

# Acute Complete Heart Block in Dogs

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A study has been conducted immediately and up to 18 days after the surgical production of complete heart block in dogs. Immediately after surgery cardiac output, coronary flow, and mean arterial pressure were reduced in rough proportion to the degree of bradycardia. In time, these measures began to return toward preoperative levels. Paralleling the diminished left ventricular work was a diminished left ventricular oxygen consumption with little consequent change in myocardial efficiency. Small rises were detected in central venous pressure. At autopsy, the only unequivocal abnormality was myocardial hypertrophy which became measurable between 2 and 18 days after operation.

**A**LTHOUGH the clinical entity of complete heart block has been recognized for almost 100 years, few studies of the cardiocirculatory alterations in this condition are available, either in man or experimental animals. Human investigations have been limited to case reports or small series with differing results in terms of cardiac output, exercise adaptation and circulation time.<sup>1, 2</sup> Complete heart block in dogs, produced by crushing the auriculoventricular junction with a special clamp, was the subject of studies by Erlanger and his associates 50 years ago,<sup>3-6</sup> but this pioneer work was oriented primarily toward an understanding of the conduction mechanism. Eyster and Swarthout,<sup>7</sup> in 1920, produced complete heart block in dogs, by heating the region of the bundle of His and measured cardiac output and mean arterial pressure.

In addition to obtaining information which might have application to a human disease entity, experimental heart block furnishes a background to study the effect of extreme bradycardia upon cardiac function.

## GENERAL METHODS

Sixty mongrel dogs were used, ranging in weight from 12 to 25 Kg., and satisfactory technical conditions were realized in 46 experiments. The dogs were given 23 to 32 mg. per kilogram of Nembutal intra-

venously, and small implementing doses were used to keep a uniform anesthetic state. Tracheostomy was performed in acute experiments. When survival was contemplated, an orally placed endotracheal tube with an inflatable cuff was used.

Heart block was produced by section of the bundle of His through a right auricular myocardotomy during temporary occlusion of the cavae (8). In acute experiments, the conditions were imposed that the occlusion be no longer than 60 seconds (fig. 1) with less than 50 cc. blood loss, measured after collection in a suction bottle. All blood loss from surgical procedures or tests was replaced promptly with whole blood. In some animals repetitive cardiac stimulation was later performed by a technique described elsewhere<sup>9</sup> after reopening the thoracotomy.

Left ventricular coronary flow in cubic centimeters per 100 Gm. myocardium per minute was measured by the nitrous oxide desaturation method<sup>10</sup> after catheterization of the coronary sinus, pulmonary artery, and femoral artery. In these animals, cardiac output was determined by the direct Fick method. A closed system spirometer was used to measure total oxygen consumption. The blood samples were analyzed for nitrous oxide by the method of Kety and Schmidt,<sup>11</sup> and for oxygen content by the manometric method of Van Slyke and Neill. Efficiency and other calculations were computed by the formulae summarized by Goodale and Hackel<sup>10</sup> after weighing the left ventricle by their method. For these computations the myocardial respiratory quotient was assumed to be 0.83. In experiments in which coronary flow was not studied, cardiac output was obtained by the dye dilution method of Stewart and Hamilton, employing a repeatedly calibrated photometer which continuously measured the dye concentration of flowing arterial blood.<sup>12</sup>

Vascular pressures were detected with inductance or capacitance type transducers, with electrical integration of the mean pressures when desired. The frequency response curve of the measuring and recording systems was flat out to 30 cycles per second when measured by recording pressures

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within a balloon during explosion. Standard limb electrocardiogram, blue dye curves (T-1824), and vascular pressures were recorded on a four-channel direct writing oscillograph.

### RESULTS

*Immediate Effects of Heart Block.* Normal dogs under Nembutal anesthesia have tachycardia (in the present series the range was 125–240 per minute), and moderate hypertension.<sup>13</sup> During occlusion of the venae cavae and right auriculotomy, the arterial pressure dropped sharply to 15 to 40 mm. Hg. Small pulses continued to appear (fig. 1A) in the arterial tracing. It was apparent, also, from the varying amounts of blood which drained from the coronary sinus ostium into the operative field, that a reduced systemic flow continued. The reduced arterial pressure and coronary flow were evidently chiefly sustained by drainage from the pulmonary vascular bed to the left heart, a factor suggested by the extreme blanching of the lungs during the period of caval occlusion. During this time the peripheral venous pressure rose to 250 to 400 mm. saline.

