ARTERIES, HEALING OF, After Ligature, Acupressure, Torsion, and Suture.—Although the introduction of the ligature is commonly ascribed to Paré, there is sufficient evidence to show that it was employed by surgeons in the earliest historic times. No mention is made of the ligature by Hippocrates, but the ancients used not only styptics and the actual cautery, but also ligature and torsion. It is highly probable that the Alexandrians were familiar with the use of the ligature three centuries before the Christian era, for Celsus (born 30 B.C.) speaks of it as a well-known fact and recommends its use. Rufus of Ephesus, a century later, makes the following mention of torsion: "Vas immissa volsella extendemus et moderate circumflectemus: at ubi ne sic quidem cessaverit [hæmorrhagia] vinculo constringemus." Archigenes and Galen both mention tying vessels for the purpose of stopping hemorrhage; the name of Antyllus also bears testimony to the skill of Roman surgeons, and in the Museum at Naples there may be seen a forceps, with sliding attachment, evidently intended to use with the ligature. We find the ligature of arteries mentioned again in the seventh century by Paulus of Ægina, whose teachings were still preserved by the Italians in the sixteenth century. In Lanfranchi's "Surgery" (1295) occurs the following passage: "Oportet te nunc aut venam ligare et ipsam de loco extrahere, et caput venæ vel arteriæ contorquere, aut ferro candente sanguinem sistere."

It is uncertain, however, whether ligatures were employed on large vessels before Paré's time. To this great surgeon is due the credit not only of fully appreciating the value of this mode of hæmostasis, but of making it a universally applicable method. At this period, the middle of the sixteenth century, the imperfect knowledge of the anatomy and physiology of the circulation prevented a due appreciation of the advantages of the ligature, and even Guillemeau, who was the champion of his friend and teacher, confined the use of the ligature to primary amputations. Although Wiseman in England, Fabricius Hildanus in Germany, Fallopius, and others favored the ligature, they were but isolated examples, and at the opening of the eighteenth century the actual cautery was still the customary method of arresting hemorrhage at the Hotel-Dieu.

