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Relationships between Physical Training and DOCA Hypertension in Rats[1] (39256)

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Until recently there were few investigations concerning the effects of a program of physical conditioning upon arterial blood pressure. Most of these studies were inconclusive or of a contradictory nature (1-5). Within the past 5 years, however, a number of investigators have reported that in man significant decreases can be obtained in both systolic and diastolic blood pressures after participating in controlled exercise programs (6-12). Reductions in blood pressure were observed in normotensive (6, 9-12) as well as hypertensive subjects (7, 8, 12). Very recently it was demonstrated that genetic hypertensive rats subjected to a training program have lower systolic blood pressures than normal rats (13). The present study was designed to extend these observations by examining the effects of a program of physical training on experimentally induced hypertension in rats. In this study rats were subjected to a swimming program before, during, or after treatment with a hypertensive regime in an attempt to prevent, delay, or alleviate the severity of hypertension.

Materials and methods. Male rats of the Sprague-Dawley strain were randomly divided into groups as shown below (Table I).

Hypertension was produced by a modification of the method described by Skelton (14). In brief, this method utilizes a unilateral nephrectomy (left), substitution of a 1% NaCl solution for drinking purposes, and 25 mg/week of desoxycorticosterone acetate (DOCA). The modification involved administration of the DOCA by a subcutaneous injection of a sesame seed oil suspension instead of implanting two 25-mg pellets every 2 weeks. This treatment will be referred to as the DOCA treatment, or hypertensive regime, in the remainder of this communication. Hypertension, for the purpose of this study, was defined as a systolic blood pressure exceeding 170 mm Hg.

Rats were trained by swimming 1 hr/day, 3 days/week. The swimming tanks were 50 cm in depth and 30 cm in diameter. Water temperature was maintained at 28 ± 1°. Three rats were placed in a swimming tank simultaneously (rats swimming three/tank have a much higher level of activity than when swimming one/tank). Rats were removed from the swimming tank after 1 hr or when exhausted. Exhauston was defined as occurring when the rat remained under water for more than 10 sec and was having difficulty in returning to the surface (15). Rats were wiped dry with towels on conclusion of each exercise episode.

Indirect systolic blood pressure was measured by use of an indirect (tail cuff) method as described by several investigators (16, 17). Blood pressure and body weights were determined every 2 weeks. The rats were sacrificed at the end of Week 12 (or Week 18 for some of the animals in the C and S-H groups). Heart weights and body weights were recorded and the heart weight/body weight ratio was calculated.

Student's *t* test was used to compare any two specific groups with respect to systolic blood pressure or heart weight/body weight ratio. The null hypothesis was rejected at the 5% level.

Results. A regular program of physical conditioning was found to affect the rate of development of hypertension in unilaterally nephrectomized, salt-loaded, DOCA-treated rats (Table II). Rats subjected to the hypertensive treatment were hypertensive (>170 mm Hg) within 4 weeks. Their blood pressure was elevated above that of the control group within 2 weeks. Rats in the groups initially subjected to the hypertensive treatment (H, HS, H-S) were not affected by the swimming program and their blood pressures behaved as if they were receiving only the hypertensive treatment.

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TABLE I. EXPERIMENTAL GROUPS

Group		Treatment and duration
1	Control (C)	Normal diet; no activity; 12 and 18 weeks
2	Swim (S)	Normal diet; swim; 12 weeks
3	Swim-hypertension (S-H)	Swim; 12 and 18 weeks; hypertension treatment after 6 weeks
4	Hypertension (H)	Hypertensive treatment; 12 weeks
5	Hypertension + swim (HS)	Hypertensive treatment; 12 weeks; swim 12 weeks; simultaneous
6	Hypertension − swim (H-S)	Hypertensive treatment; 12 weeks; swim after 6 weeks

TABLE II. MEAN SYSTOLIC BLOOD PRESSURES (mm Hg) OF THE VARIOUS GROUPS AT 2-WEEK INTERVALS

Week	C (10)[a]	S (10)	H (14)	HS (15)	S-H (14)	H-S (14)
0	133 ± 1.8[b]					
2	131 ± 1.8	139 ± 2.1[c]	165 ± 3.0[c]	152 ± 3.3[c]		
4	131 ± 5.9	140 ± 2.0	173 ± 4.5[c]	171 ± 5.3[c]		
6	128 ± 3.8	144 ± 2.1[c]	180 ± 3.2[c, d]	188 ± 4.4[c, d]		
8	135 ± 3.6	142 ± 2.8	189 ± 4.4[c]	194 ± 5.4[c]	146 ± 3.2[c, g]	193 ± 5.6[c]
10	118 ± 3.8	147 ± 2.3[c]	198 ± 4.3[c]	186 ± 4.7[c]	163 ± 2.6[c, g]	194 ± 5.2[c]
12	128 ± 4.6	146 ± 5.5[c]	185 ± 4.3[c, f]	174 ± 5.7[c]	152 ± 4.9[c, g]	191 ± 5.1[c, e, f]
14	117 ± 12.2				178 ± 7.6[c]	
16	114 ± 2.5				168 ± 6.1[c]	
18	123 ± 4.1				180 ± 9.6[c]	

[a] Number of animals.
[b] SEM.
[c] $0.01 < P < 0.05$ compared to C of that week.
[d] $0.01 < P < 0.05$ compared to S of that week.
[e] $0.01 < P < 0.05$ compared to HS of that week.
[f] $0.01 < P < 0.05$ compared to S-H of that week.
[g] $0.01 < P < 0.05$ compared to H of that week.