After closure of the auricle and release of the cavae, strong arterial pulses immediately reappeared (fig. 1A) with idioventricular rates of 25 to 67 per minute. There was, in general, a transient period of hypertension. Within a minute the arterial pressure became stable (A) with systolic pressures at about the same level as were present before the block, lower diastolic pressures than before, and consequent lower mean blood pressures (fig. 1A). Venous pressures likewise promptly returned toward control status, but generally retained an elevation of a few millimeters of saline.

Electrocardiographic confirmation of the block was obtained (fig. 1B). However, presence of block was evident at the operating table, even while the auricle was still open, because of the gross auriculoventricular dissociation and extreme ventricular slowing. In no case did a ventricular rhythm fail to start after the block.

The resulting preparation was a very stable one. In four animals the rate, cardiac output, and arterial and venous pressures were followed from 15 to 150 minutes during which time little significant change occurred in any of these

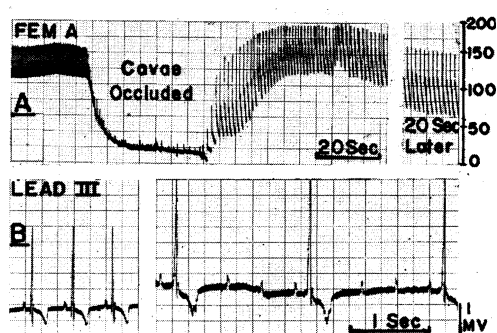


FIG. 1. A. Femoral arterial pressure before, during and after caval occlusion and section of the bundle of His. Calibration in mm. Hg. B. Electrocardiogram of sinus and idioventricular rhythm before and 15 minutes after surgically induced complete heart block. Different animal than A.

measures. Because of the tendency to maintain a *status quo*, data in subsequent experiments was usually obtained only at one to one and one half hours after the block.

*The Effect of Acute Heart Block on Cardiac Output.* Cardiac output, using either the Fick or blue-dye method, was determined in 30 dogs before and 60 to 90 minutes after complete heart block. After the operative procedure, the chest was closed with water seal drainage, so the thoracotomy had generally been closed for at least 45 minutes before post-block determinations. In some cases the pre- and post-block studies were done while the animals were on a positive pressure respirator, supplied with 100 per cent oxygen, and the results followed the same pattern as when respirations were spontaneous and with room air.

In every one of the 30 experiments, the minute output of the heart was reduced, a general conclusion which was also reached by Eyster and Swarthout.<sup>7</sup> The magnitude of the decline was related to the idioventricular rates which ranged from 25 to 67 per minute (fig. 2). The greatest number of animals had rates of from 40 to 55 per minute, and in this group the cardiac output fell quite regularly to about one half of the value previously obtained with an intact conduction system. With idioventricular rates faster or slower than this, cardiac output was curtailed less or more severely, respectively (fig. 2). After several experiments, it became apparent that the

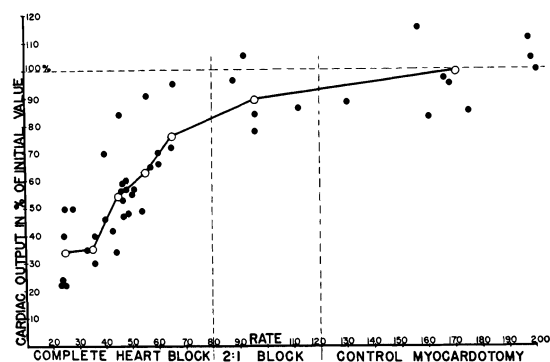


FIG. 2. Effect of complete heart block, 2:1 block, and control myocardotomy on cardiac output. Note how the magnitude of the cardiac-output fall is related to the degree of bradycardia. Values are expressed in per cent of preblock values, each animal serving as its own control.

