sults indicate that hydroxyzine stimulated release of the antidiuretic hormone in normal dogs, otherwise similar results would have been obtained in both types of animals. In addition, measurement of osmolar and "free" water clearance in 4 experiments in diabetes insipidus dogs showed no change from the control values.

Summary. Intravenous administration of hydroxyzine to unanesthetized dogs in doses of 5 mg/kg produced a decrease in urine flow following cessation of the drug in absence of any hemodynamic changes. In contrast to response in normal dogs there was no change in urine flow in diabetes insipidus animals. These results indicate hydroxyzine stimulated release of the antidiuretic hormone under conditions described here.

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Response to Stress: Differing Responses of Atherosclerotic and Normal Dog to Electric Shock or Cold.*† (25579)

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Inability to adapt successfully to stressful situations may be a factor in development of cardiovascular pathology. Although the role of the autonomic nervous system and hypothalamic-pituitary-adrenal axis in response to stress has received intensive study, the interrelations between this system and cardiovascular pathology are virtually unexplored. This report describes differing response of atherosclerotic and normal (non-atherosclerotic) dogs to stresses of electric shock and cold.

Methods. Thirty-five dogs were used. Twenty-one (9 beagles and 12 mongrels) were made atherosclerotic by maintenance on standard thiouracil and cholesterol diet (consisting of 50 mg thiouracil/kg body weight and kibble containing cholesterol prepared with ether solvent to provide daily cholesterol intake of 750 mg/kilo body weight) as previously reported by this group(1). These dogs were maintained on the atherogenic regimen for 6 months to 2 years. The remaining 14 dogs (9 beagles and 5 mongrels) served as controls and received standard kibble diet. *Electric shock.* The 21 atherosclerotic dogs and 14 normal dogs were subjected to electric shock. Each dog was anesthetized with sodium pentobarbital, after which 5 shocks were administered across frontal lobes within 15 minutes by electric shock machine delivering 450 milliamperes of 0.7 sec. duration. Urine samples were collected hourly by catheter for 3 hours prior to and 3 hours following shock treatment. Urine was analyzed for corticoids by the Heard-Sobel method(2) and for creatinine by the method of Bonsnes and Tausky(3). *Cold stress.* Four normal dogs and 4 atherosclerotic dogs were placed in metabolic cages. A minimum of three 24-hour urine collections at room temperature served as controls for each dog. Cold stress consisted of

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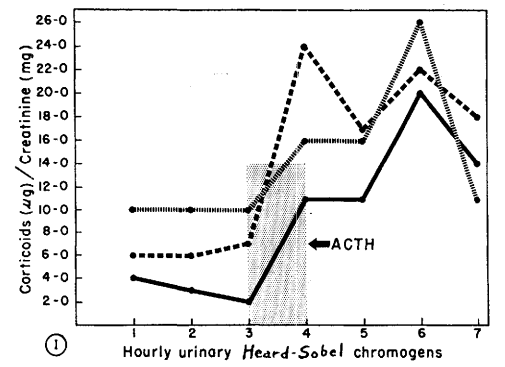

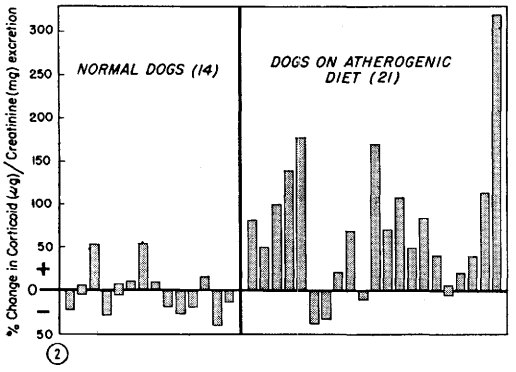

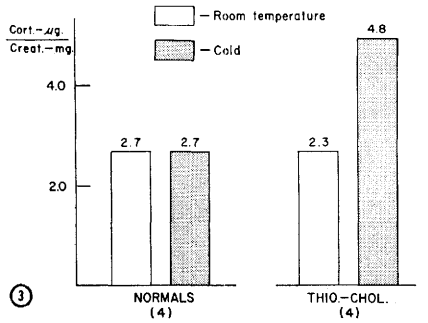

FIG. 1. Effect of ACTH infusion on corticoid excretion by 3 normal mongrels.

