# ON ARTERIOVENOUS ANASTOMOSIS AND THE MECHANICAL THEORY OF ARTERIOSCLEROSIS.[1]

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PLATES I–IV.

The function of a blood-vessel is purely mechanical and consists either in lessening the strength of the onrushing blood sent by the systole of the heart, or in assisting the blood-flow, the strength of which is diminished as it nears the periphery. Both of these functions are taken up by the elastic and muscular fibers of the media. In view of this, it is evident *a priori* that the mechanical conditions of the blood stream within the lumen of the vessels must play a certain rôle in the causation of arteriosclerosis. Nevertheless, this factor was completely lost sight of until the appearance of the first publication of Thoma (1) in 1883. This investigator was the first to indicate the importance of the increase in blood pressure on the etiology of diseases of the blood-vessels.

The wall of a blood-vessel, weakened by a degenerative process, presents little resistance to blood pressure and, as a consequence, the lesion is continually increased. But Thoma and his adherents go a step further and claim that when an artery has no preliminary degeneration of its media, a lesion of the blood-vessel wall will ensue if the blood pressure is above normal.

The proliferation of the endothelial cells of the intima, which is an early concomitant of the degenerative process of the media, is explained by these investigators by a compensatory filling-in of the depression in the wall, caused by the thinning of the diseased part of the media.

Thoma adduced the following experimental proof of this contention: when a diseased aorta is filled with melted lard under pres-

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sure, the projecting intimal nodosities disappear. Thus, a plausible explanation of the main characteristics of arteriosclerosis is offered on the basis of the mechanical theory. But while the deleterious effect of blood pressure on a previously diseased vessel wall may be self-evident, the possibility of producing arteriosclerosis by increased pressure alone needs experimental proof.

Thoma tried to approach the subject experimentally by producing in dogs an insufficiency of the aortic valve, and he claims to have observed subsequently arterial lesions. These were not identical with arteriosclerosis, consisting merely in hypertrophy of the intima. His results could not be confirmed either by Poper (2) or Jores (3).

Another experimental method was made use of, apparently with great success, by Josué, who reported, in 1903, that he had artificially produced "atheroma" in the aorta of rabbits by intravenous injections of adrenalin. Josué considered his results as an experimental proof of the mechanical theory of arteriosclerosis, since the action of adrenalin consists in raising blood pressure. Identical results have since been obtained by a great many investigators, but it is doubtful whether these results can be used in support of Thoma's theory. In the first place, spontaneous arterial lesions are found so frequently in the rabbit, that this animal does not appear to be suitable for the study of experimental arteriosclerosis. Indeed, our recent investigations (4) have shown that while only 13 per cent. of 240 rabbits showed an arterial lesion in the aorta on gross inspection, 39 per cent. of the other rabbits showed also spontaneous lesions, though in such an early stage that they could be detected only on microscopical examination. In other words, 52 per cent. of the supposedly normal rabbits had diseased blood-vessels, and this is nearly the same percentage as is usually found after treatment with adrenalin.

The microphotographs shown in Plate I, Figs. 1, 2, and 3, and Plate II, Figs. 4, 5, and 6, show that the minute spontaneous lesions are identical with the lesions found after treating rabbits with adrenalin. Furthermore, the possibility cannot be excluded that adrenalin, which is a powerful poison, may not have, besides its blood pressure-raising influence, certain toxic effects upon the organism and, consequently, upon the wall of the blood-vessel.

The same lesions were also induced in rabbits by a great many substances; some raised the blood pressure, others lowered it, and others still, like the bacterial toxins, had no effect whatever on the blood pressure.

On the other hand, all attempts to produce arterial lesions in normal dogs or other laboratory animals by injection of adrenalin failed. The following question then presents itself: is it possible to produce in dogs, by other mechanical means, conditions similar to arteriosclerosis? Carrel and Guthrie (5) have shown that the walls of a segment of a vein implanted in an artery, undergo certain changes which consist in a hyperplasia of the connective tissue of the adventitia and an increase of the number of the muscular and elastic fibers of the media. On such an implantation Stich (6) found conditions which he considers similar to arteriosclerosis. Fischer and Schmieden (7) found a slight hypertrophy of the media with an increased number of connective tissue fibers and a rather diminished number of elastic tissue fibers. The intima was thickened only in the neighborhood of the suture.

