1903

Modern Surgery - Chapter 4. Repair

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IV. REPAIR.

When a tissue is damaged, it reacts to the injury and Nature attempts to effect repair. It is held by many that inflammation is a destructive process and repair is a constructive process; that repair is constantly effected in an aseptic wound without many of the evidences of inflammation; that repair does not proceed from inflammation, but is retarded or prevented if inflammation occurs. As before stated, we agree with Adami, that inflammation is reaction to injury and the effort of Nature to repair the injury. As Adami points out, the attempt to repair may fail, the reaction to injury being excessive or not powerful enough; but even should the attempt fail, the conservative intention exists. "What is the development of cicatricial tissue but an attempt at repair? What other meaning can be ascribed to the increased bactericidal power of the inflammatory exudate as compared with that of ordinary lymph and blood-serum? Why do leukocytes accumulate in a region of injury? Why do some of them incorporate bacteria and irritant particles, and others bring about the destruction of these without necessarily ingesting them? All these are means whereby irritants are antagonized or removed, and reparation and return to the normal sought after." *

Repair is favored by good general health, asepsis of the wound, coaptation of wound edges, and rest. It is retarded or prevented by infection, gaping of the wound, frequent or forcible motion, and impairment of the general health. Albuminuria and diabetes particularly obstruct repair. R. T. Morris points out that sugar in the blood is hygroscopic, removes water from the tissues, and thus obstructs repair; and also that the wound fluids contain sugar and are good culture-media ("Med. News," June 29, 1901).

Healing by First Intention.—A wound may heal by "first intention." This mode of healing, which is known as "primary union," occurs without suppuration, and is observed in the healing of an aseptic wound. If infection occurs, primary union will not take place. The phrase "by first intention" comes down to us from the past. It was properly thought that Nature intends to repair a wound, and first intention signifies the first or most desirable way to be wished for. In a small aseptic incision, in which no considerable vessels are cut, repair will take place very rapidly after the edges have been approximated and the wound dressed. In fact, the wound edges may be firmly held together in twenty-four hours. In such a wound a small amount of blood flows from the capillaries between the edges of the wound, and this blood clots. A trivial amount of exudation and some few migrated corpuscles pass into the clot and into the tissues. The fixed connective-tissue cells and the endothelial cells of the vessels multiply, and form epithelioid cells, known as fibroblasts. The fibroblasts eat up many of the leukocytes and multiply, so that the new cells from one side of the wound finally interlace with the new cells from the other side. Nearby capillaries become irregular in outline; at certain points bulging occurs, and at these points new capillaries develop, extend into the mass of fibroblasts, and join new capillaries of the opposite side. The reparative material is now said to be organized; it has

* Adami, in Allbutt's "System of Medicine."
become granulation tissue. The fibroblasts become spindle-shaped and develop into interlacing fibers (Fig. 31). The tissue is now fibrous tissue; it contracts strongly, and finally most of the capillaries are obliterated by pressure. In such a slight wound the reaction to injury is chiefly noted in the cells of the part, and the vessels and leukocytes play but a small part in repair. The exudation is so scanty that there is practically no swelling unless some arises from venous obstruction. The vessels are so slightly affected that there is no redness. The final step in healing is contraction of the fibrous tissue and the covering of the surface with epithelium, which springs from the epithelial cells upon the edges. This final process is called "cicatrization," and consists in the formation from fibroblasts of new fibrous tissue and the contraction of the new tissue. The "immediate union" of some writers never occurs. This term means the union of microscopical parts to their counterparts without any effort at repair. A first union is effected always by clotted blood and coagulated exudate, next by proliferating cells, and finally by fibrous tissue. A wound healing by first intention exhibits no evidence of inflammation. There is some slight tenderness, but no actual pain. A certain amount of swelling arises because of exudation of fluid from the blood, and the coagulation of this fluid makes the wound edges hard. Venous obstruction leads in some cases to a considerable fluid swelling. A wound may heal by first intention even if some bacteria are present, if the part has a good blood-supply and the patient is in good health. Active leukocytes and germicidal blood-serum may prevent infection. In a more extensive incised wound many vessels are cut. After oozing ceases the vessels are closed by clots continuous with the clot between the sides of the wound. An exudation of plasma from the blood-vessels and of lymph from the lymph-spaces takes place. Leukocytes in great numbers invade the wound edges and the exudate, and the exudate clots. Thus, an infection may be surrounded and limited. This mass of blood-clot, plasma-clot, and leukocytes used to be known as "coagulable lymph." The leukocytes actively eat up the clot, and by the end of the third day occupy the space formerly occupied by the clot. The fixed connective-tissue cells and endothelial cells multiply and grow into the mass of leukocytes, eating up many of the leukocytes, and finally join the fibroblasts of the other side of the wound. Some leukocytes enter into the lymph-spaces. New capillaries form from the capillaries at the wound margins. By the end of the first week the fibroblasts begin to assume various outlines, sending out poles or branches or becoming spindle-shaped. These spindle-shaped cells become fibers, and the fibers of the new tissue interlace and strongly contract. Thus the edges are pulled firmly together. Finally new epithelium derived from epithelium at the edges forms and grows over the wound (Figs. 34–36), and exhibits the stages of repair in healing by first intention. In order to obtain primary union the surgeon must cleanse the wound and must be thoroughly aseptic; bleeding must be carefully arrested; the parts are accurately coaptated by sutures; aseptic or antiseptic dressings are applied, and special care is taken to secure rest. In a large wound special methods to secure drainage are required. In
a small wound drainage is obtained between the stitches. The use of irritant germicides in a wound greatly increases the amount of discharge and renders drainage necessary in even a comparatively small wound for the first twenty-

