surpass his control work tolerance. Despite the elevated resting auricular pressure and the marked rise during exercise this dog did not develop any clinical signs of congestive failure even after 6 months of nearly daily exhausting exercise. Right ventricular pressures were measured on several occasions, with the animal resting quietly on his side. When the animal was relaxed right ventricular systolic pressure (fig. 3C) varied from 65 to 85 mm. Hg, with presystolic pressure of 12 to 20, and a mean pressure of 28 to 30 mm. Hg. With slight excitement right ventricular systolic pressure rose to 100 mm. Hg or
more. Clear tracings of pulmonary artery pressure were difficult to obtain due to turbulence. Systolic pressure in the pulmonary artery appeared to be only 25 to 30 mm. Hg, and mean pressure 12 to 14 mm. Hg.

Respiratory patterns during exercise were essentially unchanged postoperatively in dogs 4 and 5. Heart rates likewise showed no significant difference postoperatively in dogs 4 and 5. However, after pulmonary stenosis was produced in dog 6 (60–70% of diameter occluded) heart rates were consistently higher during mild and moderate exercise than they were preoperatively, although maximum heart rates were very similar (fig. 5 and table 1).

**Effect of Pulmonary Insufficiency Superimposed on Pulmonary Stenosis.** In two dogs (dogs 4 and 5) pulmonary insufficiency was superimposed on the stenosis by damage to all three cusps of the pulmonary valve (fig. 4 and table 1). This added valvular injury did produce a small, further rise of auricular pressure at peak exercise. In neither dog was there any decrease in work tolerance, nor did signs of failure appear even after months of exhausting exercise.

**Effect of Insufficiency of Tricuspid Valve.** Tricuspid avulsion was performed on dogs 7, 8 and 9 with damage varying from destruction of one cusp, to nearly complete destruction of the valve (table 1). Resting mean right auricular pressure was elevated 75 to 130 mm. of water (table 1). In the experiment illustrated in figure 6 (middle curve) auricular pressure, which was 75 mm. of water at rest, rose another 50 mm. with the onset of exercise. Throughout the rest of the experiment the pressures paralleled the control pressures although at a considerably higher level, ending at 110 mm. of water at 5 miles per hour and 10°. In the other two dogs mean auricular pressure continued to rise slightly during graded exercise to peak values of 175 and 235 mm. of water. Heart rates tended to rise to higher levels at the lighter work loads after tricuspid avulsion, although maximum heart rates were similar. The respiratory pattern was not markedly altered after operation.
Despite this elevation of mean auricular pressure none of the dogs at this stage had any gross reduction in work tolerance, nor did any other evidence of failure appear following 3 months or more of exhausting exercise.

The changes in the right auricular pressure tracings varied with the extent of the insufficiency of the tricuspid valve. In mild insufficiency auricular pressure was elevated throughout ventricular systole, with only a slight rise in mean auricular pressure. In complete avulsion of the tricuspid leaflets right auricular pressure (fig. 3D) was nearly identical with right ventricular pressure.

Production of Chronic Congestive Failure by Combination of Tricuspid Regurgitation and Pulmonary Stenosis. Chronic congestive failure resulted when three
dogs with insufficiency of the tricuspid valve were subjected to a second operation at which the main pulmonary artery was stenosed to reduce its diameter by 50 per cent. After the second lesion was produced resting auricular pressures rose to between 165 and 250 mm. of water (table 1). The top curve of figure 6 illustrates the changes in auricular pressure during exercise in dog 7 after the second operation. With the onset of the mildest exercise (walking on the level at 1.5 mph) auricular pressure rose from 185, the resting level, to 260 mm. water. With each added increment of work the auricular pressure rose successively until it reached the remarkable height of 420 mm. water just before collapse at the relatively light work load of 3 miles per hour and 5°. Similar results were observed in dog 8. Dog 9 collapsed still sooner, 3 to 6 minutes at 2 miles per hour on the level.
In normal dogs, as mentioned above, auricular pressure fell rapidly and immediately after strenuous exercise to levels 50 to 100 mm. water below control resting values. In contrast, auricular pressure of dogs in failure fell more slowly after exercise and never went below control levels. This slower descent of venous pressure after exercise has been noted in patients with congestive failure (11). However, in our dogs this type of response was not limited to the animals in frank failure, but was also seen in dogs with severe insufficiency of the tricuspid valve, or severe pulmonary stenosis (fig. 5).

