Production of Experimental Congestive Heart Failure in the Guinea Pig.* (25262)

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To understand more clearly the basic mechanisms involved in the heart and other organs during the course of chronic congestive heart failure, there is a need further to study congestive heart failure from the viewpoint of bioenergetics(1,2,3). The adaptation of biochemical technics to such a problem requires (a) availability of fresh whole non fibrotic cardiac and other tissue for the various enzymatic and biochemical technics, (b) tissue preparations which are readily reproducible and (c) uniform development of congestive heart failure. These criteria have been met in the technic to be described herein which employs the guinea pig as the experimental animal. The basic principle of the technic is to reduce the size of the arch of the aorta by one-third by means of a ligature. The animals thus treated will develop the syndrome of congestive heart failure(4) within a period of 10 to 12 days with the sequential pattern of changes from enlargement of the left ventricle, to passive venous congestion of the visceral organs. The pathologic picture in the tissues of these animals is similar to that observed in man during the development of chronic congestive heart failure. Tissues from these animals may be subjected to technics suitable for biochemical study.

Methods and materials. An adult male Hartley strain guinea pig of approximately 400 g is anaesthetized by injecting 25 mg of Nembutal intraperitoneally. After the animal is completely anaesthetized, the hair is shaved from the chest and ventral aspect of the neck; the animal is placed in the dorsal recumbent position. A plastic catheter is inserted into the exposed trachea. Oxygen is permitted to flow at the rate of 0.3 liter per minute. A "T" tube is placed between the inflow tract and trachea in order to administer artificial respiration, if necessary, during the operative procedure. An incision is made through the skin, pectoralis major and pectoralis minor muscles in the region of the left 6th intercostal space. The chest wall is opened and self-retaining retractors are placed in the opening. The pericardial sac in the region of the pulmonary arteries is separated. A Deschamp ligature carrier, complete with black braided silk thread size 0 is placed under the aorta as close to its exit as possible. The needle is withdrawn, leaving a double thread encompassing the aorta. After the size of the aorta is ascertained by means of calipers, the ligature surrounding the aorta is closed, so that the aorta remains approximately 33% patent. The chest is closed in 3 stages, (a) thoracic cage is first closed (b) the pectoralis muscles are coaptated, (c) the skin is united. (The collapsed lung is inflated prior to closing the chest wall.) The incision surrounding the trachea is closed, the skin is united and the catheter withdrawn. Fifty mg of ascorbic acid buffered tetracycline (Squibb) is injected intramuscularly into each animal. No special treatment is required post-operatively. Electrocardiograms are taken with the aid of needle electrodes inserted into the animals' limbs and attached to a Sanborn direct writing electrocardiographic instrument.

Results. 1. *Electrocardiographic changes* observed in the guinea pig prior to and after production of congestive heart failure show a shift in axis from the normal to left as well as an increase in voltage of the QRS of 60%. In addition to the increase in voltage of the QRS there is a change in repolarization as evidenced by changes in the S-T segments and T waves. These electrocardiogram changes are indicative not only of an enlarging left ventricle but also of an enlargement of all cardiac chambers.

2. *Pathological changes*† observed in ani-

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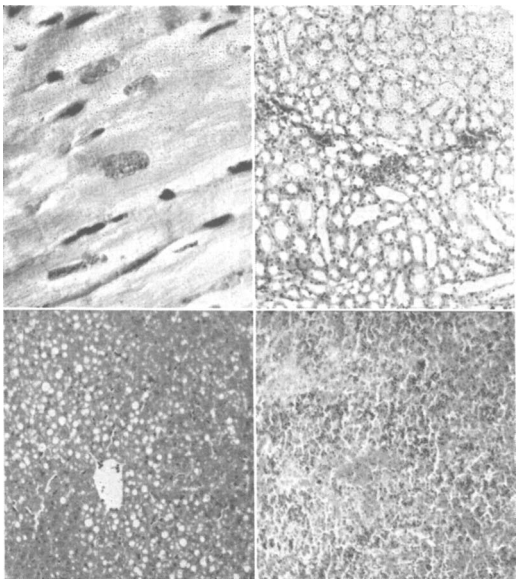

FIG. 1. Mieroscopic sections of heart (left upper corner), kidney (right upper corner), liver (left lower corner) and spleen (right lower corner) taken from 410 g guinea pig with congestive heart failure produced experimentally. Changes shown are characteristic of chronic passive venous congestion and in the heart, cardiac hypertrophy.

mals with experimentally produced congestive heart failure were typical of the classical changes described in the literature(4). Spleens taken from experimental animals were wider, thicker and heavier than normal controls. (Normal spleen weighs 0.7 g and spleen from congestive heart failure animal weight 2.85 g). Fig. 1 shows 4 microphotographs taken from sections prepared from the heart, liver, spleen and kidney of an experimental animal. Note that the changes observed are typical of congestive heart failure.

Discussion. From a biochemical viewpoint, congestive heart failure may be caused by a failure in (a) energy production, (b) energy transference or (c) energy utilization(2). The more common clinical classification of congestive heart failure suggests "forward" or "backward" failure as the 2 major classifications(2,3,5). In the method described herein, restriction of blood flow through the aorta causes a sequential pattern of changes of enlargement of left ventricle, left atrium, pulmonary edema, enlargement of the right cardiac chambers, and passive venous congestion of liver, spleen and kidneys. The changes described are manifested by (a) electrocardiographic changes, and (b) pathological changes, Fig. 1.

The technic of producing congestive heart failure presented herein offers the possibility of preparing tissue for enzyme and bio-energetic studies which was not as feasible in heart-lung preparations, or in methods previously described for producing chronic congestive heart failure(6,7). The animals in which experimental congestive heart failure is produced may be sacrificed and tissue removed from which slices, homogenates, cell-free suspensions and isolated particles may be obtained. Preliminary work on $Q^{N}_{O_2}$ values and P/O ratios on mitochondrial systems prepared from heart and liver have been obtained(8,9) and similar work is continuing.

Summary and conclusion. An operative technic has been described which causes development of congestive heart failure in the guinea pig within 8 to 12 days. Essentially the technic involves intrathoracic incision and restriction of aortic blood flow by ligature surrounding the aorta. Tissues derived from this preparation may be subjected to biochemical and enzymologic studies because of feasibility of preparing slices, homogenates, cell free suspensions and isolated particles. Preliminary biochemical work has been accomplished with this preparation.

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