four hours. During the first twenty-four hours after a large wound begins to heal by first intention the discharge of bloody serum is most plentiful, but after this period it becomes very scanty and soon ceases entirely, and can be much
diminished in quantity in the first day by the application of pressure. Warren says that after a hip-joint amputation over a pint of bloody serum flows out during the first twenty-four hours. In an aseptic wound, as a rule, one-half of the stitches are removed on the fifth or sixth day and the remainder on the eighth day, but for two weeks more the wound should be rested and supported, as the new tissue is not very resistant to infection. Aseptic fever always arises when much exudation is given out and not quickly and perfectly drained. Aseptic fever is due to the absorption of aseptic pyrogenous material (page 105). If an incised wound becomes infected, the pyogenic organisms destroy the bond of union which is forming between the wound edges by liquefying the intercellular substance. As a consequence, the wound edges are widely separated by pus.

What used to be known as "healing by blood-clot" is healing by first intention. If there is a considerable gap between the edges of an aseptic wound, and the gap is filled with a blood-clot, healing goes on in the same manner as when the gap is narrow, although more corpuscles, more exudate, and more fibroblasts are required to effect repair.

Healing by Second Intention.—Healing of a wound in which there is a large cavity in the tissue or in which the edges have gaped apart is known as healing by granulation, or healing by "second intention." It is effected in the same manner as healing by "first intention," the processes in the two cases being practically identical. As a matter of fact, in healing by granulation there is usually wound infection. As a result of infection intercellular substance is peptonized, many reparative cells are cast off, and repair can be effected only after the formation of enormous numbers of fibroblasts and the expenditure of considerable time. It requires much longer for an infected wound to heal than for an incised wound to be repaired, and an infected wound can heal only by granulation. A short time after the infliction of a wound the oozing ceases because thrombi form in the vessels and some clot gathers in tissue-gaps and interstices. Exudation begins and leukocytes migrate into the exudate and into the walls of the wound. In an hour or two the surface of the wound becomes distinctly glazed or glistening, because of the formation and coagulation of fibrin. The exudation is at first thin and red, and it becomes so profuse as to wash away the discolored fibrin coat. In a few days the discharge usually becomes purulent. The connective-tissue cells, especially the endothelial cells of the vessels, proliferate and form fibroblasts, and the fibroblasts multiply to close the wound. From adjacent capillaries new capillaries form. This formation takes place as follows: A portion of a capillary thickens and a whip-like process comes off from the thickened part. This process fuses with a second filament budded from another or from the same capillary, or runs straight out as a terminal vessel. The filaments after a time are hollowed out from within, protoplasmic tubes are formed, and endothelial cells develop from the protoplasm. In some cases a tubular prolongation comes off from a capillary directly. Fig. 37 shows the formation of a capillary. In a wound healing by granulation these newly formed capillaries run among the fibroblasts, and some of them run perpendicularly to the surface, or a loop forms and reaches the surface. The surface of a granulating wound is covered with migrated leukocytes, and directly under these are fibroblasts covering the new vascular strings or loops. Vascular strings