It is hardly possible to draw correct conclusions from this method of experimentation, since such a segment is completely severed from its vascular connection and its cellular elements are placed under unfavorable conditions of nutrition. Our recent investigations (8) lead us to suppose that such an implanted segment may ultimately become absorbed, and that a complete new tube may form around the skeleton of the implanted segment.

The conditions are nearer normal when a unilateral anastomosis is made, *i. e.*, when two vessels are united without severing the connection of either with the general circulation. Carrel and Guthrie performed the unilateral anastomosis and found that the wall of the artery contained an increased amount of connective tissue. Fischer and Schmieden, also, performed this operation twice, but they did not keep the dogs long enough to come to any definite conclusion.

In our experiments we endeavored to increase the blood pressure of a vein by anastomosing to its central end the peripheral end of an artery, thus not only preserving the circulation within the vein, but also adding to it the pressure of the arterial blood flowing from the artery. A certain number of the dogs received three to five intrave-

nous injections of adrenalin, in order to determine whether an effect could be seen in a vein already placed under unfavorable conditions of pressure. Previous to this, on two dogs a side-to-side anastomosis of the aorta and vena cava was tried, with the hope of increasing the pressure in the latter blood-vessel, but in both experiments great congestion of all the parenchymatous organs took place, and the animals died within twenty-four hours. Then, on four dogs side-to-side anastomosis was tried between the femoral artery and vein. The animals were killed two to three months later; both the artery and vein were found to be patent and the circulation perfect, but the opening made between the two vessels was completely healed and covered with endothelium.

It was then decided to resort to end-to-end anastomosis between the external carotid and the external jugular. Ten experiments were performed; a description of each is given below.

EXPERIMENT 1.—November 13, 1909 Brown female dog: anastomosis between right external carotid and external jugular.

January 5, 1910. The second operation was performed on the same animal. Anastomosis between left external carotid and external jugular.

During and before the second operation, venous pulsation could be felt in the right external jugular. The second operative field became infected; a large abscess formed, which gradually healed, leaving a suppurating sinus.

February 1. Animal killed. At the post-mortem examination the right carotid and jugular appeared thrombosed for about two and one-half inches; very fine wire could be passed through the lumen. Tissue was hard, elastic and cord-like. Microscopical examination showed growth of connective tissue in the intermediary coat of the intima and growing into the lumen of the vessel.

EXPERIMENT 2.—December 12, 1909. White and black male dog: anastomosis between right external carotid and external jugular.

January 19, 1910. The animal received an intravenous injection of 8 mm. of adrenalin.

January 23, 27, and 29. The same injection was repeated.

March 24. The animal was killed. Post-mortem examination showed a fusiform aneurismal dilatation of the vein. On gross inspection the vessel wall looked slightly thickened, but there was no evidence of a change in the endothelial lining. Microscopical examination shows no abnormality either in the intima or media of the vein. There is fibrous tissue hyperplasia in the adventitia of the vessel.

EXPERIMENT 3.—February 2, 1910. Brown female dog: anastomosis between right external carotid and external jugular. No adrenalin treatment; dog was killed March 12. Post-mortem findings the same as in experiment 2, only the vessel wall of the vein appears somewhat thicker than the vein of dog 2. Microscopical appearance was the same as in dog 2.

EXPERIMENT 4.—February 9, 1910. Brown female dog: anastomosis between right external carotid and external jugular. The dog received four injections of adrenalin. Killed April 22. Post-mortem findings were the same as in experiment 2.

EXPERIMENT 5.—February 6, 1910. Black male dog: anastomosis between right external carotid and external jugular. Four injections of adrenalin. Dog killed April 14. Post-mortem examination shows a moderate distention of the external jugular vein at its distal part. The artery and vein for a distance of half an inch on each side of the line of suture is firm, thickened, and elastic. A fine wire probe passes through the contracted lumen. Microscopical examination shows parietal organized thrombus. Connective tissue hyperplasia in the adventitia. Distal section of vein is normal.

EXPERIMENT 6.—January 19, 1910. Large, brown female dog: anastomosis between right external carotid and external jugular. Five injections of adrenalin. Killed April 7. Post-mortem examination shows normal jugular vein; no distention or thickening of the wall.

EXPERIMENT 7.—March 23, 1910. Small, brown female dog: anastomosis between right external carotid and external jugular. Three injections of adrenalin. Dog killed April 7. Post-mortem findings were the same as in experiment 6.

