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Changes in Heart Rate on Intravenous Infusion in Dogs with Chronic Cardiac Denervation.* (28352)

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It was found previously that when dogs with chronic cardiac denervation were made to exercise on a treadmill, there was a characteristic pattern of change in heart rate: a slow increase on starting to run, a maximum reached after 1½ minutes, and a slow decrease when the exercise was stopped. The maximal heart rates were proportional to the grade of work; at severe levels of work, as represented by an oxygen consumption of 65 ml/kg/min, the rate increment was 50 to 60 beats more than the pre-exercise value(1). It was found that this increase in heart rate was not affected by bilateral adrenalectomy nor was it related to the absolute value of blood temperature during the exercise(2). Studies by Blinks(3) on a number of animal species showed that distention of the right atrium in isolated heart preparations had a positive chronotropic effect. It seemed appropriate to examine the possibility that this mechanism was responsible for the increase in heart rate seen during exercise in dogs with chronic cardiac denervation.

Either 5% dextrose in physiologic saline or 6% dextran (molecular weight 40,000) at body temperature was infused intravenously into dogs in which chronic cardiac denervation previously had been performed by the neural ablation technic of Cooper and associates(4). Studies were carried out on 6 animals with proven cardiac denervation(4); 2 animals were conscious and 4 were anesthetized. In the conscious dogs, only the volume and rate of fluid infused and the heart rate were recorded. In the dogs anesthetized with sodium pentobarbital (20 mg/kg), the following were recorded: temperature and pressure of the blood within the right atrium, heart rate, esophageal pressure at the level of the atrium, and volume and rate of infusion. Prior to the time of study, bilateral adrenalectomy had been carried out in 2 animals.

Two animals were studied twice on separate occasions, once using dextrose saline and again using dextran. The data for the group are summarized in Table I. The time course of events during an infusion of dextrose saline is shown in Fig. 1, and during an infusion of dextran in Fig. 2.

Discussion and conclusions. In all cases, an increase in heart rate resulted from intravenous infusion of fluid into dogs with chronic cardiac denervation, the increments ranging from 4 to 31 beats per minute. In those cases in which it was measured, right atrial pressure increased; in individual experiments, the increase in pressure was proportional to the volume infused. In the experiments with dextran, the maximal increase in right atrial pressure preceded the maximal increase in heart rate by intervals ranging from 4 to 54 minutes. Part of this wide variation was explained by the fact that the peak of the increase in rate often was approached so slowly that it was difficult to

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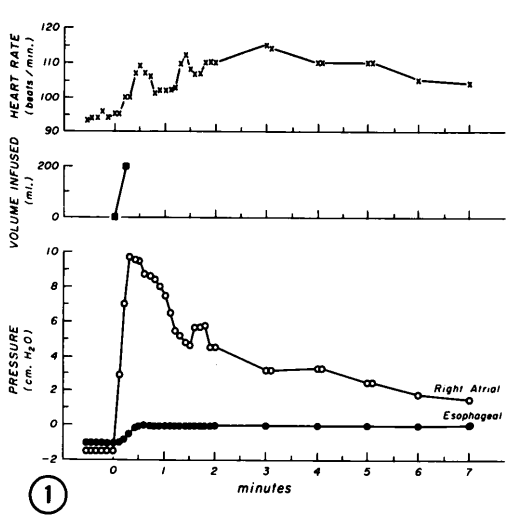
TABLE I. Effect of Intravenous Infusions on Heart Rate in Dogs with Cardiac Denervation.

Wt of dog, kg	State* of dog	Infusion fluid†	Vol infused, ml	Rate of infusion, ml/min	Delay time,‡ min	Maximal changes from control value: Heart rate, beat/min	Right atrial pressure, cm H_2O	Esophageal pressure, cm H_2O	Blood temp, °C
10.7§	C	S	500	17	—	+18	—	—	—
13.1§	A	D	400	67	4.0	+31	+ 9.4	No change	—
16.5	A	S	300	300	—	+ 4	+ 9.0	—	—
		S	300	300	—	+ 5	+ 8.5	—	—
		S	300	300	—	+ 5	+12.0	No change	—
11.1	A	S	200	800	2.5	+21	+11.2	+1.0	—
16.5	C	S	500	55	—	+16	—	—	—
	A	D	800	53	45	+31	+20.5	+1.0	No change
12.2	A	S	500	100	—	+ 8	+16.5	+3.0	—
		S	500	100	—	+ 7	+14.5	+3.5	No change
	A	D	500	86	7.0	+14	+13.5	—	—
		D	400	67	54	+13	+14.5	No change	No change

* C, Conscious; A, Anesthetized (sodium pentobarbital, 20 mg/kg).
† S, 5% dextrose saline; D, 6% dextran, molecular wt 40,000.
‡ Time from maximal right atrial pressure to maximal heart rate. Blank indicates no measurement made or recording not continued beyond end of infusion.
§ Dogs with prior bilateral adrenalectomy.

locate it precisely in relation to the time axis. In the experiments with saline, there was a clearly defined lag of 2½ minutes in the example shown in Fig. 1, but in the others the small degree of cardiac acceleration made it impossible to decide if a lag was present. Similarly, a lag between the maximal increase in venous pressure and the maximal increase in heart rate has been reported by Coleridge and Linden(5) in a study of the Bainbridge reflex in intact anesthetized dogs.



