3.

EXPERIMENTAL RESEARCHES.

EXPERIMENTAL RESEARCHES

ON

CICATRIZATION IN BLOODVESSELS AFTER LIGATURE.

BY

N. SENN, M.D.,

OF MILWAUKEE, WISCONSIN.

Extracted from the
Transactions of the American Surgical Association,
Vol. II. 1884.

PHILADELPHIA:
COLLINS, PRINTER, 705 JAYNE STREET.
1885.

EXPERIMENTAL RESEARCHES ON CICATRIZATION IN BLOODVESSELS AFTER LIGATURE.

SKILFUL treatment of hemorrhage is an infallible criterion of good surgery. Dieffenbach has well said, "From the behavior of a surgeon in cases of severe hemorrhage are we able to judge of what metal he is made." The mechanical measures employed in the management of hemorrhage have at all times constituted subjects of special interest to surgeons. Presence of mind, a steady hand, prompt action, an accurate anatomical knowledge, familiarity with the various hæmostatic agents, and clear ideas on the process of cicatrization in vessels, are prerequisite conditions of success in the treatment of the most frequent, and, at the same time, the most alarming emergency which presents itself to the surgeon—hemorrhage.

Ignorance, hesitation, and timidity, in the event of sudden, unexpected, and alarming hemorrhage, only too often mean death, while, on the other hand, the exercise of skill founded on knowledge is often the means of saving human life under the most desperate circumstances. For the benefit of suffering humanity fear of hemorrhage has deterred pretenders from performing bloody operations, which has left the cultivation of the field of operative surgery to men of skill and science.

Perhaps no branch of surgery has reached a higher degree of perfection than the treatment of injuries and diseases of the bloodvessels. The bold operations which have characterized the present era of surgery owe their inception and their legitimacy to the aseptic ligature. The aseptic ligature and the antiseptic treatment of wounds have rendered secondary hemorrhage an exceedingly rare accident after operations. Every surgeon of the late war of the rebellion is painfully aware of the frequency with which secondary hemorrhage occurred after gunshot injuries or any of the capital operations. Billroth reported 23 cases of ligation of large arteries after gunshot wounds, and of this number in seven, or 30.4 per cent., secondary hemorrhage took place. Porta collected 600 cases of ligation of large arteries, including the aorta, innominata, carotid, subclavian, axillary, common iliac, external iliac, and femoral; of this number 75, or 12.5 per cent., were followed by secondary hemorrhage. Pilz has published a table of ligation of the common carotid artery where the operation was done 158 times for hemorrhage; of these cases 35, or 33.5 per cent., suffered from secondary hemorrhage, which proved fatal in 16, or 15 per cent. How different the results of to-day! An artery is ligated, the ligature is cut short, the wound heals by primary union, and permanent obliteration of the vessel is the rule. The aseptic ligature, wherever and whenever it can be applied, has almost entirely displaced all other hæmostatic agents, and is now universally acknowledged as the safest and most reliable measure in securing provisional and definitive closure of vessels. Like all material improvements, it has met with opposition, but a more extended trial has silenced criticism. Every surgeon should be in possession of clear and definite ideas of the processes which nature employs in effecting cicatrization in bloodvessels after ligature, so as to qualify him to select and apply the various hæmostatic agents intelligently, and to measure their effect by well-defined anatomico-pathological principles.

This subject has for a long time furnished a fertile field for theoretical speculations, pathological investigations, and experimental research.

For more than forty years the doctrine has been prevalent that definitive closure of a vessel after ligature is invariably due to the formation and organization of a thrombus. The doctrine is still taught by many of our teachers and recent text-books on surgery. The object of this paper is to disprove this assertion, and to establish the fact that the production of the intravascular cicatrix is always the result of proliferation of the stable connective-tissue cells and endothelia of the walls of the vessel independently of the formation of a thrombus. The various theories which have been advanced to explain the process of obliteration in vessels will be briefly mentioned in their proper order, and the results of different methods of experimentation will be described, and, finally, the results of my own experimental work will be noticed, thus bringing the whole subject of cicatrization in bloodvessels after ligature before the Fellows of the Association for further consideration and discussion.

I. *History of the Ligature.*[1]

For a better elucidation of our subject it is necessary to briefly pass in review the history of the ligature, as it will reflect in a true light the pathological ideas entertained by surgeons at different times regarding its immediate and remote effects in arresting the circulation in a vessel after ligation.

The history of the ligature has been variable and eventful, and has always been intimately connected with the history of surgery, ever constituting a reliable barometer indicating the status, the rise and fall, in the art and science of surgery. Its use as a hæmostatic agent was not the result of reasoning or logical deduction, but was prompted by instinct. It was used and described long before the circulation of the blood was discovered. The discovery of the circulation, anatomico-pathological investigations, experimental researches, and clinical observations, have all been contributing in rescuing this invaluable agent from the dark domain of empiricism, and have secured for it a position as a remedial agent second to none in points of importance, reliability, and frequency of use.

The first account of the application of a ligature for the pur-

[1] In the preparation of this part of the paper I am greatly indebted to the following articles: W. Greifenberger, Historisch-kritische Darstellung der Lehre von den Unterbindung der Blutgefässe. Deutsche Zeitsch. f. Chir., vol. xvi. A. Adamkiewiez, Die mechanischen Blutstillungsmittel bei verletzen Arterien, von Paré bis auf die reneste Zeit. Archiv für Klin. Chir., vol. xiv.

pose of preventing hemorrhage is given by Sus'rutas, a disciple of the divine Dhavantari in his Ayur Vedas (1500 B. C.), who tied the umbilical cord in newly-born infants, with a string, eight inches from the navel previous to cutting it. A number of writers, among them Platner, Holtze, Langenbeck, and Fischer, allude to Hippocrates (460–377 B. C.) as the discoverer of the ligature. They base their opinion on the following passage from his works, translated into Latin by Fassius:[1] "Sanguinem e renis profluentem sistunt animi deliquium, figura aliorsum tendens, venæ interceptio, linamentum contortum, appositio, deligatio."

Archigenes (100 B. C.) made free use of the ligature after amputations. Celsus (30–25 B. C., 45–50 A. D.), in his works, refers to the ligature as a well-known remedy, and credits an obscure physician of the Alexandrian school with its discovery. Celsus used the ordinary linen thread, and gave particular indications for its use and manner of application. In speaking of the operation for hydrocele, he says:[2] "Nervus, ex quo testiculus dependet, præcidendus; post id venæ et arteriæ ad inguen *lino deligandæ* et infra vinculum abscindendæ sunt."

Galen (131–211 A. D.), although no practical surgeon himself, yet familiar with the literature of that day, frequently mentions the ligature, and gives particular directions to apply it to the proximal end of the bleeding vessel. For ligature material he advises silk and fine catgut. The definite closure of the vessel he attributed to the action of the tissues surrounding it, as is evident from the following quotation:[3] "Quæ namque caso in abscisis vasorum partibus coalescit, ea pro opercula est ac osculum eorum claudit." The name of Antyllus (350 A. D.) occupies such a prominent position in vessel surgery, and his method of procedure in cases of aneurism is so familiar to every student in surgery, that more than a simple allusion to his name would appear superfluous.

[1] Hippocratis medicorum omnium facile principis opera omnia quæ exstant. Frankf. ii. p. 1194.

[2] Aul. Corn. Celsi de medicina libri octo, quos ad Leon. Targæ recens, de J. H. Waldeck, Münster, 1827, p. 150.

[3] Claudii Galeni opera omnia. C. G. Kühn, Lipsiæ, 1827, T. x. L. iii. cap. xxii. p. 941.

Paulus Ægineta (625–690, A. D.) treats extensively of the ligature, quoting freely from the writings of Celsus and Galen. In practising ligation of vessels as a therapeutical measure in diverse affections he passed two ligatures beneath the vessel with the aid of a needle, cut the vessel between them, and, after permitting the requisite amount of blood to escape, closed each end of the vessel separately. Rhazes (850–922, A. D.) mentions, as a last resort to arrest hemorrhage from large vessels, the ligature which he made of strong linen thread.

The prolific writer, Avicenna (980–1037, A. D.), disposes of the subject of ligation of vessels briefly thus:[1] "Quod si (sc. vena) fuerit pulsatilis, tum melius est ut veles eam cum filio lini, et similiter si fuerit ron pulsatilis, verum tamen multoties elevatur sanguis ejus." Aneurisms he treated in accordance with the teachings of Antyllus. He limits ligation to arteries, believing that bleeding from veins is arrested spontaneously or yields to the use of the customary styptics.

Avenzoar (1113–1162 or 1196, A. D.) and Averroes (1198) were familiar with the ligature. The latter, in his commentaries on the writings of Avicenna, directs that in performing arteriotomy the vessel should be surrounded by two ligatures before it is divided.

Roland (1252), a pupil of Roger, of Parma (1214), again mentions the use of the needle in applying the ligature, a practice followed by most of the prominent Italian surgeons at that time.

Bruno, of Castel Longobrugo (1252), pointed out the difference between arterial and venous hemorrhage, and gave the advice, in case the bleeding could not be arrested by any other means, to seize the artery or vein with a small hook and carry a thread with a needle around the vessel and tie it firmly.

Guy de Chauliac (1300–1363, A. D.) prefers the ligature when the artery is deeply seated, in which case it is well brought into view, and that end is firmly tied which is placed towards the heart or liver.

[1] Avicennæ Arabum medicorum principis Canon medicinæ, ex Gerardi Cremonensis versione per Fabium Paulinum Utinensem. Venetiis apud Juntas. 1595, Lib. iv. Tract. II. cap. 17.

Lenardo Bertapaglia (died 1460) modified the intermediate ligation by passing the needle armed with a double thread not *under*, but *through* the artery, tying both ligatures firmly over each other. Giovanni Vigo (1460–1520), the founder of the school of surgery in Rome, was acquainted with the direct or immediate ligature, but gave preference to the intermediate method of ligation. Alfonso Ferri described the ligature needle used at that time in applying the intermediate ligature, which was about three inches in length and curved only at the point, with the eye at the opposite end; the point presented four sides with obtuse angles, so as to prevent injury to the vessel or its adjacent parts. This needle was armed with a double ligature, and entered about 2–3 fingers' breadth from the margin of the wound, passed underneath the vessel, and made to emerge on the opposite side of the wound, and the ligature firmly tied in several knots.

Angelo Bolognini (1508), founder of the school at Bologna, also practised percutaneous ligation of vessels, using silk as a ligature material.

Jacques Houllier (1493–1562) in wounds of the arteries relied on digital compression, and, when this failed and the vessel was deeply located, he advised that it be gently drawn forward, slightly twisted, and, after ligating both ends, divided completely at the point of injury.

In Germany we find the first mention of the ligature by Hans von Pfoloprundt. Hieronymus Brunschwig (1450–1533) practised and described Bertapaglia's method of ligation.

Hans von Gersdorf (1517), a military surgeon of great experience, frequently applied the intermediate ligature in cases of vessel wounds, but preferred styptics and the actual cautery in amputations.

Walter Ryff tied the proximal end of the vessel by isolating and seizing it with a small hook, and tying firmly with a silk ligature.

It will be seen that, up to this time, the ligature has for the most part only been used as a *dernier ressort* in cases of wounds of vessels, while styptics and the actual cautery are still relied upon as the safest and easiest methods of arresting hemorrhage. To Ambrose Paré (1517–1590) surgery owes a great debt of gratitude, not as the discoverer, but as the first and most devoted champion of the ligature. Through his influence and untiring zeal the ligature gradually found its way into popular favor, and displaced the barbarous treatment by styptics and cautery. He practised both, the immediate and intermediate ligation, according to the location of the vessel and circumstances of the case. His first operations were performed about the year 1552. In a German translation of his work on Surgery,[1] published in the year 1601, I find the following directions:—

"Wo auch dieses nicht helffen wolte, so muss man die Haeffte, wofern deren eins oder mehr vorgangen, widerumb aufſthun, und under der verletzten ader, gegen ihrem Anfang oder Wurtzel zu, mit einer Nadel und Faden durchhin fuhren, die Ader sampt einer solchen portion oder stücklein Fleisches desselbigen Orts, wie viel nemlich die Gelegenheit geben und erleiden mag, fassen und zubinden. Denn also hab ich offtmahlen sehr grosse und gewaltige Verblutungen, auch in denen Wunden, durch welche gantze Arm oder Schenkel abgehawen worden, gestillt, wie an seinem ort sol gemeldet werden. Dieses aber zu verrichten, werden wir vielmal genötiget, die ganze Haut, so über der Ader ligt, auffzuschneiden und zu entblössen. Denn wenn eine auss den Blut oder Lufftadern des Halses (Jugularium) durchschnitten were, und sich die beyde Ende, beydes hinauff und hinabwertz von einander gezogen, und also verborgen hetten, muss man die gantze Haut unter welche sie sich verschlossen, eröffnen, die Ader entdecken, mit einer Nadel und Faden darunter hinfahren, und also zusammenbinden, wie ich dan selbst vielmahl sehr glücklichen und wohl verrichtet. Du solt aber dieses Bandt oder Faden nicht eher auflösen, biss dass du sihest, das die Ader mit Fleisch überwachsen, und der Ader Mundlöchlein verstopfet sey, damit das Blut nicht widerumb und von neuwen zu rinnen anfange." For fear of secondary hemorrhage Paré favored the

[1] Wundt Artzney, od. Artzney spiegell. Translated from the Latin by Petr. Offenbach, Frankf. 1601, p. 372.

ribbon ligature, made of a number of threads; at the same time he aimed to include portions of tissue surrounding the vessel, and removed the ligature as soon as healthy granulations covered the exposed portion of the vessel. He used the ligature with a view simply to approximate the inner walls of the vessel for a sufficient length of time for union to take place, when its further presence was considered useless and even detrimental. The contemporaries of Paré were slow to acknowledge the superiority of the ligature over the rude, but time-honored cautery. On the one hand, ignorance and prejudice combined in checking progress, while, on the other, it must be acknowledged that Paré's ligature was an exceedingly imperfect thing, which, when used according to his directions, could not fail to frequently disappoint the most ardent admirer. It required centuries to establish it in the confidence of the profession.

Jacques Guillemeau (1550–1613 A.D.), Paré's pupil, friend, and successor, labored faithfully and earnestly in the interest of the cause of his illustrious master. He was one of the first who resumed the operation of arteries in their continuity for the cure of aneurism. He applied the ligature on the cardiac side, opened the sac, and allowed it to heal by granulation.

Pierre Dionis (died 1718) states that at his time the cautery was used almost exclusively at the Hôtel Dieu after amputations, although he resorted to the ligature frequently, and in some instances even practised immediate ligation. In 1733, Petit (1654–1750) writes of the ligature:[1] "La ligature cause des grandes douleurs, des tressaillements convulsifs et quelque fois la convulsion du Moignon, qui souvent est mortelle ou par elle-même ou parcequ' elle occasionne l'hemorrhagie par les mouvements extraordinairs que la malade ne peut s'empêcher de faire."

Fabricius von Hilden (1560–1634) and Scultetus (1595–1645) introduced Paré's practice into Germany. The former made use of the hemp ligature, but restricted its application to young healthy persons.

Cornelius von Solingen (died 1692) practised immediate

[1] Mém. de l'Acad. Royale des Sciences, 1733, p. 91.

ligation after the example of Dionis. Anton Nuck (died 1692) only made use of the ligature in operating for aneurism after the method of Antyllus.

In England the ligature was introduced by Wiseman (1566–1625) and was eagerly adopted after the discovery of the circulation by Harvey in 1619.

Fabricius ab Aquapendente (died 1620) applied two ligatures to arteries and divided the vessel between them, so as to allow both ends to retract.

Marcus Aurelianus Severinus (1580–1656) was the first to tie the femoral artery near Poupart's ligament.

Cesare Magati (1597–1647) followed the advice of Galen and Avicenna, and tied the vessel only on the cardiac side.

Kirkland (1721–1798) attributes the definitive closure of vessels after ligation to the inherent contractibility of the vessel wall.

White and Aikin expressed a similar view, as becomes apparent from the following passage: "That the arteries, by their natural contraction, coalesce as far as their first ramification."[1]

John Bell (1760–1820) concurred in this view, but added another important element, adhesive inflammation in the vessel wall induced by the ligature.[2]

Larrey (1766–1842) observed that in many cases after ligation no coagulum formed, and, in consequence, asserted that definitive obliteration of the vessel can take place independently of it, and is then due to contraction of the vessel wall.

Richerand (1779–1840) believed that the ligature brings the inner walls of the vessel in contact, and that direct adhesion takes place, the result of adhesive inflammation.

Garengeot (1688–1759) feared the cutting through of the ligature, and, for the purpose of preventing this accident, advised the use of a broad, ribbon-like ligature.

Claude Ponteau (1725–1775) abandoned the use of the broad ligature, but, to guard against the same evil, included within the ligature a sufficient amount of paravascular tissue.

[1] Cases in Surgery, p. 171.

[2] Discourses on the Nature and Cure of Wounds, 1800, p. 109.

Lorenz Heister (1683–1758) used a stout ligature, and tied over a small cylinder of lint to prevent premature cutting through of the ligature.

J. Z. Platner (1694–1747) made use of a similar contrivance, but always applied a double ligature with a third (reserve ligature) on the cardiac side, to be tied in the event of secondary hemorrhage.

Alexander Monroe (1697–1767) protested against the intermediate ligature, and emphasized the importance of direct ligation. He used broad ligatures, and tied only with sufficient firmness to approximate the inner walls of the vessel.

Wm. Bromfield (1712–1792) isolated the artery, drawing it out on the surface of the wound with a hook of his own construction, and which still bears his name, and applied a flat ligature.

In France, Deschamps (1740–1824) advocated the superiority of immediate ligation by means of a broad ligature, on the ground that when the intermediate ligature is used, the interposed tissues disappear very rapidly, leaving the ligature loose around the artery, thus favoring the occurrence of secondary hemorrhage.

Abernethy (1763–1831) applied a double ligature in tying an artery in its continuity, and divided the vessel between them, claiming that in doing so he was able to relieve the tension in the peripheral portion of the vessel, and, at the same time, enable both ends of the artery to retract into the tissues. He also condemned the reserve ligature, as it would necessitate more extensive isolation of the vessel, thus cutting off nutrition, and provoking a higher degree of inflammation and suppuration.

August Gottleib Richter (1742–1812) introduced the immediate ligature into Germany.

On Dec. 12, 1785, John Hunter (1728–1793), for the first time, tied the femoral artery *in loco praedilectionis* for popliteal aneurism. He applied four ligatures at short interspaces, of which number only the most distal one was tied firmly; the remaining ligatures were tied in such a manner that the lumen of the proximal end of the artery represented a cone, with the base towards the cardiac side of the vessel. Hunter anticipated that this method of operation would favor the formation of thrombus, and thus afford additional security against secondary hemorrhage. His expectations, however, were not realized, as secondary hemorrhage occurred on three different occasions, and the patient did not recover until seven months had elapsed. He did not repeat this operation, and subsequently used only one ligature.

Desault accidentally made the observation that in the ordinary method of ligation with the round ligature the two inner tunics of an artery are ruptured.

