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A Syndrome Produced in the Dog by Inclusion of Oxidized Fat in the Diet.

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The present investigation was undertaken to determine whether the chemical condition of the fat of a ration influenced the ability of an experimental animal to maintain health. McAmis, Anderson and Mendel[1] and Burr and Burr[2] have described a disease in rats due to the absence of fat in an otherwise complete diet. The syndrome is characterized by failure in growth, changes in the skin, especially of the tail and feet, and kidney degeneration. Burr and Burr[3] later reported that the disease could be prevented or cured by the feeding of linoleic acid. Evans and Lepkovsky[4] confirmed Burr and showed that glycerides of saturated fatty acids do not cure nor prevent the disease, but fatty acids containing more than one double bond have remarkable ability to improve fat-free diets. The conclusion was that certain fatty acids, essential for wellbeing, cannot be synthesized by the rat, although the rat is able to produce body fat on diets deficient in these essential fatty acids. Most of the work on fat feeding has been concerned with neutral fat or pure fatty acid. There have been a few contributions on the effects of fats altered in various ways. Powick[5] and Fridericia[6] showed independently that rancid fat destroyed the vitamin A of a ration when the fat came in contact with the vitamin-containing material.

The investigation to be reported deals with the effect on dogs of fat subjected to oxidative rancidity. A basal diet of purified foodstuffs planned to be adequate in all known dietary essentials was prepared: casein 16%, sucrose 55%, fat 25%, agar 2.5%, salt mixture 1.44%, and cystine .06%. It was very low in vitamins

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[1] McAmis, A. J., Anderson, W. E., and Mendel, L. B., *J. Biol. Chem.*, 1929, **82**, 247.

[2] Burr, G. O., and Burr, M. M., *J. Biol. Chem.*, 1929, **82**, 345.

[3] Burr, G. O., and Burr, M. M., *J. Biol. Chem.*, 1930, **86**, 587.

[4] Evans, H. M., and Lepkovsky, S., *J. Biol. Chem.*, 1932, **96**, 165.

[5] Powick, W. C., *J. Agric. Research*, 1923, **31**, 1017.

[6] Fridericia, L. S., *J. Biol. Chem.*, 1924, **62**, 471.

and was supplemented with Harris yeast concentrate and oscodal,‡ a cod liver oil concentrate. The vitamin concentrates fed were considered adequate for normal growth and wellbeing, and to insure complete consumption were given in gelatin capsules 4 hours before the rest of the ration was offered. The lard was Armour's 5-Star Brand. To produce an oxidative rancidity in the fat a stream of oxygen was bubbled through it at a temperature of 60°C. until the undiluted material showed a decided color with the Kreis test, but when diluted 1:10 with purified kerosene no color was produced.

Three control dogs receiving the basal diet with its low nitrogen (0.3 gm. N per kilo of dog) supplemented with yeast concentrate and oscodal remained in good health. Two of these dogs were used for other purposes at the end of a 4 months' control period. One is still in good health after 11 months. Four additional dogs, fed the same ration (supplemented with the vitamin concentrates), except that the neutral fat had been replaced by oxidized fat, became ill; the time of onset of the symptoms was quite variable, but the progress of the disease was strikingly similar in all affected animals. The earliest sign was a loosening and falling out of the hair; in some dogs this took place all over the body, but more frequently the hair over the face was lost first. The hair over the feet and legs was next to go, then that over the abdomen; sometimes that over the back could be pulled out by handfuls. The dogs remained lively and well during this period, sometimes even gaining weight. Within a variable time after the first loss of hair was noted, a rash appeared and spread over the body. About this time the appetite began to decline and the dogs became less lively. The stools were very black and inclined to be hard. The skin lesions became worse, ulcers appeared over the bony protuberances and rapidly became deep, sometimes exposing the bone. There was very little inflammation about them, and they did not seem to be tender. The dogs became weaker and frequently convulsive movements of the extremities were noticed. The constipation gave way to diarrhea, which was usually blood-tinged and frequently frankly bloody. The animals became weaker and finally died. The eyes remained unaffected to the end; the mouth was never involved.

The normal mouth seen in this symptom complex distinguished it from the disease produced by Underhill and Mendel[7] and from that produced by Goldberger.[8] We are led to believe that the presence of

‡ Supplied by H. A. Metz Co.

[7] Underhill, F. P., and Mendel, L. B., *Am. J. Phys.*, 1929, **88**, 589.

[8] Goldberger, J., *U. S. Public Health Reprints*, 1928, **43**, 172.

oxidized lard was in some way responsible for the syndrome of loss of hair, skin lesions, anorexia, emaciation and intestinal hemorrhages observed in our dogs. As our control dogs remained in good condition, we are convinced that this pathological condition is not due to an inadequacy in our basal ration.

Several mechanisms of action by which partially oxidized fats may bring about this syndrome may be mentioned. It might be a direct toxic effect upon the animal, though this seems unlikely. It might produce a greater need for one of the vitamins or call for a different balance between them. It is possible that the action of the oxygen on the fat destroyed some important grouping such as the unsaturated linkage shown by Burr and Burr[3] to be essential for health in the rat. The signs and symptoms presented by the dog do not resemble very closely those described for the rat, but there may be a marked species variation.

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Blood Volume in Normal Chicks and in Chicks with Nutritional Encephalomalacia.

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The cerebral lesions in the disorder of chicks described by Pappenheimer and Goettsch[1] as *nutritional encephalomalacia,* appear unquestionably to result from vascular disturbances. Oedema, hemorrhage and hyaline thrombosis of capillaries are the conspicuous initial features of the lesions and they must be due either to alteration of the vessel walls, or to a quantitative or qualitative change in the blood itself.

In attempting to analyze the problem from this point of view, it seemed of interest to determine first whether the disease producing Diet 108* leads to an alteration in the total volume of blood. This paper presents briefly experiments bearing on this phase of the subject.

Material and Technique. Eighty 2-day-old chicks were placed on Diet 108 and 20 controls of the same hatch on the natural foods Diet

[1] Pappenheimer, A. M., and Goettsch, M., *J. Exp. Med.*, 1931, **53**, 11.