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EXPERIMENTAL "WORK-ARTERIOSCLEROSIS."

BY

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The experimental work in arteriosclerosis has, up to the present, been mainly of the nature of mechanically injuring the vessels, or else by introducing foreign toxic substances into the animal body. Of the latter type much has been written in the last four years, and it has been shown that substances like adrenalin chloride, barium chloride, digitalin and nicotine, all of which produce high pressure in the arterial system, are capable of bringing about definite arterial lesions. It has also been shown that certain bacterial toxins act on the vessel walls, either by producing degenerative changes, or else in stimulating the proliferation of certain cells.

There has been a considerable controversy as to the nature of these arterial lesions, whether they were the result of the toxic substances, acting directly upon the tissue cells, or whether their mechanical effect of increasing the blood pressure was capable of bringing about these changes.

Clinically, it has been noted that in the adult, the vessels of the more active organs show hypertrophy and sclerosis earlier than in the less active parts. In right-handed persons the radial arteries are considerably more sclerosed than those on the left side, and the reverse is true in left-handed people. Similarly, those whose occupation requires them to be constantly walking around and on their feet show the most advanced arterial changes in the vessels of the legs. These facts point to the prominent part that is played by work, in the production of arteriosclerosis, but still the question arises whether in a healthy vessel increased work alone can bring about sclerotic changes, or whether it is necessary to couple the factor with the effect of toxic agents.

It was my endeavour to throw some light on this question by experimental means. I chose healthy, nine months old rabbits to carry on the experiments. The first animal was treated for one hundred and thirty days, by suspending him by the hind legs for three minutes each day. The endeavour was to increase the pressure and the mechanical stress in the arteries, without employing any drugs. By inverting the animal, the pressure in the thoracic oarta and in the arch is decidedly increased over that which normally exists in the animal. At the beginning, the animal did not seem to be worried by treatment, but later

on it showed signs of dyspnœa, and the heart beat was accelerated. Towards the end it was noted that the animal was much fatigued after each treatment.

At autopsy the following was noted:—There were no lesions in the vessels of the brain and no hæmorrhages had occurred in this organ. The carotid vessels had a remarkable appearance; the arteries were enlarged to about twice their size, and looked like sclerosed radials. There were distinct beadings on the vessels, which were most marked just above their origin from the aorta. These beadings were white in colour and encircled the vessels in transverse rings. Similar appearances were also present on the subclavian and brachial vessels. The beadings were distinctly palpable, while the vessels in general were firmer than normal. The amount of change in these arteries diminished after the bifurcation of the common carotids, though it was still apparent in some of the smaller branches.

Thorax and Abdomen.—The lungs were healthy and without change. The heart showed an enlargement of, at least, one and one-half times its normal size. The ascending aorta had its walls thickened, and was larger than normal. This increased size was apparent as far as the middle of the arch, or just beyond the opening of the left brachial. The wall felt firm and nodular, and did not collapse when its contents were removed. Opposite the 6th rib the vessel again dilated to twice its size, forming a fusiform aneurysm as far as the diaphragm. This aneurysmal dilatation had firm and brittle walls, in which concentric rings could be distinguished passing about the vessel. Below the diaphragm the aorta again became smaller, but showed thickening of its coat, which was visible as far as the right renal artery. The beginning of the cœliac axis was also sclerosed, though no changes were noted in the branches of this vessel. The renal arteries were normal in appearance, and below them the aorta, too, was without change. There was no change to be noted in the iliac arteries, nor the vessels of the legs, nor did the viscera of the abdomen exhibit any microscopical lesions.

We have, therefore, produced macroscopical changes in the aorta and its branches above the renal vessels. In these changes the aorta is chiefly involved, while the carotids and the vessels of the neck are also sclerosed. Consequent upon the weakening of the aortic wall by sclerosis, a fusiform aneurysm developed in the thoracic aorta.

Microscopical.