The resting heart rates of these dogs in failure were elevated after operation, and in two of the dogs the heart rate was relatively fixed during exercise (table 1). On the other hand, the respiration during exercise was deeper, more labored and definitely slower than during the control runs.

All three dogs with the combination of tricuspid regurgitation and pulmonary stenosis developed a syndrome similar to chronic, right-sided congestive failure as seen in man, and characterized by markedly dilated right ventricle, elevated auricular pressure and distended veins, dyspnea on exertion, decreased work tolerance, hepatomegaly, ascites, tachycardia at rest, and a relatively fixed heart rate even during exercise in two of the dogs. No frank pitting edema was demonstrated during the several months of failure. In all of the dogs in failure there was suggestive thickening of the skin overlying the paws, and one animal had questionable pitting. One dog with a very small stitch abscess at the lower end of the thoracotomy incision (and probably with some lymphatic obstruction) developed massive edema of the most dependent part of the thorax with swelling far out of proportion to the localized abscess. The systemic arterial blood pressure of the dogs remained normal.

The rate at which the clinical signs progressed differed in the three dogs. Definite ascites was apparent in dog 9 less than 2 weeks after pulmonary stenosis was performed, and while the animal was still restricted to his cage. In dog 7 ascites was not apparent 1 month after operation and did not become evident until 1 week after mild exercise was started. Dog 8 did not develop ascites until 9 weeks post-operatively, including 4 weeks of daily exercise. In order of increasing work tolerance, also, the dogs could be arranged in the same sequence, dog 9, dog 7, dog 8. The resting right auricular pressures of these dogs were as follows: dog 9, +225 to 250 mm. of water; dog 7, +185 to 215 mm. of water; dog 8, +165 to 175 mm. of water.

Figure 3D is an example of the right auricular (top) and ventricular (bottom) pressure tracings in one of the dogs with right-sided failure (dog 9). Despite the high degree of stenosis (50%) systolic pressure is not high (compare with fig. 3C). Auricular systole is forceful, and raises auricular and ventricular pressures to between 13 and 18 mm. Hg. The tricuspid insufficiency is so marked that auricular and ventricular pressures are nearly identical.

In an attempt to obtain additional evidence that the syndrome described above was due to cardiac insufficiency, two of the dogs (dogs 8 and 9) were killed for study as heart-lung preparations.3 As the preparations were being set up, it was apparent that the dogs’ blood volumes were extremely large and that a large part of this blood was pooled in the congested livers, which extended nearly to the iliac crest. Pressing the palm of the hand on the liver produced a rush of blood, and the liver shrank to nearly half the size noted when the abdomen was first opened. Both hearts showed marked dilatation of the right ventricles and right auricles.

---

3 The heart-lung experiments were performed by Dr. Otto Krayer.
As soon as the necessary cannulations were completed the reservoir was elevated in stepwise fashion (fig. 7A) until auricular pressure equaled the resting value seen during life (225–250 in dog 9). Cardiac output was then 1000 ml per minute. Elevating auricular pressure further did not increase cardiac output, indicating that the ‘limit of competence’ (leistungsfähigkeit) (12) had been reached. Under similar conditions heart-lung preparations from normal (and smaller) dogs have produced cardiac outputs as high as 1800 ml/minute with right auricular pressures less than 50 mm. water.

In these two hearts insufficiency appeared to involve both the right and left side of the heart, despite the purely right-sided lesions. Increasing the pressure applied to the ‘Starling resistance,’ thus increasing the burden on the left ventricle, led to a marked drop in cardiac output. As illustrated in figure 7B with an auricular pressure at approximately the resting level during life, (dog 8) and the ‘Starling resistance’ set to give a normal carotid artery pressure, cardiac output was 650 ml/minute. When the pressure applied to the ‘Starling resistance’ was increased by 20 mm. Hg, cardiac output fell to 450 ml while mean pulmonary artery pressure rose from 230 to 270 mm. water. At the next increment of outflow resistance the cardiac output fell precipitously. Thus, on the basis of these two preliminary experiments, it would appear that as in cardiac failure in the human, the involvement of one chamber may predominate early in the disease, but with the progression of the dis-

---

4 Also performed by Dr. Otto Krayer.
ease decompensation of both chambers becomes apparent. Further experiments are required to verify these suggestive findings.

Post-Mortem Examination. The abnormal findings in the dogs with pulmonary stenosis, and pulmonary insufficiency were limited to the heart; the rest of the organs appeared normal. The hearts were large, with dilatation and hypertrophy of the right ventricle. The columnae carnae of the right ventricle were flattened. The pulmonary artery distal to the stenosis was not dilated.