This fact was verified by Jones, who, in 1806, made a series of careful experiments to determine this point. The classical work of Jones exerted a potent influence in establishing the claims of the ligature, not only in England but wherever surgery was practised. He claimed that obliteration of an artery after ligature can take place, independently of the formation of a thrombus, by the traumatic inflammation and plastic exudation induced by the ligature. In his experiments on animals he applied several ligatures in close proximity. He called particular attention to the deleterious effects of suppuration on the process of cicatrization in the bloodvessels, and, for the purpose of guarding against this event, advised the removal of the ligatures immediately after they had ruptured the internal coats or before suppuration is established. He believed that provisional closure of the vessel is accomplished by the lacerated tissues within the lumen of the vessel, and that the healing process within the vessel is the same as in any other wound, producing the definite obliteration. In tying large arteries he advised the double ligature and division of the vessel between.

B. Travers adopted the views promulgated by Jones, but substituted the temporary for the momentary ligature. He recommended the removal of the ligature as soon as plastic inflammation is fully established, and before suppuration has time to take place. The period of time in which the ligature would accomplish this object he placed at 48 to 90 hours, according to the size of the vessel which had been ligated. Jones and Travers deserve to be called the discoverers of the temporary ligature upon a scientific basis. On Feb. 14th, 1817, Travers, for the first time, put his theory into actual practice. He ligated the brachial artery for aneurism, and removed the ligature after 50 hours. The case proved successful. The next case, the artery being the same, did not terminate so favorably; secondary hemorrhage set in and proved fatal. J. Hutchinson's case, operated upon in a similar manner, also terminated in death by recurring hemorrhages.

Sir Astley Cooper applied the temporary ligature in two instances; the results not meeting his expectations he abandoned it. Among the most formidable opponents of the temporary ligature may be mentioned Hodgson, Vacca Berlinghieri, and C. J. M. Langenbeck, who claimed that it was impossible to determine the exact length of time after which it would be safe to remove the ligature, and that the necessary manipulations for the removal of the ligature would interfere with the prompt healing of the wound.

In Italy, Antonio Scarpa (1747–1832) strongly advocated the employment of the temporary ligature. He used the broad ligature and tied over a cylinder of lint for the purpose of bringing and keeping in apposition a large surface of the inner walls of the vessel. His experiments have demonstrated that obliteration of a vessel by adhesive inflammation can and does take place without division of the inner coats. He compared the inner surface of bloodvessels with serous membranes, and credited it with the property of undergoing the same pathological changes when subjected to traumatism. He ascertained that adhesive inflammation follows about four days after the application of the ligature, while the time required for suppuration to arise requires from one to two days longer, consequently he determined the time for the removal of the ligature in accordance with the general condition of the patient. In young, robust persons he removed the ligature on the fourth day, and in old or decrepit persons he allowed it to remain for six days.

P. U. Walther asserted that definitive closure of vessels after ligation takes place within 40 hours, and urged that the ligature should be removed after the lapse of this time.

In Germany, Victor von Bruns was the next and last to bring the temporary (amovable) ligature before the notice of the profession. He removed the ligature after two or three days, according to the size of the vessel, and supports his claims for the superiority of this method of ligation by the results of a large clinical experience.

Pécot compared the methods of Jones and Scarpa by way of experiment and came to the conclusion that the round ligature, if applied with sufficient firmness to sever the inner coats of the artery, excites adhesive inflammation earlier than if the broad tape ligature is used.

Ponteau attributed great importance to the connective tissue around bloodvessels in the process of obliteration, hence he advised that an abundance of this tissue should be included within the ligature.

Delpech (1777–1832) arose against Scarpa in France, and C. J. M. Langenbeck in Germany. The latter regarded the adhesion of the inner vessel walls of prime importance in effecting permanent closure, while to the thrombus and lymph coagulum he assigned a less important rôle. The older German surgeons were in the habit of using hemp or linen ligatures. The silk ligature was first proposed in that country by Ph. Fr. von Walther. For the purpose of preventing the ill effects of the customary ligature a variety of ligature materials was proposed, such as chamois skin by Physick (1814), catgut by Sir Astley Cooper, silkwormgut by Wardrop, elastic rubber strings by Levert, tendons by Paul Eve, human hair by Porta. Metallic ligatures were brought forward as being less irritating than the ordinary ligature; gilt iron wire was proposed by Ollier, fine iron wire by B. v. Langenbeck, and silver wire by Wagner and Sims. Levert experimented with all kinds of metallic ligatures—lead, gold, silver, and platina—and always obtained primary union of the wound. Metallic ligatures were always cut short and permanently remained in the wound. Until the end of the eighteenth century the ends of the ligature were brought out through the wound. The first attempts to cut short the ligature and leave it permanently in the wound were made by Lawrence, who, in 1814, published the results of his experience. For ligatures he used fine dentist's silk. According to Samuel Cooper, however, the priority of this procedure should belong to a certain Haire of Essex, who is said to have practised it in 1786.

Hennen adopted the practice in 1813, and within four months followed it in 34 cases without observing any unfavorable results. Delpech and Guthrie also indorsed this practice. The introduction of antiseptic surgery has, however, wrought the greatest improvement in the ligature, and the founder of antiseptic surgery, Sir Joseph Lister, has also furnished us with the ideal ligature—the aseptic ligature. What has been sought for centuries has at last been found, a ligature which will arrest the circulation with safety and certainty, and a minimum amount of traumatism until the process of cicatrization is completed, and when its work is accomplished it gradually disappears by absorption and substitution.

Since the introduction of the antiseptic treatment of wounds and the aseptic ligature, surgery has received a new impulse, results have been obtained which were never realized before, operations have been performed successfully which were previously beyond the grasp of even the most ambitious, and, more than all, those horrible spectres, hospital gangrene, erysipelas, pyæmia, septicæmia, and secondary hemorrhage, which haunted the surgeons of only fifteen years ago by night and by day, have almost completely disappeared from hospital as well as private practice. For all this we are indebted to Lister. A variety of other animal tissues have been prepared into ligatures and made aseptic, and have been recommended at different times as substitutes for the catgut ligature. Among them we may enumerate silk, silkwormgut, whale and deer tendon, peritoneum, coats of bloodvessels, and nerve tissue. With the exception of the first two, all of these ligature materials, if rendered perfectly aseptic, will, after a certain time, undergo absorption, but it is questionable if any of them possess any advantage over well-prepared catgut. Czerny is entitled to a great deal of credit for the improved silk ligature. He has demonstrated that when silk is made perfectly aseptic by boiling and immersion in carbolized water it can be safely left in the tissues, where it becomes encysted.

II. *Histology of Bloodvessels.*

For our purpose it is not necessary to give a complete description of the minute anatomy of the bloodvessels, but a brief allusion to the arrangement and relations of the histological elements is necessary, with a view to study the process of cicatrization after ligation; my remarks will, therefore, apply only to vessels of such size which the surgeon is called upon to ligate. Our present knowledge of cicatrix formation in bloodvessels we owe largely to a better understanding of the structure and functions of the coats of the vessels on the one hand, and to the laborious researches concerning tissue regeneration and inflammatory tissue formation on the other. As arteries have been made more frequently the object of experiments than veins, we shall give a description of the arterial coats, and, with but few unimportant exceptions, all what can be said of the structure and obliterating processes in arteries will apply with equal force to veins. The arteries are cylindrical tubes of uniform diameter between their branches. The importance of their function demands that they should occupy such localities that would afford the greatest security against injuries from without and diseased processes within the body. In man the anatomical protection against injury and disease of the arterial system exists in a wonderful degree of perfection, the vessels, as a rule, being deeply situated in the concavities, depressions, and channels of bone, on the flexure side of joints, protected by dense fascia, supported by muscles, and, where location demands it, surrounded by a soft cushion of adipose tissue; as an additional medium of protection and source of nutrition they are accompanied everywhere by a sheath of connective tissue, which connects them loosely with the surrounding tissues.

The bloodvessels are a product of the mesoblast, and are composed of unstriped muscular fibres, elastic tissue, connective tissue, and endothelium. From an anatomical, physiological, and, I may add, pathological, standpoint, it has been customary to distinguish three coats, called respectively, according to their location: 1. Internal or Intima; 2. Middle or Media; 3. External or Adventitia. In larger arteries these coats can be separated and recognized without the aid of the microscope.

I. *Intima.*—The intima is a delicate hyaline elastic membrane. In the larger arteries it is composed of a single layer of flat endothelial cells, a delicate layer of longitudinal bundles of connective tissue, and a network of elastic tissue. His applied the term endothelium to the pavement epithelium lining the inner walls of the bloodvessels, lymphatics, and serous cavities, to distinguish it from the other varities of epithelium. As found in the vessels, Auerbach named it perithelium, and Frey suggested the simple name of primary vessel tunic. The endothelial layer is composed of eliptical or irregular polygonal cells, which are often elongated into a lanceolate shape, being continuous with the endocardium on the proximal, and the capillary vessels on the distal side. The shape of the cells is greatly modified by the degree of the distension of the vessel. The nucleus is oval, its long axis, like that of the cell, corresponding to the longitudinal direction of the vessel. In the fresh state the contour of the cell is very faint and exceedingly difficult to trace without the assistance of staining. A one per cent. solution of nitrate of silver, as first suggested by von Recklinghausen, stains the cement substance a dark brown, which imparts a well-defined outline to the irregular margins of each individual cell. If the protoplasm be at the same time stained with chloride of gold, the picture is at once rendered beautiful and perfect, illustrating the cell and its contents to perfection. The cement substance surrounding each individual cell is a lifeless substance, closely allied to the basis substance of the connective tissue, but it is not glue yielding. Some histologists (Heitzmann, Stricker, Klein) describe a network of living matter within the cell which sends delicate conical offshoots through the cement substance, thus forming a living reticulum, which connects the individual cells and permeating the lifeless cement substance in every direction. These projections were first seen and described by Max Schultze. According to Heitzmann[1] these living prolongations are capable of producing new tissue elements. The stomata or stigmata in capillary vessels are slight defects in the irregular outlines of the cement substance, and are supposed to permit the passage of the morphological elements of the blood more particularly when in a condition of inflammation. "The attachment of endothelia to the subjacent connective tissue is either direct, by means of delicate filaments penetrating the rim between the feet of the endothelia and the neighboring fibres of connective tissue; or it is indirect by means of an intervening basement layer."[2] The outer surface of this basement membrane in many instances is found to be covered by a layer of flat, polyhedral cells discovered by Czerny by means of silver staining. These cells may be regarded as endothelia. These endothelial or endothelioid cells may bear important relation to the subject of regeneration of endothelia. Frey[3] acknowledges that we are as yet ignorant concerning the reproduction of endothelia, while Wendt[4] attributes to the vascular endothelia the still higher function of being converted into elements identical to leucocytes after separation by desquamation. This process has been actually observed by Altmann in the serous endothelia of the exposed mesentery of a frog.[5] The absence of a direct blood supply does not appear to deprive them of a sufficient nutritive supply by means of which they receive their own nourishment, and which imparts to them the power of reproduction and to assume an active part in various pathological processes. In large arteries immediately underneath the lining endothelium there is a special connective-tissue membrane variously designated as striated internal coat (Kölliker), inner-

[1] Microscopical Morphology of the Animal Body in Health and Disease. New York, 1883.

[2] Ibid. page 318.

[3] Handbuch der Histologie und Histschemie des Menschen. Leipzig, 1874, p. 147.

[4] The Bloodvessels. Satterthwaite's Manual of Histology. N. Y. 1881.

[5] Archiv für Mikrosk. Anatomie, vol. xvi. p. 3.

most longitudinal fibrous coat (Remak), and internal fibrous coat (Eberth). In the adult this layer is distinctly fibrillated. Embedded in this membrane are lodged numerous branching corpuscles, containing large, conspicuous nuclei and so-called granulation-bodies. Wendt regards the granulation bodies as matrix-cells for the regeneration of desquamated endothelia. Talma has described similar bodies, but regarded them as the product of endothelia, instead of *vice versa*. This inner connective-tissue membrane is prolonged into the smaller arterial branches in the form of a single layer of branched cells being interspersed between the endothelial lining and the elastic membrane of the intima. The elastic membrane of the intima consists of a network of longitudinal fibres. In the larger arteries this membrane is laminated, the lamina being (longitudinal) fenestrated elastic membranes, between which pass (longitudinal) networks of elastic fibres.

II. *Media.*—The middle coat consists of unstriped muscular fibres, elastic and connective tissue. In vessels of small or medium size, there is a preponderance of muscular over elastic elements, in the larger trunks the reverse condition obtains. The muscular tissue consists of smooth nucleated muscle fibres arranged in concentric layers, and disposed transversely or obliquely around the vessel. Bardeleben maintained that an inner longitudinal muscular coat exists in all large and middle-sized arteries. The muscular elements are arranged in layers or groups, the interspaces being occupied by connective tissue and elastic fibres arranged in networks. The complicated relations of the elastic fibres in this coat have caused no little confusion in giving a description of it.

Henle describes four distinct layers. The middle coat is distinctly separated from the intima by the interposition of the internal elastic coat. The external elastic coat of the media consists of a close network of delicate elastic fibrils anastomosing with similar reticula from the adventitia. The third layer of the elastic tissue fills the interspaces between the muscular layers in the interior of the middle coat. A small amount of connective tissue is found in this coat chiefly accompanying small bloodvessels when they permeate it. The elastic fibres are usually arranged transversely to correspond with the direction of the muscular fibres, but some of them especially those in immediate contact, and intimately connected with the fenestrated membrane of Henle, are arranged in a longitudinal direction. The great degree of elasticity possessed by the arterial coats is usually wrongly attributed singly to the existence of the elastic tissue, and Hyrtl[1] very properly remarks that all of the tunics share this property in common with the elastic tissue, otherwise the remaining tissues would suffer a certain amount of distraction during the expansion of the vessel. The circular direction of the muscular fibres, and the same direction of the bulk of the elastic fibres of the middle coat, predispose to the laceration of this coat in ligating an artery by means of a round ligature when firmly applied; but, as some of the fibres are arranged obliquely and longitudinally, complete division occurs but seldom, and only on the application of considerable force. The principal elements of this coat, in common with the same tissues in other localities in case of injury or disease affecting their structure, do not possess the power of reproduction or regeneration. The loss of tissue is filled in by cicatricial tissue, and solutions of continuity are invariably repaired by connective tissue.

III. *Adventitia.*—The external coat, the adstitia of Haller, is the simplest in structure, being composed of interlacing bundles of connective tissue, commingled with elastic lamellæ of varying thickness. The external coat serves as a nidus for the nutrient vessels, the vasa vasorum. These vessels only in exceptional cases (Henle) arise from the trunk which they supply, but are usually recurrent vessels from the nearest branches. Hyrtl has called attention to the fact, that even the smallest of these vessels are accompanied by two veins. He has never seen these vessels extend beyond the adventitia. Frey asserts that the media receives vessels from the adventitia. In the outer coat the vessels resemble the capillaries in the connective tissue only forming a more dense vascular network.

[1] Lehrbuch der Anatomie des Menschen, Wien, 1878, p. 140.

Klein locates the vasa vasorum as follows: "The media and adventitia of large vessels (arteries and veins) contain a special system of nutrient bloodvessels, vasa vasorum; the arterial and venous branches of these lie chiefly in the adventitia, occasionally also in the part of the media; the capillaries generally penetrate into the media and near the intima, only seldom also into the latter (Köster). In the microscopic arterial branches we meet with capillary vessels, as a rule only in the adventitia."[1]

Flint says: "A tolerably rich plexus of vessels is found in the external coats of the arteries. These are called vasa vasorum, and come from the adjacent arterioles, having no direct connection with the vessel on which they are distributed. A few vessels penetrate the external of the middle coat, but none are ever found in the internal coat."[2]

Lymph-spaces are present as intercommunicating interfascicular spaces, containing connective-tissue cells, in all coats of arterial and venous trunks. Most histologists take it for granted that the ultimate distribution of nerve-filaments from the cerebro-spinal centres and the sympathetic reach only the adventitia and media. Cohnheim's researches, however, tend to prove that the finest axis-fibrilli of the nerves terminate in the epithelial layers. The termination was described by some observers as a plexus between the epithelia, while others (Pflueger, Flemming) claim that the axis fibrilli penetrate the body of the epithelium and may terminate in its nucleolus. Heitzmann has traced the terminal filaments into the cement substance between the epithelia. From the foregoing anatomical consideration, it is evident that the intima, although devoid of bloodvessels, yet receives sufficient nutritive supply which renders it capable to regenerate its own elements in case of loss, and to assume inflammatory changes under the same circumstances and in the same manner as other tissues occupying the same relative position to the vascular system. I will append a short abstract of the microscopical description of veins as given by

[1] Atlas of Histology, Phila. 1880, p. 144.
[2] The Physiology of Man, N. Y. 1866, vol. i. p. 245.

Raab as an introduction to his paper "On the development of the cicatrix in bloodvessels after ligation." His studies were made on veins of dogs. On making a longitudinal and a transverse section through a vein, the endothelial cells appear as an exceedingly delicate seam which, from the greater prominence of the nuclei towards the lumen of the vessel, presents a slightly wavy appearance. The endothelial cells are not in direct contact, but each is surrounded by a zone of cement substance which fastens the cells among themselves and to the subjacent tissue. This cement substance, according to Julius Arnold, is a remnant of the protoplasm from which the original cells were formed. The nucleus containing a number of nucleoli is located near the centre of the cell. On section this nucleus presents the outlines of a half ellipse, the long axis of which is in contact with the vessel wall. The distance between two nuclei of neighboring cells amounts to three or four times their longest diameters, and from this it is easy to estimate the area of a protoplasmic plate. As carmine stains only the nucleus, the contour of a cell can only be traced after staining the specimen with nitrate of silver. The endothelia are either rhomboidal or polygonal in shape. Isolated cells can be obtained in most perfect condition from veins which have been immersed for some time in a one per cent. solution of chloride of sodium, lime-water, or Mueller's fluid. For silver staining, the valves are best adapted; they can be spread on the object glass without any special preparation and show most beautifully the mosaic arrangement of the cellular layer. On the outer side of the endothelial lining a framework of elastic tissue is found. The strongest fibres of this network are arranged in concentric rows in regular order, parallel with the long axis of the vein, while the smaller fibres take a diagonal or radiate course. In this elastic network are found bundles of connective tissue crossing each other in all directions. These fibres are very dense immediately beneath the endothelial layer, and are intimately interlaced with the elastic tissue; towards the periphery they are more loosely arranged. An elastic membrane, which in the arteries completely separates the endothelial from the muscular layer, does not exist in the veins. In transverse sections of a vein, the longitudinal elastic fibres appear as light, round, or oval objects between the loose wavy connective-tissue bundles, and in the spa es surrounding them an occasional spindle or stellate cell with a large nucleus may be seen. Muscular tissue is not to be found in the superficial cutaneous veins of dogs. It is also absent in the internal jugular and femoral veins. The adventitia consists of loose connective tissue and firm elastic fibres, separated by a distinct space from the middle coat.

III. *Intermediate Ligature, Ligature en masse.*

All of the older surgeons were in fear of a too early separation of the ligature, and aimed to prevent secondary hemorrhage as the result of such an occurrence by including adjacent tissues, thus protecting the vessel against undue pressure. The object of this practice was simply to apply the ligature as a provisional mechanical agent to arrest the flow of blood in a vessel without any theory as to the permanent closure of the vessel. The ligature was passed underneath, with points of entrance and exit some distance from the vessel and firmly tied. This method was practised by Paré, and through his influence and example it was adopted by all of the prominent surgeons until nearly the end of the 18th century. Guillemeau, Thévenin, Garengeot, LeDran, Louis, Dionis, and Petit were faithful followers of Paré, and with few unimportant modifications followed his directions to the letter. Since the definitive closure of vessels has been made an object of study and experiment this method of ligation has been abandoned and is only resorted to in exceptional cases where isolation of the vessel or vessels is impossible from the nature or location of the wound.

