Provisional report on healing of arteries after ligature / by J. Collins Warren.

PROVISIONAL REPORT 19.

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HEALING OF ARTERIES AFTER LIGATURE,

BY

J. COLLINS WARREN, M. D.

AT A MEETING OF THE

BOSTON SOCIETY OF MEDICAL SCIENCES,

HELD MARCH 20, 1883.

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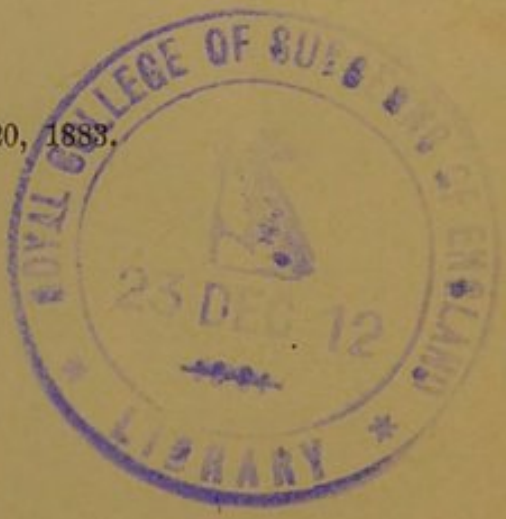

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THE HEALING OF ARTERIES AFTER LIGATURE.

[The accompanying statement embodies the results of several years of experimental investigations on animals and the examination of specimens taken from the human subject. Owing to the inability of the writer to prepare an elaborate paper at the present time, he has been obliged to content himself with publishing this brief summary of remarks made at the meetings of the Boston Society for Medical Sciences during several successive seasons, and reported in their records of March 20, 1883.]

Investigators who have interested themselves in the process of repair in arteries have considered the question usually from some special stand-point such as "the organization of the thrombus," "the part played by the white corpuscles," "the endothelium," etc. The object of this paper is to study the various pathological changes which occur in and around the vessel from the time the ligature has been applied until the process of cicatrization has fully completed itself.

These changes may be compared not inaptly to those which occur in long bones after fracture. In both we find an external and an internal callus, the former having only a provisional existence in the case of arteries, and subsequently giving place to a ligamentous union of the divided fragments, the latter undergoing such changes in the later stages of the process that the canal or lumen of the vessel is imperfectly reëstablished by the so-called "canalization" of the thrombus. In the mean time the walls of the vessel, like the cortical bone, have undergone certain changes which enable them to participate in the final process of repair.

When a large artery is tied in its continuity, the intima and a portion of the media are usually ruptured, and the adventitia is gathered into a dense tendinous-like sheath around the constricted ends. The first noticeable change is the formation of the thrombi and the development of a granulation-like mass of cells about the ligature, which if it has been cut short is completely enveloped by them. This appears to proceed from the connective tissue which surrounds the vessel, the peri-adventitial tissue. When the injury done by the constricting ligature is slight this new formation will be less in quantity, but if the coats of the vessel have been considerably bruised and a certain amount of extravasation has taken place, or the ligature has created irritation, the surrounding inflammatory tissue will form a well-marked callus. When one end of the ligature is left uncut or suppuration has taken place, the surrounding callus is imperfectly developed and secondary hæmorrhage is more likely to occur. Following the development of this tissue, we find it extends some distance up and down the sides of the divided vessel in the periadventitial tissue, the round cells of which it is composed invading only the superficial layers of the adventitia ; at the point of ligature, where the fibres of the outer wall are densely packed, the cells at first do not penetrate at all ; they follow the ligature as it cuts its way through, and indeed appear to exert a solvent action on the resisting fibres of the adventitia. As the walls thus liberated retract, the cells penetrate through various clefts and spaces, and eventually make their way into the clot and contribute more or less to the development of the internal growth. When a double ligature has been placed upon a vessel these cells find their way into the isolated central portions at the retracted ends and not through the walls directly as some investigators have supposed, and gradually disintegrate the various coats, invading them eventually from every point. The process, however, is a slow one, and requires several weeks for its accomplishment. If the

artery has been properly removed from the body we find this growth forming a callus-like ring at the ligatured spot, in size about twice the thickness of the vessel. This was shown particularly well in the femoral artery of the dog killed on the tenth day. At the end of a month evidences are still present of such a cicatricial mass of tissue, but at three months a slender cord only unites the peripheral to the proximal end.