Ascending Aorta.—The aortic wall was hypertrophied, the thickening occurring in the intima and possibly in the media. The media, where it was apparently thickened, was normal in structure and showed the

alternating layers of elastic fibres and muscle tissue. The intima, where thickened, showed the hypertrophy to be in the muscle elements (of the musculo-elastic layer). There was no connective tissue proliferation to be found. With the intimal thickening there was everywhere a process of degeneration accompanying it. This degeneration in the mildest form occurred close to the internal elastic lamina, and, in the more advanced types, extended closer to the endothelial surface. The muscle cells themselves were degenerating and disintegrating, leaving areas of non-cellular debris. These areas showed many spicules of crystals like those of calcium salts. Many of the cells were vacuolated as if containing drops of fat. In one area the media, too, showed degeneration where the muscle cells were entirely wanting, while the elastic bands were thrown into prominence by a darker blue staining, due to a calcification. Fractures were occasionally seen in the elastic laminæ. Remarkable cells were found between these calcified elastic bands. These cells were large with a spherical media and lay in a homogeneous looking matrix with vacuoles about them. One was reminded of the appearance of cartilage cells, though definite cartilage was not to be made out.

A study of these sections convinces one that the muscular changes are primary. The rupture and changes in the elastic fibres are secondary.

Descending aorta just above diaphragm.—The vessel wall was in its greatest extent narrowed. Only short stretches of normal looking aortic wall were seen. The rest of the wall showed a hypertrophied intima, in which the musculo-elastic layer was thickened, while the media was much narrowed. The middle zone of the media showed a band of calcification almost encircling the vessel. There was a narrow strip of media on both sides of the calcified band, which showed the muscle cells wanting to a great extent, while the elastic fibres lay more closely together. The adventitia nowhere showed change. In the calcified band of the media no cells were to be made out. This degenerative change in the descending aorta resembled that produced in the aorta by adrenalin chloride.

Carotids.—In the carotids the changes found were principally located in the intima. The media showed no changes in any part, save such as is produced by the compression of the thickened intima and slightly fatty degeneration along the border of the internal elastic lamina.

The intima was in parts normal, consisting of a single layer of endothelium lying upon the internal elastic lamina. In other parts there was a thickening of this membrane to that exceeding the thickness of the media. This thickened portion of the intima was made up of a

superficial and circularly disposed layer of connective tissue (possibly of endothelial origin), while beneath this was a thick layer of longitudinally disposed muscle fibres, with extensive fatty degeneration in them. In this deeper layer of the intima many of the muscle cells had entirely disappeared, leaving behind a granular debris mixed with minute fatty granules. In some places this thickened intima occupied one-half the circumference of the vessel.

We have, therefore, in this experiment been able to reproduce by physical means two kinds of changes in the arterial walls. The one is isolated in the media without intimal change and consists of a purely degenerative process, with death of the muscular elements and calcification of the involved areas, including the elastic fibres. The other change is isolated to the intima, and consists mainly of a proliferation of the tissue, while a secondary fatty degeneration has occurred in the newly formed tissue.

In the lesions of the first type involving the media there has also occurred the production of aneurysm. This, as we have previously pointed out, is the common result of severe degenerative changes in the media.

I believe, therefore, that we may conclude from these experiments that work plays a very important rôle in the production of arteriosclerosis of different characters, and that even in vessels of different histological structure sclerotic changes can be brought about by increasing the work of the artery. And further, as a consequence to certain changes, degenerative in character, taking place as the result of increased work in the media of the vessels, aneurysms may result.

We understand from Professor J. J. Mackenzie that Dr. Harvey of Toronto, working at Cambridge, has by different methods of increasing arterial pressure obtained marked changes in the arteries. As to the character of these changes, we have no information beyond that they are arteriosclerotic. We gather from Professor Mackenzie's letter that this paper has just been presented to the Royal Society of London.