IV. *Immediate or Direct Ligature.*

The experiments of Jones led the way to the immediate or direct ligature. Jones and his followers placed great stress on the laceration of the inner tissues of an artery by the circular constriction of the ligature in effecting provisional and definitive closure of the lumen of the vessel. The simple round ligature was gradually adopted by all surgeons who aimed at division of the internal coats by the ligature. The size of the ligature has also undergone considerable modification. Bell used fine oiled ligatures which he supposed would apply themselves accurately to the artery. Some united from two to as many as eight (Arndt) ligatures into one string.

Lisfranc used moderately broad ligatures, but he claimed that in tying the knot they were changed into round cords and would as effectually divide the inner coats as the round ligature. Velpeau used ligatures proportionate in size to the vessel to be ligated. Hodgson used the fine round ligature. Lawrence spoke highly of the use of very fine silk, dentist's silk, in tying arteries of any size. A. Cooper also was in favor of the round single ligature. The circular constriction of Jones, with a single round thread, by degrees won the favor of surgeons and has firmly maintained its position as the best method of ligation until the advent of the aseptic ligature. The advantages presented by this method during its pre-antiseptic period were: 1. Effective and safe provisional closure of vessel. 2. Promotion of process of definitive closure of vessel. 3. It favored the spontaneous elimination of the ligature by diminishing the amount of tissue included in the loop of the ligature.

V. *Scarpa's Aplatissement.*

Scarpa's ligature was intended by its author to fulfil the two essential indications in obliterating the lumen of a vessel: 1. To arrest the circulation temporarily by mechanical pressure without lacerating the tissues of the vessel. 2. To approximate and keep in constant and accurate contact a comparatively large surface of the inner vessel walls for union to take place by adhesion. His leading idea was that the intima resembles serous surfaces, and for rapid union to take place only a moderate amount of irritation is necessary, and that the injury inflicted by the circular ligature is too severe to obtain the most desirable result. He used ligatures two lines in width and tied over a small cylinder of linen. The ligature is usually expelled spontaneously about the fifteenth day, but if this is not the case and it is loose upon the vessel it should be removed at this time. Scarpa's theories found many admirers, who introduced modifications in the operation to suit their individual ideas. Förster substituted for the cylinder of linen, charpie and cork, Deschamps agaricus, Desault small plates of wood, Cline cork, and Roux small rolls of diachylon plaster.

In England this practice was advocated by Crampton, and in France it was represented more particularly by Boyer and Roux. Some exponents of the theory of aplatissement, while believing in the doctrine, objected to the introduction of foreign bodies into the wound, which they regarded not only as useless but injurious to the healing of the wound. Jameson used ligatures made of strips of raw chamois skin, which he claimed would by their pliability and elasticity hold in approximation the inner vessel walls without inflicting injury to its tissues. Without means to prevent suppuration it can be readily understood that the expectations held by the originator of this method of ligation and his followers were not realized, and it was by degrees displaced by the round ligature.

VI. *Double Ligature.*

The double ligature is mentioned by Celsus and Ætius, Rolandus of Parma speaks of the double ligature as applied to the vena organica (jugularis). John Bell and Maunoir not infrequently applied two ligatures in close proximity. In ligating arteries in their continuity Abernethy always applied the double ligature after isolating the vessel freely, claiming that even if the intermediary isolated portion sloughs the ligatures will successfully guard against secondary hemorrhage. As an important advantage of this method he mentions that the vessel can be divided between the ligatures which relieves tension and allows both ends of the artery to retract into the tissues—occupying then the same favorable position as vessels divided during an amputation. The double ligature has been frequently employed in experiments for the purpose of studying the process of cicatrization in bloodvessels, after ligature, and will be again referred to in that connection.

According to time, ligatures may be classified into: 1. Momentary; 2. Temporary; 3. Permanent. The first two varieties aim at obliteration of the lumen without loss of continuity of the vessel, while until recently the permanent ligature was always expected to divide the artery before it could be eliminated as a foreign body from the wound.

VII. *Momentary Ligature.*

A series of experiments on animals made by Jones satisfied him that frequently definitive closure of an artery takes place by drawing the ligature tightly and removing it at once. The rupture of the internal coats in many instances produced satisfactory closure by mechanically interfering with the circulation, and causing the formation of a thrombus, the definitive obliteration following as the natural consequence of the traumatism. To insure these results more constantly, he made several of these circular constrictions in close proximity, so as to inflict a greater amount of traumatism, and procure a larger surface for cicatrization. Jones called attention to the superior advantages offered by this method of ligation over all other methods, as it would secure obliteration of vessels without incurring the necessity of leaving a foreign substance in the wound. Unfortunately, however, the results obtained were so uncertain that he did not dare to recommend its adoption in practice. In many instances, as late as the third or fourth day, the artery was found permeable, a sufficient proof that the operation with all its other advantages lacked reliability.

Porta made fifty experiments with the momentary ligature on dogs, sheep, and goats, with the result that in only ten partial or complete obliteration of the vessel by thrombus or lymph-coagulum followed, while in all of the remaining cases only division of the inner coats could be demonstrated.

Maunoir attempted to accomplish the same object by different means. He crushed the internal coats of arteries with a forceps of his own construction, and expected the same series of changes to occur in their interior as the result of the laceration of tissue, but his results must have been equally unsatisfactory, as the procedure does not appear to have been adopted to any extent in practice.

VIII. *Temporary Ligature.*

The temporary ligature was introduced for the purpose of obviating the deleterious effects of the presence of a foreign body in the healing of a wound, and the process of cicatrization in the bloodvessel. While the ordinary ligature remained for a period of time varying from three to twenty days, it has been argued that the average time necessary for the ligature to remain is much less, hence various contrivances were invented which were intended as substitutes for the ligature, and which could be removed with greater facility after the necessary time had elapsed, such were the pressure forceps designed by Deschamps, Desault, Percy, Assolini, Kœhler, Porter, Billroth, L'Estrange, Richardson, Crampton, Nunnelly, Wolfe, Jeoffresson, and Speir. A similar function and sphere was assigned to the percutaneous acupressure of Middeldorpf, the ansa fili metallici of B. v. Langenbeck, the filo-pressure of Dix, the ansa hæmostatica a tergo of Schmitz, and more recently the amovable ligature of V. v. Burns. The laborious researches of Jones prepared the way for the temporary ligature. Travers believed with Jones that vessels are obliterated by inflammatory adhesive exudation and union between the inner coats, but affirmed that the inflammatory process requires a longer period of time to secure the requisite firmness in the adhesions. His first experiments were directed towards ascertaining the length of time required for a sufficiently firm adhesion to take place. The experiments were made on carotids of horses and asses. The ligature was applied either in the form of a loop or tied over a tape placed parallel with the artery for the purpose of facilitating its removal. The ligature was removed after one, two, and six hours, and the animal killed from twenty to thirty hours after the operation. In fifty per cent. of the cases, where the ligature remained for one hour, the vessel was not obliterated. In all cases where it was allowed to remain from two to six hours, the experiment proved successful. From these experiments he concluded that six hours is the longest time required for the ligature to remain, and that at this time definitive occlusion has always been accomplished.

With a view to determine whether the closure of the vessel is perfect at this time, or whether this is effected after the removal of the ligature, he made another series of experiments, dividing the artery on the peripheral side after removing the ligature. These experiments satisfied him that definitive closure takes place *after* the removal of the ligature, and is effected by an exudation of plastic lymph. If the ligature remained for twelve hours, and the artery was cut on the peripheral side, no hemorrhage followed its removal. He reduced his theory to practice by ligating the brachial artery in a man suffering from aneurism, and removed the ligature fifty hours after the operation. No hemorrhage followed, and the patient recovered. He next tied the femoral artery for popliteal aneurism, and removed the ligature twenty-seven hours later. Pulsation soon returned below the seat of operation. The disappointment due to the failure in this case deterred him from giving the temporary ligature further trial, and he returned to the ordinary ligature. This method was tested by a few English surgeons, but, not meeting with more encouraging results, was soon completely abandoned. Scarpa, in Italy, was the next advocate of the temporary ligature. His pathological views regarding the use of the ligature and the process of obliteration of vessels, as well as his method of ligation, are given elsewhere.

Delpech claimed that a few days after ligation, the ligature is found loose on the vessel, and consequently could exert no influence for good, and therefore should be removed like any other foreign body, so as not to interfere with the normal healing of the wound.

Velpeau also regarded the temporary ligature with favor. P. U. Walther studied the effects of the temporary ligature on animals. With a ligature-instrument of his own device, he aimed to divide the inner coats of the vessel, and removed the ligature after forty-eight to seventy-two hours, when definitive closure was always found perfect.

N. R. Smith constricted the vessels with an iron wire passed through a silver tube, and found arteries of the fourth and fifth size obliterated after six hours. The femoral artery was found permanently closed after two days. Victor v. Bruns originated his method of filo-pressure in 1868.[1] The silk ligature which he used was passed around the artery and brought out of the wound through a silver canula with a crossbar, to which it was fastened. Arteries of the size of the radial he found closed after eighteen hours, while larger arteries required from one to three days. For six years this method was used exclusively in all cases requiring ligation in Bruns's clinic with entire satisfaction. Only in two cases did secondary hemorrhage occur; in one instance the common carotid was ligated during an operation for the removal of a cancerous tumor of the thyroid gland, the ligature was removed on the fifth day; in the second case the femoral artery was ligated, and the ligature removed on the third day. The great objections against the temporary ligature always have been, that the wound could not be completely closed, or had to be reopened at the time of removal of the ligature, thus increasing the risks of suppuration, and preventing primary union of the wound, circumstances which the ligature was intended to obviate. Absence of suppuration and primary union of the wound are the most reliable safeguards against secondary hemorrhage after any method of ligation, and any method which cannot secure these results with some degree of certainty, must be considered as faulty in principle and practice, and this can be said without hesitation against the temporary ligature as described above. The aseptic animal ligature must

[1] Paul Bruns, Die temporäre Ligatur der Arterien, Deutsche Zeitschr. f. Chir., B. V., S. 327.

be considered as a temporary ligature in every sense of the word, only that the material of which it is composed is removed by healthy active granulations instead of by the hand of the surgeon, an advantage which it would be difficult to overestimate, and which neutralizes all valid objections against the temporary ligature. The ligature of the future, then, will be the aseptic animal ligature.

IX. *Permanent Ligature.*

The permanent ligature is composed of a material which will remain for the most part unchanged in the tissues of the body, and is either permanently retained (encysted) or spontaneously expelled. Before the aseptic ligature came into use, the ligature usually cut its way through the remaining tissues of the artery in from three to twenty days, by a process of molecular death, and was spontaneously expelled, thus destroying the continuity of the vessel in every instance. Hodgson held that the ligature as usually applied divides the two inner coats of the vessel, and destroys the vitality of the circular constricted portion of the adventitia, which separates like any other slough and comes away in the loop of the ligature. The same explanation is given by Guthrie, Brodie, and Gross. Bruns, however, maintains that the constricted portion under the pressure of the ligature undergoes molecular necrosis, a process necessarily attended by suppuration. He also claims that in animals, if the ligature is cut short, it cuts through the tissues and is encysted in the cicatrix. Porta studied the future fate of ligatures in the wound experimentally. He made 300 experiments, using catgut, silk, hemp, linen, and horse-hair ligatures, cutting them short. The animals were killed from a few days to three years after the operation. Of the 300 ligatures, 64 were completely absorbed (of 80 catgut, 33; of 120 silk, 19; of 50 linen, 10; of 40 horse-hair, 2). Of the 236 ligatures which remained in the wound, only 26 were found lodged in an abscess cavity. He claimed that the ligature destroys the continuity of the vessel by interstitial absorption.

P. U. Walther in his numerous experiments with the temporary ligature found the adventitia divided in only one case. He removed the ligatures at variable periods of time (1 hr.–110 hrs.) after operation. P. Bruns[1] made fifteen experiments to determine the effect of the ligature on the coats of vessels, and confirmed the observations of Walther. If the constricted portion of an artery is examined some time after the application of the ligature, it is not always easy to determine whether complete division has taken place or not. A few days after ligation the artery in close proximity to the ligature is thickened, the swelling on each side effacing the depression made by the ligature, and shutting the ligature out of sight. The traumatic peri-arteritis produces a connective-tissue proliferation which covers the ligature and both ends of the artery in a similar manner as the provisional callus after fracture surrounds the broken ends of the bone. If the inflammation does not proceed beyond the process of tissue formation, the granulation tissue is converted into cicatricial tissue, which forms an additional connecting medium between the ends of the artery, and by forming at the same time a capsule around the ligature, the latter becomes permanently encysted. If the end of an artery is tied, the vitality of the ligated stump will depend on the manner in which the wound heals; if suppuration takes place it will in all probability separate as a slough, and with the ligature will escape with the wound secretions; if, on the other hand, the wound heals by primary union it will either remain in organic connection with the vessel and form new vascular communications with the adjacent tissue, or in the event of a cutting through of the ligature it may still retain its vitality and remain in the tissues, or finally it may be removed by gradual absorption. John Bell and Otto Weber were convinced that the end of the ligated vessel invariably separates and dies. There is, however, good reason to believe that the ligated artery stump in the absence of suppuration will retain its vitality and will again unite with the surrounding tissues from which it receives its nutrition. P. Bruns made a few experiments in this direction.

[1] Op. cit.

Experiment No. 1.—Double ligation of carotid artery of a dog; division of artery between ligatures. The animal was killed, and parts were examined fourteen days after operation. The ends of the artery were separated 2 ctm., the interspace was bridged over by a band of connective tissue in which were embedded both ligated stumps a short distance from the closed ends of the artery.

Experiment No. 2.—Vessels and operation the same. The separated ends of the artery embedded in the intermediate connective-tissue string.

Experiment No. 3.—Femoral artery, operation the same. Local conditions the same, only that the bridge of new connective tissue was larger and firmer. The separated ends of the artery somewhat reduced in size.

Experiment No. 4.—Femoral artery, operation the same. Separated pieces much smaller, and incorporated in the newly formed connective tissues.

In all of these experiments it appears that the ligature cut its way through the tissues of the artery, thus completely separating the ligated stumps, and still they retained their vitality through the influence of the surrounding living tissue. The ligatures were undoubtedly drawn very tight, and as the operations were done without antiseptic precautions the reaction was in excess of what is necessary to obtain obliteration of the vessels, and these circumstances will go far towards furnishing an explanation of the uniformity with which the constricted portion of the vessel gave way under the ligature. The use of the aseptic ligature and antiseptic wound treatment tend to preserve the continuity of the ligated vessel, as has been abundantly proved by clinical experience and experimental research. In many of my specimens it can be seen that weeks and months after the operation the ligatures remained in their original location and occupied the same relative position to the vessel as immediately after the operation, the ligature in every instance where suppuration was prevented being surrounded or encapsuled by a dense capsule of connective tissue. If under antiseptic precautions the end of an artery is ligated, the stump of the artery retains its vitality in a similar way, and is nourished in the same manner as the pedicle after ovariotomy, with the only difference that in the former instance the local conditions are perhaps more favorable for the preservation of the vitality of the ligated parts.

X. *Aseptic Ligature.*

In his first communication to the profession on this subject Lister alludes to the advantages of the aseptic ligature as follows: "If the antiseptic ligature be employed it merely inflicts a wound or injury upon the vessel, without introducing any permanent cause of irritation. The injured part, therefore, becomes repaired after the manner of a subcutaneous wound without passing through the process of granulation and suppuration, which is induced by the employment of the ordinary septic ligature."[1] It may now be truly said that some form of aseptic ligature is used at present by almost every surgeon, and that, while the merits of the antiseptic treatment of wounds are still denied by many, few or none would dare to use the ordinary ligature without realizing that their duty towards their patients had not been conscientiously discharged. Perhaps no other surgical procedure has ever enjoyed the confidence of the whole profession throughout the civilized world to the same extent as the aseptic ligature. This universal faith in the reliability and safety of the aseptic ligature is only a natural outgrowth of the superior results following its use. Protracted suppuration in wounds, the result of retained ligatures, secondary hemorrhage, and suppurative inflammation of vessels have been gradually diminishing in frequency, and bid fair under the influence of the aseptic ligatures to be almost completely expunged from the future category of wound complications. Nussbaum very appropriately remarks: "Catgut is without doubt Lister's greatest discovery."[2] And again: "How pleasant it is to cut the liga-

[1] London Lancet, April 3, 1869.

[2] Leitfaden zur antiseptischen Wund-behandlung. Stuttgart, 1879, S. 23.

tures short and leave them unconcerned to their fate in the wound! In ovariotomies, etc., their value cannot be overestimated. The manner in which catgut adheres to an artery, forming connections with it and the surrounding tissues, assisting at the same time in forming a firm ring around the coats of the artery, are exceedingly welcome occurrences, guarding against secondary arterial hemorrhage in ligating in the continuity of a vessel, and rendering even the application of a ligature in close proximity to a large collateral branch devoid of danger. All this silk cannot do." Before the introduction of antiseptic surgery suppuration at the seat of ligature was almost a necessity. As suppuration interfered seriously with the hyperplastic processes in the tissues of the arterial tunics, secondary hemorrhage was of frequent occurrence, because the adhesion between the surfaces of the interior of the vessel walls were not sufficiently firm to resist the intra-arterial pressure at the time of the separation of the ligature. It was on this account deemed necessary by the older surgeons in deligating an artery in its continuity to apply the ligature at least an inch distant from the next collateral branch so as to favor the formation of a thrombus. The aseptic ligature marks a new era in the surgery of blood-vessels. Ligating a vessel under antiseptic precautions presents the following advantages:—

1. The ligature remains undisturbed in the wound, becoming either absorbed or encysted after having fulfilled the purpose of a provisional hæmostatic.

2. Prompt obliteration of the vessel takes place by proliferation of new tissue elements from pre-existing cells independently of the formation of a thrombus, in fact thrombosis is often wanting. The constricted portion of the vessel does not necrose, it is infiltrated like the catgut with living tissue.[1] Bardeleben makes a similar assertion.[2]

In all operations with the aseptic ligature the small size of the clot and its frequent entire absence is in remarkable contrast

[1] C. Hueter, Grundriss der Chirurgie, 1880, B. I. p. 146.

[2] Berl. klin. Wochenschrift, 1875, No. 29.

with the results observed after the ordinary septic ligature. The importance of the thrombus as an active agent in the definitive closure of vessels has vanished before the brilliant results obtained with the aseptic ligature. John A. Lidell, in speaking of vein ligature, says: "If a ligature of animal origin, such as carbolized catgut, has been applied the approximated walls grow directly together, and the ligature itself disappears by absorption or is replaced by new connective tissue."[1]

A discrepancy of opinion still exists regarding the time in which the catgut ligature is absorbed. The results of experiments in this direction have not been uniform. Lister ligated the carotid artery of a calf with carbolized catgut, and on examining the parts, thirty days after operation, he found only small portions of the ligature remaining, the rest absorbed and its space occupied by new tissue.