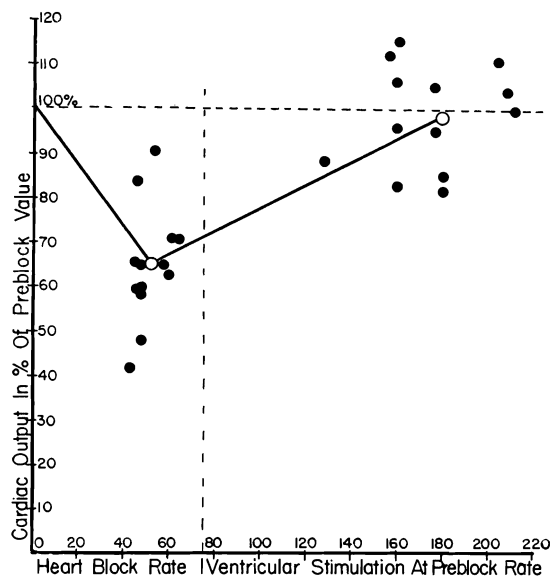


FIG. 3. Cardiac outputs, expressed in per cent of preblock values, in 13 dogs in which complete heart block was produced and ventricular stimulation then conducted at the same rate as had been present before the lesion. Note the fall in output after block, with subsequent restoration to preoperative values during ventricular pacemaking.

cardiac output with idioventricular rhythm could be roughly predicted, by the fraction  $\frac{\text{block rate}}{90} \times \text{control cardiac output}$ .

In five animals, 2:1 heart block was inadvertently produced, with rates of 85 to 112 per minute. In these animals, cardiac output was reduced an average of only 10 per cent

(fig. 2). In nine other cases, the right auricle was opened during a 60-second caval occlusion in exactly the same manner as in performing a block, but without section of the bundle of His. In these controls the cardiac output was essentially unaffected (fig. 2).

The foregoing data is strong evidence that the decreases in minute output of the heart were due specifically to the extreme bradycardia resulting from section of the bundle of His. To further rule out the possibility of nonspecific effects due to the operative procedure, ventricular stimulation, at the rate of the preblock heart beat, was performed in 13 animals with complete heart block. Such repetitive stimulation restored the cardiac output to levels present before the block (fig. 3).

In order to follow any further alterations in cardiac output in the later postoperative period, seven dogs were studied 2 to 18 days after establishment of complete heart block. In this group, all pre- and postoperative determinations were done by the Fick method, in conjunction with coronary flows. The results are shown in figure 4, and for comparison, the data obtained acutely under identical test conditions is included. Three dogs were studied 48 hours after the heart block and then sacrificed. The cardiac output had returned on the average to 70 per cent of preoperative values, in contrast to a general 50 per cent reduction found acutely (fig. 4). This improvement coincided with larger stroke volumes. In four other dogs, similar studies were done 10 to 18 days postoperatively. In these animals the minute output of the heart averaged about 80 per cent of the preblock figures (fig. 4). Comparative stroke volumes had also increased.

To generalize, it has been shown that after heart block, the cardiac output is acutely reduced to an extent dependent upon the degree of rate slowing. Bradycardias as low as 90 beats per minute are attended by stroke-volume increases of such a magnitude that the cardiac output is not greatly affected. With idioventricular rates slower than this, further stroke volume increases evidently do not occur, and cardiac output is diminished as the fraction  $\frac{\text{idioventricular rate}}{90}$ . This state of reduced out-