The contrast between the two methods at that time was not indeed as great as it would seem to-day. A glance at Paré's plates shows the forceps as an instrument of rude pattern and clumsy make; no attempt was made to isolate the vessel; veins, nerves, and arteries being included in one knot. No wonder that surgeons had a "horrid apprehension of compressing the nerves," and that Petit, with whom modern investigation on the healing of arteries may be said to have begun, actually proposed compression as a substitute for the ligature. It was he who first called attention to the agency of the thrombus in checking bleeding, the blood around the end of the vessel being termed the *couvercle*, and that found within the lumen the *bouchon*. The retraction and contraction of the vessel were soon recognized by Morand, who also called attention to the rupture of the inner walls by the ligature. Pouteau, of Lyons, thought that the swelling of the tissues surrounding the mouth of the vessel was as important a factor as any other in bringing about the arrest of hemorrhage, and he devised what has since been called the mediate ligature. This was, however, a return to obsolete methods, and a protest was soon raised against its brutality. In England, Gooch and Kirkland dwelt strongly upon the action of the vessel wall, and the former showed that the sides even became adherent for some distance, the vessel shrinking into a cord. White even thought that the clot was injurious and should be removed; John Bell, on the other hand, thought that the extravasated blood in the tissues compressed the vessel, which subsequently receded by adhesive inflammation. Hunter gave a great impetus to the study of the process of repair in arteries through his views on healing by first intention. He first enunciated a theory, which has since led to much discussion, concerning the organization of the thrombus and its vascularization, which he likened to the changes seen in the embryo of the chick; but he also believed in a direct adhesion of the arterial walls. It was due to him, also, that the subsequent establishment of a collateral circulation was recognized. To Jones, however, has been pretty generally accorded the credit of producing the classical work upon this subject. By a large and varied series of experiments on animals he was able to give a complete account of the macroscopical appearances showing injuries to arteries, which account, in the main, holds good to-day. He found that when a large artery was divided it retracted into its sheath, and contracted slightly at its extremity (a coagulum forming within the sheath and external to the vessel, and appearing like a continuation of the artery); and that later a slender and conical coagulum formed within the vessel, being only partially adherent to its walls. Permanent occlusion, he says, is effected by the inflammation of the wall, the vasa vasorum pouring out lymph which, according to the theory of that day, became organized, that is, was endowed with an independent power of forming tissue. As the external clot was absorbed it was replaced by this coagulated lymph, the vessel in the mean time contracting up to the first branch, a delicate ligament being eventually all that remained. In partial division of the vessel, this writer tells us, a coagulum forms between the vessel and its sheath at the point of injury, and the wound in the wall is closed with coagulated lymph, which subsequently forms outside as well. Wounds less than one-fourth the circumference of the vessel in animals are capable of healing so as to occasion little or no obstruction in the canal, and rarely do such injuries lead to aneurism—a curious fact noticed by all subsequent experimenters. If the artery be surrounded by a tight ligature the middle and internal coats will be completely divided as if by a knife, the external coat remaining entire, upon the strength of which coat very much depends. He speaks of the "ulceration of the ligature," which expression at the present time, when both ends of the knot are cut short and it is allowed to heal in, conveys a false impression of the nature of the subsequent changes. The process of repair is essentially the same as that already described. He was inclined to attach too little importance to the thrombus, or internal coagulum, as he called it; and in ordinary accidents he thought it contributed nothing to the suppression of hemorrhage. Jones' views were generally accepted, but, since he differed essentially from Hunter respecting the rôle played by the internal thrombus, this question now became the chief subject of discussion, one party maintaining that the thrombus was organized and formed the cicatricial tissue; the other believing that this function was performed by the walls of the vessel, which were supposed to be united by an adhesive inflammation. In France the majority favored Hunter's views, though Andral believed with Cruveilhier in the correctness of the latter theory, as did also Guthrie in England. In Germany opinions were about equally divided until Stilling, by an elaborate series of researches, the most extensive since those of Jones, seems to have definitely settled the question that the thrombus did become organized. Guthrie also established the fact that a longitudinal slit in human arteries of medium size, as the temporal, may heal without obliteration of the vessel, and that in vessels of considerable size hemorrhage may be arrested without aid, the power and influence of the heart over the circulation through the arteries being greatly overrated; a fact also observed by Velpeau.

With the rise and progress of histological research the question of the organization of the thrombus was subjected to new tests. Schwann, in 1838, had developed his "cell theory," that it was only through the intervention of cells that further development could take place, and not, as Henle still maintained, through an amorphous blastema formed from coagulated lymph, which could be directly changed into new tissue.

Rokitansky called attention to the changes taking place in vessels which had been excluded from the circulation owing to a change in the current of the blood, as the umbilical arteries and the *ductus Botalli*, and he pointed out that the process was the same in ligatured vessels. It was not, in the opinion of this writer, through the intervention of a thrombus, but through a collapse in the walls and their subsequent fusion by the deposition of a new layer, that obliteration took place. Virchow, who was at first more or less influenced by the views of Hunter, as he became convinced of the power of cell action and inaugurated the theory of "*omnis cellula e cellula*," discarded the views of Schwann and Henle, and saw in the white corpuscles of the thrombus the organizing elements. Although he conceded that the vessels in the thrombus might be developed from the vasa vasorum, still he did not think that the presence of the cellular elements of the new tissue could be explained by a primary growth inward of the cells from the vessel wall. Both he and Rokitansky recognized that the spaces filled with fresh blood were not new-formed vessels, but channels hollowed out by the blood current which are to be distinguished carefully from the vascularization of the thrombus. This process was termed by Virchow the "sinus-like degeneration"; the term "cavernous metamorphosis" has also since been applied to it by Rindfleisch. The latter likened the thrombus to a tissue, of which the white corpuscles were the cells and the red corpuscles and fibrin were the matrix and the gradual series of changes of the white corpuscles into connective-tissue cells were described both by him and by O. Weber, who also thought that new blood-vessels were formed by them which subsequently united with the vasa vasorum. It was by these observers that the theory of the organization of the thrombus received its fullest elaboration.

