

found by Westerfeld and Richert(2) to be a better test object than liver tissue for the unidentified liver residue factor. This may help to explain the difference in response observed with the 2 tissues on the same treatment.

No significant differences between intestinal enzyme activity of the dietary treatments other than the control group were noted. Since the supplements supplied varying levels of molybdenum (0.05-0.35 ppm), it was assumed that a saturation level has been reached similar to that observed in the rat(12).

The response of liver xanthine dehydrogenase activity to the added supplements was less consistent than that observed in intestinal homogenates. The liver enzyme activities of the groups fed the higher level of sodium molybdate (0.30 ppm) and the U.G.F. mixture (added Mo 0.35 ppm) were significantly higher ($P < 0.01$) than the activity noted in the livers of birds fed distillers dried solubles supplying 0.05 ppm of molybdenum. When xanthine dehydrogenase activity was expressed on a nitrogen basis the differences observed above were quantitatively less, but still statistically significant ($P < 0.05$).

The ratio of enzyme activity to liver molybdenum content was more erratic than that reported in turkey poults(4). However, a correlation of 0.617 ($P < 0.05$) was found to exist between the results of the two determinations.

Summary. 1) Growth of chicks was significantly improved by the addition of distillers dried solubles, sodium molybdate or a

mixture of unidentified factor sources. Removal of the molybdenum from the ash of distillers dried solubles resulted in the same growth rate exhibited by the control group. The ash of this product produced a 9.1% increase in growth; which was not quite significant. 2) Bone ash values were not affected by the dietary treatments. Intestinal xanthine dehydrogenase activities were significantly increased in all cases except the "molybdenum-free" distillers dried solubles ash-fed group.

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Cold-Pressor Responses in Families of Rabbits with Spontaneous Hypertension.* (23220)

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For the past 5 years we have bred rabbits with spontaneous hypertension(1). A high percentage of their progeny inherit the hy-

pertension(2). We recently began raising families of control rabbits under the same conditions as those of the spontaneously hy-

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pertensive group. Controls are offspring of rabbits chosen at random from normotensive laboratory stock. They are from the same strains that show spontaneous hypertension—New Zealand and Dutch.

We set out to see whether spontaneously hypertensive rabbit families differed from normotensive laboratory stock in their blood pressure response to cold stimulation. Hines and Brown developed a cold-pressor test in humans to evaluate what they term vascular reactivity(3), and we adapted this test for rabbits in the present study. Hines and Brown showed that persons with hypertension or normotensives with a family history of hypertension tend to have a greater blood pressure response to the cold-pressor test than persons with no personal or family history of hypertension(4). Progeny of the spontaneously hypertensive rabbits used in this study will be referred to as "selected" animals and controls as "unselected" animals.

Methods. Cold-pressor test. Results from cold-pressor tests are meaningful only if the conditions, *i.e.*, stimulus and environment, of the tests are identical(3,5). Our procedures were standardized and all conditions rigidly controlled. Further, to insure that the response would be solely to the stimulus applied, the animals were sedated with pentobarbital (Nembutal—Abbot Vet) 15 mg/kg. *Cuff method.* The abdominal cuff method of McGregor(6) is used routinely to determine arterial blood pressures in our colony of rabbits (2) and was used in the first series of cold-pressor tests. Experience with the cuff method has shown that diastolic pressure probably cannot be determined with an accuracy greater than ± 10 mm Hg, but systolic pressure may be obtained with an accuracy of ± 4 mm Hg. Therefore, only systolic pressures are reported from these tests. After a set of control blood pressure readings was obtained, the sedating dose of pentobarbital was injected into the marginal ear vein. Blood pressure fell immediately, then gradually rose and stabilized within 27 to 45 minutes. This stable pressure under sedation will subsequently be referred to as the *basal* pressure. At this time animals were relaxed, had normal pupils and a corneal reflex. If handled

gently the sedated animals offered no resistance, and ordinary laboratory sounds did not evoke any response. When the basal condition had been achieved, the ears were completely immersed in a beaker of ice water (2° to 4°C) for exactly 60 seconds. Systolic and diastolic pressures were determined every 10 to 15 seconds during the "cold minute" and for 2 minutes after the ice water was removed. *Intra-arterial method.* In a second, smaller series of cold-pressor tests, femoral arterial pressure was recorded with a #24 needle connected to a Statham P-23A pressure transducer. Oscillographic records were made at a film speed of 0.4 inch/second. The femoral artery was exposed after subcutaneous infusion of 1% procaine; the recording needle was inserted 30 to 35 minutes after Nembutal injection. Pressure recorded 10 to 30 seconds *before* immersing the ears in ice water was considered the basal pressure (see above). The needle remained in the artery throughout the "cold minute" and for 2 minutes afterwards. Both systolic and diastolic pressures were measured to within ± 2 or 3 mm Hg, and both pressures are reported. *Calculation of response to cold-pressor test.* The value for maximum systolic or diastolic pressure response obtained from an intra-arterial record was the difference between the highest pulse (or pulses) of the basal pressure and highest one(s) recorded during the "cold minute." The time at which the highest pressure first occurred during the "cold minute" was not necessarily the same for systolic and diastolic pressure. Maximum response was obtained *during* the "cold minute" in 35 of 40 tests by the intra-arterial method. Since only 5 maximum responses occurred after the "cold minute" (longest time was 115 seconds from time of ear immersion), we felt justified in disregarding these and based all results on the maximum response during the "cold minute." Since pressure determinations by the cuff method were intermittent (every 10 to 15 seconds), maximum responses obtained beyond the "cold minute" were included in the results. (The longest time to a maximum response was 103 seconds after immersion of ears.)