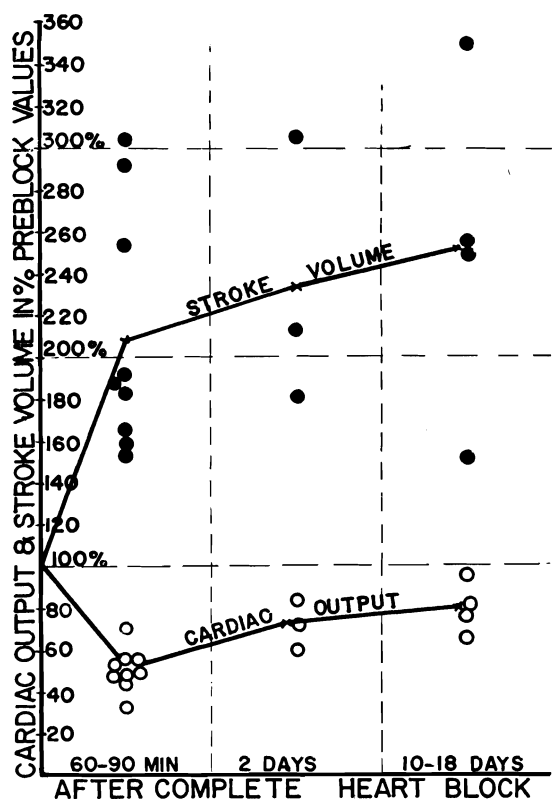


FIG. 4. Changes in cardiac output and stroke volume in animals studied one to one and one half hours, two days, and 10 to 18 days after surgically induced complete heart block. Results are in per cent of preoperative values, each animal serving as his own control.

put is quite stable for the first few hours. Within 48 hours, the cardiac output begins to return toward control values, subserved by increasing stroke volume. This compensation continued with time, but even after 10 to 18 days, the cardiac output was still only 80 per cent of preoperative values.

*The Effect of Acute Complete Heart Block on Total Oxygen Consumption and Systemic Arterial-Venous Difference.* As might be expected, the metabolic requirements of dogs with complete heart block were not greatly changed. The total oxygen consumption one to one and one half hours after the block was in most cases slightly reduced, averaging 90 per cent of the preblock uptake (fig. 5). In the dogs studied after 2 to 18 days, total oxygen consumption averaged 15 to 20 per cent greater than preoperatively. This elevation was prob-

ably a nonspecific effect such as is frequently noted clinically after major surgical procedures.

With the minimally altered oxygen consumption and reduced cardiac output, tissue oxygen needs were met by an increased extraction of oxygen from the blood (fig. 5). Acutely, the average arterial-venous difference was doubled. At 2 and 18 days, a progressive decline in the arteriovenous difference occurred coincident with the return toward normal of the cardiac output. In no animal, however, did the arterial-venous difference return completely to normal (fig. 5).

*The Effect of Complete Heart Block on Arterial Pressure.* A few minutes after complete block was established, systolic pressure usually stabilized at about the same level as had been present with the preoperative sinus rhythm (fig. 1), an observation which had been previously recorded by Erlanger.<sup>3</sup> The diastolic pressures with the slowed rate were considerably reduced with the development of large pulse

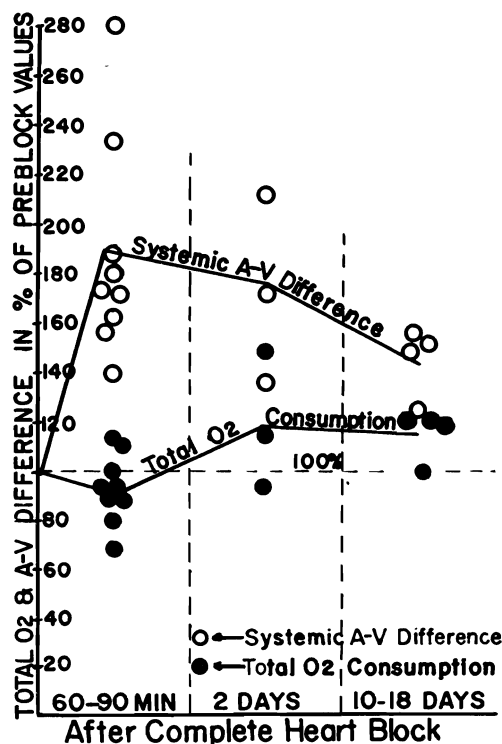


FIG. 5. Total oxygen consumption and arterial-venous difference at different times after surgically induced complete heart block. Results are in per cent of preoperative values, each animal serving as his own control.