or loops coated with fibroblasts are called granulations (Fig. 39 shows a granulating surface). When the discharge becomes purulent, many leukocytes and fibroblasts are destroyed, inflammation increases, exudation becomes profuse, and cellular multiplication widespread and rapid in order to make up for the cells lost by microbial action. Gradually the gap is filled. As it is being filled the older fibroblasts in the deeper layers of the edges and base of the wound are converted into cicatricial, fibrous, or scar tissue. (Fig. 38.) As the granulations rise to a higher level at the surface the area of fibrous tissue becomes broader at the base and margins, and this young fibrous tissue contracts. By contracting it draws the edges of the wound nearer together and thus lessens the area of the surface which must be covered with epithelium. When the granulations reach the level of the cutaneous surface the epithelial cells at the margin of the wound proliferate, and young epithelial cells, constituting a bluish or opalescent film, grow over the granulations. Epithelium comes only from epithelium. Granulations are never converted into epithelium. The epithelial covering comes only from the epithelium at the wound margins, unless there be epithelial remains in the wound; for instance, an undestroyed papilla,
sweat-duct, or hair follicle. The process of covering the surface with epithelium is known as epidermization. The epidermization of a large area always consumes considerable time and sometimes Nature fails to accomplish it. In such cases skin-grafting is employed (q. v.). Before, during, and for a time after epidermization the fibrous tissue of the walls and base of the wound contracts. Thus the wound margins are pulled and held nearer together, the gap to be bridged is diminished in size, the danger of tearing apart of the epithelial coat is lessened, many capillaries are destroyed by pressure, and the scar becomes firm, white, and puckered. Cicatrization consists in the conversion of immature connective tissue into mature fibrous tissue and in the contraction of the new fibrous tissue. If infection is severe, destruction will exceed repair and healing will not occur. In such a case there is coagulation necrosis of granulation tissue, and the wound becomes covered with tissue remains (aplastic lymph). If granulations rise above the cutaneous level, healing will not take place, because the epithelium cannot then grow over the raw surface. A wound in this condition is said to possess exuberant granulations, or proud flesh. In some cases the granulations are pale from insufficient blood-supply, and in others edematous from venous congestion. Contraction of the fibrous tissue may be insufficient because there is adhesion to deep unyielding fascia or to periosteum. Excessive contraction, so often seen after burns, often produces terrible deformity. The scars or cicatrices of burns contain much elastic tissue. Infected wounds and ulcers heal by second intention.

Healing by Third Intention.—This consists in the union of two granulating surfaces, the granulations of one side fusing with the granulations of the other side. It is seen in the union of collapsed abscess-walls. The surgeon occasionally seeks to obtain union by third intention by approximating two granulating surfaces. If the surfaces are aseptic, he will often succeed. The process follows what is known as secondary suturing. It is not unusual to pack a wound with iodoform gauze to control oozing. When this is done it is customary to pass the sutures, but not to tie them. After a few days the gauze is removed and the sutures are tied. This plan renders healing much more rapid than could be obtained by the process of healing by second intention.

Healing of Subcutaneous Wounds.—Blood fills the tissue-gap and the blood clots. Plasma exudes and corpuscles migrate into the clot and the tissue about it. The clot is eaten up by the leukocytes. The connective-tissue cells and the endothelial cells of the adjacent tissue proliferate and form fibroblasts, and fibroblasts multiply and replace the clot. The area of fibroblasts is vascularized by the formation of new capillaries, and fibrous tissue forms and strongly contracts.

