

raised, slightly irregular patches were seen. These areas varied in number, size, and height, but were present in all animals after the first week. In the slightest reactions found, a number of these granuloma were noted along coronary vessels and over the auricles. In the more extensive disease, patches were found over the epicardium of the ventricles, and lastly over the inner layer of the pericardial sac. In the later and more severe reactions, the entire heart was a nodular mass enclosed in a thickened sac. The fluid varied in amount and color; it was usually cloudy yellow in the later groups, but not infrequently hemorrhagic. Although loose fibrinous adhesions were occasionally noted, no dense adherence of the 2 layers developed. Cultures made in 12 animals were positive in 8.

Microscopically, the pericardium showed edema and increased vascularity in those with slight reaction. The tubercles showed round conglomerations with large macrophages in the center, epithelioid cells and lymphocytes in the surrounding zone and occasional giant cell formation. Capillary proliferation was

noted in some areas. No acid-fast stains were done.

The radiographic studies were not particularly satisfactory although gross enlargement could be noted at times. The electrocardiographic tracings frequently showed T wave changes, but were not diagnostic.

Discussion. At the time of sacrifice, anesthesia was obtained and the chest opened so that cardiac action might be observed directly. In those animals with the more severe reaction, no constrictive pericarditis had developed, but restriction of cardiac activity was evident. Based on the uniformly positive results obtained in this series, and the similar findings by Kinoshita, further studies over longer periods of observation should be carried out, to obtain more information regarding tuberculous pericarditis.

Summary. Tuberculous pericarditis was produced in sensitized rabbits by the intrapericardial injection of live bovine tubercle bacilli.

1. Kinoshita, S., *Ann. Tuberc. Tenri.*, 1955, v6, 64.

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Experimental Hypertension in Rats Produced by Dietary Condiments. (23029)

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Blair(1) reported that, in a group of persons undergoing routine physical examination, he had observed some degree of correlation between occurrence of hypertension with excessive use of condiments in the daily diet. He reported 50 cases, presenting the theory that excessive use of spices and condiments, especially pepper, mustard and ginger, is a common cause of hypertension; and stated his opinion that hypertension may be produced experimentally in animals by repeated feeding of these spices and condiments, and also that the damage produced may be irreversible. In pilot experiments (in cooperation with J. E. Owens, unpublished data) it

was found that rats, maintained on diets to which pepper, mustard and ginger had been added, developed hypertension. However, due to circumstances beyond his control, this work was not pursued further. Personal correspondence led to resumption of our studies on experimental hypertension.

Methods. Female rats (200-250 g) were used. Blood pressure was determined by photoelectric plethysmographic method of Kersten *et al.*(2). Each value recorded represents the average of at least 4 consistent readings in a single test period. Initially, the condiments were mixed in powdered breeder's diet. Later, for reasons to be discussed, a

TABLE I. Systolic Blood Pressure of Rats on Diets Containing Condiments.

Diet	Mean systolic blood pressure* (mm Hg) $\pm$ S.E.			
	Initial	7 mo	10 mo	12 mo
Control	122 $\pm$ 7.5		115 $\pm$ 7.1	
I		154 $\pm$ 11.9	122 $\pm$ 11.4†	174 $\pm$ 7.6†
II		152 $\pm$ 9.7	165 $\pm$ 6.3	156 $\pm$ 10.4
III		171 $\pm$ 7.4	173 $\pm$ 15.0	164 $\pm$ 4.5

* Blood pressure averages from 5-7 animals, except (+). Value for each animal an avg of at least 4 consistent readings.

† Avg of 2 animals, only survivors at 12 mo.

‡ Only experimental value not significantly different at 1% level.

commercial producer* cooperated in supplying a standard diet in which the condiments were mixed before extrusion of the pellets. All condiments were standard table grade, obtained from a wholesale grocery supply house. Diet I contained 2% pepper. Diet II contained 1% each of mustard and ginger, and Diet III contained 2% pepper, 1% mustard and 1% ginger. Blood pressures and weight of each animal were obtained periodically. At the end of one year, representative animals were sacrificed for a complete gross and microscopic histopathological study.