Czerny operated on rabbits, and examined the parts from one to thirty days after operation. After a number of days the ligature was always found loose on the vessel, softened and infiltrated with cells. Fillenbaum applied a double ligature to the carotid artery of a dog, and killing the animal fourteen days subsequently found only microscopical remnants of the ligatures. Schurhardt experimented with guinea pigs, and if the ligature was allowed to remain for five weeks, only traces of it remained. P. Bruns[2] operated on dogs four times, tying the femoral and axillary arteries, no antiseptic precautions being used, and the specimens were examined after ten days. In two cases catgut ligatures had undergone but little change; in the third case the ligature could not be detected with the naked eye, but the microscope showed traces of it; in the fourth case a double ligature had been applied to the femoral artery four ctm. apart, and in this instance the proximal ligature showed no change, while of the distal ligature only the knot remained. He also ligated the carotid artery three times and examined specimens after twenty days had elapsed, and found only in one instance traces

[1] Injuries of Bloodvessels. The Intern. Encycl. of Surgery, vol. iii. p. 211.

[2] Die temporäre Ligatur der Arterien, Deutsche Zeitschr. f. Chirurgie, B. V.

of the ligature on making longitudinal section of the vessel. In two cases he examined the ligatures after thirty days, the carotid and axillary arteries being the vessels tied, and found only microscopical traces. In four more operations he tied the axillary and femoral arteries, and examined after forty days, and on careful examination found traces of the ligature only in one case, while in the remaining three the microscope revealed only traces. From these experiments he concluded that the catgut ligature from the first to the tenth day is either not changed at all, or that the changes are not constant; absorption is constant from the twentieth to thirtieth day, and after the fortieth day only microscopical remnants can be found.

M. Arnaud, in a series of careful experiments, gives these results in regard to the absorption of carbolized catgut ligatures :—[1]

Catgut disappeared once in	4 days
" " twice in	7 "
" " once in	9 "
Catgut distinctly visible once in	4 "
" " " "	9 "
" " " "	11 "
Catgut visible but softened and infiltrated once in .	16 "

The time required for absorption, although variable in the same animals and in the same locality, will depend on: 1. The quality of the ligature; 2. The size of the ligature; 3. The nature of the tissue with which it is kept in contact; 4. The presence or absence of suppuration. P. Bruns claims that catgut is dissolved by pus, hence it will disappear in a shorter time in wounds that suppurate. In my experience I have observed the contrary. In suppurating wounds I have seen the catgut remain unchanged for an exceedingly long time, and after weeks have seen the ligature come away in the secretions, having undergone but little change. The absorption of the catgut ligature is accomplished by a process of softening and infiltration of cellular elements, and is consequently accomplished in the

[1] Richard Barwell, Aneurism, Encycl. of Surgery, New York, vol. iii. p. 442.

shortest space of time, in wounds where the process of granulation is not impaired by suppuration.

The immediate and remote effects of the catgut ligature on the vessel also deserves consideration. The impression prevailed at one time, that the catgut ligature does not destroy the continuity of the artery. This assertion has, however, met with opposition.

P. Bruns,[1] in his experimental work, has made special search in this direction in 13 ligations of arteries in their continuity. In the three specimens obtained ten days after operation, he found the artery completely severed in one instance, while in the other two cases a fine thread of adventitial tissue was found in the loops of the ligatures. In the remaining ten cases, where only traces and microscopical remnants of the ligatures could be found, three different conditions of things presented themselves. In three cases the vessel was completely divided in the same manner as after using the ordinary ligature, only the intermediate space between the vessel ends was less than after using the silk ligature, the space measured only from 1½ to 3 mm., and was filled in with connective tissue. In six cases a solution of continuity had apparently not taken place, and its existence was ascertained only by close examination. The place of ligature presented a somewhat prominent circular ring; on making a longitudinal section, the intima and media were found severed, and their margins directed towards the interior of the vessel, shutting off its lumen on both sides by a concave or funnel-shaped end. The interspaces between both blunt ends was occupied by a solid intermediary substance about the thickness of the ligature and continuous with the adventitia. The intermediary substance was composed of young connective tissue interspersed with particles of the catgut ligature. In one case the continuity of the vessel was perfect, all of its coats being entire. Evidently the ligature was not tied with the same degree of firmness as in the other cases. The lumen was only narrowed by the ligature and rendered impermeable by a thrombus.

[1] Op. cit.

Bruns is willing to admit, that in case the catgut ligature is drawn only sufficiently tight to interrupt the circulation, all of the coats of the artery remain intact during the healing process, and the continuity of the vessel is preserved in the strictest sense of the word. In the cases where division of the vessel took place, and a bridge of connective tissue, corresponding to the diameter of the ligature, formed, he also asserts that *practically* this process may be regarded as similar to the process of healing without loss of continuity of the vessel-tunics.

Stimson[1] agrees with Bryant, that the catgut ligature not only primarily divides the two inner coats of an artery like the ordinary silk ligature, but that subsequently the adventitia also gives way under the pressure of the ligature, thus completely interrupting the continuity of the vessel. They affirm that the bridge of intermediary connective tissue may impart an appearance as though no division had occurred. The results of my experiments have demonstrated to my satisfaction that it is not necessary to tie with sufficient firmness to divide any of the arterial coats, and yet prompt obliteration of the artery will ensue, and that in such instances the coats of the vessel are transformed into a solid string of connective tissue, the best possible result which can be obtained after ligature. Even in case the ligature is tied with sufficient force to rupture the inner coats, the constricted adventitia may retain its vitality, and form a part and parcel of the intermediary connective tissue uniting the two ends of the vessel; and still further, if the vitality of the adventitial coat is suspended, and it is removed by a slow process of molecular disintegration and absorption, it is replaced by tissue elements which are converted into a similar tissue, thus practically preserving the continuity of the vessel. In the event of suppuration, the advantages of the aseptic catgut ligature are lost, and the ligature escapes with the discharges either entire and unchanged, or in fragments after it has undergone softening and disintegration. Ligatures made of any other animal tissue rendered properly aseptic are disposed of in the wound in a

[1] The Antiseptic Catgut Ligature, Amer. Journ. Med. Sciences, 1881, p. 131.

similar manner as catgut, and it has not been proved that any of them possess any advantages over the well-prepared catgut ligature.

Mr. Barwell,[1] in tying large arteries, uses a broad ligature made of the strong middle coat of the ox's aorta. His idea is to approximate the intima without rupturing it. In sixteen cases of ligation of large vessels it proved successful. In one case of ligation of the femoral artery, hemorrhage occurred from a small vessel near the ligature at the time of operation; at the request of Mr. Barwell, two more ligatures were applied within an inch of the first ligature, and the case terminated favorably. Mr. Barwell still maintains the novel belief that his ligature material is not absorbed, but is organized and becomes a part of the living tissue around it. Aseptic ligatures made of materials which are not capable of being absorbed remain in the wound and are encysted. All of these ligatures are more prone to destroy the continuity of the vessels than animal ligatures, but they do not do so invariably. Czerny's silk, for example, which is used next in frequency to catgut, is infiltrated with cellular elements, and, after a long time, is partly absorbed and completely encysted.

XI. *Thrombosis after Ligature.*

One of the most serious objections against the prevalent doctrine of obliteration of vessels through the instrumentality of an organized thrombus, is the fact that, in many instances, coagulation of the blood fails to take place after tying a vessel with a ligature, and that primary union of its inner walls has been frequently demonstrated without thrombus formation. The conditions which determine intravascular coagulation after ligature are still not well known. Alexander Schmidt has shown that fibrin as such does not exist in blood, but that it is the product of a union between two substances, the fibrinogen and paraglobin, under the influence of a fibrin ferment, and he has

[1] International Encylopædia of Surgery, New York, vol. iii.

further shown that fibrinogen is contained in the plasma of the blood in solution, and that the fibrinferment and paraglobin are a product of the white corpuscles of the blood. Only after dissolution of the white corpuscles are paraglobin and fibrinferment set free, and can act on fibrinogen. Consequently, as long as the integrity of the white blood-cells is preserved, coagulation cannot take place. As fibrin does not pre-exist in the blood, it is the product of chemico-vital changes which take place before and during the process of coagulation. During coagulation the vitality of the morphological elements in the thrombus is lost as the white blood-corpuscles lose their identity, and their protoplasm unites with the fibrinogen contained in the serum and produces the fibrin. The endothelia lining the intima as long as they retain their vitality prevent the spontaneous death of the white blood-corpuscles, and this prevents the formation of fibrin.

Virchow attributed coagulation to the diminished motion or arrest of the current of blood in the vessel, but this cause has been found insufficient in itself to produce a thrombus provided the endothelia retained their normal qualities. Baumgarten has shown that a column of blood can be kept in a fluid condition for weeks within a vessel between two aseptic ligatures. If after several weeks the blood was allowed to escape through an incision in the tied portion of the vessel it coagulated the same as blood drawn from any other locality, showing that it had not lost its coagulating properties by its long confinement between the ligatures. This interesting phenomenon can only be explained by assuming that the aseptic ligature preserves the vitality even of the torn inner coats which successfully prevents loss of vitality of any of the white blood-cells. Some twenty years ago the famous experiments of Bruecke demonstrated that living tissues resist coagulation, and Baumgarten's experiments certainly most beautifully substantiate this assertion. It is a well-known fact that coagulation takes place with the greatest degree of certainty and becomes more extensive in proportion to the magnitude of the traumatism inflicted by the ligature and the degree and extent of the subsequent inflammation.

Until recently the universal belief prevailed that foreign substances introduced into the circulation invariably produce coagulation. This doctrine has also been successfully refuted. Zahn's investigations have demonstrated beyond all possible doubt that coagulation only follows the introduction of substances which have not been properly disinfected. He introduced aseptic pieces of glass and rubber, and never observed coagulation following this procedure.

Hueter, in speaking of thrombosis in veins, refers to our subject as follows: "Whether by following antiseptic precautions the formation of a thrombus can be prevented with the same degree of certainty as in the case of arteries remains an open question. It is certain, however, that septic infections favor coagulation in veins."[1] Of this latter assertion clinical experience furnishes abundant proof. It is more than probable that during the progress of many of the infectious diseases, many of the lining endothelia of the intima are destroyed, and that the white corpuscles coming in contact with dead tissue lose their vitality and produce thrombosis. But even under the old pre-antiseptic treatment thrombus formation was by no means a constant result after ligation. Walther, in 28 experiments to determine this question, found a thrombus in both ends of the vessel 18 times. In one case there was no thrombus on either side of the ligature, and in one only on the cardiac side, while in the remaining 8 cases the thrombus was found only in the distal end of the artery.

Porta has made the largest number of experiments to ascertain the relative frequency of thrombus formation after ligature. In 250 cases of ligation of large arteries in animals in which the vessels were examined for this purpose, he found in 35 cases no traces of a thrombus, and yet he observed only 3 cases of secondary hemorrhage after 400 ligations.

Schumann[2] made 54 experiments on dogs and rabbits with a

[1] Grundriss der Chirurgie, 1880, vol. i. p. 148.

[2] Virchow u. Hirsch's Jahresb. 1874, vol. ii. p. 377.

view to study the provisional and definitive closure of vessels after ligature. Thrombus formation had only occurred in 32 per cent. of the cases, and the coagulum in all of these cases was usually small. It is evident from these statistics that thrombus formation after ligature frequently fails to take place, and that in this event closure of the vessel is effected by tissue proliferation from the vessel tunics. It would hardly appear reasonable to assume with Kocher, that in these cases a thrombus so minute in size as to elude detection by the naked eye might still exist, and perform the difficult task of obliterating the lumen of the vessel.

XII. *Organization of Thrombus.*

By organization of a thrombus we understand that some of its morphological elements retain their vitality and power of tissue proliferation. In this sense the term is used by all authors who have attributed to fibrin, white blood-corpuscles and red blood-corpuscles the property of being converted into connective tissue. If the intra-vascular thrombus possesses this quality, it is certainly an exception to the general rule, as extravasations of blood in any other locality of the body are never known to undergo organization. Under the most favorable circumstances they are destined to succumb to retrograde metamorphosis leaving eventually nothing but hæmatoidin crystals as landmarks of their former existence.

Serous membranes afford a favorable surface for rapid absorption of blood, so much so that the peritoneal cavity has been utilized for the purpose of performing transfusion of blood. Copious effusions of blood into joints are usually promptly absorbed, leaving no permanent ill results as far as the functions of the joints are concerned. Immense extravasations into the cellular tissue about the seat of fractures, or the result of other injuries, are completely absorbed in a remarkably short time, provided suppuration is prevented. The anterior chamber of the eye, from the peculiar anatomical structure of its walls, is an exceedingly favorable locality for successful tissue transplantation, as has been demonstrated by Dorremal and Goldzieher, and yet every oculist can testify to the fact that extravasations of blood in this locality never undergo organization, but are usually promptly removed by absorption. As an additional factor, it may also be mentioned that the intra-vascular thrombus is located disadvantageously as far as organization is concerned, the intima and media separating it from the nearest vascular supply. The assertion made by Lister that bloodclots in wounds under the antiseptic treatment become organized, certainly does not correspond with facts. If bloodclots in the interior of the tissues of the body, safely protected from any possible source of infection, invariably disappear by absorption, there is no good reason to believe that they will undergo any other changes when located in wounds. The clot itself is not organized, but simply serves the useful purpose of furnishing a favorable soil for the lodgement and propagation of new tissue-elements from the adjacent wound surfaces. In this sense the organization of the clot is accepted by Volkmann.[1] He believes that the blood clot between the broken ends of the bone in compound fractures serves primarily the purpose of a soft cement substance which, under the protection of antiseptic precautions, is gradually displaced by substitution, and its space occupied by permanent tissue.

XIII. *Formation of Cicatrix in Bloodvessels after Ligature.*

The ligature fulfils a twofold object: 1. It constitutes the most scientific and reliable provisional hæmostatic, interrupting at once the physiological function of the vessel at the point of application. 2. It brings the vessel walls in mutual contact, and, by maintaining uninterrupted apposition for a sufficient length of time, it induces an active tissue proliferation which is destined to produce definitive obliteration of the lumen of the vessel. The immediate effect of the ligature in arresting the

[1] Die Behandlung der complicirten Fracturen. Volkmann's Sammlung klin. Vortraege. No. 134.

circulation was well known even to those who first resorted to its use, but the secondary changes, the definitive closure of vessels by cicatrization, has been a subject concerning which there has prevailed the greatest diversity of opinion and which still remains a prolific object for study and investigation. The researches of Jones laid the foundation for an intelligent and rational study of the process of cicatrization in bloodvessels after ligature. Various theories have been advanced which were intended to furnish an explanation of the process of obliteration, or to point out the particular tissue which supplies the material for the cicatrix. The production of cicatricial tissue within the bloodvessels has been attributed to: 1. Adhesive inflammation and plastic exudation at the seat of ligature without reference to any histological changes. 2. Fibrin. 3. White blood-corpuscles. 4. Red blood-corpuscles. 5. Immigration corpuscles. 6. Connective tissue. 7. Endothelia.

XIV. *Formation of Cicatrix by Adhesive or Plastic Inflammation.*

The existence of adhesive inflammation has always been recognized as an important element in effecting permanent closure of a vessel after ligature. Under this head will be mentioned the pathological views of older writers who studied the process of cicatrization independently of any accurate histological knowledge.

Celsus believed that the definitive obliteration of the vessel was due to retraction of the artery and tumefaction of the connective tissue around it. Galen asserted that permanent closure takes place by a cicatrix which closes the wound in the vessel, believing that the arterial walls unite only in exceptional cases. Ponteau regarded the inflamed para-vascular tissue as the most important element in the obliterating process. John and Benjamin Bell believed that an artery is occluded by a plastic exudation which takes place from its inner walls and the divided ends. Scarpa, who compared the tunica intima with serous membranes, and attributed to it the same tendency to assume inflammatory changes and form speedy and firm adhesions, commits himself on this subject as follows:[1] "The union of the two opposite sides of an artery, as I have mentioned several times, only takes place by means of the adhesive inflammation, to excite which, and in order that it may produce the desired effect, it is necessary that the artery be not insulated too much, or beyond the limits of the ligature; that the degree of pressure be such as to put and keep the two opposite sides of it in complete and firm contact, that the irritation caused by the pressure be sufficient to produce inflammation in the proper coats of the artery without their passing immediately into a state of mortification from a want of vitality. If this degree of pressure be too small, the artery does not inflame sufficiently and is not obliterated, but is rather wasted slowly and then bursts; if the pressure be too great, and especially upon an artery insulated in a greater space than is requisite for the ligature, it mortifies, ulcerates, and opens before the sides of it have adhered to each other, both at the place of ligation and for a certain space above and below it."

Porta placed great stress on the importance of primary union of the wound, and the appearance of an external plastic ring at the seat of the ligature, in securing permanent occlusion of a vessel. He also pointed out how suppuration would interfere in obtaining the most favorable results after ligation. Jones and Travers almost ignored the importance of the thrombus in effecting closure of a vessel, and assigned to the traumatic inflammatory exudation almost exclusively the function in accomplishing this object. They claimed that the ligature acts as an irritant to the walls of the vessel, plastic exudation taking place into its lumen, the torn intima and media becoming adherent, thus permanently closing the canal.

Kirkland and White maintained that the coats of arteries near the ligature unite by plastic lymph, and that the coagulum is not only useless but may prove detrimental by interfering with such union.

[1] A Treatise on the Anatomy, Pathology, and Treatment of Aneurism, trans. by Henry Wishart, 1808, p. 277.

After Virchow in his researches on thrombosis and embolism had demonstrated that the intima is not susceptible of inflammation, pathologists again turned their attention to the importance of the thrombus as an active agent in the process of cicatrization. Rokitansky,[1] in opposition to Virchow, again claimed that the final obliteration of an artery can take place without a thrombus in a similar manner as in the vessels of the umbilical cord and the ductus Botalli.

Ph. Von Walther[2] says that the tunics of injured arteries inflame in a similar manner as other wounded organs. The phlogistic exudation takes place first in the external coat, somewhat later in the middle coat, and latest on the free surface of the internal tunic.

Cruveilhier, Castleman, and Foerster also ignored the importance of the thrombus, and pointed to the tissues of the vessel-walls as the active agents in the obliterating process. All of the authorities who mention adhesive inflammation as the means by which vessels are permanently closed, assign to the thrombus only an unimportant or entirely passive rôle, but at the same time they do not point out the particular tissue element which is supposed to furnish the material for the cicatrix. Later researches have aimed to limit the process to some special structure and to study and demonstrate the minute processes by which obliteration is accomplished. In one of our recent American text-books on surgery, the process of obliteration in an artery is described as follows: "The permanent closure and final and complete obliteration of these vessels (arteries) is effected by their continued contraction, by the effusion of fibrin within and around the vessels, and at length by the conversion of all their coats into simple cords of connective tissue. Even these latter may in the course of time disappear."[3]

[1] Handbuch der Speciellen pathologischen Anatomie. Wien, 1844, p. 616.

[2] System der Chirurgie. Carlsruhe u. Freiburg, 1843, B. i. p. 253.

[3] Hamilton, The Principles and Practice of Surgery, 1879, p. 176.

XV. *Formation of Cicatrix from Fibrin.*

All pathologists who ascribe to any of the pre-existing morphological elements of the thrombus the active part in the process of cicatrization, as a matter of necessity consider the presence of the thrombus essential in the process of obliteration.