The dogs in chronic, right-sided congestive failure had large amounts of ascites, without pleural fluid or gross pitting edema, although the tissues appeared wet and thickened. All organs were markedly congested. The hearts were enlarged with such striking dilatation of the right ventricle that the hypertrophy of the right ventricular myocardium was somewhat masked. However, the columnae carnae were nearly obliterated. The heart weight/body weight ratios of all the dogs in this series were well above normal for dogs of this size (0.0091-0.0122) (13).

DISCUSSION

The study of the pathogenesis of congestive failure in man is accompanied by numerous handicaps, many of which would be obviated if the syndrome could be reproduced in dogs. Our purpose was to produce a relatively stable reduction of cardiac competence in dogs by known and graded degrees of valvular damage, and to study the relation of these lesions and of exercise to auricular pressure, work tolerance, and the development of chronic, congestive failure. The operative lesions were limited to right side of the heart because 1) it seemed likely that failure of the less muscular right ventricle could be produced more readily than failure of the left ventricle, 2) congestive failure was desired with minimum involvement of the lesser circulation, and 3) pressure measurements could be made in the right heart more easily and frequently, and with little trauma. The results of the investigation are summarized in more succinct form in table 2 for the sake of discussion.

In the normal dog (table 2) mean right auricular pressure (with respect to atmospheric pressure) did not change significantly during exercise, which was intense enough to raise cardiac output fourfold or more (14). The constancy of auricular pressure does not indicate that the net filling pressure remains unchanged, for intrathoracic pressure tends to fall during exercise on the treadmill. A drop of 50 mm. water in mean intrathoracic pressure during strenuous exercise was observed in one normal dog (and also in one dog with pulmonary insufficiency). However, the increase in net filling pressure during exercise is not only difficult to measure quantitatively, but even in the heart-lung preparation cardiac output may double with a rise of auricular pressure of only a few millimeters of water (12). Hence, the relative constancy of mean auricular pressure during exercise is not surprising.

In the dogs with valvular damage the average values for resting mean auricular pressures varied over a wide range—from 10 to 203 mm. water. During peak exercise auricular pressure in these dogs varied from 5 to 363 mm. water. The dogs with valvular lesions fell into the following four general categories, and remained within a given category during months of daily, exhausting exercise. 1) Normal resting, mean auricular pressure, without elevation during exercise, and normal exercise tolerance (pulmonary insufficiency). 2) Normal or slightly elevated resting, mean auricular pressure, with further elevation during exercise, and normal exercise tolerance (one exception) (pulmonary stenosis or pulmonary stenosis plus pulmonary insufficiency). 3) Moderate elevation of resting, mean auricular pressure, with further rise during
exercise, and normal exercise tolerance (tricuspid insufficiency).

4) High resting, mean auricular pressure, with sharp and marked rise during light exercise, and reduced work tolerance. The dogs in this group developed right-sided congestive failure (tricuspid insufficiency plus pulmonary stenosis).

In agreement with clinical findings we have noted that valvular lesions (e.g., pulmonary insufficiency) may be present in the dog without elevation of venous pressure at rest, and even during exhausting exercise. Exercise tolerance was normal in the dogs with pulmonary insufficiency and no signs of congestive failure appeared. This evidence, if confirmed, may have important clinical implications relating to the surgical conversion of severe pulmonary stenosis into pulmonary insufficiency.

In fact, vein grafts (without valves) have been used by Donovan (15) to shunt blood from the right ventricle into the distal pulmonary artery, bypassing an experimentally occluded pulmonary artery. These dogs also had grossly normal exercise tolerance.

### Table 2. Summary of Effects of Valvular Lesions on Right Auricular Pressure, Exercise Tolerance and Development of Congestive Failure