FIG. 2. Effect of electric shock stress on corticoid excretion of normal dogs and dogs on atherogenic diet.

FIG. 3. Urinary corticoids and creatinine of normal and thiouracil-cholesterol treated dogs before and after cold stress.

maintenance of dogs in "cold room" at 0° for 24 hours. *ACTH infusion.* To determine whether output of urinary corticoids as identified by Heard-Sobel method furnishes a measure of ACTH-dependent activity, 3 normal dogs were infused with ACTH (one unit/kg in 100 cc saline solution) for an hour, and urine specimens were collected before, during, and after infusion period. In each case, infusion of ACTH caused an increase in corticoid/creatinine ratio (Fig. 1) indicating that methods used to determine urinary corticoids were detecting ACTH-dependent activity.

Results. With Electric Shock. Dogs on atherogenic diet showed a greater response than normal dogs to stress of electric shock, as indicated by higher excretion of corticoids relative to creatinine (Fig. 2).

With Cold Stress. In no instance was urinary corticoid activity of the normal dog increased by exposure to cold, Contrariwise, the 4 atherosclerotic animals each exhibited a marked increase in adrenocortical activity (Fig. 3).

Discussion. Although basal output of normal and atherosclerotic dogs was approximately the same, our study demonstrates that dogs maintained on an atherogenic diet for 6 months to 2 years exhibit a greater response to stress produced by electric shock or by cold than occurs with normal dogs. Our experiments do not indicate the locus of altered hypothalamic-pituitary-adrenal response to stress. Some controvery exists as to whether the adrenal gland of the hypothyroid animal is more responsive to ACTH and to stress than the adrenal gland of normal animal. Hess and Finerty(4), using ascorbic acid depletion in the rat, interpret their observations to indicate that this is the case. However, according to Eik-Nes and Brizzee(5) the adrenal of the thyroidectomized dog has a lower basal corticoid output and is less responsive to ACTH. It is also possible that thiouracil exerts an effect upon the hypothalamic component of stress response. In support of this, Martini demonstrated that propylthiouracil produces distinct histologic change in cells of the anterior hypothalamus and neurohypophysis(6).

A hypothyroid condition may be present in human atherosclerosis. For review see (7). In line with this observation, serum cholesterol levels are usually elevated in myxedema(8). Similarly, in the dog the hypothyroid state is necessary to produce atherosclerosis(9). The serum cholesterol level apparently bears some relationship to nervous apprehension or anxiety(10-13). Myasnikov(14)

found evidence in rabbits that drugs acting directly upon the central nervous system exert a modifying influence on serum cholesterol and on development of experimental atherosclerosis. Raab(15) recently reviewed literature showing relationship of neurohumoral agents to atherogenesis, while Vedeneeva(16) obtained histologic and electrocardiographic evidence of development of myocardial infarctions several days after administration of a large dose of adrenalin. These observations tending to implicate the neuroendocrine system in pathological deposition of lipid material in vascular walls may be related to older findings of Hausberger(17) more recently confirmed by Sidman and Fawcett(18) that lipid mobilization from, and deposition in, fat depots depends upon intact innervation to these areas.

The influence of the nervous system upon development of experimental atherosclerosis has not been studied as extensively as the possible importance of endocrine and dietary factors. The effect of chronic cardiovascular pathology upon integrative functions of the neuroendocrine system is virtually unexplored.

Our results indicate that, at least in the dog, such pathology—produced by prolonged period on an atherogenic diet—is associated with an altered hypothalamic-pituitary-adrenal response to stress. Further work is needed to clarify the site and mechanism of this altered reactivity.

Summary. Dogs maintained on an atherogenic diet to 2 years exhibited a greater response to electric shock or cold stress than did normal control animals.

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Antimicrobial Effect of Abalone Juice. (25580)

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Meat of the abalone (*Haliotis refescens*) (1) has been a common food item in China for many generations. A familiarity with the characteristics of this sea animal, which has access to a wide variety of organic material of biological origin led the author to consider it as a potentially valuable source of material in which to search for an antimicrobial agent. The investigation reported here indicates that there is, indeed, an effect of abalone upon growth of *Staphylococcus aureus* and to some extent also upon the course of experimental poliomyelitis in mice although the mechanisms involved are obscure.