Attention had, however, already been called, both in France and in Germany, to the action of the lining membrane of the vessel, and the views of the above-mentioned writers were further strengthened by an important communication from His, who showed that the endothelium was of an essentially different origin from the epithelium of the skin and mucous membranes, and belonged rather to the group of connective substances.

Waldeyer thereupon concluded that the endothelium was capable of producing a young connective tissue within the vessel, which tissue was subsequently vascularized by vessels springing from the vasa vasorum, and that the thrombus was absorbed as this tissue grew into it. The same thing, he thought, occurred in the blood clot in extravasation, the process of organization always taking place at the edges only.

The investigations of Recklinghausen on the wandering cells, and of Cohnheim on the passage of the white corpuscles through the walls of blood-vessels, turned the discussion into a new channel. The theory of the organization of the thrombus was now virtually abandoned, and the dispute, as to the origin of the cells found in the thrombus, now lay between those who derived such cells from the endothelium and those who assumed that they had wandered in through the walls of the vessels. While the views of Cohnheim, as to the origin of the new cells in inflamed tissues, were adopted by a large number of pathologists, there were still many who believed that the pre-existing cells of a part were capable of proliferation.

The study of endarteritis appears to have convinced most observers that the growths which eventually obliterate the smaller vessels arise from the internal tunic. A growth of mucous tissue is sometimes seen under the endothelium; at other times its upper layer also appears to be involved; and, if coagulation of the blood occurs, the cells may grow into the clot so formed. According to Cornil and Ranvier, a further growth of such tissue in larger vessels will lead to a breaking down of the media, and to a growth of cells outward into the adventitia. A number of observers have found a new formation of vessels in the obliterated artery produced by the force of the blood current forming a channel. Around such spaces may be seen newly formed elastic laminæ, constituting a newly developed wall for the new vessel, which thus does the work of a collateral branch. Analogy would suggest a growth also of the internal tunic in vessels after ligature, and Cornil and Ranvier, indeed, consider the two processes identical.

The weight of opinion latterly has been decidedly in favor of the activity of the inner tunic of the vessel in the healing process after ligature. Such is the view of those who have studied the subject in this country during recent years. Shakespeare derives the new formation from the endothelium and subjacent cells of the intima. A collection of these cells is to be found at the point of ligature at the end of the first twenty-four hours, forming a cushion upon which the clot is seen to be resting. To this new growth Shakespeare gives the name "plastic clot." The thrombus, or "fibrinous clot," takes no part in the process, but is pushed up by the plastic clot, in which latter signs of vascularization begin to show themselves as early as the sixth day, communication being effected with the vasa vasorum between the fifteenth and thirtieth days.

Senn finds that the cicatrix is the exclusive product of connective-tissue and of endothelial proliferation, and that permanent obliteration takes place in an artery in from four to seven days. This would imply a reliance chiefly upon the intima for the production of the new tissue.

Thoma has elaborated the views of Rokitansky on the analogy with the closure of the umbilical arteries and the *ductus Botalli;* and he has described the formation of a hyaline and fibrillated connective tissue in the deeper layers of the intima, as a compensatory endarteritis occurring at birth in that part of the arterial system specially concerned in the fetal circulation, in the arterioles of the kidneys in chronic nephritis, and in the stumps of arteries after ligature. The closure of an artery, he says, whether it occurs physiologically or as the result of an operation, depends upon the slowing of the current. It begins with a contraction of the media; if this contraction be enough to restore the normal rapidity of the circulation, further changes are confined to an atrophy of the muscular wall sufficient to correspond with the diminished calibre and diminished tension. If this change does not suffice, it is supplemented by a compensatory thickening of the intima. The observations of Schultz respecting the shape of the cicatrix in an arterial stump, on its elongation or thickening upon one side of the vessel according to the proximity of a branch, are in this way explained.