Early changes are seen in the proximal thrombus, well advanced already on the fourth day. In the carotid of a dog an abundant growth of young tissue was found budding from the ruptured ends of the media, and spreading in various directions throughout the clot, attaching itself to the wall at various points, and leaving spaces or meshes still occupied by the blood clot. As these fragments of clot become disintegrated and disappear, spaces are left into which blood eventually circulates, and the so-called "canalization" of the thrombus is effected. By the fifteenth day the new tissue has become very abundant, and has the appearance of granulations growing into and replacing the thrombus. By the end of a month we find but fragments of the thrombus remaining, and the granulations now present themselves to the lumen of the vessel. We find here a free communication between the spaces which separate these granulation-like masses and the lumen and an injection mass can be forced successfully for a considerable distance into them. The vessel walls are in the meanwhile undergoing certain changes. There is unquestionably a proliferation of the cells of the intima. This can be conveniently studied in those specimens where the distal thrombus is small, or in the space between two ligatures; the amount developed, however, is not sufficient to supply but a small fractional part of the internal callus. The rôle played by the endothelium appears to be one which furnishes a new endothelial covering to the cicatricial tissue and a lining to the new vessels that have been formed. Wherever the intima has been ruptured and the media

exposed we find an intimate connection existing between it and the new tissue; at an early stage of the process cells are seen springing from the muscular layers and projecting into the thrombus; later one sees elongated spindle cells, like those forming the muscular layer, projecting from this layer into the newly-formed tissue, sometimes singly, sometimes in bundles, and occasionally occupying a considerable space.

At the point of ligature the elastic lamina appears frayed out, and is seen extending in various directions through the new tissue; the media begins by the end of the second week to retract, as also does the adventitia, leaving a space through which vessels eventually find their way, and communicate with those coming down from the lumen.

At the end of three months the cicatricial process is completed, the external callus has disappeared, and is replaced by a cord of connective tissue which joins the two ends of the vessel, now widely separated from one another. No traces of the thrombus are to be found, except a few pigment granules. A cicatrix, more or less voluminous, according to the size of the vessel and the situation of the ligature, is seen.

In the femoral artery of a large dog a very beautiful example of this was seen. The cul-de-sacs of the two ends were occupied by a semilunar mass of tissue, with its concavity towards the lumen. On the surface of this cicatrix was seen a thin layer of endothelium; beneath this was a crescent-shaped layer of cells, the horns extending up some distance on the sides of the vessels. These cells were parallel to one another and to the arc of the circle made by the layer. On a careful examination they were found to resemble more closely the *muscular* fibre cell than any other. The long prolongations and the staff-shaped nuclei were demonstrated by various methods of staining. A special series of stainings with aniline dyes and examination under Zeiss's oil immersion showed a close resemblance between these nuclei and those of adjacent

muscular cells. Cross sections were confirmatory of this view. Below this layer was the body of the cicatrix, which consisted of interlacing fibres of connective tissue dotted over with masses of blood pigment. Through this tissue a large vessel made its way from the fundus of the cul-de-sac, rapidly diminishing in size and breaking up into branches, which anastomosed freely with a series of capillary vessels which lay between the slightly retracted walls of the vessel, and communicated with others in the slender ligament.

We see here an explanation of the immunity of cicatrices of this kind from aneurismal dilatation which occurs so frequently after wounds of vessels. The protective influence of the thrombus insures the development of a tissue closely resembling the three layers of the vessel wall, and having all the powers of resistance which they possess.

In the larger vessels of the human subject, where there is less muscular and more elastic tissue, the new muscular tissue is not so evident, but the connective tissue is greatly increased in quantity, and extends for a long distance into the lumen of the vessel. This was seen in a ligatured carotid artery of a man who died four years after the operation.

To summarize briefly, the ligatured artery is invested by a protective layer of new tissue formed from the periadventitial tissue, which, if well developed, gives great security against hæmorrhage until the permanent cicatrix has grown sufficiently strong. This may be likened to the provisional callus of bone. There is also an internal growth or callus formed from several sources, namely, the intima to a slight extent, the media more largely, also from cells finding their way from the periadventitia at a late stage through the retracted ends of the vessel. The thrombus is a mere passive structure, takes no part in the growth, but is protective, and affords an excellent medium for the new tissue to germinate in. When the provisional part of the inter-

nal callus has disappeared we find remaining a cicatrix closely resembling the three coats of the artery, and affording by virtue of its peculiar structures an equally effective resistance to the pressure of the blood column. The ligament which unites the two ends of the vessel represents in part the residue of the external callus, but also a portion of the walls of the vessel which have been absorbed during the inflammatory process. A vessel successfully ligatured in its continuity cannot, therefore, be said to have been "ulcerated" into two separate portions, but must be conceived of as a hollow tube which has solidified into a solid columnar mass of tissue a considerable portion of which subsequently shrinks into a cord.