John Hunter maintained that the fibrin in the clot is capable of undergoing organization, and is the active agent in producing permanent closure of a vessel after ligation. He based his assertion on the examination of a thrombus taken from a crural artery which he injected from the lumen of the vessel and found that it contained a network of vessels. To satisfy himself that organization of the thrombus takes place, he applied a double ligature to the carotid artery of a dog, and on examination of the specimen some time afterward he verified his conclusion. Gendrin, who repeated the experiments of Hunter, says: "If a quantity of blood is included between two ligatures in an artery or vein, it coagulates, and, as is well known, the serum is absorbed and a slight inflammation takes place in the walls of the vessel. The different parts of the thrombus are decolorized, a thin layer of coagulated lymph diffuses itself over the inner walls of the vessels which effects adhesion between thrombus and vessel-walls, the thrombus finally undergoes organization and cicatrization."

Andral supposed that he had demonstrated in a satisfactory manner that fibrin in cases of pleuritic exudations and pseudomembranes is converted into connective tissue, and his teachings were generally accepted. Henle also claimed that fibrin is converted into connective tissue, and that it constituted the most important element of the thrombus. Zwicky, a pupil of Henle, was the first to give an accurate microscopical description of the appearances in vessels after ligation. In accordance with the views of his preceptor, he asserted that the blood corpuscles only play a passive part in the process of organization of the clot.

As late as 1872, Billroth writes: "Coagulated fibrin may, by aid of cells, be transformed into connective-tissue inter-cellular substance, although I cannot decide whether this be due to a true metamorphosis, or to a gradual substitution of cell protoplasms for disappearing fibrin."[1]

It is almost unnecessary to say that at the present time no one can be found who claims that fibrin is capable of being transformed into connective tissue, but that wherever found it invariably disappears after a time by molecular disintegration and absorption. Physiology teaches us that fibrin does not pre-exist in living blood, but that it is formed as the result of chemico-vital changes during coagulation, hence we would *a priori* conclude that such a substance is not capable of being elaborated into tissue endowed with a higher degree of vitality.

XVI. *Formation of Cicatrix from White Blood-Corpuscles.*

After Virchow had shown that adhesive inflammation of the intima is incompatible with its structure, pathologists again turned their attention to the thrombus as the active medium of the process of obliteration. The organization of the thrombus now became a favorite study. Stilling and Zwicky not only claimed that the thrombus undergoes organization, but they were also among the first to describe a vascular network in the thrombus; the vessels, according to their observations, communicating with and originating from the lumen of the vessel. Virchow, Billroth, and O. Weber referred the organization of the thrombus to the presence in it of the white blood-corpuscles. Czernay and Schuman attributed it to the same cause. They traced step by step the part taken by these corpuscles in the process of organization of the clot. Pirogoff, Thierfelder, Gerstäcker, and Boner, studying the fate of the white blood-corpuscles in subcutaneous tenotomies, found them capable of transformation into new connective tissue.

[1] General Surgical Pathology and Therapeutics, trans. by C. E. Hackley, New York, 1872.

The conclusions at which O. Weber arrived may be summarized as follows:—

1. The red blood-corpuscles and fibrin of the clot disintegrate and disappear by absorption.

2. The colorless blood-corpuscles in the clot, a few hours after the application of the ligature, enter into a transformation into spindle-shaped cells.

3. After a few days the projections thrown out by these cells may be seen to unite with each other, and, by arranging themselves in rows, plainly assume the shape of new vessels.

4. The youngest vessels are formed in the peripheral portion of the clot.

5. During the third and fourth weeks the vascularization of he thrombus is completed, the vessel having formed anastomoses with the vasa vasorum of the adventitia. At the point of ligature where the intima and media have been lacerated, the vessels of the adventitia enter the thrombus directly; further from the ligature they penetrate through the two inner coats and enter the thrombus.

6. About the fiftieth to the sixtieth day the thrombus is traversed everywhere by vessels, more especially at the periphery. A large vessel is often found in the centre of the clot.

7. During the process of cicatrization, the vessels in the thrombus disappear, the lumen of the vessel becomes narrower, and is finally completely obliterated.

8. The cicatricial tissue is the exclusive product of the white blood-corpuscles.

9. The white blood-corpuscles multiply very rapidly by segmentation.

10. The endothelia of the new bloodvessels in the thrombus are produced exclusively from the white blood-corpuscles.[1]

Kocher[2] has studied the organization and vascularization of the thrombus after ligature, and sustains the views entertained

[1] V. Pitha u. Billroth's Chirurgie, i. 1.

[2] Ueber die feineren Vorgänge bei der Blutstillungdurch Acupressur, Ligatur und Torsion, Archiv f. Kl. Chirurgie, B. xi. S. 660.

by Weber. He injected the vessels from the lumen of the artery, and examined transverse sections under the microscope.

I will give the description of one of his specimens: On December 24, 1867, he ligated the right carotid artery of a dog, and dusted finely powdered cinnabar over the exposed portion of the vessel to indicate subsequently the exact location of the ligature. The animal was killed January 11, 1868. The operation wound was healed. The vessel was injected with gelatine stained with Berlin blue, and hardened at first in a solution of chromate of potassa, and subsequently in alcohol; after it was sufficiently hardened it was thoroughly dried and inclosed in a coating of paraffin for the purpose of making microscopical sections. The decolorization of the thrombus was more complete near the ligature than towards the free lumen of the vessel. The proximal end of the thrombus was adherent only to one side of the vessel, so that the injection material penetrated the other side between vessel-wall and thrombus. From the free surface of the central end of the thrombus a central vessel of considerable size was seen to enter the thrombus; from it smaller vessels branched off and penetrated the thrombus in different directions, forming a beautiful network of capillary vessels, which left no doubt in his mind that the channels were real blood-vessels and not an artificial product. Wherever the thrombus was adherent to the intima, the latter showed small vessels from the adventitia, while the free surfaces of the intima remained non-vascular. Nearer the ligature the vascular network from the adventitia was more fully developed, supplying numerous branches to the inner coats of the artery. The torn intima at the seat of ligature was arranged in folds, its free and irregular margins sending prolongations into the thrombus. The media was also divided by the ligature, so that the thrombus penetrated between its fibres. While the vascularity of the vessel-wall increased towards the ligature, the vessels in the thrombus became smaller in the same ratio, to disappear completely near the ligature. These appearances satisfied him that the vascular supply of the thrombus is derived directly from the free lumen of the vessel, while the vasa vasorum increase in size and number, and distribute branches to the inner tunics over an area corresponding with the adherent portions of the thrombus. He agrees with O. Weber that canalization of the thrombus initiates organization. He also made a number of experiments where the conditions for thrombus formation were exceedingly unfavorable, by tying arteries in close proximity to a large collateral branch. In all cases where the experiment proved successful, he found the two inner tunics ruptured, and in every instance no direct union of the lacerated tissues, but cicatrization was always the result of a thrombus, which in some instances was exceedingly small, almost microscopical in size. For the purpose of proving that the tissues of the arterial coats take no active part in the process of obliteration, he made the following experiment: The right carotid artery of a dog was tied December 24, 1867, in two places, 2 ctm. apart, the blood in the intermediate space having been squeezed out between two fingers before tying the peripheral ligature. Cinnabar was dusted over the vessel in the wound. The animal was killed January 11, 1868. The wound was healed. The vessel on the cardiac side was closed by an extensive adherent thrombus. Between the ligatures the vessels contained a very small adherent thrombus, the greater portion of the lumen being empty. Transverse section through this portion of the artery revealed the star-shaped lumen of the vessel, the folds of the intima being in contact but not adherent. No proliferation of the vessel-wall or the epithelium could be observed. The staining material was found diffused in the para-vascular connective tissue and the outer layers of the adventitia, but had failed to reach the inner tunics or lumen of the vessel. This experiment convinced him that the intact vessel-wall does not participate in the obliterating process. His numerous acupressure and torsion experiments showed that wherever obliteration of the vessels take place it is due to injury done to the intima, however slight that may be, followed by thrombosis, vascularization, and organization of the thrombus, and cicatrization by transformation of the white blood-corpuscles into cicatricial connective tissue, which finally approximates the inner vessel-walls, and holds them in permanent contact. He denies the possibility of direct union between the surfaces of the intima without the intervention of a thrombus. The views so strongly advocated by Virchow, O. Weber, and Kocher have been indorsed for the last forty years by a majority of the most prominent pathologists, and have found their way into most of our text-books.

Paget writes: "The artery between the ligature and the nearest collateral branch contracts and in some instances obliterates the whole portion of the vessel, losing its anatomical features, and is gradually converted into a fibrous string. The colorless blood-corpuscles in the clot elongate into spindles, or form stellate corpuscles, such as are seen in young connective tissue, forming by anastomoses a network which traverses the clot in all directions."[1]

Paget, however, recognizes the part performed by the vessel-walls, as he further states: "The clot, with the aid of the plastic inflammatory exudation, becomes firmly adherent to the inner walls of the vessel." Billroth, after his description of organized thrombi, accounts for the presence of the embryonal connective-tissue cells in the following manner: "After having abandoned the idea of proliferation of stable tissue-cells in inflammation, we can no longer talk of a proliferation of the intima in the old sense. But whence come, then, these newly-formed cells? I have no doubt that they originate from the white blood-cells, which have been partly inclosed in the thrombus, partly may have wandered into it, according to the observations of von Recklinghausen and Bubnoff."[2]

XVII. *Formation of Cicatrix from Red Blood-Corpuscles.*

The remaining pre-existing histological elements in the thrombus, the red blood-cells, have been considered as passive elements by the preceding authorities, destined to undergo granular degeneration and to disappear by absorption. A few

[1] Lectures on Surgical Pathology, 1870.

[2] General Surgical Pathology and Therapeutics, trans. by C. E. Hackley, A.M., M.D. N. Y. 1872, p. 108.

pathologists, however, among them Rindfleisch, Adreef, and Koslowsky, assign to them an active part in the organization of the clot, for the reason that they have observed that instead of undergoing molecular disintegration they gradually lose their coloring material, and by a series of successive changes they are transformed into white blood-corpuscles and become endowed with all the intrinsic vital properties possessed by these elements. They maintain for the red blood-corpuscles the same active rôle in the organization of the clot and process of cicatrization as has been assigned to the white blood-corpuscles.

XVIII. *Formation of Cicatrix from Immigration Corpuscles.*

Soon after the discovery of the wandering corpuscle this element was supposed to be the principal agent in the process of tissue regeneration and in the formation of pathological products. The obscure and much vexed question of obliteration of vessels after ligation found a ready interpretation by assuming that these wandering corpuscles, endowed with inherent properties to produce new tissue, would penetrate the walls of the vessel and enter its lumen, and there, by being converted into connective tissue, would effect definitive closure. The functions previously attributed to the pre-existing white blood-corpuscles in the thrombus was now assigned to immigration corpuscles by a number of observers. von Recklinghausen adopted this theory, and was soon followed by one of his pupils, Bubnoff, who wrote a lengthy and interesting article on this subject.[1] In order to prove that cells enter the vessel from without he tied the jugular vein in animals, and applied finely powdered cinnabar to the vessel at the seat of ligature before closing the wound. From the well-known capacity of the white blood-corpuscles to absorb finely divided substances, he expected that they would absorb some of these minute granules of the coloring material and convey them into the vessel, which would, on subsequent examination, render their identification in the lumen an easy matter,

[1] Ueber die Organization des Thrombus, Centralbl. f. d. Med. Wiss. 1867, No. 48.

and furnish positive proof of their passage through the vessel walls. He was not disappointed in his expectations, as in all of his experiments he found on microscopical examination corpuscles charged with granules of cinnabar in the interior of the vessels. His results led him to adopt the following conclusions: The colorless blood-corpuscles in the thrombus lose their property to migrate after coagulation has taken place, consequently they take no active part in cell-proliferation. The organization of the thrombus is, to a great extent, accomplished by cells which enter the veins from without. Most of the cells are derived from the vasa vasorum and the adjacent para-vascular spaces.

Kocher repeated these experiments on arteries, but failed to find the same results.

Thiersch objects to the conclusions advanced by Bubnoff, claiming that the discovery of cells containing granules of cinnabar in the interior of the vessels is no proof that the cells entered from without, as the coloring material might have entered the vessel with fluids passing through spaces in the vessel-walls without the assistance of any morphological elements. Raab admits that leucocytes do penetrate the coats of veins, but does not believe that they take any part in the obliteration of the vessel. Durante, Cornil and Ranvier, have demonstrated that leucocytes traverse the walls of a vessel only when this has been tied with a double ligature causing death of the included vessel, and that leucocytes travel only through this dead tissue. Klein[1] claims that endothelial cells are converted into leucocytes, and that these are instrumental in the process of cicatrization. Seuftleben[2] has demonstrated beyond all doubt that leucocytes do enter the walls of veins which have been separated from all vascular connections. He removed sections of veins, disinfected them thoroughly, tied both ends firmly, and introduced them into the peritoneal cavity of living animals. He killed the animals at variable periods after the operation and found these

[1] The Anatomy of the Lymphatic System, London, 1873, I.

[2] Ueber den Verschluss der Blutgefässe nach Unterbindung, Virch. Arch., B. 77, S. 421.

bloodless transplanted pieces of vein-tissue in most instances adherent and encysted. Even after a comparatively short time he found the interior of the vein occupied by masses of epithelial cells, spindle-shaped cells, round and even giant cells. The last mentioned cells were evidently intended to accomplish the work of absorption of the transplanted tissues. To all of these cells Seuftleben assigned an extra-vascular origin.

N. Schultz[1] studied the influence of the migration corpuscles in cicatrization in bloodvessels by applying a double ligature and excluding the blood from the intermediate portion of the vessel. He operated on arteries. In examining specimens a short time after operation he scraped the intima, and observed incipient degenerative change in the endothelia and no attempt at proliferation. In specimens two days old he found white blood-corpuscles in the lumen of the intermediary portion of the vessel which he believed entered from without, and which are eventually converted into connective tissue. In specimens 128–155 days old, the vessel between the two ligatures consisted of a string of loose connective tissue in which no trace of the original tissues of the arterial coat remained. Cicatrization progressed more rapidly in the femoral than in the carotid arteries. In case only one ligature is applied he also observed no proliferation on part of the endothelial cells, but in this instance he believed that the process of organization and cicatrization of thrombus is due to the presence of the white corpuscles in the thrombus.

Uhle and Wagner[2] credit the wandering corpuscle at least with a part of the work required in the obliteration of a vessel. Their description of the cicatrix formation commences with the following allusion to this subject: "The organization of a thrombus is certainly not effected by an exudation on the inner surface of the walls of a vessel, nor by the white blood-corpuscles contained in it; perhaps at least in part it is due to the white blood cells circulating in the blood, and which gain entrance

[1] Ueber die Vernarbung von Arterien nach Unterbindungen u. Verwandungen, Deutsche Zeitschr. f. Chir. ix.

[2] Handbuch der allgemeinen Pathologie, Leipsig, 1876.

into the vessel from the vasa vasorum, or by cells which originate outside of the vessel walls, and by permeating them enter the lumen of the vessel." Billroth, after speculating on the origin of the white blood-corpuscles, says that they may spring from connective tissue or a protoplasm analogous to connective tissue, and he believes that they may traverse the living walls of vessels, as he has performed Bubnoff's experiment successfully on the carotid artery of a dog.

One of the strongest arguments in favor of the tissue-producing function of the wandering blood-corpuscles is advanced by Ziegler.[1] His experiments consisted in introducing under antiseptic precautions into the living tissues of animals, two glass plates with a capillary space between them. On examining the specimens at different intervals of time he found the space between the glass plates at first filled with white blood-corpuscles which were subsequently transformed into connective tissue and bloodvessels. The results of these experiments have made Ziegler an ardent advocate of the doctrine that the wandering corpuscle is the principal tissue-producing element in all regenerative and pathological formations. Every one must admit that these experiments are both ingenious and beautiful, but the deductions may lead to erroneous conclusions, as the experiments do not preclude the possibility of the entrance of embryonal connective-tissue elements from the wounded surfaces surrounding the glass plates. In many instances the obliterating process is accomplished in such a remarkably short time that this theory would hardly apply, and until more positive evidence is furnished we must seek for a more satisfactory explanation.

XIX. *Formation of Cicatrix from Endothelia.*

The majority of the older authors who maintained that direct and primary adhesion of the inner walls of the vessel takes place after ligature, attributed this occurrence to a plastic exudation

[1] Experimentelle Untersuchungen über die Herkunft der Tuberkel elemente, Würzburg, 1875.

upon the free surface of the intima. In entertaining this idea, they must have necessarily assumed that the tissues of which the intima is composed are capable of entering into tissue proliferation subsequent to the traumatism inflicted by the ligature. This doctrine was annihilated by Virchow, who taught that the intima does not respond to any amount of stimulation, and that, if the irritation is increased to a certain degree, necrosis of the intima takes place as a constant and unavoidable result. For a long time it was claimed that the intima takes no active part either in the organization of the thrombus, and the process of cicatrization. The advancements made in histology and the experimental investigations which have characterized the history of medicine for the last forty years have thrown new light upon the subject. The important part taken by stable tissue cells in all regenerative and pathological changes is again fully realized by the most competent observers, and the presence of inflammatory changes in the intima after ligature is now fully established.

His[1] pointed out the difference between epithelia and endothelia, and showed that the latter originate exclusively from the mesoblast, belonging, therefore, to the series of connective-tissue formations possessed, like all analogous structures, of the common property of being capable of entering into tissue proliferation. As early as 1824, Rokitansky taught that primary union of the vessel-walls and definitive obliteration could take place independently of the formation of a thrombus. He believed that the surfaces of the intima adhere nearest to ligature, and the process of obliteration proceeds from this point to where collateral circulation is established. The vessel obliterates as it has no further physiological function to perform. He was never able to discover any vessels in the thrombus.

Cohn[2] was the first to assert that obliteration of a vessel after ligation is due to proliferation of the endothelial lining of the intima. Lancereux in France and Förster in Germany adopted his views.

[1] Die Haüte und Höhlen des Körpers, Basel, 1866.

[2] Klinik der embolischen Gefässkrankheiten, Berlin, 1860.

Waldeyer, who is a firm believer in the endothelial origin of the intra-vascular cicatrix, describes the process of organization of the clot after ligature as follows: "The intima is rendered vascular from the media. From the intima loops of capillary vessels project into the thrombus accompanied by an envelope of delicate spindle-shaped cells from the endothelial lining, which constitute the basis of the future connective tissue."[1]

Thiersch[2] has studied experimentally the process of obliteration in small vessels in wounds of the tongue of the Guinea pig. At the point of injury, both in arteries and veins, he has witnessed the rapid production of endothelial cells to which he attributed the most important function in the organization of the clot and obliteration of the vessel.

Czernay[3] claims that organization of the clot is complete five days after ligation. Although he refers this process to the presence of white corpuscles which accumulate in the thrombus and the vessel-walls, he satisfied himself that the endothelia at and near the seat of the ligature multiply with great rapidity.

Baumgarten[4] has made some very interesting experiments to establish a proliferation capacity of the endothelia. He asserts that obliteration of a vessel takes place without the intervention of a thrombus, as when the column of blood is excluded between two ligatures. He operated on rabbits by applying a double ligature both by excluding the blood in the intermediate portion of the vessel, or by leaving it between ligatures. In both instances he obtained prompt obliteration of the vessel. In case the blood was excluded from the vessel, he observed a cellular product in the lumen of the vessel a few days after operation; these cells he believed to be the product of endothelial tissue proliferation which was most marked in the immediate vicinity of the ligatures. The modified endothelia are

[1] Zur pathologischen Anatomie der Wundkrankheiten, Virchow's Arch. vol. xi. p. 379.

