were killed and were similarly weighed, autopsied, and examined for trichobezoar.

Of the rats in Group I receiving the basic sugar caries-producing synthetic diet, a total of 21 died before the end of the 14-week period, giving a mortality rate of about 40%. Postmortem examination of all Group I rodents consistently showed trichobezoar formation. The size of the trichobezoars varied somewhat, but in those rats that died during the experiment they were apparently of sufficient size to interfere effectively with gastric emptying. These trichobezoars were at least as large as one-half of the stomach volume, and some were so large as to fill the stomach completely. Multiple trichobezoars were found in several of the rats, but no more than three were found in any one animal. All other organs appeared normal on gross examination.

Of the Group II animals receiving the basic sugar caries-producing diet with the addition of 10% cellulose, all lived the full 14 weeks and appeared quite normal in contrast to the moribund appearance of the previous group. Autopsy of these rats showed no evidence of trichobezoar formation, and all organs and tissues were grossly normal.

Comparison of the weight gains of the rats (Table 1) indicates the marked difference between the two major groups. This difference was shown to be significant by comparison of subgroups IA and IIA according to accepted statistical methods (*2*). Since an analysis of the weight gains of the rats showed no significant difference between A and B, A and C, and B and C within both major groups, it was felt that Groups I and II, as a whole, could logically be compared for weight gains by analysis of the control subgroups IA and IIA. As seen in Table 1, only those rats of Group I which survived the full 14 weeks were used for evaluation. The t value between the control subgroups demonstrates that there is a significant difference in the weights gained, indicating that the cellulose may have been the responsible factor.

The possible effects of the oxalates on trichobezoar formation may be discounted by comparison of trichobezoar distribution among the subgroups of major groups I and II (Table 1). Since the trichobezoars were distributed equally throughout the control rats and rats receiving oxalates of Group I (100% trichobezoars), and none was found in the three subgroups of Group II, it may be assumed that the oxalates played no role in trichobezoar formation.

The consistent appearance of trichobezoars in rats on a synthetic diet without cellulose, compared with its absence in those animals on a synthetic diet with cellulose, seems to point fairly conclusively to the advantage of this type of inert material in the diet.

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An Experimental Syndrome of Fatty Liver, Uric Acid Kidney Stones, and Acute Pancreatic Necrosis Produced in Dogs by Exclusive Feeding of Bacon

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In the experiments to be described,[1] 9 dogs were fed on fat bacon exclusively. Two of these died after 2½ and 3 months, respectively. On postmortem examination they showed a severe fatty degeneration of the liver without significant changes in other organs.

Five dogs lived for periods varying between 5 and 7 months after the bacon diet was begun. At first these animals did well, but soon their appetite declined; they vomited occasionally and had to be fed forcefully. Occasionally they suffered from diarrhea. There was severe weight loss, and a peculiar kind of skin sores developed on the front and hind legs. Although the general condition became very poor and remained so for weeks, death occurred suddenly and often unexpectedly.

The postmortem examination of these animals revealed characteristic findings. The liver showed extensive fatty infiltration. In most cases only a few normal liver cells remained. These were located at the periphery of the lobules. Four of the 5 dogs had stones in the pelvis of the kidneys, in the ureters, or in the bladder which varied in size from a pinhead to a cornseed. They were thin and flat, sometimes round or polygonal in shape, and were of a greenish-yellow or brownish color. The bladder showed an apposition of stony material on the mucosa. The stones burned completely on heating and dissolved in alkali. Dried and powdered, the material gave a strong murexide reaction. Eighty-five per cent of the dry weight of the stones could be accounted for as uric acid. When the stones were dissolved in dilute ammonia, the solution filtered, and hydrochloric acid added, typical crystals of uric acid appeared.

In addition to these findings, 4 of the 5 dogs showed macroscopic and microscopic severe changes in the pancreas. The first animal showed extensive necrosis of the

[1] These experiments were carried out in the period 1938–40. With the German invasion of the Netherlands and the ensuing shortage of food, they had to be discontinued, and publication of the results was consequently delayed.

parenchyma cells; the next two had necrosis plus edema of the gland, with infiltration of polynuclear leucocytes and hemorrhages inside the septa; the fourth dog showed only pancreatic hemorrhages, without much necrosis or infiltration. Accompanying this acute pancreatic disease, all 4 dogs had fat necrosis of the adipose tissue around the pancreas and in the mesentery and omentum. These fat necroses had the typical aspect of white specks which is so characteristic of the fat necrosis that accompanies acute pancreatitis in the human. Three of the 5 dogs showed recent hemorrhages in the mucosa of the stomach or small intestine.