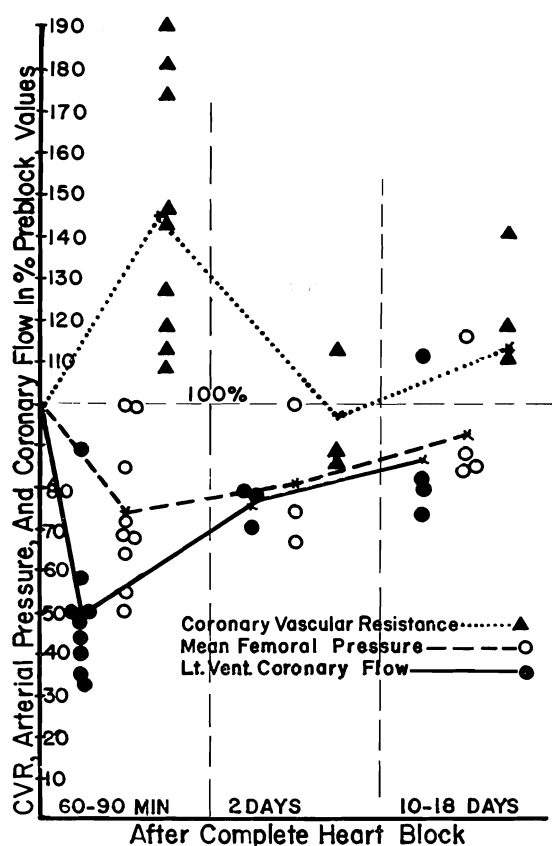


FIG. 6. Changes in left ventricular coronary flow, mean femoral pressure, and coronary vascular resistance (CVR) at varying times after surgically induced complete heart block. Results are in per cent of preoperative values, each animal serving as his own control.

pressures (fig. 1). Mean arterial pressures were consequently reduced (fig. 6) in agreement with earlier data of Eyster and Swarthout.<sup>7</sup> The decline in mean arterial pressure was roughly proportional to the degree of rate reduction. During the first 18 postoperative days, a gradual elevation of mean (fig. 6), diastolic, and systolic pressures occurred. In only two of the seven cases shown, however, did complete restoration of the mean pressure to preblock levels occur (fig. 6).

*The Effect of Complete Heart Block on Left Ventricular Coronary Flow and Coronary Vascular Resistance.* Sixty to 90 minutes after completion of the block, the coronary flow was reduced in all dogs studied, with an average decline of 50 per cent (fig. 6). The diminution

in coronary flow was greatest in the animals with the slowest rates. In the animals studied at two days, coronary flow had returned to 75 per cent of preoperative values, and in 10 to 18 days a further return toward but not to preblock values had taken place (fig. 6). In the animals studied during the first one and one half hours after block, the arterial-coronary sinus extraction was in every case slightly reduced. The intact controls had an average extraction of 11.3 volumes per 100 cc. and the acutely blocked dogs had an average extraction of 9.2 volumes per 100 cc. This change was less pronounced in the animals observed from 2 to 18 days. In the latter group, average extraction in the preoperative controls was 10.8 volumes per 100 cc., and after block was 9.9 volumes per 100 cc.

Coronary vascular resistance was computed in arbitrary units from the formula

$$\frac{\text{mean arterial pressure}}{\text{coronary flow/sec./100Gm. left ventricular muscle}}$$

One to one and one half hours after the operative procedure, some degree of coronary vasoconstriction, relative to the preblock status, was evident in all the animals studied (fig. 6). In the 2 to 18 day group of animals, however, the coronary vascular resistance was not greatly altered in comparison to previously performed control studies on the same animal (fig. 6).

*The Effect of Complete Heart Block on Left Ventricular Work, Oxygen Consumption, and Efficiency.* Left ventricular work was computed from cardiac output times mean femoral pressure. The calculation ignores the work done in imparting velocity to blood, a factor which is ordinarily less than 2 per cent of total work. This kinetic factor may be increased with the pronounced bradycardia and large stroke volumes<sup>14</sup> seen with complete heart block. Although it is unlikely that the kinetic work becomes any greater than 10 per cent of the total ventricular work, it is possible that the work calculations were falsely low to this degree. It has been previously noted in this study that both mean femoral pressure and cardiac output were reduced. Work, the product of these determinations, was reduced in the manner

shown in figure 7. Acutely, left ventricular work was diminished to one third of the preblock value. With temporal passage, work returned toward control values. From 10 to 18 days after the heart block, the work had returned to an average of 80 per cent of preoperative figures (fig. 7).