[2] Ueber den Verschluss der Gefässe bei Acupressur, Centralbl. f. d. med Wissensch., 1868, No. 50.

[3] Von Pitha u. Billroth's Handbuch der Chirurgie, vol. i. part ii.

[4] Ueber die sogenannte Organisation des Thrombus, Centralbl. [illegible]., 1876, No. 34.

converted into fibroblasts (Neumann) and spindles of connective-tissue cells. When a thrombus was present, the granulation tissue gradually displaced the thrombus, and was finally converted into vascular connective tissue. The vascularization always took place by vessels from vasa vasorum. The ligatures were tied with sufficient force to divide the two internal coats. By applying an irritant to the outer surface of veins, he also noticed after twenty-four to forty-eight hours proliferation from the endothelial lining of the intima. The endothelia enlarged and assumed a cuboidal shape, showing conclusively that they participated in the inflammatory process which affected the entire thickness of the vein-walls. For one of the most valuable contributions to our knowledge of cicatrization in blood-vessels after ligature we are indebted to Fritz Raab.[1] His experiments were made on dogs, and always under antiseptic precautions. The sheath of the vessel was opened at two places from 1–4 ctm. apart, and after tying the proximal ligature in the case of arteries, and the distal ligature in case of veins first, the blood was squeezed out of the vessel before tying the second ligature, securing thus a bloodless space between them. He cautioned against opening the sheath extensively for fear of producing necrosis in the intermediate section of the vessel. As ligature material, silk was used which was always cut short. If the ligature cuts through or the wound does not heal promptly, a funnel-shaped sinus remains which leads to the ligature, and in all of these cases the portion of the vessel-walls towards the wound was found destroyed.

Experiment No. I.—Carotid artery; intermediate portion of vessel between ligatures two ctm. Animal killed after 12 days. At seat of ligature, artery, vein, and vagus blended in a spindle-shaped indurated mass of connective tissue. Vessel, between ligatures, completely obliterated. Adventitia slightly infiltrated with cells. Media and intima normal. Endothelial lining changed into several layers of oblong spindle-shaped cells. Where surfaces of intima were brought into apposition the lumen was found obliterated. Remnants of blood-cells were also found which had remained in

[1] Ueber die Entwickelung der Narbe im Blutgefäss nach der Unterbindgung.

contact with inner walls of vessel. No vessels in the endothelial layers except at the seat of ligatures where intima and media had been circularly divided. Silk ligatures not infiltrated with cells. Under ligatures, fibres of adventitia remained intact. Proximal coagulum two ctm. in length, between folds of intima new endothelial formations.

Experiment No. II.—External jugular vein; ligatures four ctm. apart. Animal killed on 12th day. Around vein some induration. On distal side thickening of vein-walls; lumen smaller, containing a brittle red brown coagulum. Between ligatures, and two inches on proximal side, the vessel was transformed into a fibrous cord. Between ligatures all coats of vessels changed. Endothelia multiplied and converted into spindle-shaped cells; between them embryonal connective-tissue cells and round cells. No vessels except close to ligatures where vessels from vasa vasorum had penetrated the interior of the vein.

In commenting on these cases he gives his views concerning the formation of the intra-vascular cicatrix. Slight irritations will produce remarkable morphological changes in the endothelial cells. The walls of the veins do not require a great amount of traumatism to produce these results. During the first forty-eight hours after ligation, marked changes are observed which gradually extend from seat of ligatures to a certain distance, and it is immaterial whether the vessel contains blood or whether it has been rendered bloodless between ligatures. The first changes in the endothelia consist in an enlargement of the nuclei which imparts to the intima an increased wavy appearance. Later, the nuclei enlarge towards the periphery of the cells, displaying the protoplasm so that the protoplasmic spaces are diminished. The cells at this time assume a polyhedric or rounded contour. The naked eye now detects a loss of the glossy surface of the intima. Similar changes can be observed in the endothelial lining of small arteries and veins in inflamed tissue. The sharp contour of the nuclei is lost as soon as the cells have attained a certain size. The protoplasm is interspersed with fine molecules which aggregate at three or four points, and the cell soon contains from three to four nuclei.

Other smaller or pyriform or spindle-shaped cells are found in immediate contact with the large cell. These new cells originate from nuclei, and leave the cell-wall by the budding process. These small or daughter-cells are found in the lumen of the vessel on the surface of the endothelial layer. They become flattened, and eventually assume the shape of the old cells. They are variable in shape, according to the stage of development and locality in which they are found. In the folds of the intima they are flat, spindle-shaped, and elongated; on the surface, towards the lumen of the vessel, round or polyhedral. The proliferation takes place in the bloodless space as rapidly as when a thrombus is present. The obliterating process is completed earliest near the ligatures. In veins the round cells are most numerous, while in the arteries the flat spindle-shaped cells predominate. As the connective tissue is in closer proximity to the endothelial cells in veins than in the arteries, the proliferating process cannot be observed so satisfactorily as in the latter vessels. For the same reason the proliferation of endothelia begins later in arteries, and the process is accomplished less rapidly. At first the proliferation is witnessed in the folds of the intima in the shape of spindle-shaped cells which fill the spaces between the elevations forming bridges from one fold to another. While in the normal intima the endothelial lining consists of two or more layers of cells, in the inflamed intima an amorphous mass is found which is interspersed with cells of high refractive power. These new cells accumulate in great numbers, and finally perforate the endothelial lining into the lumen of the vessel. Heubner found the same conditions in examining specimens of endarteritis in vessels of the brain. In contradistinction to Heubner, Raab considers the cells on the surface of the endothelia as new productions. The nutritive supply for the endothelia is not derived from the blood circulating in the vessels, but is derived from the vasa vasorum of the adventitia.

The cement substance liquefies and gradually disappears during active proliferation. If the inner surfaces of a vein or artery are kept in mutual contact primary union takes place at once by means of long spindle-shaped cells which are the product of the endothelial cells. The space between the surfaces of the intima occupied by these cells is finally completely obliterated and the inner coat is transformed into one tissue. If a thrombus is present the embryonal cells of the intima send prolongations into the thrombus which unite with similar projections of other cells, thus forming a complete network of protoplasmic strings permeating the entire coagulum. Upon these strings new nuclei appear. These nuclei are the product of an aggregation of molecules, the connecting strings between the nuclei become narrower and eventually disappear, setting free the nuclei as new tissue elements. Some of the large spindle-shaped cells divide into two or more cells. The spindle-shaped cells arrange themselves into bundles with spaces between them which contain blood-corpuscles; these spaces may easily be mistaken for new bloodvessels. The endothelial product is not supplied with vessels until the tunics participate in the process, when vascularization takes place from the vasa vasorum. Obliteration can take place by tissue derived exclusively from the intima, but all coats of the vessel assist in the process from the beginning. The connective tissue immediately beneath the swollen endothelial cells is rendered loose and succulent, the spaces between the individual bundles are widened and an occasional cell is seen in them. Towards the periphery of the vessel the spaces between the elastic tissue fibres are also widened and active infiltration of cells is also witnessed here. These cells, like the endothelia, send out projections in the form of long strings of protoplasm, forming networks with the connective-tissue interspaces. The connective tissue between elastic fibres proliferates. The connective and elastic tissue spaces are populated with cells of various shapes and sizes. We find here cells in all stages of division, large, round, polygonal, and pyriform shaped, containing in their interior from two to four smaller cells. Around the vessels of the adventitia round lymphoid cells appear which infiltrate all the tissues of the vessel. The microscopical appearances resemble in many respects the picture presented by the inflamed tissue in the cornea or cartilage. Finally the new tissues perforate the endothelial layers and enter the lumen of the vessel, and mingle with the products of the endothelial cells, forming a common cicatricial tissue as the elements are being converted into connective tissue. Vessels of the adventitia enter through the coats of the vessel into its lumen, but the principal vascular supply of the intra-vascular tissues is derived from vessels which enter near the ligature through the spaces made by the circular division of the inner coats by the ligature. The ligature not only produces circular division of the inner coats but also longitudinal lacerations of the intima. The extent and degree of laceration of the walls of the vessel are in direct proportion to the amount of granulation tissue which is formed subsequently. Under the most favorable circumstances direct union of the inner surface of the intima takes place exclusively by endothelial proliferation without a granulative thrombus. Where this result is not obtained the granulation tissue is formed first, and advances from the seat of ligature towards and into the lumen of the vessel where it unites with the endothelial product and produces the tissue which has heretofore been known as the organized thrombus. The granulation tissue is composed at first of cells, later of cells, fibres, and vessels, and finally the number of cells is diminished and the connective tissue is increased, when the vessel is reduced in size being ultimately converted into a string of connective tissue.

Riedel,[1] studied the process of cicatrization in bloodvessels experimentally in the same manner as the preceding author and arrived at similar conclusions. He used catgut in place of silk, and dogs and rabbits were made the objects of his experiments. The space between the ligature was made bloodless by isolating the vessel, raising it from its bed, and placing a spatula underneath. In two of the specimens the interior of the intervening portion of the vessel was found obliterated. One specimen was obtained 9 days and the other 63 days after ligation. In the former specimen the endothelial proliferation appeared in the

[1] Die Entwickelung der Narbe im Blutgefäss nach der Unterbindung, Deutche Zeitschrift für Chirurgie, vol. vi. p. 450.

shape of spindle-shaped connective-tissue cells which filled only two-thirds of the lumen of the vessel. In the second specimen the connective tissue in the interior of the vessel was distinctly fibrillated. The elastic layer of the intima had suffered in many places a loss of continuity to give passage to bloodvessels from the media into the thrombus. In the next experiment two ligatures were applied one ctm. apart, including a column of blood. The animal was killed on the ninth day. In place of the white blood-corpuscles in the red thrombus large cells containing from one to three nuclei were found; the cell contents were either granular or round globules of a yellowish color. The identity of these globular masses with the red blood-corpuscles deprived of the greater part of their coloring matter was unmistakable. Some of these large cells appeared shrunken, with irregular surfaces, denoting incipient disorganization. While these cells were found uniformly present throughout the intervening portion of the vessel, the endothelia, half way between the ligatures, remained unchanged. Nearer the ligatures the endothelial layer was much thickened, filling completely the longitudinal folds of the intima. On the surface of the thickened endothelial lining were thin flat cells, and behind these new endothelial cells were seen the embryonal connective-tissue cells arranged irregularly with a variable amount of intercellular or cement substance. In other transverse sections, through portions of the vessel between the ligatures, could be seen springing from the parietal proliferation of the endothelial layer delicate processes penetrating the thrombus and reaching into the interior of the vessel and uniting with similar processes from the opposite side. These processes carried with them a layer of endothelia. At a right angle with these processes could be seen similar structures, thus dividing the interior of the vessel into spaces lined with endothelia. As the ligatures are approached these spaces grow smaller, containing in their interior well preserved red corpuscles and the large cells previously described. Any active part on part of the blood-corpuscles in this process could be safely excluded, and cicatrization could be referred exclusively to the action of the endothelial cells. The question presented itself whether the same process takes place in a thrombus not included between ligatures. To furnish a satisfactory answer, a thrombus, 27 days old, in the femoral artery of a dog was examined. The appearances presented were identical. The network of vessels in the thrombus communicated directly with the vessels of the media. Injections made into the lumen of the vessel sometimes followed processes from the lining of the vessel and filled the spaces in the thrombus. About the seat of the ligatures the external coats were actively engaged in aiding the processes of cicatrization. The connective tissue proliferates, the new cells being directed in such manner that they point towards the lumen of the vessel. They approach the intima accompanied by bloodvessels, penetrate the *membrana fenestrata*, and unite directly with the endothelial formations. The spaces in the *membrana elastica* of the intima increase in size as the ligatures are approached so that in place of circular necrotic pieces of tissue large cicatrices are formed. Ligatures always produce necrosis of tissue underneath. A thrombus, 12 days old, showed the endothelial proliferation in the form of cells corresponding to the windings of the elastic intima. The membrane projected into the lumen of the artery. The conical end of the thrombus is also covered with endothelial cells.

It is a well-known fact that connective tissue can be transformed into endothelial cells, as has been repeatedly observed in the formation of new synovial sacs. A thrombus not included between ligatures receives its first vascular supply from the lumen of the vessel. When blood is included between two ligatures, a scanty network of vessels reaches the lumen of the vessel from without.

Uhle and Wagner[1] testify positively to the importance of the functions of the endothelial cells and connective tissue in intravascular cicatrization in the following language: "In all probability the most important structures in the process of organization are the endothelial cells and connective tissue of the intima.

[1] Handbuch der allgem. Pathologie. Leipsig, 1876.

These proliferate within a few hours after ligation, and are first transformed into spindle-shaped cells, and later into connective tissue and vessels. As early as six or eight days after the formation of the thrombus, especially towards its periphery, it is traversed by a network of young capillary vessels which increase rapidly for the next few days. During this time the fibrin and blood-corpuscles disintegrate in the same manner as the so-called dissolution of the thrombus. The new vessels in the thrombus and intima enter into communication with the original and new vessels of the media and adventitia, and thus a genuine circulation is established throughout the entire thrombus; later an anastomosis is formed between the vessels in the thrombus and the lumen of the vessels. Reparative changes are initiated at first in the immediate vicinity of the ligature. After four to six weeks the circulation in the thrombus is completed, when the vessels again gradually disappear, the cement substance grows firmer, the red blood-corpuscles and fibrin, which still may remain are absorbed. At last only a minute connective-tissue string remains which can only be recognized by the aid of a microscope."

Cornil and Ranvier[1] have carefully investigated the part taken by the endothelia in cicatrization within bloodvessels after ligature. The following is a summary of their observations: Within 24 hours after ligation a clot forms in the central end which reaches to the nearest collateral branch. At this time the endothelia are swollen and granular, containing a round nucleus and frequently several nuclei. On the following day the thickening of the intima is well marked, especially near the ligature. The thickening of the internal coat is due to a proliferation of cells which appear spindle-shaped, but in truth they are flat. They resemble endothelia or cells of connective tissue swollen by inflammation. On the eighth day the internal coat puts forth low elevations, nipple-like in shape, which are particularly well marked at the point of ligation. By the 12th to the 15th day these elevations on the cardiac side of the ligature

[1] A Manual of Histology, by Shakespeare and Simes. Philadelphia, 1880.

penetrate into the blood clot, accompanied by capillary blood-vessels which run parallel to the axis of the elevations. In longitudinal sections it is seen that, at the place of implantation of these projections, the middle coat of the artery has disappeared so that they appear to spring from the external coat. Their vessels are derived from the vasa vasorum. The clot disappears before the new tissue, the spaces between them being occupied by discolored red blood-corpuscles, granules, and a few white corpuscles, an appearance which simulates blood channels as described by O. Weber.

I will mention a few recent American authors who assign to the endothelia an important, if not essential, function in the formation of the intra-vascular cicatrix.

Shakespeare[1] has made a number of experiments to determine what histological elements are active in the obliteration of vessels after ligation, and his views are summarized in the following: An acute endarteritis follows ligation, during which the endothelia and other cellular elements of the intima multiply with great rapidity. The inflammatory changes are most marked near the ligature. New cells are usually flattened and more or less endothelial in appearance. Among these large endothelioid cells are a considerable number of lymphoid cells and a few red blood-corpuscles. The cement substance holding these elements together, is sometimes structureless, sometimes granular, and occasionally slightly fibrillar. In a few days the walls of the plastic clot begin to bud and put forth granulations which encroach upon the space between the inner surface of the vessel and the blood clot, and upon the blood clot itself. The granulations by pressure and absorption remove the clot. The granulations have much the same structure as granulation tissue in any other part of the body. They are covered by a layer of endothelial cells. The base of the granulations rests upon the elastic lamina of the intima which, up to the 20th or 25th day, remains unchanged, forming a sharp boundary between the middle coat of the artery and the proliferation of the intima.

[1] Cornil and Ranvier's Manual of Histology, p. 322.

There is usually no indication of its perforation by capillary loop from the vasa vasorum. As the projections of granular tissue approach each other, sinuses are formed in which the blood circulates and supplies capillary vessels which at this time are formed at the bottom of the plastic clot. At the same time capillary varices form in the embryonal tissue of the outer coats of the vessel in the neighborhood and at the location of the ligature. They receive their blood from the vasa vasorum. In a few days the two capillary systems form a communication with one another by means of connecting loops which perforate the space between the injured elastic membrane of the intima at the point of ligature. The granulation tissue undergoes cicatrization and contraction which obliterate the vessel. The author describes at some length the laminated structure of the thrombus, and it is evident that the vascular networks in the thrombus were simply spaces between the lamina which were occupied by the pre-existing blood corpuscles in the thrombus, and that vascularization took place exclusively from the vasa vasorum.

Agnew[1] believes that the production of the new tissue may be accomplished by white blood-corpuscles, endothelia, and migrating corpuscles.

Lidell[2] holds that the thrombus undergoes organization, but attributes the definitive closure to adhesive inflammation of the inner and middle coats, the plastic exudation from the adventitia adding additional strength to the walls of the vessel. In speaking of the same process in veins he says: "Again, veins may, and often do, undergo repair after ligature without any inflammation whatever, whether adhesive or otherwise, as Mr. Travers was the first to show."

Wyeth[3] takes a more advanced ground and regards the endothelia as the essential element in effecting definitive obliteration. He writes: "The permanent occlusion is due to new-formed tissue springing from the normal cells of the intima."

1 The Principles and Practice of Surgery, vol. i. p. 155.

2 Injuries of Bloodvessels, Intern. Encyclop. of Surgery, 1883, vol. iii.

3 Surg. Diseases of the Vascular System, Intern. Encyclop. of Surgery, vol. iii. p. 351.

Heitzmann says: "Occlusion of ligated vessels is due mainly to endothelial proliferation, and vascularization of the thrombus starts in the inflamed intima."[1]

The fact that endothelia are endowed with sufficient vitality to proliferate new tissue is, however, not based alone on the observations of practical surgeons and experimental research, it is also supported by pathological processes which affect the inner tunics of the vessel. Virchow, in his experiments on embolism, introduced triangular pieces of rubber into the right heart through the external jugular vein. After four weeks he found the piece of rubber impacted in a branch of the pulmonary artery encysted in a vascular capsule composed of spindle-cells and flat-cells, evidently products of the endothelial lining. The inflammatory changes which occur in the endothelia of serous membranes have been studied by Rindfleisch, Klein, and Cornil and Ranvier. Kundrat selected for his investigations the peritoneum, Chapman the pericardium, and Albert the synovial membranes. Ponfick has called special attention to the rapid changes which take place in the endothelia during the acute stage of infectious diseases, and Heubner has assigned to them a special susceptibility for the syphilitic virus. Although O. Weber[2] takes it for granted that thrombosis and organization of the clot are the two essential conditions which precede and accompany the definitive obliteration of a vessel, he states distinctly that he has seen the endothelia repeatedly in a condition of so-called cloudy swelling, which would indicate that he has witnessed the first stage of progressive tissue metamorphosis in these structures—the first stage of inflammation.

Friedländer[3] has described a heretofore unknown affection of the arterial coats which he has called "arteritis obliterans." The affection is located in the intima of arteries of medium and smallest calibre and results in stenosis and sometimes complete obliteration of the vessel. The process is inaugurated by the

[1] Microscopical Morphology of the Animal Body in Health and Disease, N. Y. 1883.