<table>
<thead>
<tr>
<th>VALVULAR LESIONS</th>
<th>AURICULAR PRESS. (av. figures in mm. water)</th>
<th>EXERCISE TOLERANCE</th>
<th>CONGESTIVE FAILURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td>NORMAL</td>
<td>NO</td>
</tr>
<tr>
<td>Pulmonary insufficiency</td>
<td>+6^1</td>
<td>-13</td>
<td>NORMAL</td>
</tr>
<tr>
<td>Pulmonary stenosis</td>
<td>+10^1</td>
<td>+5</td>
<td>NORMAL</td>
</tr>
<tr>
<td>(Total)</td>
<td>+13^2</td>
<td>+42</td>
<td>NORMAL</td>
</tr>
<tr>
<td>Pulmonary stenosis and pulmonary insufficiency</td>
<td>+3^0</td>
<td>+94</td>
<td>NORMAL</td>
</tr>
<tr>
<td>Pulmonary stenosis and pulmonary insufficiency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tricuspid insufficiency</td>
<td>+112</td>
<td>+178</td>
<td>Normal</td>
</tr>
<tr>
<td>Tricuspid insufficiency and pulmonary stenosis</td>
<td>+203</td>
<td>+363</td>
<td>Marked reduction</td>
</tr>
<tr>
<td></td>
<td>(Lowest)</td>
<td>(Lowest)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>+165</td>
<td>(+355)</td>
<td></td>
</tr>
</tbody>
</table>

^1 Dog 2 omitted (see table 1). ^2 Dog 6 included in averages. Figures for this dog with more severe stenosis are in parentheses.

ance, and no signs of congestive failure appeared over a period of 18 months despite the pulmonary regurgitation. Since diastolic pressure in the pulmonary artery is relatively low, the amount of regurgitation through an insufficient pulmonary valve is probably not great. During exercise the amount of blood regurgitated may even be less than at rest, because pulmonary artery pressure does not rise during exercise (16, 17), and the tachycardia reduces the time available for retrograde flow.

Pulmonary stenosis (less than 50% reduction of diameter), or pulmonary stenosis plus pulmonary insufficiency, with little or no rise of resting auricular pressure, did produce an elevation of central venous pressure during severe exercise. However, the rise of auricular pressure to between 40 and 90 mm. water (table 2) during exercise was not associated with any gross reduction of work tolerance, nor did congestive failure supervene after 3 to 6 months of exhausting exercise. One dog with severe pulmonary stenosis (dog 6) had a more pronounced rise of auricular pressure during exercise, and a temporary reduction in work capacity following operation. Three months later exercise tolerance was normal. The studies of experimental pulmonary stenosis in dogs agree with clinical experience in man because
pulmonary stenosis is compatible with survival to adult life and frequently the lesion may be an accidental finding at autopsy. Furthermore, the exercise tolerance of six of Dow’s patients (18) was grossly normal, and only two had physical limitations on moderate exertion. During mild to moderate exercise cardiac output of the four patients tested rose normally. In one case, a vigorous athletic boy, right auricular pressure rose from 8 mm. Hg (109 mm. water) to 20 mm. Hg (272 mm. water) while cardiac output increased from 7.2 to 12.1 liters per minute. The patient had no evidence of congestive failure.

On the other hand congestive failure (right-sided) was the most common cause of death in Greene’s (19) series of cases of pulmonary stenosis proved at autopsy. His figure of 26 deaths from congestive failure in 68 cases of pulmonary stenosis seems very high. Many patients with pulmonary stenosis go through life without limitation of activity, and die of unrelated causes. These may not come to autopsy in as large numbers as those with frank congestive failure, and failure may develop only in the most severe cases of stenosis. Whether failure will supervene in dogs with pulmonary stenosis exercised over longer periods of time is now under investigation.

Tricuspid insufficiency in the dog likewise stimulates tricuspid disease in man, with elevated venous pressure, normal resting cardiac output (20, 14), absence of physical limitations and of peripheral edema. Resting auricular pressure in the dogs with tricuspid insufficiency averaged over 100 mm. water (table 2), and rose to nearly 200 mm. during exercise. Despite this elevation of mean auricular pressure, no signs of congestive failure were observed after 3 months of daily exercise. These observations agree with those of Altschule in man (20). He has stressed the theoretical importance of tricuspid disease since it causes a high venous pressure which may persist for years without giving rise to peripheral edema. He has suggested that this finding negates the concept that cardiac edema is due solely to failure of the right ventricle with consequent rise in venous pressure.

Chronic, right-sided congestive failure regularly resulted, however, from the combination of tricuspid insufficiency with pulmonary stenosis (reduction of diameter to 50%). The syndrome was characterized by dilated right heart, elevated auricular pressure and distended veins, dyspnea on exertion, decreased work tolerance, hypervolemia, hepatomegaly, massive ascites and tachycardia. True cardiac insufficiency is suggested also by the heart-lung preparations. At this advanced stage, the left side of the heart, as well as the right, appeared to be in failure despite the fact that the initial lesions were purely right-sided.

