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The Effect of Pitressin (Vaso-pressin) upon the Heart.

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It has been pointed out by one of us[1] that pitressin (Vaso-pressin) caused a marked drop in blood pressure and decreased pulse rate in the unanesthetized dog. The decreased pulse rate we then believed to be of vagal origin. The present work is a continuation of these earlier experiments.

The effect of the drug upon the heart was noted by recording the electrical potential changes in the action current by the string galvanometer in leads I and III, although usually only the latter lead was employed. Unanesthetized dogs were used. The pitressin was injected intravenously in small doses 0.1 to 0.5 cc. and in some cases followed by the injection of atropine sulphate in doses of 0.2 mgm. or more per kilo. In other experiments the atropine was injected intravenously before the pitressin and other experiments were performed on animals in which the vagi had been severed under ether anesthesia a sufficient time earlier for the animals to have recovered.

In a series of unanesthetized dogs the effect of pitressin upon the blood pressure and pulse rate was studied by means either of a mercury monometer or of a membrane monometer. The pulse rate was counted before, during and following the fall in blood pressure. Other conditions were similar to the above described experiments.

[1] Gruber, *J. Pharm. Exp. Therap.*, 1929, xxxvi, 155.

The effect of pitressin upon coronary flow was studied in excised perfused rabbit's hearts.

Results. The electrocardiographic studies in the normal unanesthetized dog shows the heart slowed, 10 to 15 seconds after the injection of pitressin. This slowing was quickly followed by an acceleration which was subsequently followed by marked slowing of the heart, which persisted for several minutes. During the period of excessive slowing high branching of the T-wave occurred with a marked increase in the height of the wave. In some animals in which the T-wave appeared inverted in the control electrocardiogram it was changed to an upright T-wave after pitressin administration. If atropine in doses sufficient to paralyze the vagi is injected in such animals partial heart block is noted, *i. e.,* P-waves appear in the record without ventricular complexes. In most instances the P-waves following such treatment are inverted or diphasic in character and remain so even though atropine tachycardia is established.

An injection of atropine before the injection of pitressin did not prevent the slowing of the heart completely. Neither did the fact that the vagi had been cut. In such hearts pitressin appears very much more toxic. In all animals high T-waves were observed. In some high branching of the T-waves, shifting pace-maker, nodal rhythm, many ventricular extra systoles, paroxysmal ventricular tachycardia and even ventricular fibrillation were encountered.

The blood pressure records as well as the electrocardiogram of the heart beat show the slowing of the heart beat to be mainly of central origin as it disappears quickly after the injection of atropine sulphate and does not occur to the same degree in animals in which the vagi are cut or paralyzed by atropine. Likewise the acceleration disappears to a large extent by either cutting the vagi or administrating atropine. The acceleration occurs during the fall in blood pressure and is mainly, though not wholly, a compensatory phenomenon, an attempt on the part of the body to maintain a normal blood pressure.

The coronary vessels of rabbits constrict when exposed to pitressin. Moderately high concentration of pitressin injected into the perfusate, suddenly slows the perfusion flow, requiring considerable time for its recovery.

Most of the electrocardiographic changes noted, especially the high T and high branching of the T-waves, we believe can be accounted for by the asphyxia of the heart muscle and accumulation of products of metabolism through coronary vaso-constriction.