As to the cause of formation of the thrombus, Cohnheim takes the ground that it is due to an injury to the endothelium; the old view that it might be produced merely by a slowing of the current not holding good, for even in marasmic thrombi we find slight injuries to the internal membrane; moreover, a ligature may be put around the vessel without producing coagulation, provided the endothelium be not injured. Baumgarten thought to avoid formation of a thrombus by keeping the wound aseptic, but we find no other such observations recorded.

The shape of the thrombus is usually represented as ovoid, the apex, which is unattached, being directed toward the lumen of the vessel; the proximal thrombus is usually longer and always broader than the distal thrombus. Bryant explains the ampulla-like dilatation of the proximal end by the more rapid coagulation of blood here, which coagulation is attributed by Lister and Callendar to the greater turmoil into which the blood is thrown on the cardiac side by impinging against the obstruction, the churning process leading to the deposit of fibrin more or less pure; but they also agree that the deposit of blood clot is favored by slowness of movement, as on the distal side in the lower extremity when the anastomosis is not free.

It will be observed that those histologists who have interested themselves in the repair of arteries have considered the question usually from some special standpoint, such as the "organization of the thrombus," the rôle of the white corpuscles, of the wandering cells, or of the endothelium. We shall now undertake to follow 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 been fully completed. 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, in both there

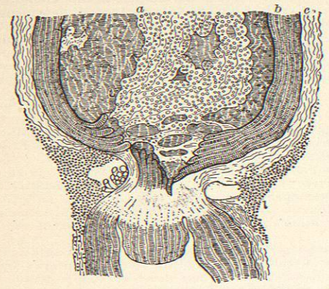

FIG. 319.—Ligatured Vessel. *a*, Proximal thrombus in ampulla-like dilatation of the vessel; *b*, media; *c*, adventitia; *l*, site of ligature. (Drawn from author's specimen.)

is a growth of tissue which has only a provisional existence, and in both the dense walls subsequently undergo certain changes which enable them to take a tardy but important part in the final cicatrization. In arteries, however, the external callus produces a ligamentous union only between the two fragments.

When a large artery is tied in its continuity, the intima and a variable portion of the media are usually ruptured, and the adventitia is gathered into a dense tendinous sheath around the constricted ends. The first noticeable change is the formation of the thrombi, which are usually developed within the first twenty-four hours, and the accumulation of a granulation-like mass of cells about the ligature, which, if it has been cut short, is completely enveloped by them. This growth appears to proceed from the periadventitial tissue, and varies according to the amount of injury done by the ligature to the vessel walls, or to the irritation which it produces. If the coats of the vessel have been unnecessarily bruised and a certain amount of extravasation has taken place in consequence, or if the ligature itself, for some cause, has created irritation, the surrounding inflammatory tissue will form a well-marked callus. If an excessive irritation has been produced, the growth of this protective tissue may be retarded, or it may be destroyed and the danger of hemorrhage correspondingly increased. Following the development of this external growth, we find that it extends some distance up and down the sides of the vessel in the periadventitial tissue, the round cells of which it is composed invading only the superficial layers of the adventitia; the breadth of the growth is, of course, greatest at the point of ligature; in length it reaches usually to a point on a level with the ends of the two thrombi; when fully developed it is consequently spindle-shaped (Fig. 319). At the point of ligature, where the fibres of the outer wall are densely packed (Fig. 319, *l*), the wandering cells do not penetrate during the first few days; but just above and below the ligature they may be found already invading the media as early as the second day; occasionally the apex of a pyramidal-shaped mass of such cells will have reached the thrombus. These cells appear to exert a solvent action on the bunch of fibres projecting from the ring of the ligature, which thus becomes gradually liberated from all connection with the vessel, the two ends of which now retract and leave the knot embedded in the centre of the callus. The fibres of the ligature itself soon become infiltrated with cells, and by the tenth day they may have already disappeared, or, if its resisting powers are greater, may remain encysted for some time. The period which the ligature requires for this separation varies greatly according to the size of the vessel and character of the ligature, and is longer in man than in animals. If the artery has been properly dissected out, this external growth will be observed forming a callus-like ring, in which the two ends of the vessel are embedded, in size about twice the thickness of the vessel, and it can still be seen well developed at the end of two months (Fig. 320). In the specimen from which the accompanying drawing was taken the ligature had caused suppuration about it, and had formed a fistulous track at the fundus of which some fibres were found still remaining. By the end of three months the external callus has disappeared, and only a slender cord unites the peripheral to the proximal end.