Resting mean auricular pressure in the dogs with failure varied from 165 to 250 mm. water, with a sharp rise to between 350 and 400 mm. during light exercise. Ascites was prominent, but frank pitting edema did not appear, nor was it present in Bolton and Starling’s (1) dog with spontaneous congestive failure. A striking clinical feature of patients with tricuspid disease in failure, according to Levine (21), is the predominance of ascites and enlargement of the liver without peripheral edema, a clinical picture we have observed in dogs.

The role of the elevated auricular pressure in the pathogenesis of the syndrome described above is still obscure. We found, as did Landis et al. (8), that minor decreases in cardiac competence, which were not apparent at rest, led to an elevation of central venous pressure during strenuous exercise. However, conspicuous abnormalities of venous pressure at rest and during exercise appeared in animals with normal exercise tolerance and without gross fluid retention. In general, the higher the
resting venous pressure, the greater the rise during exercise, although there were exceptions. Whether the development of the signs of congestive failure is associated with the elevation of resting auricular pressure above a critical resting level, e.g. 165 mm. water, or above a critical level during exercise, e.g. 300 mm. water, is not clear. To help in assessing the relative importance of the cardiac and extracardiac factors in the pathogenesis of congestive failure studies are now in progress on 1) cardiac output, 2) venous gradients, and 3) renal excretion of sodium. In such analyses the availability of animals with graded resting auricular pressure and graded elevation of auricular pressure during exercise should be most helpful.

**SUMMARY**

In the present study we have attempted to investigate the relation of valvular lesions and of exercise to auricular pressure, exercise tolerance and the development of congestive failure in the unanesthetized dog. In this initial approach to the problem the valvular lesions were limited to the right side of the heart for reasons already enumerated. The valvular lesions were a) insufficiency of the pulmonary valve, b) pulmonary stenosis, c) combined pulmonary insufficiency and pulmonary stenosis, d) insufficiency of the tricuspid valve, and e) the combination of tricuspid insufficiency and pulmonary stenosis. The effects of these operative lesions on auricular pressure and work tolerance of the dogs may be summarized briefly as follows:

1) Pulmonary insufficiency alone had remarkably little effect on auricular pressure or work tolerance even after months of daily strenuous exercise. 2) Pulmonary stenosis of less than 50 per cent of the diameter produced a slight rise in resting auricular pressure, with further rise during exercise. Work capacity was normal. Superimposed pulmonary insufficiency produced only minor changes. One dog with severe pulmonary stenosis had a resting auricular pressure of 100 mm. water. The auricular pressure rose progressively during exercise to 330 to 400 mm. water. Exercise capacity was temporarily reduced to a slight extent after operation, but soon returned to normal. 3) Tricuspid insufficiency elevated resting auricular pressure by 75 to 135 mm. water, with slight to moderate increases during exercise. Here again work tolerance was normal and no signs of failure appeared after 3 months or more of daily exhausting exercise. 4) The combination of tricuspid insufficiency and pulmonary stenosis produced a syndrome similar to chronic, right-sided congestive failure as seen in man, and characterized by dilated right heart, elevated auricular pressure and distended veins, dyspnea on exertion, decreased work tolerance, hypervolemia, hepatomegaly, ascites and tachycardia. That true cardiac insufficiency was present was suggested by heart-lung preparations.

It is a pleasure to thank Dr. Eugene M. Landis for his advice and criticism. We also wish to express our appreciation to Drs. Otto Krayer for performing the heart-lung experiments, to Charles A. Hufnagel for his surgical advice, to Joseph R. DiPalma for his aid in the preliminary experiments, and to Mr. Franklin W. Smith for his technical assistance.

**REFERENCES**

4. Fishman, A. P. Personal communication.
14. BARGER, A. C., V. RICHARDS, J. METCALFE AND B. GUNTHER. To be published.
15. DONOVAN, T. J. Personal communication.
16. RILEY, R. L., A. HIMMELSTEIN, H. L. MOTLEY, H. M. WEINER AND A. COURNAND. Am. J.
18. DOW, J. W., H. D. LEVINE, M. ELKIN, F. W. HAYNES, H. K. HELLEMS, J. W. WHITTENBERGER,
   1: 207, 1950.
19. GREENE, D. G., E DE F. BALDWIN, J. S. BALDWIN, A. HIMMELSTEIN, C. E. ROH AND A. COUR-