The group of rats subjected to a 6-week swimming period prior to the hypertensive treatment (S-H) also developed hypertension when exposed to the treatment, but required 8 weeks of such treatment to become hypertensive instead of 4 weeks. It is interesting to note that the group subjected only to swimming also had blood pressures above normal within 2 to 6 weeks. The blood pressure appeared to stabilize, however, at this new and higher level.

Both physical training and DOCA hypertension have been found to result in cardiac hypertrophy (18, 19). This was confirmed in the present study and indicates that the swimming program produced a training effect. However, it is apparent that a greater degree of cardiac hypertrophy is created by the hypertension treatment than by swimming. Also, the two effects may be additive since 6 weeks of simultaneous swimming and hypertensive treatment produced a greater degree of cardiac hypertrophy than the hypertensive treatment alone.

TABLE III. HEART WEIGHT/BODY WEIGHT RATIOS AT 12 AND 18 WEEKS

Group	12 Weeks mean (10^{-4})	18 Weeks mean (10^{-4})
C	21.06 ± 0.05	21.62 ± 0.46
S	23.12 ± 0.63[b]	
H	30.83 ± 1.03[a, c, f]	
H-S	30.23 ± 0.50[e, a]	
HS	33.02 ± 0.10[d, a]	
S-H	28.73 ± 0.48[a]	31.21 ± 1.26[a, g]

[a] $P < 0.01$ compared to control (12 weeks).
[b] $P < 0.05$ compared to control (12 weeks).
[c] $P < 0.01$ compared to S.
[d] $P < 0.05$ compared to H-S.
[e] $P < 0.05$ compared to S-H (12 weeks).
[f] $P < 0.01$ compared to HS.
[g] $P < 0.01$ compared to control (18 weeks).

Discussion. The present study indicates that physical training, if initiated before application of a stressor capable of rapidly elliciting hypertension, can delay development of hypertension. The swimming program has no effect on the rate of development of hypertension if it is initiated concurrently with, or after treatment with, the hypertensive regime. These results are somewhat different from those of Tipton *et al.* (13). They reported that the systolic blood

pressure, in spontaneously hypertensive rats, was lower if the animals were subjected to training. We were not able to achieve any reduction in pressure. The difference in hypertensive models used in the two studies may explain the differences in results.

The mechanism by which the development of hypertension is delayed is unknown. The mechanism(s) responsible for the development of hypertension itself is controversial. An increased reactivity of the resistance vessels may be caused by structural thickening (20) or the vascular smooth muscle may exhibit increased sensitivity to constrictor stimuli (21). These two concepts are not mutually exclusive; in fact, Berecek and Bohr have shown that in renal hypertensive rats the resistance vessels exhibit changes in both structure and smooth muscle sensitivity (22).

In order to lower blood pressure in hypertension then, either the structural or sensitivity changes or both would need to be reversed. Little evidence is available with regard to structural alterations. One can only speculate from indirect evidence that changes in smooth muscle sensitivity to catecholamines might be altered by training. Certainly such a change appears to occur in cardiac muscle of trained rats (19). Crews and Aldinger found after training rats with a swimming regime that the isometric systolic tension response of the heart to epinephrine was less than that of the sedentary controls. This would appear to indicate a decrease in sensitivity of trained cardiac muscle to catecholamines. It is tempting to speculate that such a change might also occur in the smooth muscle of the resistance vessels of trained rats.

Finally, the increase in systolic arterial blood pressure which occurred in the control group subjected to regular swimming (S), may be due to the stress associated with swimming. Herd found that with application of a stress there was a transient increase in arterial blood pressure (23). If the experimental animals were exposed to the stress several times per day, and for several days, the increase in blood pressure was no longer transient, but remained elevated, even in the absence of application of the stressors. Swimming is not the usual means of locomotion for a rat; hence, regular exposure to such an event may be regarded as a stress and thus may result in a sustained increase in blood pressure.

Summary. Swimming, if undertaken for 1 hr/day, 3 days/week for 6 weeks prior to treatment with DOCA, unilateral nephrectomy, and salt-loading, delayed the development of hypertension in rats. If the swimming were undertaken concurrently with or after initiation of treatment with the above hypertensive regime, then it was without effect on the level of blood pressure attained or the length of time required to attain a given blood pressure. Swimming in itself resulted in a significant increase in arterial blood pressure. Previous training, such as swimming, may delay the development of hypertension through an alteration in vascular structure or smooth muscle sensitivity. The increase in blood pressure noted in physically trained rats may be a consequence of the training regime itself acting as a stressor.

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