Already by the fourth day changes are noticed within the vessel. Observing the proximal thrombus we find an increase in the number of white corpuscles, particularly near the point of ligature, not in an isolated mass, but mingled with red corpuscles. Masses of coagulated fibrin with young cells (white corpuscles of clot, wandering cells from arterial coats, and rarely also peri-arterial tissues) are attached to the frayed ends of the media which have been cut by the ligature, and are more or less inverted. The endothelial cells, when not firmly compressed by the thrombus, as in the distal end, are in a state of activity, undergoing proliferation to a moderate extent. Occasionally, loop-like masses of cells may be seen projecting into the clot, or a delicate anastomosing network of stellate or spindle-shaped cells; but the total amount of this cell growth is small as compared with the size of the thrombus. In the mean time, in the second week, masses of granulation cells are seen infiltrating that part of the wall which is separating or has already separated from the ligature. Even at this period, with the external growth carefully dissected away, as is the custom in museum specimens, the vessel appears to have united by first intention, that is, by a direct union of the media and intima side to side. But the infiltration and softening continue until the walls are separated and expand, like the petals of a rose, yielding before the advancing growth of granulation tissue. The deeper portions of the clot are now infiltrated with two growths; the more superficial (that is, the portion nearest the open lumen of the vessel) is composed of tissue grown from the intima and media and wandering cells, and the deeper is composed of vascular granulation tissue which has pushed its way in from without. Viewed at the third week, the ends of the vessel will be found expanded and the space between them filled with well-formed granulations, such as are seen on the surface of a healthy wound. A portion of the thrombus, sometimes a large portion, has not been infiltrated, but is attached firmly to the top. A longitudinal section of such a specimen gives a striking illustration of what is understood as "healing by scabbing." As the clot shrinks the spaces left between the granulations, which have now rolled over one another in cloud-like masses, become continuous with the open

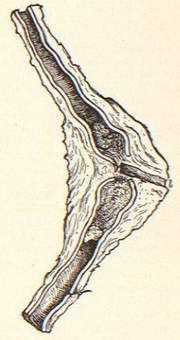

FIG. 320.—Carotid Artery of Horse Two Months After Ligature. *l*, Sinus at site of ligature; the ends of the artery have separated, but are enclosed in a firm callus. (Drawn from author's specimen.)

lumen of the vessel, and the so-called "canalization" of the thrombus is thus effected. An injection mass can be forced from the vessel for some distance into these spaces, but as yet they do not communicate with the vessels of the granulation tissue. This communication usually does not occur until the second month, that is, until the provisional growth has reached its period of highest development. The vessel walls have in the mean time been undergoing certain changes. A proliferation of the cells of the intima, as has been noticed by so many observers, unquestionably takes place; but the amount developed is not sufficient to supply more than a very small part of the provisional tissue. The cells, however, have begun to grow before the other tissue has made its way into the vessel, and at this period serve the purpose of attaching the thrombus to the walls of the vessel, but even in this work they are aided by other cells from the media. They also furnish a new endothelial covering to the permanent cicatrix, and a lining to the new vascular spaces that have been formed. When the elastic lamina has been ruptured (and this is frequently seen on the sides of the vessel near the ligature, and also here and there higher up as far as the thrombus extends), we find an intimate connection at such points of the media with new growing tissue within the vessel. In the second week, cells may be seen springing from the media and growing into either the clot or a clump of cells attached to the inner wall. The cells are round and spindle-shaped, frequently in bundles. Evidences of cell activity in the media are abundant, and in some specimens in animals a proliferation of the muscular cells through the whole thickness of the media is observed, giving a considerable increase to the width of this layer. The elastic lamina is frayed out at its divided end, and glistening elastic fibres are seen extending downward into the external growth as the two ends of the vessel gradually retract from each other. At the end of three months the provisional tissue has been absorbed, and we find the walls united by a permanent cicatrix which joins the sides of the vessel, still somewhat separated from each other. It consists, in medium-sized arteries, of a crescent-shaped mass of tissue, the concave side of which faces the lumen, while the horns run up on either side of the vessel. One horn may be long and the other short,

