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The early stages of the spontaneous arterial lesions in the rabbit.

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Since the first publication of Josué in 1903, who succeeded in producing artificial arterio-sclerosis by intravenous injection of adrenalin, a great deal of work has been done on the subject. Successful results were reported by treating animals with digalen, barium chloride, hydrastin, nicotine and a number of other substances. The lesions thus produced resemble closely the atheromatous degeneration in the human aorta.

The site of the lesion is usually the ascending portion or the arch of the aorta. The process occurs primarily in the media of the vessel wall and consists in necrosis of the smooth muscle cells, thickening and breaking up of the elastic fibers, and the appearance of calcareous deposits in the diseased areas.

All these successful experiments with the production of artificial arterio-sclerosis were obtained only in rabbits. All efforts to produce similar results in other laboratory animals failed. The question consequently suggested itself whether the success with the rabbit is not due to the frequency of the spontaneous occurrence of this disease in the animal. Indeed several reports were made on the spontaneous occurrence of arterio-sclerosis in the rabbit. A. B. Miles makes a most remarkable statement in this respect. In 61 rabbits treated with adrenalin he found arterial lesions in 17 animals, which represents 27.86 per cent., while of 49 normal rabbits he found the same condition also in 17 animals, which represents 34.77 per cent. R. M. Pearce found spontaneous arterial lesions in 6 per cent. of animals. M. C. Hill found the lesions in 15 per cent. of 210 animals examined.

All these investigations show that while spontaneous lesions are met with in rabbits the percentage of the diseased vessels is far lower than the percentage of the lesions found after treatment with adrenalin and the other substances. But since all the investigations arrived at their conclusions only by gross inspection, the

question very naturally presents itself whether spontaneous lesions could not be found more frequently if every vessel which appears normal were examined microscopically. It seems plausible *a priori* to suppose that before a lesion develops to such a degree that it may be noticed on gross inspection, the beginning of it may be so minute as to be discovered only by microscopical examination.

With this aim in view, 240 rabbits were examined. All these animals were used for laboratory purposes, mainly for obtaining blood-serum, and no toxic substance of any kind was introduced into these animals. On gross inspection of the aorta of these 240 rabbits, 31, or 13 per cent., had gross lesions and these were not examined any further. Of the remaining 209 animals, every arch of the aorta (the part of the aorta which is most frequently affected with spontaneous and arterial lesions) was examined microscopically. The specimens were hardened in formalin, imbedded in celloidin or paraffin, and stained with hematoxylin-eosin and Weigert's elastic tissue stain. Of the 209 vessels examined, 78, or 37.3 per cent., presented minute lesions visible under the microscope. The lesions showed either the degeneration of the media including the muscular and fibrous tissue coat with the elastic fibers preserved, but thickened and tortuous, or the same degeneration of the media with loss of muscular and elastic fibers and deposition of calcium. In other vessels, again, the main condition was proliferation of the endothelial cells of the intima.

Thus in our investigation we found in 52 per cent. of the examined rabbits arterial lesions of different degrees or development. This percentage corresponds very closely to the percentage of the diseased vessels found after adrenalin or other treatment.

While the results of this research cannot prove with absolute certainty that in some cases arterial lesions may not be produced solely by the injections, the possibility seems to be great that the treatment frequently only enhances or ripens an early stage of arterial disease that existed in the vessel before treatment. It would seem, therefore, that the rabbit is not a suitable animal for the study of experimental arterio-sclerosis.