EXPERIMENT 8.—December 4, 1909. Black female dog: anastomosis between right external carotid and external jugular. Four injections of adrenalin. Dog killed April 7. Post-mortem examination shows aneurismal dilatation of vein for about half a inch above anastomosis. Beyond this point the vein is not markedly dilated. Dissection of the artery and vein shows aneurismal dilatation in vein to be due to mechanical impact of arterial blood against the wall of the vein. No abnormality in the intima or media is seen on microscopical examination.

EXPERIMENT 9.—February 23, 1910 Medium-sized, white male dog; anastomosis between the right external carotid and external jugular. No adrenalin injection. April 22, dog killed. The result of the post-mortem examination was the same as in dog 8.

EXPERIMENT 10.—March 9, 1910. Light, bushy, female dog: anastomosis between the right external carotid and external jugular. Four injections of adrenalin. Dog killed April 22. Post-mortem findings were the same as in experiment 8.

Analysis of these experiments shows that not in a single instance did the vessel wall of the external jugular undergo the degenerative process characteristic of arteriosclerosis, though the pressure exerted on its wall must have been considerable, since at one end there was a stream of arterial blood from the carotid, and at the other end the normal venous circulation pressing against the carotid. Moreover, in several instances the animal received from three to five injections of adrenalin. The dilatation that was found

in six out of the ten experiments is not identical with the usual condition of aneurism, since the vessel wall does not show any degeneration and retains its elastic lamina (Plate III, Figs. 7 and 8). Only at the level of the suture was there a noticeable hyperplasia of the intima. This was apparently due to the irritation caused by the silk suture acting as a foreign body. The thickening of the walls of veins, found occasionally on gross inspection, is due to connective tissue proliferation of the adventitia caused by the stripping off of the adventitia during the operation (Plate IV, Fig. 9). The obliterative endarteritis found in experiment 1 is due to an infection which took place after the second operation on the same dog, and in experiment 5 it occurred subsequently to the primary operation.

Consequently, as a result of our investigation, the conclusion must be drawn that arteriosclerosis cannot be artificially induced in a previously healthy blood-vessel by a change in the blood pressure alone, and that the thickening of the wall and the other changes noticed in such vessels is probably due to changes in the adventitia caused by the operative procedures.

## EXPLANATION OF PLATES.

### PLATE I.

FIG. 1. Aorta of normal rabbit. Hematoxylin-eosin, low-power: small area of degeneration in media reaching intima. Lime deposits.

FIG. 2. Aorta of normal rabbit. Hematoxylin-eosin, high-power: small area of degeneration in media reaching intima. Lime deposits.

FIG. 3. Aorta of normal rabbit. Hematoxylin-eosin: two areas of degeneration in media. Lime deposits.

### PLATE II.

FIG. 4 Aorta of normal rabbit. Weigert's elastic tissue stain: two areas of degeneration in media. Same specimen as Fig. 3.

FIG. 5. Aorta of normal rabbit. Hematoxylin-eosin, low-power; minute nodule in the intima.

FIG. 6. Aorta of normal rabbit. Weigert's elastic stain: minute nodule of the intima shows no elastic tissue.

### PLATE III.

FIG. 7. Anastomosis between external carotid and external jugular The two figures to the left show dilatation of the vein split open. The third specimen shows that the dilatation of the vein reaches only above the valve. The fourth specimen is the same as the first before opening.

FIG. 8. Dog 3. Anastomosis between carotid and jugular. Hematoxylin-eosin, low-power, longitudinal section: in the middle of the section is the line of anastomosis; artery to left, vein to right.

## PLATE IV.

FIG. 9. Dog 3. Anastomosis between carotid and jugular vein. Hematoxylin-eosin: connective tissue proliferation in adventitia.

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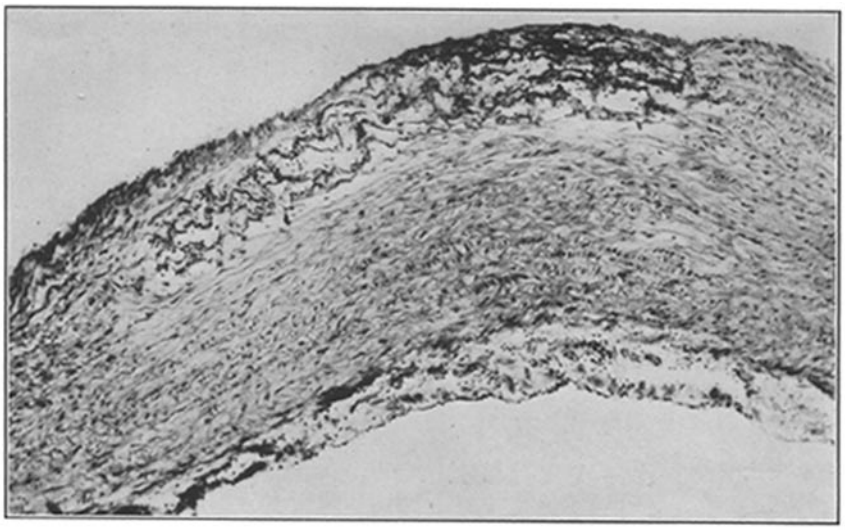