[2] V. Pitha u. Billroth's Handb. d. allg. u. spec. Chir. vol. ii. div. ii. part i.

[3] Ueber Arteritis obliterans. Centralblatt f. d. med. Wiss. No. 4, 1876.

appearance of numerous round-cells between the innermost lamellæ of the elastic layer and the endothelial lining. The cells increase in size, intercellular substance is formed, and the new product presents all the characteristic appearances of granulation tissue with an abundant supply of new vessels, some of which are of considerable size. The proliferation may be limited to small points, or it may involve the entire circumference of the vessel. The new-formed tissue is generally converted into dense connective tissue, seldom undergoing fatty or calcareous degeneration. A physiological process very similar to the one described takes place during the occlusion of the *ductus arteriosus Botali* in the vessels of the umbilical cord after birth, and in the arteries and veins of the uterus after parturition. Analogous changes are observed in the small vessels in tissues which are the seat of chronic inflammation. Heubner has described it as it occurs in the vessels of the brain, but he was wrong in asserting that it was caused by the specific effect of the syphilitic virus. Regarding the source of the cellular elements, he mentions three probabilities: 1. Either they are the product of the endothelia of the intima; 2. They originate from white blood-corpuscles in the lumen of the vessel which must pass through the endothelial lining of the vessel; 3. Or leucocytes from the vasa vasorum.

Friedländer is inclined to the belief that they are derived from all of the three sources.

Winiwarter[1] reports a case of spontaneous gangrene of the foot in a man 57 years of age, who presented no symptoms of atheromatous degeneration of the vessels. On submitting the vessels of the amputated member to a thorough microscopical examination, he found a proliferation of endothelial cells of the intima in the arteries and veins, which had produced narrowing, and, in some places, complete obliteration of their lumen. He found the proliferation most active in small vessels which are composed exclusively of endothelia. The endothelia increase

[1] Ueber eine eigenthuemliche Form von Endarteritis und Endophlebitis, Archiv f. klinische Chirurgie, vol. xxiii. p. 206.

in size and assume a cuboidal shape, and as the proliferation advances the endothelial lining is thickened by additional closely packed layers of cells. In examining transverse sections of the smallest arteries, he observed the following appearances: The endothelial cells are arranged in concentric layers; towards the lumen of the vessel they are spindle-shaped and partly converted into connective tissue. In places where the vessel is not entirely obliterated, its lumen often appears irregular in outline, owing to the greater activity of tissue production in some portions of the inner walls of the vessel than in others. The media is also thickened partly by the increase of muscular fibres, and partly by cell infiltration from the intima. The cellular thrombus in the interior of the vessel is organized, and the cellular elements are gradually converted into connective tissue which completely and permanently obliterates the vessel, transforming it into a round string of connective tissue. In the interior of such strings, deposits of a homogeneous substance may be seen which indicate that retrograde metamorphosis of the cellular elements has occurred in place of organization into connective tissue. The same conditions were also found in veins.

Baumgarten[1] has found the vasa vasorum included in the ligature in ligating large vessels, a favorable locality to study this process. The inflammatory process begins in the adventitial structures, and extends by continuity to the endothelial lining, where proliferation takes place promptly and with considerable activity. Giant-cells may originate from endothelia, and, in case of very minute vessels, a single cell may block the calibre of the vessel completely. The endothelial cells, in the course of time, are changed into spindle cells, and finally into connective tissue. The round cells found in the media and adventitia undergo the same transformation.

Cornil and Ranvier[2] have seen several times cases of acute circumscribed endarteritis in the form of patches as an isolated lesion. Multiplication of the endothelia on the surface of the

[1] Ueber chronische Arteritis u. Endarteritis, Archiv f. path. Anatomie u. Phys., vol. lxxiii. p. 90.

[2] A Manual of Histology, by Shakespeare and Simes, Phil. 1880, p. 307.

internal coat is peculiar to acute endarteritis, while in the endarteritis preceding atheromatous degeneration, the proliferation takes place in the deepest layer of the intima. Multiplication of cells takes place by division of nuclei. A careful study of the new elements demonstrates that they spring from the intima. Periarteritis always coexists. The external coat produces granulation tissue. In the middle coat proliferating elongated cells of smooth muscle are seen, while the elastic fibres are broken down and absorbed.

As a last witness we will hear Heitzmann[1] concerning the endothelia when subjected to irritation and in a condition of inflammation, without alluding to the peculiar views on protoplasm entertained by this author. Endothelia being formations of living matter, are susceptible of undergoing rapid changes under the influence of irritation. The process is always secondary to affections of the subjacent vascular connective tissue. The inflammatory changes in this tissue as in every other consist in an increase of tissue. The endothelial cells in the initial stage become coarsely granular, or assume the "condition of cloudy swelling." The coarse granules increase in size, and constitute the inflammatory elements in all stages of development, reaching the highest development in the nucleated cells. The endogeneous new formation of elements within the epithelia was first maintained by Remak in physiological, and afterward by Buhl, Rindfleisch, and others in pathological conditions, and its existence thoroughly proved by L. Oser. In opposition to the supposition that the corpuscles visible in the endothelia had immigrated from without, Oser demonstrated the origin of inflammatory corpuscles *within* the epithelia. Heitzmann corroborates this view. A sufficient number of competent and reliable authorities have been cited, and enough has been said to prove that the vascular endothelia, when subjected to a sufficient degree of irritation, are susceptible of assuming inflammatory changes, and capable of proliferating new tissue elements which, if not the only reparative material, at least render essen-

[1] Loc. cit.

tial assistance in the process of cicatrization after ligature. It is important, however, to remember that the process of endothelial proliferation is secondary to the inflammatory changes which take place in the vascular connective tissue. The periarteritis and mesoarteritis which immediately follow ligation are attended by the formation of new bloodvessels which penetrate the intima, bringing the endothelial lining in direct contact with the circulation, which places the endothelia under the same conditions of nutrition and subject to the same pathological processes as any other vascular organs.

XX. *Formation of Cicatrix from Connective Tissue.*

The formation of the intra-vascular cicatrix from connective tissue has been frequently mentioned as the cause of the definitive closure of vessels since the introduction of the circular ligature by Jones. It was urged that the division of the two inner coats by the ligature and the curling inward of the lacerated tissues towards the lumen of the vessel would not only allow of the adventitia being brought in contact, but would also create a wound surface which would heal in the same manner as wounds in any other locality. The important function performed by the connective tissue in repairing solutions of continuity in any part or organ is well established and recognized by all authorities. The connective tissue is more widely diffused throughout the entire body and its susceptibility to undergo embryonal changes in a remarkably short time is as well known as its capacity to produce various types of tissue. It is the tissue which is invariably present in all cicatricial formations. This tissue is present in all coats of the arteries and veins; it accompanies bloodvessels wherever they go, hence it is only reasonable to assume that it plays an important part in the reparative process in vessels after ligation.

Kölliker and Eberth claimed that the connective tissue between the endothelial lining and the elastic layer of the intima proliferates and renders material assistance in the permanent closure of vessels.

Durante believed that when only one ligature is applied, obliteration of the vessel takes place by proliferation of the intima; when the double ligature is used the media and adventitia assume this office.

Reinhardt, after declaring that the thrombus remains passive after ligature, asserts that obliteration of the vessel takes place by an exudation or blastema from the adventitia.

Auerbach,[1] under Köster's directions, studied the obliteration of vessels experimentally on dogs and rabbits after single and double ligation. In using the double ligature he compared the results obtained by excluding the column of blood in the intervening vessel with those cases where blood was included between the ligatures. He ascertained that those vessels furnish the most favorable conditions for obliteration where the intervening portion was moderately filled with blood. The first changes observed in the coats of the vessel after ligation was an inflammatory infiltration in the adventitia proceeding in a central direction toward the lumen of the vessel. The acute stage is followed by a chronic granulation process which is established almost exclusively in the adventitia and intima. The inflammatory infiltration appears earliest at the seat of the ligature and reaches here the highest degree of development. The intima is supplied with vessels from the adventitia. The definitive obliteration of the vessel is due entirely to connective-tissue proliferation from the intima. The endothelia, although they manifest an attempt at progressive metamorphosis, do not produce new tissue. In case the adventitia is injured or removed prior to operation no changes occur in the two inner coats.

Roser[2] asserts that obliteration of an artery often takes place without a thrombus, and that the essential structure in this process is the adventitia. After the two internal coats have been severed by the ligature the external coat is brought in contact, and union takes place in the same manner as in other wounds.

[1] Ueber die Obliteration der Arterien nach Ligaturoo. Dissertation, Bonn, 1877. Virchow u. Hirsch's Jahresb. 1878, vol. i. p. 233.

[2] Zur Theorie der Blutstillung u. d. Nachblutungen. Arch. f. klin. Chir., vol. xii. p. 223.

As a frequent cause of secondary hemorrhage he mentions that small traumatic aneurisms sometimes form at the seat of ligature in the sac of the adventitia which rupture, and that in case of ligation of the artery in its continuity the tension exerted by the vessel increases the danger of rupture. In healthy animals occlusion of an artery takes place in a satisfactory manner even if it is tied in the immediate vicinity of a large branch. The same can be said of arteries which are ligated after amputations. Only in exceptional cases does obliteration take place through the medium of a thrombus.

For the most thorough investigations respecting the definitive closure of vessels after ligation from connective-tissue proliferation, we are indebted to Tschausoff.[1] His experiments were made on dogs. The specimens for microscopic examination were hardened in Mueller's fluid for two to three weeks and subsequently immersed for two to three days in absolute alcohol, and finally a few days in turpentine, and for the purpose of making sections, they were incorporated in a cylinder composed of wax and stearin. He has carefully traced the tissue changes in specimens from 1 to 120 days old. In specimens three days old he noticed an increase in the size and number of the vessels in the external coat. At this time the connective tissue of the intima has undergone considerable development, the fibres being directed transversely to the lumen of the vessel and in immediate contact with the endothelial lining. In a thrombus of the brachial artery obtained eight days after ligation he found in transverse sections the vessels of the media and adventitia, and, to a lesser extent, of the intima stained blue from colored injections. The new connective-tissue formation of the media and intima at some points had gained entrance into the lumen of the vessel, reaching as far as the centre of the thrombus at certain places. In a specimen of the brachial artery nine days old the lumen of the vessel near the ligature was found completely filled with new connective tissue. In a specimen of the femoral artery of 18 days all the tissues of the vessel showed a beautiful network

[1] Ueber den Thrombus nach der Ligatur. Arch. f. klin. Chirurg.

of capillary vessels which were derived from the external coat. The original structures of the intima and media were at many points observed by the new formative tissue. The endothelial layer at some places was preserved, at some points indistinct, and at others completely obscured. The lumen was filled with a compact mass of organized tissue. In a thrombus of the brachial artery 20 days old the proliferation of connective tissue was seen to project beyond the endothelial lining of the intima. In a thrombus of the brachial artery 25 days old the endothelial lining was seen to be almost completely covered by new tissue in some places, while at others it was either indistinctly visible or somewhat thickened. The new connective-tissue fibres in the intima and media were disposed transversely, obliquely, and longitudinally. The lumen of the vessel was completely closed by new connective tissue, the most recent formation corresponding to the centre of the vessel, while vascularization increased in a peripheral direction. In a specimen of the carotid artery 32 days old all tissues of the vessel-walls were stained by the injection fluid. The endothelial layer was covered partly or completely with organized exudation material; near the ligature the endothelial cells had completely disappeared, and the fibres of the intima and media could no longer be seen. Lumen of vessel completely obliterated. Remains of thrombus consist of pigment granules. In a specimen of the femoral artery 40 days old only the external coat was discernible. The endothelial layer was expanded, infiltrating the intima. In a specimen of the femoral artery 50 days old the endothelial layer was obscured by new connective-tissue fibres; lumen near ligature obliterated.

In a specimen of the carotid artery 60 days old the endothelial layer was found mostly covered with embryonal connective tissue, and at some points somewhat thickened. In a preparation of the femoral artery, obtained 120 days after operation, the lumen occupied by a thrombus was not obliterated, but near the ligature the vessel was completely closed. The vessels in the walls of the artery were reduced in size and number. Endothelial layer in some places displaced by new tissue, at other points it can be distinctly seen. The young connective tissue in the lumen of the vessel is defined by the plicated endothelial layer, and adheres all around to the inner walls of the vessel. No vessels can be seen in the intra-vascular cicatrix. In commenting on these specimens, Raab alludes to the constancy with which inflammatory exudation takes place at the seat of the operation and ligature. The thrombus varies in size, and frequently does not reach as far as the nearest collateral branch. As a rule, the central thrombus is larger than the peripheral. Three to four weeks after ligature adhesion of the inner walls of the vessel takes place near the ligature by connective-tissue proliferation. The blood-corpuscles in the thrombus become granular, disintegrate, and are absorbed. Dissolution of the thrombus commences where organization of new tissue begins, that is, near the ligature and in the peripheral portion of the clot. That the pre-existing tissues in the coats of the artery are active in the process of obliteration is made evident from the fact that the walls of the vessel are invariably very much thickened. Tissue proliferation in the coats of the vessel could be observed in cases where no progressive changes could be recognized in the thrombus. No attempt at organization ever took place prior to the fourth day. Vascularization of the inner tunics is attended by an active connective-tissue proliferation; the new tissue advances in a central direction and finally gains entrance into the lumen of the vessel. The best possible proof of the importance of the vessel walls in the process of obliteration is furnished by the fact that tissue proliferation takes place within them, independently of the formation of a thrombus. The connective tissue, wherever found in the tunics of the vessel, takes part in the process, the endothelia, and muscle fibres of the media take no active part. The endothelial layer is perforated by the new connective tissue, or is pushed before it towards the centre of the lumen of the vessel. The final disposition of the endothelia and muscular fibres probably consists in atrophy and absorption.

With the evidence before us we are certainly not warranted in assuming with Tschausoff that the endothelia are not susceptible of tissue proliferation under such conditions as are created by the ligature. Endothelia and connective tissue have one common embryonal origin, and their relations are such that in the vessel-walls changes in one are very apt to extend to the other. Connective tissue can be transformed into endothelia, and there is no well-founded reason why the reverse should not occur. Even Tschausoff, who explains the whole process of cicatrization from a standpoint that the connective tissue is the only active element, volunteers the assertion that on several occasions he has seen the endothelial lining thickened, which certainly would imply tissue increase from pre-existing cell elements.

After having excluded fibrin and the morphological elements of the blood within and without the walls of the vessels, as active agents in accomplishing definitive obliteration of the vessel after ligature, we are prepared to impute to the endothelial cells, and the connective tissue in the vessel-walls, the rôle of active agents in the formation of the intra-vascular cicatrix. Both of these histological elements are transformed into embryonal tissue which in turn is changed into mature connective tissue. The tissue proliferation is initiated at the point of greatest irritation, the seat of traumatism, and in the vascular adventitia; from these points it extends towards and into the lumen of the vessel. This process of tissue proliferation is attended by the formation of new vessels from the vasa vasorum, which permeate all tunics of the vessel and supply the intra-vascular thrombus of embryonal tissue, which is finally converted into perfect connective tissue, and results in the definitive closure of the vessel. After the function of the vessel has been permanently abolished all remaining histological elements from non-use and cicatricial compression undergo atrophy and eventually disappear completely by absorption, leaving only a string of connective tissue to indicate the extent of the obliterated vessel. The vessels in the cicatrix, after having accomplished the purpose for which they were intended, gradually disappear, an occurrence which is followed by contraction and atrophy of the cicatrix itself.

XXI. *Primary Union in Bloodvessels after Ligature.*

By the healing of a wound by primary union we understand rapid repair without suppuration. · Used in this sense the term could be appropriately applied almost to every case of ligation of vessels if the operation were done under antiseptic precautions. As applied to vessels after ligature this term however conveys another and still more significant meaning: it implies union between the inner surfaces of the lumen of an artery or vein independently of the formation of a thrombus. The importance of guarding against suppuration, and of securing primary union of the wound, has been repeatedly alluded to as conditions which favorably influence the process of cicatrization in vessels. All conditions which impair normal healthy tissue proliferation at the seat of ligature affect unfavorably the reparative process after ligature. Atheroma of the tunics of the vessel, excessive inflammation and suppuration cannot fail to exert a deleterious influence upon the reparative process in the walls of the vessel after ligature. From what we have gleaned from the literature on thrombosis, tissue proliferation, and regeneration, we are justified in asserting that obliteration of a vessel after ligature takes place promptly without a thrombus, and further that the only function of the thrombus consists in furnishing a favorable soil for the development and maturation of the tissue which grows into the lumen of the vessel from the stable cells of its tunics, and which is destined to furnish the cicatricial tissue for permanent obliteration. Experiment and clinical observation furnish abundant evidence that closure of vessels frequently does take place without thrombus formation. The many cases of successful lateral ligation of large veins with preservation of the lumen of the vessel also speak in favor of primary union. H. Braun[1] collected fifteen cases of lateral ligature of veins, of which number ten proved successful. Eliminating the thrombus as an active agent in the obliterating process, we can say that union between the tissues which are brought in contact by the

[1] Verhandlungen der Deutschen Gesellsch. für Chirurgie, 1882.

ligature takes place by tissue proliferation from the walls of the vessel itself. In its true sense direct or primary union never takes place, as in all instances closure is effected by granulation and cicatrization. In case the inner tunics are severed by the ligature, the lacerated surfaces are brought in contact with the adventitia, and repair takes place as in any other tissues which are largely composed of connective tissue, the process extending from both sides of the ligature where endothelia assist in the process of cicatrization. If, on the other hand, the continuity of the vessel is not destroyed by the ligature, and the intima is brought in contact, the connective-tissue proliferation perforates the endothelial lining, and the elements of the latter join in the reparative process by being converted into embryonal and subsequently into connective tissue. The first inflammatory changes in endothelia are observed near the seat of the ligature about the third day, and the use of the temporary ligature has demonstrated that in arteries about the size of the radial, even when the internal coats are ruptured, three to four days are necessary for sufficiently firm adhesions to take place to resist the intra-arterial pressure.

While vascular tissues may unite firmly after twenty-four to forty-eight hours, as in wounds about the face or scalp, it requires from four to twelve days for the tissues of the vessel-walls to unite with the same degree of firmness. In the inner tunics of the vessels vascularization from the vasa vasorum must take place before tissue proliferation can advance to the requisite extent.

In conclusion, we can say that wounds in bloodvessels invariably heal by granulation and cicatrization, and that when a ligature is applied the definitive intra-vascular cicatrix is formed in a similar manner.