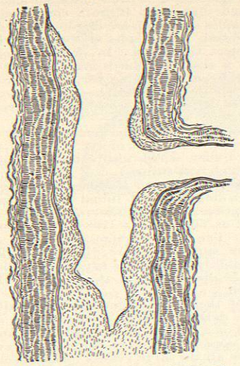

FIG. 321.—Carotid Artery of Dog Four Months After Ligature, showing shape of cicatrix as modified by the presence of a branch. (Drawn from author's specimen.)

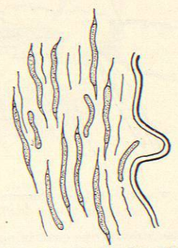

FIG. 322.—New Muscular Cells in the Cicatrix; from the femoral artery of a dog three months after ligature. (Drawn from author's specimen.)

the crescent being placed somewhat excentrically. The longer horn may be sometimes thickened (see Schultz and Thoma), as in Fig. 321, if a branch lies opposite to it. In the largest vessels the cicatricial tissue occupies a considerable portion of the calibre of the vessel.

On the surface of the cicatrix is seen a thin layer of endothelium; beneath this, in medium-sized vessels, there can be seen a layer of delicate, tapering, spindle cells with staff-shaped nuclei, forming a continuous layer from one horn to the other. They run parallel to one another and to the arc of the circle made by the crescent, and resemble in all respects muscular cells; in short, a genuine muscular layer is found here (Fig. 322). Beneath this layer is a mass of cicatricial connective tissue which plugs the space lying directly between the ends of the retracted walls (Fig. 323). The cicatrix is pierced by a vessel of considerable size which rapidly tapers to a point and anastomoses with a capillary network, ramifying both in the cicatrix itself and in the ligamentous band outside. This central vessel, which in larger cica-

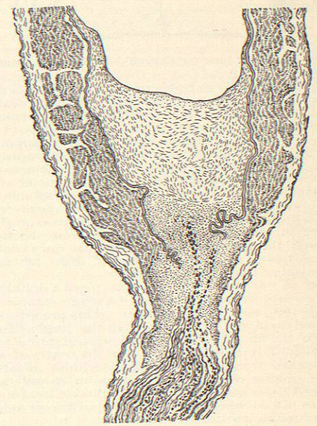

FIG. 323.—External Iliac Artery of Man One Hundred and Thirty Days After Ligature: formation of permanent cicatrix. (Drawn from author's specimen.)

trices becomes tortuous and gives to the cicatricial tissue a "cavernous" appearance, may be regarded as the unobliterated residuum of the lumen.

We find in this anatomical peculiarity of the cicatrix an explanation of its immunity from aneurismal dilatation. The protective influence of the thrombus enables the process of cicatrization to complete itself before the cicatrix is called upon to withstand blood pressure, and it is then armed with a muscular coat (as is the normal vessel wall), which acts not unlike a levator ani muscle in sustaining and modulating the force of the blood column.

The ligament which unites the two ends of the vessel represents, in part, the residue of the external callus; it has become much elongated by the retraction of the two ends. During the healing process, a small portion of the vessel walls has become disintegrated by the new growth, and a portion has atrophied and has been absorbed, the remaining walls have shrunk greatly by retraction, and their calibre has been filled to a greater or less extent by a cicatricial tissue; so that the vessel has