Healing of Wounds in Non-vascular Tissues.—In a trivial injury of the cornea a few leukocytes gather from the lymph-spaces and a few of the fixed cells proliferate. When the cornea is distinctly wounded, an increased
flow of lymph occurs. The nerves are irritated, vessels adjacent to the cornea distend, and many leukocytes invade the lymph-spaces. The corneal corpuscles multiply and alter in shape. The product of the process may be transparent if fibrin is absorbed and leukocytes pass away, for proliferating corneal corpuscles form transparent tissue. The surface epithelium is replaced by proliferation of the deep layer of corneal epithelium. If the wound has penetrated the posterior portion, it is filled by proliferating epithelium from the membrane of Descemet. In a severe injury of the cornea endothelial cells and corneal corpuscles proliferate, vessels grow in from the corneal margins toward the seat of inflammation, fibrous tissue forms, and permanent opacity results.

Repair in cartilage, if it occurs at all, is very slow and is accomplished in the same way as repair in the cornea. Any marked injury is repaired by white fibrous tissue, furnished by the cells of the perichondrium, and the scar is permanent.

**Cell-division.**—The multiplication of connective-tissue cells in repair may be by direct, but is usually by indirect, cell-division. Direct cell-division consists in division of the nucleus followed by division of the entire cell. Indirect cell-division, or karyokinesis, takes place after remarkable changes in the nucleus. The membrane of the nucleus disappears; the nuclear network becomes first close and then more open; and the cell becomes round, if not so before. The network of the nucleus, now consisting of one long fiber, takes the shape of a rosette; next it takes a star form—the aster stage; two sets of V's next form—the equatorial stage; an equatorial line appears and widens, and each set of V's retreats toward a pole. Thus two new nuclei are formed, each polar V passing in inverse order through the previous changes of shape, and the protoplasm of the original cell collecting about each nucleus (Fig. 40).

**Repair of Nerve.**—A nerve-fiber consists of a core known as the axis-cylinder, which is the essential element in function. About the axis-cylinder is an almost liquid material, known as the medullary sheath or white substance of Schwann, or myelin. The myelin is surrounded by a firm sheath known as the neurilemma (sheath of Schwann, primitive sheath, neurolemma). On its inner surface, or between it and the white substance of Schwann, are nuclei which are supposed by some to be peripheral nerve-cells (neuroblasts). The neurilemma is absent in the brain and cord. The continuity of the white substance of Schwann is interrupted at frequent intervals, and these breaks in the myelin are called nodes of Ranvier. Numbers of fibers of the kind just described, bound into bundles by connective tissue and surrounded by a fibrous sheath, constitute a nerve. It is known that a nerve may be regenerated and completely regain function after division; that regeneration is strongly favored by suturing the ends together; and that if the ends of a divided nerve are more than one inch apart, regeneration will rarely take place unless they are sutured together. The method by which regeneration is effected has been much disputed and is still involved in uncertainty. If a nerve is divided, the peripheral segment at once loses its function and then undergoes degeneration (Wallerian degeneration). The degeneration begins within twenty-four to forty-eight hours and affects the entire peripheral segment. The axis-cylinder perishes, the myelin runs into globules and is absorbed,
leaving an almost empty sheath; the nuclei of the inner surface of the neurilemma proliferate for a time, but cease to do so before the myelin is completely absorbed. The sheath shrinks and looks empty, but here and there are collected masses of proliferated nuclei and protoplasm. The common view is that regeneration takes place as follows: The nuclei again proliferate and form a mass of protoplasm within the old sheath, which protoplasm joins the proximal segment. Such a protoplasmic fiber has "conduction and irritability" (Raymond's "Human Physiology"), but there is as yet neither myelin nor axis-cylinder. "The fiber is responsive to mechanical stimuli, but not to induction shocks, which latter property returns only after the axis-cylinder is developed. The medullary substance later appears and forms a tube; and still later the axis-cylinder is formed, having its origin in the central end of the nerve" (Raymond's "Human Physiology").