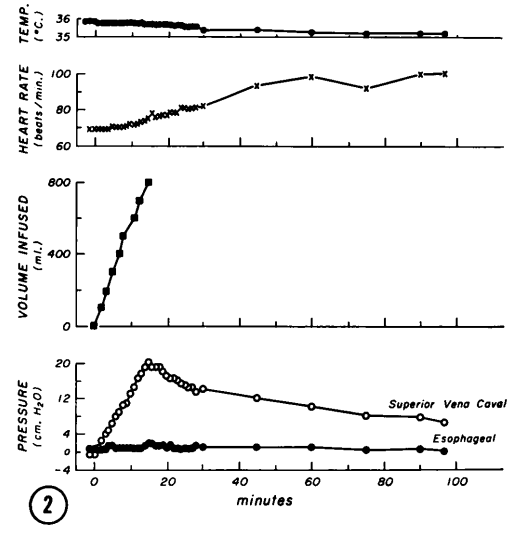


FIG. 1. Effect of intravenous infusion of 200 ml of 5% dextrose saline at body temperature on heart rate and esophageal and right atrial pressures in a dog (11.1 kg) with chronic cardiac denervation.

FIG. 2. Effect of intravenous infusion of 6% dextran (molecular weight 40,000) at body temperature on heart rate and esophageal and right atrial pressures in a dog (16.5 kg) with chronic cardiac denervation.

When exercised, dogs with cardiac denervation achieve a maximal heart rate in 90 to 100 seconds. An increase in the transmural atrial pressure, due to an increase in depth of respiration and in return of blood to the heart, might be expected to develop early in exercise and to be sustained throughout the period of work. In the experiments shown in Fig. 1 and 2, the maximal transmural atrial pressures were achieved in 15 seconds and 15 minutes, respectively, but the corresponding maxima in heart rates did not occur until 2½ and 45 minutes later, at which times the transmural pressures had declined considerably from their maximal values. Although the early increase in heart rate shown in Fig. 1 suggested that rate of change of pressure might play some part in the cardiac acceleration, at the maximal mean right atrial pressure shown in Fig. 2, there was a peak-to-trough excursion of 14 cm of H_2O in the right atrial pulse.

These data suggest that it is unlikely that either increases in absolute level of the transmural atrial pressure or in rate of change of this pressure are the factors responsible for the increase in heart rate during exercise in the dog with chronic cardiac denervation.

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Corticosterone in Lymphoma-Bearing Rats.* (28353)

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In lymphoma-bearing rats, glucocorticoids and potassium appear to have opposing effects upon the lethal and tumor-necrotizing properties of capsular polysaccharide from *Klebsiella pneumoniae*(1-3). Lethal and tumor-necrotizing effects of the lipid-free polysaccharide were inhibited by cortisol and corticosterone(2) but minute quantities of potassium, injected intravenously, augmented these biologic properties(3). However, glucocorticoids did not nullify the polysaccharide-potentiating action of potassium (3). Since altered biosynthesis of corticosterone, the major glucocorticoid of the rat, could have some bearing on these interrelationships, corticosterone in the plasma and urine was determined by 2 procedures in control and in lymphoma-bearing rats.

Materials and methods. Eight young, male Holtzman rats bearing subcutaneous Murphy-Sturm lymphomas(1) of 35-40 mm diameter (approximately 2 weeks following implantation) and 8 control rats, each 180-220 g body weight, were placed in individual cages and urine collected for 24 hours as 3 refrigerated 8-hour samples which were later pooled. During the collection period the diet of Purina Laboratory Chow, lettuce and water was withheld. Immediately following collection of urine, the animals were killed by neck clamp(4), blood withdrawn from the heart into heparinized syringe and plasma separated by centrifugation.

Urine samples, adjusted to pH 1.0 with HCl, and plasma samples were processed by procedures for extraction and purification of corticosterone as described by Moncloa, Peron and Dorfman(5). However, the final extracts were further purified by paper chromatography in toluene/propylene glycol(6), the zones containing corticosterone eluted with absolute ethanol, and the dry residues of these eluates partitioned between n-hep-

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