Left ventricular oxygen consumption was calculated from the formula

$$\text{coronary flow} \times \text{coronary oxygen extraction} \times \text{left ventricular weight.}$$

As will be described subsequently the animals acquired varying degrees of myocardial hypertrophy after a few days. In all cases in which the animals were kept for 10 to 18 days, the preoperative weight, for use in the computation, was estimated by the method of Goodale and Hackel.<sup>10</sup> Postoperative calculations were based on the actual postmortem left ventricular weights. It is evident from a glance (fig. 7) that left ventricular oxygen consumption closely paralleled the work load of the left ventricle. Acutely, oxygen consumption sustained an abrupt fall, with a subsequent return toward preoperative levels.

Left ventricular myocardial efficiency was calculated from

$$\frac{\text{actual work}}{\text{work equivalent of oxygen used}}$$

Because of the well known tendency of the isolated heart to function more economically at slowed rates,<sup>15, 16</sup> it was anticipated that myocardial efficiency would be increased in animals with an idioventricular rhythm. This was not the case, although in chronically blocked dogs with complete return to preoperative work level, rises in efficiency have been noted.<sup>8</sup> With the close relation between work done and left ventricular oxygen utilization, the average efficiency was changed very little in the present series (fig. 7), either acutely or in 2 to 18 days. In actuality, a slight decline in efficiency was seen, possibly related to falsely low work values (see above).

*The Effect of Complete Heart Block on Right Auricular Pressures.* Sixty to 90 minutes after completion of the block, right auricular pressures were taken in six animals. In every case

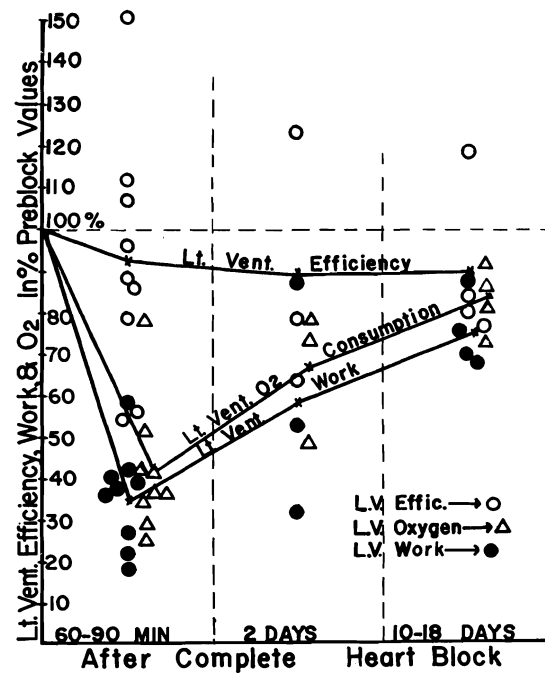


FIG. 7. Changes in left ventricular work, oxygen consumption, and efficiency at varying times after section of the bundle of His. Results are in per cent of preoperative values, each animal serving as his own control.

a small elevation of pressure occurred, ranging from 10 to 30 mm. saline. The right auricular pressure was recorded pre- and postoperatively in the four dogs followed 10 to 18 days, with pressure increases of 20, 20, 30, and 50 mm. saline.

*The Influence of Miscellaneous Factors on Idioventricular Rate.* The investigations of Erlanger<sup>3</sup> on the effects of acute asphyxia, acute exsanguinating arterial hemorrhage, and distal stimulation of the cut vagus nerve were repeated in 4, 3, and 2 dogs, respectively. In confirmation of the earlier work, significant rate changes were not noted with any of these procedures.