Degeneration takes place in days, but regeneration requires months. Regeneration takes place by the multiplication of pre-existing nerve-fibers and not by the transformation of connective tissue into nerve structure. The ends of a divided nerve, it is true, are united by connective tissue formed by the proliferation of fibroblasts, but this connective tissue is only a bridge to carry nerve elements across the gap between the proximal and peripheral segments. The new axis-cylinder of the peripheral segment is a prolongation of the old axis-cylinder of the proximal segment, projected in the following manner. A fiber, which is at first devoid of myelin, is prolonged from a proximal axis-cylinder; it divides into many cylinders, which pierce the granulation tissue between the ends and enter into the empty sheaths of Schwann of the distal segment or insinuate themselves between these sheaths (Ranvier, Réclus, Senn). The above is the view entertained by those who teach that the new axis-cylinders come entirely and only from the prolongation of old axis-cylinders of the proximal segment, and that the distal segment is passive in the process until "neurotised" (Vanlair), and that regeneration is impossible in the distal segment unless it is in approximation with the proximal segment or within easy reach of the prolongations of the axis-cylinders from above. Another view is that the axis-cylinders, myelin, and neurilemma are formed from cells which exist in the distal segment, and that juvenile axis-cylinders and medullary sheaths are formed in the peripheral portion and then effect a junction with like structures of the central segment. The last-mentioned view is advocated by Mayer and Eichhorst, Tizzoni, Cattani, and others, and Ballance and Stewart have recently published a most valuable monograph advocating it ("The Healing of Nerves"). The views of Ballance and Stewart may be set forth as follows: When a nerve-trunk is divided, the peripheral segment degenerates whether it has been sutured to the proximal segment or not, and the portion of the proximal segment near the wound also degenerates. The injury produces at once an effusion of blood, migration of leukocytes takes place into and about the wound at the proximal segment, but leukocytic invasion of the entire distal segment is noted. After three days connective-tissue cells begin to replace the leukocytes, and after two weeks the excess of leukocytes is no longer observed, proliferated connective-tissue cells having taken their place (page 94, "Healing of Nerves"). The proximal segment in the neighborhood of the wound and the entire distal segment are invaded by proliferating connective-tissue cells. The connective-tissue cells
completely absorb the fatty myelin and axis-cylinders. The cells of the neurilemma actively multiply, and connective-tissue cells lying among chains of neurilemma cells become spindle-shaped and “the degenerated nerve-trunk therefore becomes hard, fibrous, and cirrhumed” (Ballance and Stewart on the “Healing of Nerves,” page 95).

In the proximal end of a divided nerve an “end-bulb” is formed. This was long supposed to be due to the prolongation of nerve-fibers from the central fibers and a turning backward because they cannot cross the gap. As a matter of fact, the ends of the divided fibers curl up; on and in this scaffold-like arrangement new fibers are placed, they having been produced by the neurilemma cells which have taken on “neuroblastic function” (Ballance and Stewart). When a nerve has been sutured, the earliest signs of regeneration “occur at the end of three weeks” (Ballance and Stewart). Short lengths of new fibers are laid down within old neurilemma sheaths. The new axis-cylinder “is seen to consist in the deposition along one side of a spindle-shaped neurilemma cell, of a thin thread which grows in length until it projects beyond the limits of the parent cell and stretches on toward its next neighbor in the same longitudinal row” (Ballance and Stewart). The new medullary sheath is “laid down by a process of secretion” (Ballance and Stewart) along the sides of the neurilemma cells.

Ballance and Stewart go on to point out that if the central theory of regeneration is true, not a trace of regeneration could occur in the distal segment when the two segments have not been united by sutures, and yet such regeneration does occur, although slowly, the new axis-cylinders and medullary sheaths not attaining full size. “Evidently some stimulus afforded by the conduction of impulses is necessary in order to permit of their full development” (Ballance and Stewart). In the notable study quoted at such length are some experiments on the “conduct and fate of transplanted nerve.” When the gap is wide between the two ends, a portion of fresh nerve-trunk may be inserted to bridge it. The transplanted piece degenerates; it is invaded by leukocytes, and proliferating connective-tissue cells, medullary sheaths, and axis-cylinders are destroyed, but regeneration may subsequently occur; “but when it does occur, it is not from the activity of the cells of the graft itself” (Ballance and Stewart). Blood-vessels enter the degenerated graft at each end and they are accompanied by chains of neurilemma cells, which form axis-cylinders and medullary sheaths. The graft is merely a scaffold (Ballance and Stewart).

The studies of Ballance and Stewart persuade us that regeneration does occur in the distal part independently of the proximal part, although full development does not take place unless there is a junction with the central part. As to the exact method of regeneration we still feel somewhat uncertain. When we remember that the nerve-fibers of the spinal cord are devoid of neurilemma and that the cord can regenerate, we must conclude that regeneration can take place in the cord without the aid of neurilemma cells, and must infer that the same may be true in a nerve.

