

EXPERIMENTAL STUDIES IN CARDIOVASCULAR PATHOLOGY

XIV. EXPERIMENTAL ATHEROMATOSIS IN MACACUS RHESUS MONKEYS *

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Little information is available on the occurrence of "spontaneous" arteriosclerosis in primates. Fox¹ found arteriosclerotic lesions of atheromatous or sclerotic type in only 8 of 796 monkeys studied, and concluded that arterial disease is not a prominent process in the species used. None of the affected animals was a rhesus macaque so commonly used in laboratory work. Kawamura's efforts² to produce cholesterol atheromatosis experimentally in 3 monkeys of the species *Macacus fuscatus* gave a negative result. One of these monkeys received 2 egg yolks daily for 150 days, while the other 2 were fed a total of 1,350 gm. and 1,650 gm. of anhydrous wool fat, respectively, within 300 days. Corwin³ noted in 1938 that all attempts to elicit the condition known as cholesterol arteriosclerosis in monkeys were unsuccessful.

In a critical evaluation of these observations consideration must be given to the fact that monkeys in general are herbivorous animals, which, under normal dietary conditions, show a low tendency toward arterial cholesterol deposition. Only rabbits, when exposed over prolonged periods to an abnormal and excessive intake of cholesterol causing a considerable rise in the level of their blood cholesterol, have so far developed a cholesterol atheromatosis (Hueper⁴). Ssolowjew⁵ reported, moreover, the occurrence of lipid deposits in the aortic intima and media of suckling rabbits, which he attributed to the exclusive milk diet consumed by the rabbits during their early life and which he compared with the lipid spots often seen in human babies for the same reason.

In view of the fact that primates are phylogenetically closer to man than any other species and that *Macacus rhesus* monkeys are extensively used in laboratory work, it seemed to be pertinent to attempt once more to produce atheromatosis in these animals, utilizing the observations made in suckling rabbits in the experimental conditions to be employed.

EXPERIMENTAL PROCEDURE

Two young *Macacus rhesus* monkeys, born in the Warner Institute for Therapeutic Research, were used in the experiments. One was 5 months old and the second was 6 months old at the start of the experiment. Both had just been weaned and had been placed on a diet

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consisting of carrots, apples, oranges, and bread, with a daily supplement of approximately 90 cc. of milk into which one fresh egg was beaten and which was divided between the two monkeys. The male monkey, which weighed 1.4 kg. at the start of the experiment, in addition received daily by mouth 10 cc. of a 2.5 per cent solution of cholesterol in Mazola oil. The solution was injected into an orange or soaked into bread so as to make it more palatable. After 18 weeks on this management the daily dose of 2.5 per cent cholesterol in oil was raised to 15 cc. This dose was maintained for 20 months, when the animal at the age of 2 years and 5 months was sacrificed by the intracardial injection of 20 cc. of a 4 per cent formaldehyde solution.

The female monkey, which weighed 900 gm. at the start of the experiment, was given 5 cc. of cholesterol-oil daily for a period of 5 months. The dose was then raised to 10 cc. and maintained at this level for the remaining 8 months, at the end of which time the animal, when 18 months old, was sacrificed in the manner described. Both monkeys showed a steady gain in weight during the observation period. The male monkey weighed, at the end, 3.1 kg., whereas the female monkey weighed 1.4 kg. Their appetites were good throughout and they were always lively and playful while under the special dietary regime.

The autopsies showed essentially normal organs in both animals. The histological examination of the internal organs (lung, heart, liver, spleen, pancreas, adrenal, kidney, testis, thyroid) did not reveal any abnormalities. The inferior vena cava of the female monkey had a small area in which the endothelial cells were swollen and had proliferated. The aorta of this animal exhibited similar endothelial changes in the thoracic portion (Fig. 1). In the male monkey similar reactions were more extensive and more widely distributed in the aorta. Several transverse sections showed a crowding of the endothelial cells which were swollen in places and cuboidal. In one level of the ascending part, the endothelial cells were forming a stratified coat of slender cylindrical cells (Fig. 2). The aortic branches and the large and small arteries of the parenchymatous organs were normal.

The histological examination of the internal organs, the aorta and its branches of a monkey 7 months old, continuously nursed by its mother for the entire length of its life and succumbing to pneumonia, did not reveal any abnormal vascular reactions of the type described.

COMMENT

The observations reported indicate that *Macacus rhesus* monkeys do not readily react to a prolonged nutritional intake of excessive amounts of cholesterol with the formation of atheromatous aortic

lesions, even when exposed to such a dietary regimen during an early period of life. The endothelial aortic lesions, however, may represent proliferative responses to the cholesterol ingested, since similar endothelial reactions have been found in dogs following the repeated intravenous injection of other atheromatogenic substances, such as hydroxyethylcellulose solution (Hueper⁶) and after a prolonged oral administration of excessive amounts of cholesterol (Hueper⁷). They may thus represent early atheromatous reactions.

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[*Illustrations follow*]

DESCRIPTION OF PLATE

PLATE 268

FIG. 1. Aorta with proliferated and swollen endothelial cells.

FIG. 2. Aorta covered by a cushion of stratified, slender endothelial cells.