*The Effect of Complete Heart Block on Heart Weight.* At autopsy, 2 to 18 days after section of the bundle of His, various portions of the heart were weighed. In all cases the left ventricle was weighed after dissection by the method of Goodale and Hackel.<sup>10</sup> In three animals sacrificed after 48 hours, the left ventricular weight was essentially that predicted on the basis of body weight (fig. 8). In

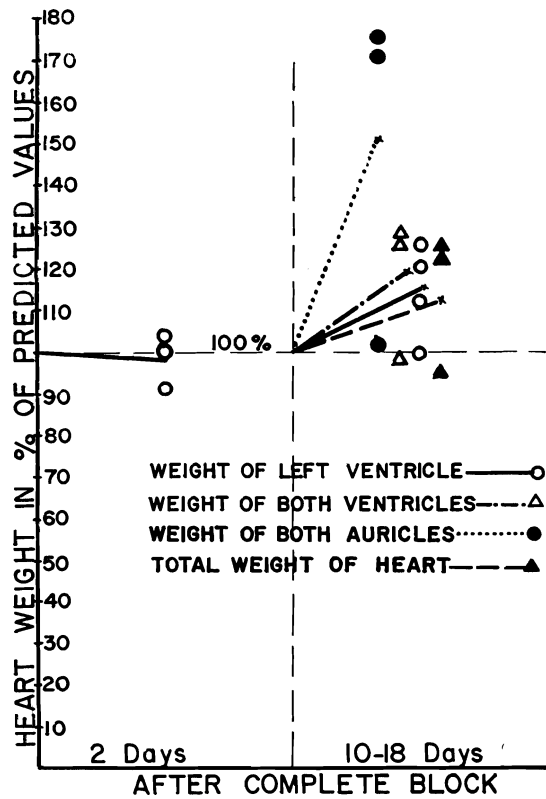


FIG. 8. Changes in heart weight. Note dogs sacrificed after 48 hours had no hypertrophy. Heart weights were abnormally high in animals sacrificed after 10 to 18 days. The percentage values were obtained by dividing the actual post mortem heart weights by the weights predicted on the basis of body weight.

the four animals sacrificed after 10 to 18 days, left ventricular weight was greater than predicted in three cases, with increases from 13 to 25 per cent. In three of the 10 to 18 day series, the total heart weight, weight of both auricles, and weight of both ventricles were also determined and the measures were compared with the values predicted by the method of Herrmann.<sup>17</sup> In two of these three dogs, the weight measures were greater than would have been expected in normal dogs (fig. 8), the exception being the animal which had similarly evidenced no left ventricular hypertrophy.

*Autopsy Findings.* In all animals kept for 48 or more hours, gross examination was conducted, and tissue kept for microscopic study. Except for myocardial hypertrophy (see above) no gross abnormalities were noted. The tricuspid

valves were examined with care, since the section of the bundle of His was through the base of this valve. In all cases, injury to the tricuspid was either not present or trivial. All other valves were uninjured. In every case, sections of the myocardium, lung and liver were made. In one dog, which was sacrificed 12 days after surgery, equivocal evidence of early passive congestion of the liver was reported, but in all other cases the tissues were normal.

#### DISCUSSION

The present work, together with a companion chronic study,<sup>8</sup> permits the integrated outline of the natural history of complete heart block in dogs. Immediately, there is a reduction in cardiac output, coronary flow, and mean arterial pressure, with subsequent gradual return toward preblock values. Full compensation may never occur, in which case right and left sided congestive heart failure results.<sup>8</sup> Some dogs have an evident full restoration of cardiac reserve, but this usually requires several months.<sup>8</sup> In the present study, cardiac hypertrophy was not demonstrable after two days, but was present 10 to 18 days after induction of complete heart block. In the chronic study<sup>8</sup> in which all animals were studied at least six weeks after operation, every animal had cardiac hypertrophy.

#### SUMMARY

A study has been conducted on the effects of surgically induced complete heart block, acutely and for as long as 18 days postoperatively. Idioventricular rates ranged from 25 to 67 per minute. Immediately after the production of the lesion, cardiac output, coronary flow, and mean arterial pressure were reduced, in rough proportion to the degree of bradycardia. At this time the cardiac output could be restored to the preoperative levels by electrical stimulation of the ventricles at the same rate as had been present before the block.

