development of this type of hypertension. Further study is required to elucidate the mechanism of this hypertension. One possibility which suggests itself is that the hypertension is due to the synergism between large quantities of salt and the endogenous secretions of the adrenal cortex. We are inclined to doubt this view, for work now in progress indicates that "salt" hypertension is not abolished by bilateral adrenalectomy, in contradistinction to hypertension of the Goldblatt type. Another possible interpretation is that the development of renal hypertrophy may result in a relative renal ischemia with the evocation of hypertension of the Goldblatt type. We consider this view unlikely, for we have noted no significant lesions in the kidneys of our hypertensive animals beyond the hypertrophy.

Although, as noted above, there is considerable evidence that arterial hypertension of several types is associated with a disturbance in extracellular fluid, an exact characterization of the changes in the extracellular fluid in hypertension has not been made, nor are we at present in a position to state the nature of the changes in the body fluids which occur in animals watered with hypertonic saline solutions. Further investigations in these directions will be required before it will be possible to attribute any etiological significance to body fluid alterations in hypertension.

Summary and Conclusions. (1) In 3 experiments, systolic blood pressure measurements were made on 27 control rats and on 31 animals watered with hypertonic sodium chloride solutions for a period of 6 weeks.

(2) The animals watered with hypertonic saline solutions developed an arterial hypertension after a latent period of one to 4 weeks. At autopsy this was found to be associated with an hypertrophy of the heart and kidneys relative to body weight.

(3) Some possible mechanisms for the development of this hypertension are discussed.

(4) The substitution of hypertonic sodium chloride solutions for the drinking water affords a simple, inexpensive, and dependable method for the production of arterial hypertension in the rat.

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Relation Between Pantothenic Acid and Response to Growth Hormone in the Adult Rat. (17584)

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The experiment reported here was originally designed to test the response of rats on high fat and high carbohydrate diets to anterior pituitary growth hormone. During the course of the experiment it was discovered that the diets were deficient in pantothenic acid. This circumstance, when coupled with the injection of growth hormone, produced results that seemed sufficiently interesting to report.

Methods. Adult female rats of the Sprague-Dawley strain were used in this study. There were 7 rats in each group. One group was placed on a high fat, and the other group on a high carbohydrate diet. Each high fat animal was pair fed with a high carbohydrate animal of similar body weight. Differences in caloric value of equivalent amounts of the fat and carbohydrate sources were taken into account in the paired feeding in order to insure isocaloric intake between the animals of each pair. Both diets contained 20% protein as casein, inorganic salts, Wesson oil, cod liver oil, tocopherols, and B vitamins in excess. The high fat diet contained 37% Crisco and the high carbohydrate diet 74% sucrose. The rats were allowed a preliminary

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The Effect of Pantothenic Acid Deficiency on the Response to Pituitary Growth Hormone.

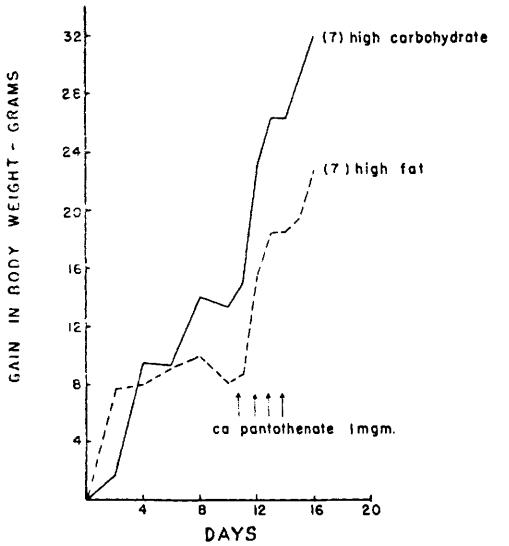

FIG. 1.

An experiment illustrating the essential nature of pantothenic acid in the body weight response of adult female rats to growth hormone. See text for details.

period of 2 weeks on these diets in order to become accustomed to them. During this period it was established that the weight curves of both groups had "plateaued," and that both groups were maintaining approximately equal weights. There then followed an experimental period of 16 days during which each rat received a daily intraperitoneal injection of 1.0 mg of a crystalline anterior pituitary growth hormone.† Body weight was measured daily and increments over the control weights were determined.

Results. In Fig. 1 are presented the results of the experiment. Each curve represents the average weight gain over the control value, for the group. The solid line represents the high carbohydrate group, and the dashed line the high fat group. During the first week of the experiment the animals of both groups showed a definite gain in weight in response to the growth hormone administration. However, in the second week it was noted that both groups were not gaining as rapidly as before and were not completely consuming their ration. Indeed they started to lose weight and show signs of a deficiency of one of the B vitamins. There was porphyrin encrustation of the whiskers and fur on the top of the head, red painful feet, bloody encrustation about the external nares, and general loss of luster and matting of the coat. These signs were much more marked in the animals on the high fat diet. It is to be noted that their weight curve dropped below that of their high carbohydrate pairs. An examination of the diet at this time revealed that pantothenic acid had been omitted. Accordingly each rat was given an intraperitoneal injection of 1.0 mg of calcium pantothenate on the eleventh day and for 3 days thereafter. It is evident from the figure that both groups showed a dramatic increase in weight gain after this vitamin. This specific response, coupled with a complete disappearance of the other clinical signs of the deficiency, would seem to establish the existence of a true pantothenic acid deficiency.

Discussion. It should be emphasized that the results presented herein are those of a single experiment. Nevertheless they indicate that, under the circumstances of this experiment, a deficiency of pantothenic acid was produced in adult female rats whose weight curves had "plateaued". Under ordinary conditions a deficiency of pantothenic acid is difficult, if not impossible, to produce in an adult rat. Apparently when such an adult animal is induced to grow again at a rapid rate, as after the injection of growth hormone, the requirements for pantothenic acid are sufficiently increased to produce signs of a deficiency of that vitamin if sufficient supplies are not available. Furthermore if the animal is on a high fat diet under these conditions the requirements for pantothenic acid are still greater, and hence the degree of deficiency is more severe. The reasons for this effect of fat are not immediately obvious; however they might be explained on the basis of the carefully performed experiments of Forbes and his associates.(3) These workers studied the relative efficiency, in terms of nitrogen retention,

† The authors are indebted to Dr. I. M. Bunding of Armour and Company for the generous supply of growth hormone.

3. Forbes, E. B., Swift, R. W., Elliott, R. F., and James, W. H., *J. Nutrition*, 1946, v31, 203.

of high fat, as versus low fat diets. They found that the diet high in fat caused the retention of more nitrogen than the low fat diet, when the protein intake was the same in both instances. Thus the energy made available by the combustion of fat caused more protein to be synthesized than the energy from an equicaloric quantity of another source. Therefore the animals on a high fat diet, who were receiving growth hormone at the same time, were getting a double stimulus to their protein synthetic process. This would put a greater strain on their reserves of pantothenic acid than that experienced by the animals on the high carbohydrate diet, and thus produce a more severe deficiency.

Lipmann and his associates (1,2) have clearly demonstrated that pantothenic acid exists in the tissues in the form of a coenzyme that is vitally concerned in acetylation reactions. They have studied these reactions extensively in the case of the acetylation of sulfanilamide in the liver. They believe that in the process of acetylation there is an intermediate stage in which the carboxyl group is phosphorylated, and thus "activated", as a preliminary to condensation. Since this process of acetylation of sulfanilamide represents the synthesis of a peptide bond, and since coenzyme A is necessary for its normal occurrence, it is logical to assume that pantothenic acid, in the form of this coenzyme, is involved in the reactions leading to the synthesis of proteins. Under conditions where there is an exaggerated rate of protein synthesis, as after the administration of the growth hormone, the rate of synthesis is depressed if adequate amounts of pantothenic acid are not available.

Summary. It has been shown that the adult female rat, whose growth curve has "plateaued", can be made to develop an acute pantothenic acid deficiency when stimulated to grow rapidly by the continued injection of anterior pituitary growth hormone. The deficiency, so produced, develops more rapidly and is more severe if the deficient diet is high in fat. It is concluded that pantothenic acid is required for the synthesis of protein in the body.

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1. Lipmann, F., and Kaplan, N. O., *J. Biol. Chem.*, 1946, v162, 743.
2. Lipmann, F., Kaplan, N. O., Novelli, G. D., Tuttle, L. C., and Guirard, B. M., *J. Biol. Chem.*, 1947, v167, 869.

Use of Radioactive Phosphorus to Determine Volume of Blood Replaced in Replacement Transfusion. (17585)

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Replacement transfusion has been advocated recently in the treatment of acute leukemia and acute renal failure. (1-3) The volume of blood replaced by such a procedure may be calculated mathematically if the mixing of blood in the body behaves as it would in a simple mechanical system. The agreement of a determination (using differential Rh typing) of the volume of blood replaced in a case of erythroblastosis fetalis (4) with a mathematically derived value supports this concept. Since the technic of labeling erythrocytes with radioactive phosphorus (5) provides a simple and widely applicable method for the determination of blood volumes, it was decided to evaluate the usefulness of this technic in the

1. Bessis, M., *Aquisition Med. Recentes*, 1948, v1.
2. Bessis, M., *Paris Med.*, 1948, v24, 304.
3. Bessis, M., and Bernard, J., *Bull. Acad. Med.*, 1947, v131, 615.
4. Wallerstein, H., *Am. J. Dis. Child.*, 1947, v73, 19.