FIG. 1.

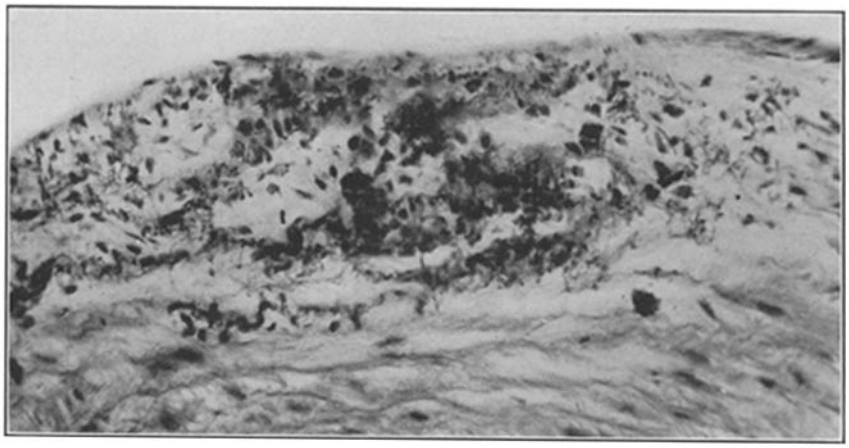


FIG. 2.

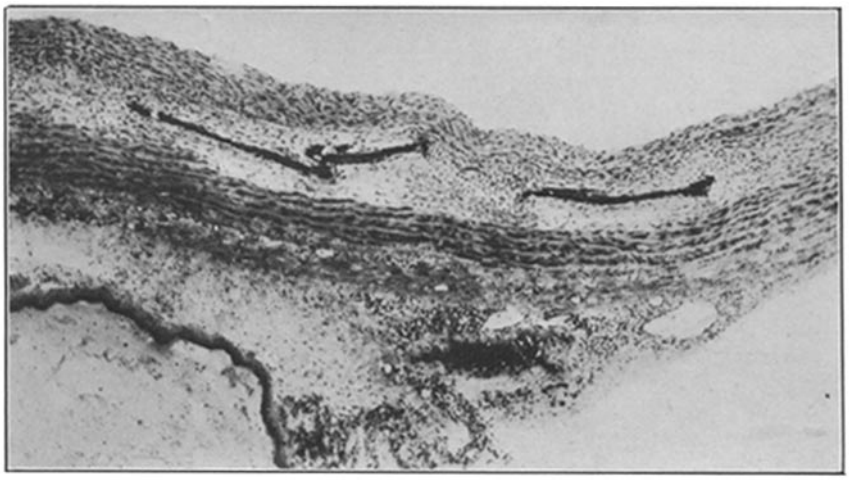
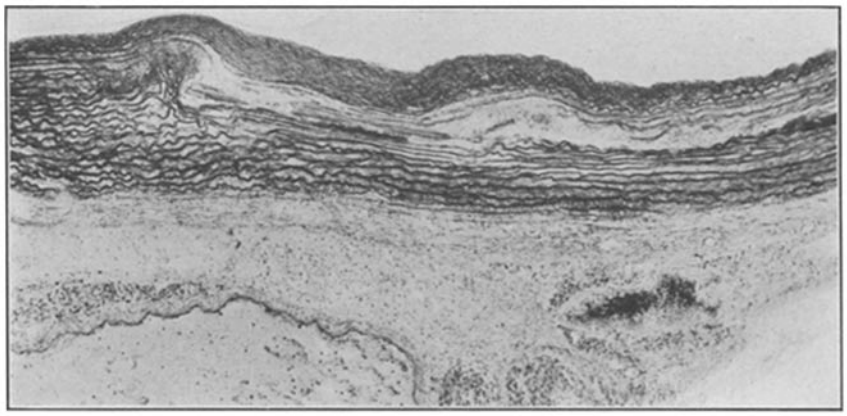


FIG. 3.