Results. The original powdered diets produced a high incidence of respiratory involvement, presumably because of irritant qualities of the powdered condiments, which were inhaled during feeding. Before the pellets were obtained, several deaths with pulmonary symptoms occurred. This respiratory involvement was no longer observed when the pellet diet was instituted.

Table I shows average blood pressure readings obtained during the experimental period, for all diets. The average control value obtained before diets were instituted was 122 mm Hg $\pm$ 7.48. One group was maintained continuously on Diet I (pepper) for one year. It will be noted that there was a decline in blood pressure level at 10 months to essentially normal values. From then until the end of the year all rats lost weight, 3 died, and the 2 which survived were sacrificed for pathological study. Their final pressures before autopsy were 168 and 180 mm Hg.

Another group was maintained on Diet II (mustard and ginger) for one year. These animals showed a similar rise in blood pres-

sure (Table I), but did not exhibit a secondary decline as observed with Diet I. They did not lose weight, and appeared healthy through the experimental period.

Animals on Diet III (pepper, mustard and ginger) were started earlier, and were studied in somewhat greater detail. The average blood pressure after only 8 weeks on the diet was 167 mm Hg. Withdrawal to non-condiment control diet for 3 weeks was accompanied by a decline to 157 mm Hg. Return to Diet III for 5 weeks elevated the pressure to 168 mm Hg. Thereafter, temporary withdrawal did not reverse the pressure trend, and after a cumulative total of 8 more weeks of intermittent use of Diet III the average blood pressure was 176 mm Hg. At that point the group was permanently withdrawn and kept on control diet. Throughout a period of 7 months the mean blood pressure values averaged 171 mm Hg (range 165-183) over 14 periodic readings. The last reading at 16 months was 172 mm Hg. This implies that a permanent hypertensive state had been established. The use of experimental anti-hypertensive drugs produced a lowering of blood pressure to the same extent as obtained in rats with experimental renal (Grollman) hypertension.

Pathologic findings. Kidney samples from each diet series were submitted for histological examination. Two rats were from Diet I, 3 from Diet II and 3 from Diet III.

Grossly, kidneys from rats fed the above-mentioned diets exhibited some congestion but were otherwise essentially negative. There was no evidence of cortical atrophy, surface scarring or vascular sclerotic changes. Blocks of tissue from these organs were fixed

* The Vi-D-Co., Marion, Ind.

in formalin and stained with hematoxylin and eosin for general topography, with Schiff's Periodic Acid for changes in basement membrane and capsule, and with Unna's Orcein stain for changes in elastica of blood vessels.

Microscopically, the parenchyma, stroma and the renal-vascular apparatus exhibited no changes compatible with any drug action. The tubular system was essentially negative, no abnormal changes were seen in the elastica of blood vessels and the PAS reaction was within normal limits. Final diagnosis was "essentially negative kidney findings."

Discussion. It would appear that mustard or ginger contains some factors capable of producing changes leading to a hypertensive state in the rat, while pepper has a factor which is less effective, though possibly additive when combined with other condiments. As a collateral observation, it was noted that the fur of the animals on Diets II and III was much softer to the touch than normal rats, while those receiving pepper failed to show this effect. The benefit probably derived from additional sulfur available in the mustard. All groups exhibited a temporary reluctance to accept the diets, but soon resumed normal intake as judged by an essentially normal growth curve. The latter part of the year for the pepper group was the only exception to this, and the cause of their decline is not known at present.

Future experiments may explore the possibility of extraction of the condiments in an attempt to isolate a single identifiable factor which will induce the hypertensive state.

In view of the essentially negative findings in the examinations of the kidneys, the authors are still at a loss to explain the mechanism of action in the production of hypertension.

Summary. Continued feeding of pepper, mustard and ginger in various diet combinations results in appearance of a statistically significant hypertension in rats. The greatest elevation occurred in a diet containing all 3 condiments; the hypertension from this diet persisted for months after the diet was discontinued. Other combinations were less effective, and work is continuing to determine if any single representative contains the necessary and sufficient factor for the production of hypertension.

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1. Blair, J., *Med. Record*, 1948, May, p. 1.

2. Kersten, H., Brosene, W. G., Jr., Ablondi, F., and Subba Row, Y., *J. Lab. and Clin. Med.*, 1947, v32, 1090.

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