**Repair of the Spinal Cord and Brain.**—Can the spinal cord regenerate? Many observers have doubted it. But there is no doubt of the fact that sometimes, after the subsidence of an acute myelitis or the relief of a pressure which produced complete and prolonged paralysis, there is a return
of functional power. It is usually assumed that restoration is possible in fibers which have not been hopelessly damaged, but is not possible in those which have been destroyed; but, as Gowers says, there are cases in which "we can scarcely believe that the axis-cylinders retain their continuity, although conducting capacity is ultimately restored." Clinical evidence indicates strongly that the pyramidal fibers may regenerate. Mills says ("The Nervous System and Its Diseases"): "Nerve-tracts in the spinal cord and brain have power to regenerate, but this is not so great as in the peripheral nerves, and yet even old cases of compression of the spinal cord may make great improvement after a long time, largely through the regeneration of the columns of the cord." Mills affirms that although nerve-cells sometimes appear to regenerate, the destruction in these cases was not complete.

When axis-cylinders have been destroyed in the cord and yet some power returns, we ask ourselves if this occurs because new fibers have grown down from above. Gowers says that such a growth has been proved to occur in the lower animals, but has not as yet been demonstrated in man; although specimens have been described which strongly suggest such an occurrence in the human subject. That the cord can regenerate was recently proved. Dr. Francis T. Stewart, of Philadelphia, sutured a completely divided spinal cord and an extraordinary restoration of function took place (Francis T. Stewart and Richard H. Harte, in "Phil. Med. Journal," June 7, 1902). This case is commented on at some length in the section on Injuries of the Spinal Cord.

Many claim that a brain injury cannot be followed by repair with restoration of function; some think that complete regeneration can take place; others, that partial regeneration may occur. Vitzon and Tedeschi even believe that nerve-cells in the brain can regenerate. It seems probable that extensive injuries are not repaired, but slighter ones may be, new ganglion-cells and neuroglia being formed. Tedeschi describes the process of repair after a wound of the brain as follows: Degeneration occurs and a limited focus of necrosis forms and then the adjacent tissue shows evidences of repair. Capillaries form from the endothelial cells, glia tissue from the neuroglia, ganglion-cells present karyokinetic changes, and some nerve-fibers appear in the scar (Senn's "Principles of Surgery").

Repair of Muscle.—It has long been taught that the repair of muscle by muscle is impossible, and, as a matter of fact, it does not take place if the ends of a divided muscle are separated to the extent of an inch or more. When a muscle is divided transversely by a considerable cut, the ends retract and a wide space is left between them. Blood flows into the space between the ends and also between individual fibers of the injured muscle, and the blood clots.
Exudation of plasma occurs and migration of corpuscles takes place. Fibroblasts are produced by proliferation of connective-tissue cells and a mass of fibroblasts soon replaces the blood-clot. Granulation tissue is formed by vascularization of the mass of fibroblasts, and granulation tissue is converted into scar tissue, but not at all into muscle. After slight injuries a trivial amount of muscular regeneration does occur by the multiplication of living muscle-cells, but not by metamorphosis of fibroblasts. Fibroblasts are incapable of a transformation into muscular tissue. When the ends of a divided muscle are separated to a slight degree or when they have been brought together and sutured, some muscular regeneration occurs. After an injury some of the muscular fibers wither, perish, and are absorbed. The process of regeneration arises from the remaining fibers. The nuclei of the muscle-fiber proliferate and so do the nuclei of the perimysium. The muscle-cells are called myoblasts and the nuclei of the perimysium are called sarcoblasts. About the juvenile muscle-cells a deposit of protoplasm takes place (Weber). The embryonal cells gradually become spindle-shaped and muscular fiber is formed by cellular fusion or by elongation of individual cells.

The above remarks refer to striated muscle. Unstriated muscle fibers are repaired solely by "indirect multiplication of their nuclei" (Senn).
If a muscle has been divided, it should be sutured. This process insures more rapid repair and secures a better functional result, and is followed by much muscular regeneration.

**Repair of Tendon.**—When a tendon is divided, the ends retract, and the sheath, as a rule, becomes filled with blood-clot. The blood-clot is rapidly removed, fibroblasts replacing it. This new tissue arises from the sheath, and the cut ends of the tendon do not participate in the process. Granulation tissue is formed; this is converted into fibrous tissue, and after a time the fibrous tissue becomes true tendon. If no blood-clot forms in the sheath, the walls of this structure collapse and adhere, and the separated tendon-ends are held together by a flat fibrous band formed from the collapsed sheath (Warren's "Surgical Pathology").

**Repair of Bone.**—When a bone is broken, a blood-clot quickly forms in the medullary cavity, between the broken ends and under and outside the periosteum. Leukocytes invade and destroy the clot. The cells outside the periosteum, the cells of the periosteum and of the medullary tissue, particularly the endothelial cells, proliferate and produce cells which are practically fibroblasts. The osteoblasts in the medullary tissue and in the deeper layers of the periosteum multiply and are distributed through the mass of fibroblasts. The osteoblasts may form bone directly or may form cartilage first. Some teach that fibroblasts can be converted into bone; others positively deny such a conversion. The point is not settled, but it is well to remember that in myositis ossificans a muscle is converted into bone, and hence it is probable that fibroblasts formed from periosteum and medullary tissue will be much more prone to undergo such a development. During regeneration the bone ends soften and are partially absorbed by osteoclasts. These cells are large osteoblasts which have lost the power of bone production and furnish a secretion which dissolves osseous matter. The excess of callus is finally absorbed by osteoclasts. (For a more extended description see Repair of Fractures.)

**Repair of Blood-vessels.**—If an artery is cut across and ligated, a clot forms within its lumen and about its divided end, and the circulation in the vessel at this point is permanently arrested. The proximal clot, it used to be thought, always reaches the first collateral branch. This statement was true before the days of asepsis; it is not always true now. Often a clot stops far short of the branch above. Exudation of plasma and migration of corpuscles take place from the vasa vasorum. The clot becomes filled with leukocytes, which gradually destroy it, and it plays no active part in repair. Fibroblasts form by the multiplication of the cells of the vessel wall and the clot is now replaced by fibroblasts. The fibroblasts are converted into granulation tissue, granulation tissue becomes fibrous tissue, the fibrous tissue contracts, and the artery is converted into a fibrous cord (Fig. 133). Warren insists that the muscle-cells of the middle coat play an active part in repair. Usually, when a ligature is applied to an artery in continuity, a deliberate attempt is made to rupture the internal and middle coats, in order to permit of contraction and retraction above and below the seat of ligature, and a turning inward of the inner coat. Such a sequence of events happens when an artery is completely divided across and not tied, and favors the rapid formation of a clot.

Ballance and Edmunds ("Ligation in Continuity") maintain that repair
Repair

is obtained most rapidly when the artery is tied with two ligatures, the vessel at this point being deprived of blood, but the internal and middle coats being kept intact. Cell-proliferation forms a spindle-shaped mass of new cells and the lumen is obliterated at the seat of ligation by fibroblasts obtained from the fixed cells of the wall of the artery. Senn advocates the employment of two ligatures, not placed side by side as in the method of Ballance and Edmunds, but so applied as to include "a bloodless space about half an inch in length" (Senn's "Principles of Surgery"). When a lateral ligature is applied to a vein or when a small wound in a vein or artery is sutured, the circulation in the vessel is not completely cut off, a thrombus of small size is formed on the vessel-walls, the fixed cells of the vessel-wall proliferate, and a scar of fibrous tissue effects repair. A completely divided vein heals as does a completely divided artery (Fig. 134). The clot after the aseptic application of a ligature to a vein may be of slight extent, but in some cases the proximal clot reaches the first collateral branch and in others goes far above it.

Repair of Skin.—The fibrous structure is repaired by fibrous tissue. Hair follicles, sweat-glands, and sebaceous glands are not reformed. The epithelial layer is regenerated by the proliferation of adjacent epithelial cells. Lymphatic tissue can regenerate either from the fatty tissue, the divided ends of the lymph ducts or both structures. The kidney and testicle can undergo some regeneration. The liver and spleen can undergo considerable regeneration.