Results. The cuff method was used on 56

TABLE I. Maximum Systolic and Diastolic Responses to Cold-Pressor Test, Recorded by Intra-Arterial or Abdominal Cuff Method, in Unselected and Selected Rabbits.

		Max. systolic response		Max. diastolic response	
	No. trials	Mean (mm Hg) and S.D).	Avg time to max. resp. (sec.)	Mean (mm Hg) and S.D.	Avg time to max. resp. (sec.)
Intra-arterial method					
Unselected	23	8.4 ± 4.1	43	7.0 ± 4.7	44
Selected	17	16.5 ± 8.9	39	13.4 ± 6.6	38
Cuff method					
Unselected	26	8.7 ± 4.9	40		
Selected	108	14.8 ± 6.2	38		

Calculation of Fisher's "t" values showed that the means of maximum systolic responses for unselected and selected rabbits by both abdominal cuff and intra-arterial methods are "very significantly different" ($p = <.001$), and the means of maximum diastolic response by intra-arterial method are "significantly different" ($p = <.01$).

selected and 15 unselected rabbits. Two tests were carried out on most animals 1 to 6 days apart, and the results compiled from all the determinations. If an animal struggled during the test, the results were discarded. A total of 108 tests on selected, and 26 on unselected, were successful. For the intra-arterial method, 15 selected and 15 unselected rabbits were used. Most of the unselected animals were tested 2 times and some 3, but only 23 tests were considered satisfactory. The others were discarded because the recorded pulse wave was damped. Only 2 repeats were successful in the selected group giving a total of 17 tests. Some of the animals were used for both cuff and intra-arterial tests.

The averages and p-values for maximum pressure responses and time (seconds) to maximum response are given in Table I for both intra-arterial and cuff tests. Selected rabbits had "significantly" higher mean maximum pressure responses than unselected rabbits in both series of tests. Although values overlapped, some selected animals had maximum responses above the highest ones in the

unselected group.

Table II shows that selected animals had a greater average maximum systolic response than unselected rabbits at any given basal pressure range. Additionally, it can be seen that there was no correlation between maximum systolic response and the basal systolic pressure for either group. The same was true in repeat tests on single animals. For example, a cold-pressor test was repeated by the cuff method 3 times at 5 minute intervals in an unselected rabbit. The systolic responses were 6, 4, and 5 mm Hg with basal pressures of 130, 123, and 116 mm Hg, respectively.

In a group of 5 rabbits, 2 or 3 cold-pressor tests were repeated at 5 to 15 minute intervals. The magnitude of response to each test by a single animal was similar, not differing by more than 6, and usually by only 1 or 2, mm Hg. On the other hand, the magnitude of response to tests made from 1 to 6 days apart was not necessarily the same in a given animal, differing by as much as 30 mm Hg.

The cold-pressor responses of 5 selected

TABLE II. Average Maximum Systolic Pressure Response of Selected and Unselected Rabbits with the Same Basal Systolic Pressures—Intra-Arterial Method.

	Basal systolic pressure* (mm Hg)					
	91-100	101-110	111-120	121-130	131-140	151-160
Unselected	10 (1)†	7 (5)	8.5 (6)	7.5 (6)	9.5 (5)	
Selected	24 (1)	13 (3)	16 (7)	16 (3)	15 (2)	29 (1)

* Avg basal pressure for selected and unselected groups was 120 and 119 mm Hg, respectively.

† No. of animals.

animals with consistently high[‡] systolic pressures were compared to those of 5 selected animals with consistently low[§] systolic pressures. There was no apparent relationship between these levels of blood pressure and the magnitude of response to the test.

Discussion. We previously pointed out certain cardiovascular characteristics of spontaneously hypertensive rabbits similar to those found in human essential hypertension (2). The most obvious similarities are elevation and lability of systolic and diastolic pressures. In the present study another cardiovascular characteristic of human essential hypertension was demonstrated by progeny of rabbits with spontaneous hypertension, *viz.*, as a group they showed a "significantly greater" average blood pressure response to the cold-pressor test than rabbits from normotensive families.

The intra-arterial records showed that maximum variation in heart rate during the cold-pressor test was only 5% of the basal rate. Thus, the mechanism for large pressure responses in selected rabbits was probably not attributable to changes in cardiac output.

The selected animals sometimes responded with pressure increases 2 to 3 times those of the unselected group. This difference in responsiveness to the cold-pressor test was not correlated with a higher starting or basal level

of pressure (Table II) in selected animals, but rather it seems to be a characteristic of the animal. Further evidence that an increased cold-pressor response in selected animals is a characteristic of these rabbits and not dependent on the presence of elevated pressure is that those with consistently normal pressures showed greater blood pressure increases than did unselected normotensive rabbits.

Summary. (1) Blood pressure responses to cold-pressor test were studied in progeny of spontaneously hypertensive rabbits. These animals were both hypertensive and normotensive. Controls were offspring of rabbits chosen from normotensive laboratory stock. (2) Average maximum blood pressure response to cold stimulation of progeny of spontaneously hypertensive rabbits was quantitatively greater than in the control group. This difference in responsiveness was not attributable to difference in basal (starting) pressure. (3) It is concluded that increased pressure response to cold is a characteristic of progeny of spontaneously hypertensive rabbits.

$\ddagger > 150 \text{ mm Hg}$ $\S < 130 \text{ mm Hg}$	{	as determined by routine cuff measurements 2 or 3 times a month from age 3 or 4 months. Ages of animals at time of tests ranged from 7 to 10 months.
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