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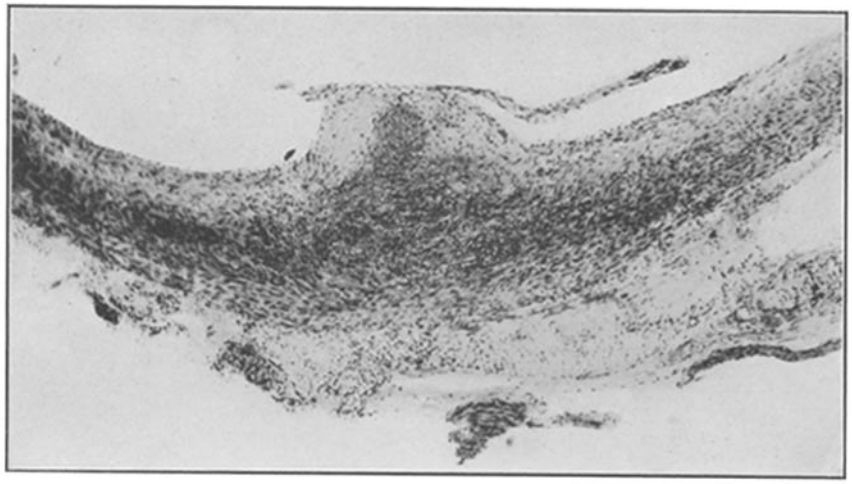

FIG. 5.

FIG. 6.

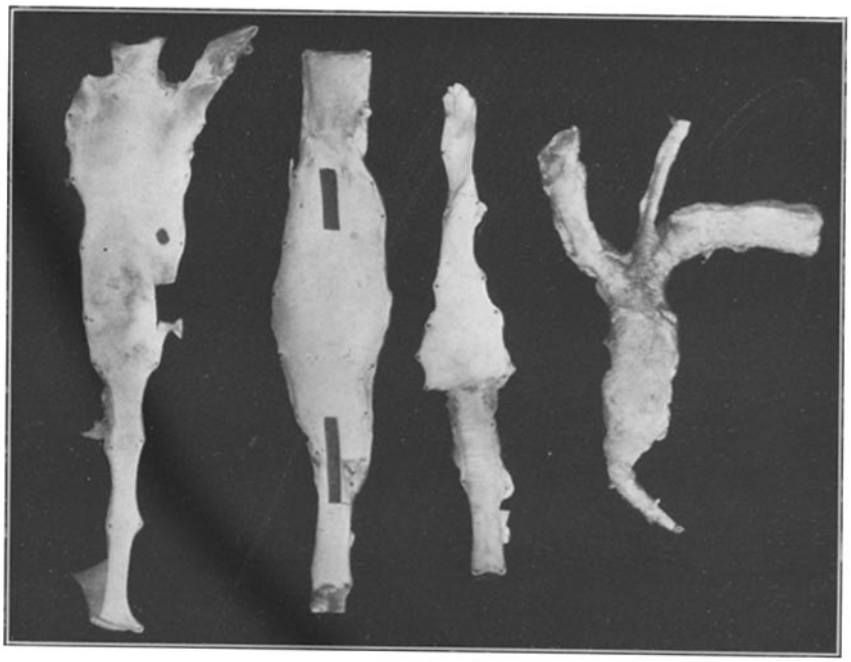

FIG. 7.

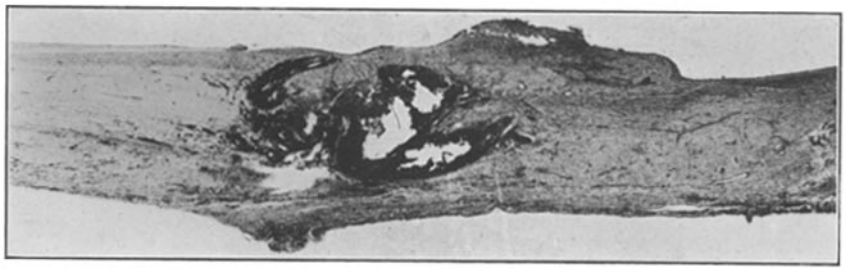

FIG. 8.

FIG. 9.