The total oxygen consumption of animals with complete heart block remained essentially unchanged. With the minimally altered oxygen need, metabolic demands were met by an increased extraction of oxygen from the blood,

with a consequent widening of the arterial-venous difference.

With the passage of time, these measures gradually returned toward values which had been present before operation, although even at 18 days cardiac output, coronary flow, and mean femoral pressure were still low, and the arterial-venous difference widened. During this period, elevations in central venous pressure, of from 20 to 50 mm. water, occurred.

All animals observed for two days or longer were autopsied and histologic sections made of the liver and lungs. No gross abnormalities were detected. One dog had histologic evidence of early passive congestion of the liver. After 48 hours, myocardial hypertrophy was not present, but after 10 to 18 days increases in heart weight were found in three of four animals.

#### SUMMARIO IN INTERLINGUA

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#### REFERENCES

- <sup>1</sup> LEQUIME, J.: Le debit cardiaque. Acta med. scandinav. Suppl. **107**: 164, 1940.
- <sup>2</sup> ALTSCHULE, M. D.: Physiology in Diseases of the Heart and Lungs. Cambridge, Harvard University Press, 1949.
- <sup>3</sup> ERLANGER, J.: On the physiology of heart block in mammals with special reference to the causa-

- tion of Stokes-Adams disease. J. Exper. Med. **8**: 8, 1906.
- <sup>4</sup> — AND HIRSCHFELDER, A. D.: Further studies on the physiology of heart block in mammals. Am. J. Physiol. **15**: 153, 1906.
- <sup>5</sup> — AND BLACKMAN, J. R.: A study of relative rhythmicity and conductivity in various regions of the auricles of the mammalian heart. Am. J. Physiol. **19**: 125, 1907.
- <sup>6</sup> — AND —: Further studies on the physiology of heart block in mammals. Heart: **1**: 177, 1910.
- <sup>7</sup> EYSTER, J. A. E. AND SWARTHOUT, E. C.: Experimental determination of the influence of abnormal cardiac rhythms on the mechanical efficiency of the heart. Arch. Int. Med. **25**: 317, 1920.
- <sup>8</sup> STARZL, T. E. AND GAERTNER, R. A.: Chronic heart block in dogs. A method for producing experimental heart failure. Circulation, in press.
- <sup>9</sup> —, — AND WEBB, R. C., JR.: The effect of repetitive electrical cardiac stimulation in dogs with normal hearts, complete heart block, and experimental cardiac arrest. Circulation **11**: 952, 1955.
- <sup>10</sup> GOODALE, W. T. AND HACKEL, D. B.: Measurement of coronary blood flow in dogs and man from rate of myocardial nitrous oxide desaturation. Circulation Research **1**: 502, 1953.
- <sup>11</sup> KETY, S. AND SCHMIDT, C. F.: The determination of cerebral blood flow in man by the use of nitrous oxide in low concentrations. Am. J. Physiol. **143**: 53, 1945.
- <sup>12</sup> FRIEDLICH, A., HEIMBECKER, R. AND BING, R. J.: A device for continuous recording of concentration of Evans blue dye in whole blood and its application to the determination of cardiac output. J. Appl. Physiol. **3**: 12, 1950.
- <sup>13</sup> CORCORAN, A. C. AND PAGE, I. H.: Effects of anesthetic dosage of pentobarbital sodium on renal function and blood pressure in dogs. Am. J. Physiol. **140**: 234, 1943.
- <sup>14</sup> REMINGTON, J. W. AND HAMILTON, W. F.: The evaluation of the work of the heart. Am. J. Physiol. **150**: 292, 1947.
- <sup>15</sup> STARLING, E. H. AND VISSCHNER, M. B.: The regulation of the energy output of the heart. J. Physiol. **62**: 243, 1927.
- <sup>16</sup> COHN, A. E. AND STEELE, J. M.: Influence of frequency of contraction of isolated mammalian heart upon consumption of oxygen. Am. J. Physiol. **113**: 654, 1935.
- <sup>17</sup> HERRMANN, G. R.: Experimental heart disease. I. Methods of dividing hearts; with sectional and proportional weights and ratios for two hundred dog's hearts. Am. Heart J. **1**: 213, 1925.