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Observations on cholesterol-fed guinea pigs.

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The following experiments were done to test the possibility of the production of atheroma of the aorta in guinea pigs by cholesterol feeding, and also to test certain theories which have been advanced as to the importance of factors, other than the cholesterol, in the production of this type of atheroma.

Four guinea pigs were fed on daily doses of 0.1 to 0.5 gm. of cholesterol dissolved in cotton seed oil for periods of 18 to 72 days. These animals, like rabbits similarly fed, show an enlargement of the adrenals, and an abundant deposit of anisotropic fat in the liver and spleen, the situation of this fat being similar to that previously described in these organs in the rabbit. An occasional guinea pig in this and the following experiments showed focal areas of degeneration in the cortex of the adrenal with a deposit of calcium. The aortas show no gross lesions. Microscopically there are found small patches of fatty infiltration in the intima and upper media. The characteristic proliferation and subsequent degeneration seen in the rabbit were entirely lacking. The feeding periods were too short to conclude that such tissue reaction might not ultimately result. One guinea pig which received 20 g. of cholesterol in 72 days (15.1 g. in the last 40 days) would seem however quite comparable with a rabbit, previously reported, which showed pronounced atheroma after receiving 13.7 g. in 37 days. From these experiments and others which follow it can at least be concluded that a longer period and larger doses are necessary for the production of an atheroma in the guinea pig than in the rabbit.

A guinea pig receiving 13.4 g. cholesterol without oil in 51 days showed some adrenal enlargement, but no anisotropic fat could be found in liver, spleen, or elsewhere. Knack, because of failure to produce atheroma in a rabbit with cholesterol alone, concludes that previous injury to the aorta is necessary before a deposit of

anisotropic fat occurs, and that such injury is produced by oil. If such injurious effect is exercised by cotton seed oil, it is also exercised by various oils which have been used as vehicles in the administration of cholesterol, and also by some substance in egg yolk other than cholesterol. A rabbit may moreover be fed large daily doses of cotton seed oil over a long period without the production of any demonstrable lesion of the vessels. It would therefore seem more probable that the importance of the fat lies in the fact that it supplies to the diet of these animals, normally low in fat, an essential factor for the formation of esters, and thus enables the absorption of cholesterol in large amounts, and possibly also that it facilitates the formation of some compound with cholesterol, in the process of metabolism, which is toxic to the vessels.

Anitschkow and Aschoff believe that the production of atheroma in cholesterol-fed rabbits is aided by raising the blood pressure by mechanical or chemical means. Since the production of cholesterol atheroma in rabbits is so rapid without resort to artificial means of changing the blood pressure, the guinea pig seemed a more suitable animal for testing this theory. A guinea pig received daily doses of cholesterol in oil, 12 gm. in all, for a period of 82 days. During the last 32 days of the feeding he was suspended head down for 15 to 40 minutes daily. Another received 4.7 g. in 44 days and was suspended 20 to 40 minutes daily for the last 38 days. The distribution of the fat was the same as in the preceding experiments, the amount deposited in the aorta was not greater, and tissue reaction was similarly lacking. The same negative results were obtained in 2 guinea pigs receiving daily subcutaneous injections of pituitrin during the feeding.

Four guinea pigs were put on a feeding of cholesterol in oil 26 days after the last of 2 injections of uranium and continued on this feeding for 43, 80, 83, and 88 days. Since it is believed that the cholesterol kidney lesions previously described by the author in rabbits are dependent on a preëxisting spontaneous nephritis, it was hoped in this way to obtain similar lesions from the deposit of cholesterol in the interstitial lesions of chronic uranium nephritis. The kidneys of all these guinea pigs showed a small amount of anisotropic fat, while in only one of the above reported 9 guinea pigs could any of this fat be found in the kidneys. The fat was

present in a few large cells, probably of endothelial type, in the scars, but the lesions seen in rabbits were not obtained. There was also some fat in the glomerular tufts. The latter observation might be considered as evidence that uranium produces a vascular lesion and that such a preëxisting lesion facilitates the absorption of anisotropic fat as argued by Knack. The deposit of fat in the aortas of these animals however was not increased.

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Lesions produced in rabbits by repeated intravenous injections of living colon bacilli.

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Of a series of rabbits injected intravenously with a strain of colon bacillus every 3 or 4 days over considerable periods, the 7 animals which withstood this treatment longest, namely 88, 98, 102, 113, 115, 116, and 142 days, showed pronounced lesions in the kidneys, spleen, and liver. In the kidneys there is produced a hyaline and fibrous thickening of the vascular loops of the glomeruli with the formation of hyaline bodies in the tufts and occasional adhesions between the tufts and glomerular capsules. The tubular epithelium shows more or less degeneration and many casts are present in the tubules. The interstitial connective tissue shows a beginning cellular thickening, apparently not due to the spontaneous nephritis frequently seen in rabbits.

The livers show in certain cases central necroses with hyaline degeneration of the liver cells about these areas and elsewhere. In two cases there is deposited between the rows of liver cells in the middle and peripheral portions of the lobules a homogeneous amyloid-like substance. The livers in all cases show a more or less marked cellular increase of the periportal connective tissue—the latter possibly a spontaneous lesion.

The spleens show a fibrous thickening of the reticulum of the pulp with some hyaline formation. The most striking lesion is a formation of connective tissue with much amyloid-like material about the peripheries of the Malphigian bodies, in cases almost replacing these structures.