One other dog was fed 10,000 units of vitamin A and 5 mg of vitamin B_1/day in addition to the bacon diet. These vitamin supplements were unable to modify the course or the ultimate outcome of the experiment. This dog, which died after 7 months, had a fatty liver and acute necrosis with hemorrhages in the pancreas, fat necrosis in the omentum, and uric acid kidney stones, just as did the animals that had not received any supplement.

The last dog received 25 gm of raw liver daily for 13 months. At the end of this time it was still in perfect condition. The liver supplement was then replaced by 25 gm of raw pancreas daily. After 5 months on this supplement the animal died in a cachectic condition. Postmortem examination showed fatty degeneration of the liver. The pancreas showed hemorrhages and areas of inflammation. There were fat necroses in the omentum, and both kidneys contained uric acid stones. It appeared, therefore, as if 25 gm of raw liver had protected the animal, whereas 25 gm of raw pancreas had been unable to do so.

The severe fatty infiltration of the liver was obviously due to the combination of a high fat content of the diet and a lack of lipotropic factors. The finding of kidney stones consisting of uric acid is remarkable. The normal end-product of purine metabolism in dogs is not uric acid but allantoin, and only small amounts of uric acid normally appear in the dogs' blood and urine. Mann and his associates (*1*) have shown that the transformation of uric acid into allantoin in the dog takes place in the liver. In the liverless dog uric acid accumulates in the blood and is excreted into the urine. The same was found when the liver was damaged by chloroform or phosphorus intoxication. It seems likely, therefore, that the severe fatty infiltration of the liver had impaired its function in our animals and had acted as chemical hepatectomy. Moreover, many of the dogs had a low urinary output with a high concentration of solids and a very high urinary acidity. All these factors may have contributed to the precipitation of uric acid and the formation of stones in the urinary tract.

The hemorrhagic pancreatic necrosis in these animals had apparently occurred as a terminal event. Its explanation is uncertain. From the microscopical aspect one got the impression that the inflammation and hemorrhage had spread along the septa. In some of the sections the lumen of the pancreatic ducts appeared blocked by a material that could not be identified. It seems possible that obstruction of the ducts by this material has been the primary event after which necrosis, hemorrhage, and inflammation of the gland followed. Whatever the pathogenesis of the acute pancreatic necrosis may have been, it is interesting to note the association of acute pancreatic disease with fatty degeneration of the liver in these dogs. It is well known from human pathology that acute pancreatic necrosis occurs as a complication in patients with disease of the gall bladder and bile ducts, in alcoholics, and sometimes in diabetic coma. Fatty degeneration of the liver is a common feature in all these conditions. These experiments suggest that the presence of a fatty liver may play a part in the pathogenesis of acute pancreatic necrosis.

In a further communication the effect of the diet on blood and urine chemistry and blood morphology will be presented.

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Photochemical Oxidation of Nicotine in the Presence of Methylene Blue

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The photochemical oxidation of nicotine in the presence of methylene blue produces a compound which has not been completely characterized. During the course of this investigation, it was learned that a similar, if not identical, product had been isolated by W. G. Frankenburg (*1*) from the alkaloids of fermented tobacco. It was therefore deemed advisable to disclose our findings simultaneously.

If an aqueous solution of *l*-nicotine is irradiated in the presence of oxygen and a small amount of methylene blue, a rapid oxidation of the nicotine takes place which, in the dark, comes to a standstill. The effective wave length (around 6,700 A) coincides with the maximum absorption of the dye, and thus the "light-excited" dye can serve as a hydrogen acceptor, as shown by its rapid bleaching. The leuco methylene blue formed is reoxidized and serves continuously as a hydrogen acceptor. The oxygen required for the reoxidation of the reduced dye or, in terms of total effect, for the oxidation of nicotine thus serves as a means to follow the rate of the reaction.

An adaptation of the manometric technique of Warburg and Negelein (*3*) was used. White light of high intensity was passed horizontally through the glass wall of the water bath and reflected on the bottom of the vessel by a mirror placed at 45° under the respirometers. In general, 20 mg of the compound to be studied was dissolved in 1.5 cc of water and placed in the main chamber,

[1] One of the laboratories of the Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture.