transplant; but if the olive oil is digested with pancreatin, and the neutralized digest (neutralized with Na_2CO_3) applied to the mucosa of the Thiry fistula, the pancreatic transplant is stimulated.

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Studies on inorganic salt metabolism. II. The effect of the sudden alteration of the acid-base balance of the diet on dogs.

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During the course of a study on inorganic salt metabolism in dogs which has been in progress in this laboratory for the past 4 years, it has frequently been observed that convulsions, usually followed by death, occur in the experimental animals after the sudden alteration of the acid-base balance of the diet. The convulsions appear to result from an increase in the acid or alkali content of the diet beyond the limit of tolerance of the animal as well as after the sudden reversal of the dietary reaction. The nutritive condition of the dogs has been excellent, there having been no known dietary fault other than a disproportion of its acid-base balance. The onset of the symptoms has been sudden, the attacks, which are characterized by marked twitching, clonic contractions of the limbs, rapid respiration, gasping for breath and excessive salivation, are of short duration, as a rule. The animals recover quickly and appear to be hungry, eating with relish any food that may be available. From the standpoint of our studies, no significance was at first attached to these observations, the condition being attributed to other causes. It occurred, however, with such frequency, and the convulsive attacks were so similar in the various animals affected, that it seemed there must be some common underlying cause. In order to determine whether or not a disturbance in the acid-base balance of the diet was an etiological factor in producing this condition the following experiment was planned:

Five large adult dogs, 4 females and 1 male, ranging in age from 3 to 8 years, and 2 puppies, 5 months of age were used. All of the animals appeared to be in excellent physical condition. The adult dogs had been used for breeding in the laboratory kennels and had never been known to have had a convulsion. The puppies had been under close observation since birth and appeared to be normal. All of the adult dogs, Nos. 1, 5, 7, 8, and 9, were fed bread, meat and potato, the latter predominating in order to make the diet potentially alkaline. Bitches Nos. 8 and 9, who were sisters, 3 years of age, were given sodium carbonate to further increase the alkalinity of the food mixture, and No. 8, beef suet in addition. Puppies Nos. 107 and 109 had developed rickets spontaneously but had apparently entirely recovered on a diet consisting of bread, milk, meat, butter fat, orange juice, bone ash and hydrochloric acid. No change was made in their food other than an exchange of acid and alkali.

Bitches Nos. 5 and 7, which were 5 and 7 years of age, respectively, were first observed in convulsions about 4 weeks after the bread, meat and potato diet was started. No. 7 became pregnant during this time and had frequent convulsions during the gestation period. At the time of delivery she had a severe attack, went into a coma and was chloroformed 24 hours later. Bitch No. 5 had occasional convulsions during a period of 4 months, but seemed to suffer no permanent ill effects. She also became pregnant and died in a severe attack just before the completion of the gestation period. Dogs Nos. 1, 8, and 9 were not known to have had an attack during the first 5 months on the alkaline diets. The soda was discontinued and an amount of rice equivalent in caloric value to the potato used was substituted for the latter. The animals were watched as closely as possible, but no evidence of convulsions was observed until about the third week after the change in diet. The attacks increased in frequency and severity and finally resulted in the death of all the animals. Puppy No. 107 was suddenly changed from an acid to an alkaline diet by substituting sodium carbonate for hydrochloric acid. Five days later he went into convulsions and died. Puppy No. 109 was gradually changed from an acid to an alkaline diet by first omitting the hydrochloric acid and adding soda in small but gradually increasing quantities. No convulsions were observed during a period of 7 weeks. The diet was then changed to bread, meat and rice in the same proportions used in the other experiments. After

23 days he went ito convulsions which occurred with great frequency until his death 4 days later. Dog No. 1, a large, vigorous male weighing about 80 pounds, proved to be the most resistant of all the animals. His appetite was good and he appeared to be in excellent condition throughout the experimental period. On the day of his death the convulsive seizures started at 10 a. m. and continued without cessation until 3:30 p. m., when he died. His behavior throughout and post mortem findings were typical of all of the animals and will be reported as representative of the group.

Post mortem examinations, which were kindly made by Dr. K. F. Meyer, Director of the Hooper Foundation, showed marked injection of all of the organs, stomach mucosa and subcutaneous tissue, with numerous hemorrhagic areas throughout the body. The heart was greatly enlarged and showed many hemorrhagic areas in myocardium and endocardial lining. The brain was injected and contained small hemorrhages at the base and in the cord, from which a quantity of bloody exudate escaped. The lungs showed terminal pneumonia. Blood failed to coagulate after several hours standing.

No explanation of the phenomena observed will be attempted until histological studies of all of the tissues have been completed. Certain observations on blood and urine which have been made and are now being repeated and extended indicate, however, a profound disturbance in the acid-base balance of the body fluids. On the alkaline diets the H ion concentration of the urine was greatly decreased although the ratio of ammonia nitrogen to total nitrogen was well within normal limits. When the diet was changed from a potentially alkaline to a potentially acid one by the substitution of rice for potato, the increase in acidity was reflected in an increase in the ammonia content of the urine while the H ion concentration was only slightly increased. A few days before death, without any change whatsoever in the diet, the ammonia content of the urine continued to drop until the ammonia nitrogen to total nitrogen ratio was even higher than that observed on the alkaline diet. The reaction of the urine became steadily more alkaline.

These observations indicate a progressive failure of the body mechanism to maintain acid-base equilibrium. The deeply injected organs, greatly distended blood vessels and numerous hemorrhagic areas throughout the body suggest an alteration in the

permeability of the endothelial lining of the vessels. Loeb[1] in his studies on the selective diffusion in living organisms, made on the eggs of the marine fish *Fundulus,* showed that salts accelerate the rate of diffusion of dissociated alkalies and retard the rate of dissociated acids. He also showed they have no retarding influence on the rate of diffusion of non dissoviated acid and perhaps also of non dissociated alkali, and concludes that this probably has some bearing on secretions. It appears that the rate of diffusion of ions through membranes, which is undoubtedly influenced by the concentration, as well as proportions of salts in the body fluids, may have a direct bearing on such conditions as rickets, tetany, so called bronchial tetany, which frequently occurs in rickety babies, hemophilia, certain allergic conditions, spasmophilia, faulty kidney function and many other disorders, the etiology of which is unknown. Experiments are now under way, which we hope will throw more light on the phenomena observed, and will be published in detail, with complete histological studies, at a later date.

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The cholesterol content of the hair of the albino rat.

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The data reported herein represent a preliminary study of the lipoids in the hair of the albino rat.

The hair of young normal rats was found to contain 4.5 per cent total lipoids. The total cholesterol content of these lipoids, determined by the digitonin method, was found to be 11.9 per cent, and of this amount 80 per cent consisted of free cholesterol and 20 per cent of combined cholesterol. The amount of lecithin present was calculated from the phosphorus content of the lipoids and amounted to 0.8 per cent of the total lipoids. In a previous communication[1] attention was called to the fact that the lipoids of the human skin contained as much as 20 per cent of total cholesterol. Work is now in progress which will determine the nature of the lipoids in the hair of rachitic rats.

[1] Loeb, J., *J. Gen. Physiol.*, 1922, v, 231.

[1] Eckstein, H. C., and Wile, Udo J., *J. Biol. Chem.*, 1926, lxvii, 59.