XXII. *Experiments.*

After many trials the sheep was selected as the subject of most of the experiments, as it was found that this animal presented the most favorable conditions for these operations. All operations were done under antiseptic precautions as far as circumstances would permit. The surface was shaved, thoroughly cleansed, and disinfected with a five per cent. solution of carbolic acid. Irrigation with a three per cent. solution was used occasionally during the operation, and always before closing the wound. The wounds were invariably completely closed with a continuous catgut suture, and hermetically sealed with salicylated cotton and iodoform collodium. The vessel sheath was always opened to the extent of one inch or more, and the artery or vein completely isolated to the same distance, when two ligatures were placed underneath the vessel. The proximal was tied first in tying arteries, and the distal in the case of veins, the vessel was made bloodless by placing the second ligature in close contact with the first and by making traction upon both ends, and sliding the loop to the required distance, when the return of blood was prevented by an assistant compressing the vessel between the thumb and index finger until the ligature was tied. If any doubt remained as to the bloodless nature of the intervening space, these manipulations were repeated before tying the second ligature. In tying the ligatures it was aimed not to injure the internal coats but simply to approximate the inner surfaces of the intima so as to effect provisional closure of the vessel. The ligatures were usually applied about one-half to one inch apart. With the exception of the temporary all ligatures were cut short. In removing the temporary ligatures the collodium dressing and suture were removed, and the vessel drawn towards the surface of the wound by making gentle traction on the ligature ends when the loop of the ligature was carefully cut with small curved scissors. After the necessary examination the wound was irrigated, closed, and dressed in the same manner as before. As an anæsthetic, ether, chloroform, or bromide of ethyl were used. The anæsthesia produced by the last was always of very short duration, while ether appeared to offer the greatest immunity against accidents. The illustrations are of natural size, and represent the whole specimen as removed from the animal and a cross section through the middle of the intervening portion. The two perpendicular lines at the extremities of the specimen show the location of the ligature, while the middle line denotes the place of the cross-section. I desire, in this place, to express my gratitude to my friend Dr. H. M. Brown, of Milwaukee, for the valuable aid rendered in preparing the illustrations for this article.

Double Ligation of Arteries.

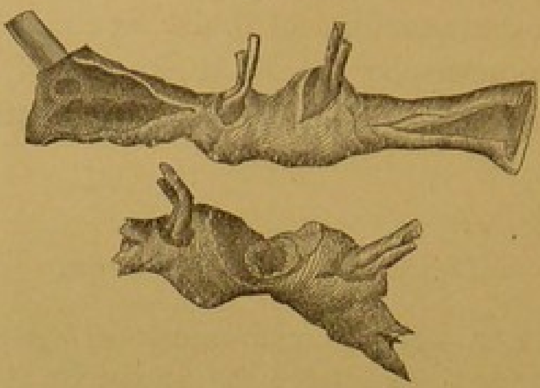
Experiment No. 1.—Right common carotid ligated with medium sized catgut. Animal died from the effects of the anæsthetic six hours after operation. Proximal thrombus two inches in length; non-adherent. Minute distal thrombus in the folds of the intima. Inner coats of the vessel not injured by the ligatures. No appreciable changes in walls of vessel.

Experiment No. 2.—Left common femoral artery ligated with coarse catgut, the distal ligature immediately above the profunda. Animal killed 24 hours after operation. Proximal thrombus, none. Minute distal thrombus. Loop of ligature covered by swollen adventitia. Lumen of profunda not closed by thrombus.

Experiment No. 3.—Right common iliac ligated with braided silk. Distal ligature immediately above bifurcation. Animal killed 3 days after operation. Proximal thrombus, none. Minute mural thrombus in external iliac artery. No thrombus in internal iliac. On removing proximal ligature vessel was found closed beneath it, while the intermediate portion of vessel remained pervious. Loop of ligature covered by granulation tissue.

Experiment No. 4.—Right femoral artery tied with coarse catgut. Animal killed 7 days after operation. Proximal thrombus extending to next collateral branch, three-fourths of an inch above the ligature; non-adherent, and filling only partly the lumen of vessel. Distal thrombus minute. Intervening portion of vessel filled with an adherent mass of granulation tissue. Ligatures softened and covered by granulation tissue. On removing central ligature lumen of vessel was found to be completely and firmly obliterated by direct adhesion between the surfaces of the intima (Fig. 1).

Fig. 1.



Experiment No. 5.—Right femoral artery ligated with medium sized catgut, proximal ligature, immediately below the profunda. Animal killed 8 days after operation. Proximal thrombus about one inch in length, small, non-adherent, and not extending into the profunda, this vessel remaining pervious. Filiform peripheral thrombus. Intervening portion patent and adherent to surrounding tissues. Ligatures almost completely encysted ; vessel under proximal ligature obliterated.

Experiment No. 6.—Right femoral artery ligated with coarse braided silk. Animal killed 10 days after operation. Small globular proximal thrombus. No peripheral thrombus. Intervening portion and ligatures inclosed by a fibrous capsule. Underneath distal ligature vessel walls adherent. Intervening portion on the side corresponding to the external surface is covered by a thick layer of granulation tissue.

Experiment No. 7.—Left common carotid ligated with silkworm-gut ligature. Animal killed 11 days after operation. Proximal thrombus three inches in length ; one circumscribed mural adhesion. Distal thrombus, none. Ligatures completely encysted in a spindle-shaped, fibrous capsule inclosing the intervening portion. Circular intravascular cicatrix underneath the peripheral ligature. Intervening portion patent. The inner tunics are not ruptured.

Experiment No. 8.—Right carotid ligated with coarse catgut. Animal killed 12 days after operation. Ligatures and intervening portion surrounded by a fibrous capsule. Proximal thrombus conical, and nearly one inch in length. Circumscribed points of adhesion near ligature. No peripheral clot. Circular cicatrix closing the vessel completely and firmly underneath the distal ligature. Intervening portion patent.

Experiment No. 9.—Right femoral artery ligated with medium-sized silk ligatures. Animal killed 13 days after operation. A large abscess communicated with the seat of the operation, the walls of the abscess surrounding both ends of the vessel. The intervening portion is much shrunken and completely necrosed and separated. Both ends of artery firmly closed. The proximal end contained a very small thrombus. The cicatricial tissue surrounding the artery had drawn the ends together so as to give the appearance as though the artery had suffered no loss of continuity.

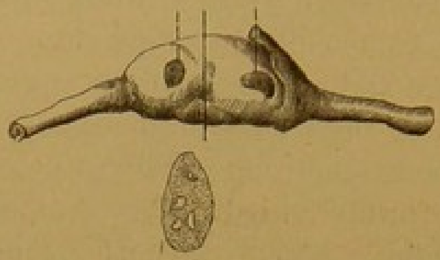
Experiment No. 10.—Left carotid tied with coarse catgut. Animal killed 14 days after operation. No thrombus. Ligatures and intervening portion surrounded by a firm, fibrous capsule. Ligatures completely encysted, but remaining quite firm. A firm, circular cicatrix completely obliterating the artery underneath the proximal ligature. Inner coats not injured. Walls of intervening portion much thickened, and its lumen near distal ligature much contracted.

Experiment No. 11.—Right carotid tied with coarse catgut. Animal killed 15 days after operation. Proximal thrombus nearly 3′ in length, almost filling the lumen of the vessel, but non-adherent. No distal thrombus. Ligatures and intervening portion of vessel completely encysted. Size of catgut unchanged. Inner tunics not injured. Obliterating circular cicatrix underneath distal ligature. Lumen of intervening portion diminished in size, and its walls thickened.

Experiment No. 12.—Left carotid ligated with fine silk. Animal killed 18 days after operation. Small proximal thrombus. No distal thrombus. The intervening portion and ligature completely encysted. Lumen of vessel immediately above the distal ligature closed by a firm cicatrix. Lumen of the intervening portion reduced in size. Folds of intima filled with granulation tissue.

Experiment No. 13.—Subcutaneous artery of thigh of sheep ligated with medium sized catgut. Sheep killed 21 days after operation. No thrombi. Ligatures and intervening portion surrounded by spindle-shaped mass of connective tissue. Lumen of intervening portion of vessel completely obliterated (Fig. 2).

Fig. 2.

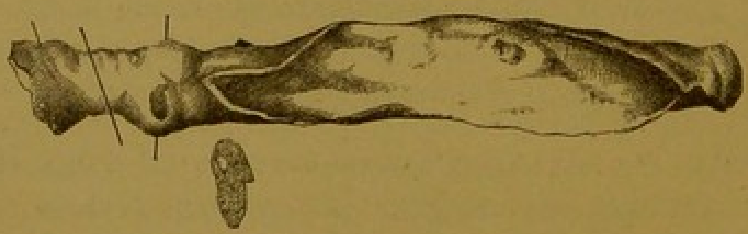


Experiment No. 14.—Right common carotid ligated with fine catgut. Animal killed 21 days after operation. No thrombus. Intervening portion, ligatures, and pneumogastric nerve surrounded by a firm capsule of connective tissue. Lumen of intervening portion contracted and filled with granulation tissue, more near proximal ligature. Only the knot of the peripheral ligature remains. Firm union underneath the ligature.

Experiment No. 15.—Left carotid tied with silkworm ligature. Animal killed 25 days after operation. No thrombus. Ligature unchanged and encysted. Coats of intervening portion of vessel thickened. Circular cicatrix underneath the proximal ligature, which has cut through the greater portion of the vessel-walls. Intervening portion permeable. Intima presents a roughened appearance.

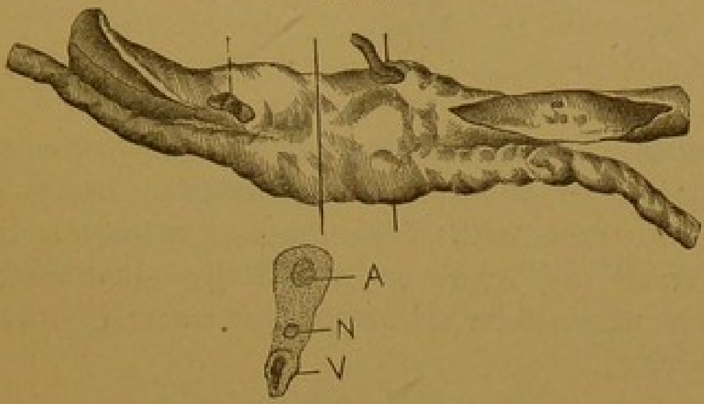
Experiment No. 15½.—Right femoral tied with fine silk. Animal killed 35 days after operation. No thrombus. Ligatures encysted. A firm, fibrous mass between ligatures, in which the lumen of the artery, much reduced in size and nearly obliterated, could be identified. Vessel pervious to points of ligation (Fig. 3).

Fig. 3.



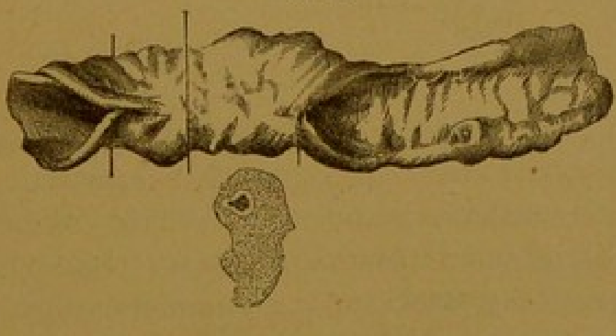
Experiment No. 16.—Right carotid. Catgut ligature. Animal killed after 39 days. No thrombus. Ligatures encysted. Knots distinctly visible. Artery obliterated one-half inch above the peripheral ligature. Below, vessel pervious to near ligature. Transverse section between ligatures shows a mass of connective tissue in which the obliterated artery can be distinctly seen (Fig. 4).

Fig. 4.



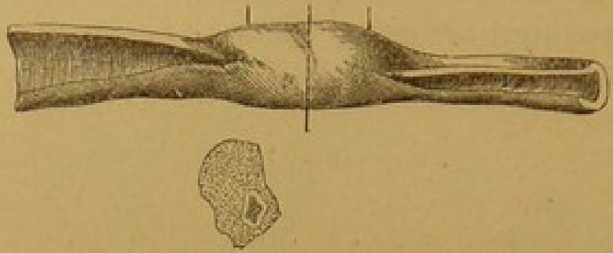
Experiment No. 17.—Right femoral ligated with coarse silk Animal killed 49 days after operation. No thrombus. Ligatures encysted. Artery on either side of ligatures obliterated to a distance of one-sixth of an inch. Section between ligatures reveals the vessel in a mass of cicatricial tissue, somewhat reduced in size, its lumen filled with a mass of organized tissue (Fig. 5).

Fig. 5.



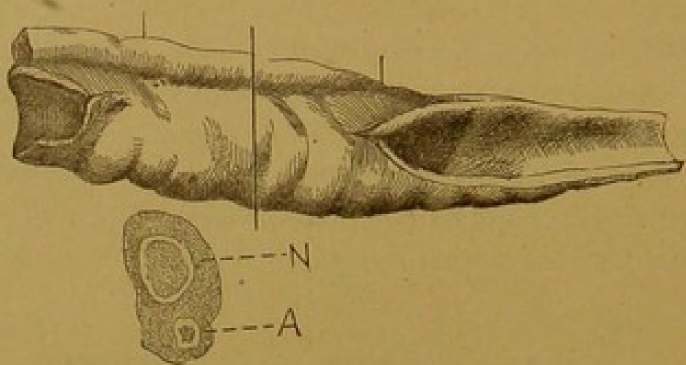
Experiment No. 18.—Left femoral tied with coarse braided silk. Distal ligature just above profunda. Animal killed 50 days after operation. No thrombus. Ligatures encysted. On the proximal end the artery is obliterated to a distance of one-eighth of an inch above ligature. Intervening portion converted into a solid string of connective tissue in which the remains of the artery can still be recognized (Fig. 6).

Fig. 6.



Experiment No. 19.—Right femoral; medium-sized catgut. Animal killed after 52 days. No thrombus. Artery pervious to ligatures. No traces of the ligatures can be found. Intervening portion of vessel and vagus surrounded by a spindle-shaped mass of connective tissue in which no distinct traces of the vessel can be found (Fig. 7).

Fig. 7.

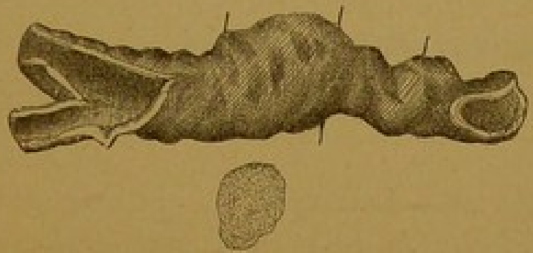


Experiment No. 20.—Right femoral; silkwormgut ligature. Animal killed 55 days after operation. No thrombus. On proximal side vessel obliterated to a distance of one-third of an inch; below, three-fourths of an inch from the ligature. Ligatures have apparently cut through the vessel, and are completely encysted. Intervening portion surrounded by a large mass of connective tissue in which the closed lumen of the vessel can plainly be seen.

Experiment No. 21.—Right femoral. Medium-sized silk, distal ligature just above profunda. Animal killed after 68 days. Profunda converted into a fibrous cord. In the deep femoral remnants of a thrombus about one-half of an inch in length. Vessel obliterated to same distance. Ligatures cut through. One of them imbedded in a mass of cicatricial tissue in which the intervening portion of the vessel could not be recognized. A small abscess communicated with the seat of the operation through which one of the ligatures must have escaped.

Experiment No. 22.—Left carotid of goat tied with catgut. Animal killed after 80 days. Proximal end of vessel obliterated to within the next collateral branch, one-third of an inch below ligature. Distal portion of artery obliterated to same extent, to within one-half of an inch of its bifurcation. Ligatures completely disappeared, and intervening portion converted into a solid string of connective tissue (Fig. 8).

Fig. 8.



Experiment No. 23.—Right femoral of goat tied with silk. 90 days. Artery pervious to within one-half of an inch on each side of the ligatures. Ligatures probably cut through the vessel, and completely encysted. Intervening portion of vessel transformed into a solid mass of connective tissue about the size of the vessel.

Experiments with the Double Temporary Ligature on Arteries.

Experiment No. 24.—Right common carotid of goat tied with coarse catgut; removed 25 hours after operation. Animal killed 10 days after ligation. At the time the ligatures were removed the circulation in the vessel was interrupted. On examination the artery and the vagus were found surrounded by a copious mass of cicatricial tissue. Interiorly, the vessel corresponding to the seat of the ligatures is filled and occluded by a small white thrombus projecting into the distal portion of the vessel. Cicatricial tissue in lumen continuous with the para-vascular connective tissue.

Experiment No. 25.—Left femoral of goat. Coarse catgut. Removal 24 hours after operation. Animal killed 9 days after ligation. On removal of ligatures circulation not interrupted. Ligated portion of vessel considerably smaller. Lumen not obliterated. Inner walls of vessel at the seat of operation studded with minute patches of exudation material, the result of recent endarteritis.

Experiment No. 26.—Left carotid. Coarse catgut; removed 48 hours after operation. Animal killed 10 days after ligation. On removal of ligatures circulation in vessel not interrupted. An abscess with thick walls communicates with the vessel. The vessel surrounded by a thick fibrous capsule. No thrombus. Lumen of vessel between seat of ligatures narrowed by a copious plastic exudation on that part of the vessel which is in immediate contact with the abscess.

Experiment No. 27.—Left carotid. Silk ligature; removed 48 hours after operation. Animal killed 14 days after operation. Circulation not interrupted. Post-mortem appearances the same as in No. 25.

Experiment No. 28.—Left carotid. Silk ligature; removed 72 hours after operation. Animal killed 35 days after operation. Circulation, on removal of ligatures, interrupted. Proximal clot 1⅓ inch in length with circumscribed points of adhesion. Distal clot none. At seat of operation vessel very much contracted. Lumen filled with remnants of a small clot and granulation tissue.

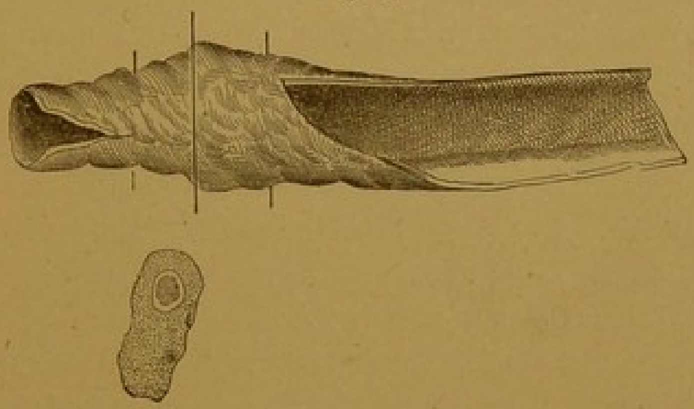
Experiment No. 29.—Left carotid. Silk ligature; removed after 72 hours. Animal killed 35 days after operation. Circulation interrupted. Suppuration followed the removal of the ligatures. Proximal thrombus about 2′ in length. Coats of vessel very much thickened. Thrombus adherent by plastic exudation from inner vessel-walls. Distal thrombus very minute. Intervening portion separated at one end, projecting into the abscess cavity. Both ends of the artery permanently obliterated, united, and brought into close approximation by a mass of cicatricial tissue.

Experiment No. 30.—Right carotid. Silk ligature; removed 72 hours after operation. Animal killed 28 days after ligation. Removal of ligatures followed by suppuration. No thrombi.

Both ends of the vessel permanently obliterated and brought into close contact by a mass of cicatricial tissue in which no trace of the intervening portion can be found. Ligated portion of vessel has probably sloughed, and escaped with the contents of the abscess which communicates with the seat of the operation.

Experiment No. 31.—Right common carotid near subclavian. Coarse catgut. Ligatures removed 6 days after ligation. Animal killed 16 days after operation. Circulation completely arrested on removal of ligatures. No thrombi. Vessel, at seat of ligatures, surrounded by spindle-shaped mass of connective tissue, in a transverse section of which the artery can be readily identified, its lumen being filled with embryonal connective tissue (Fig. 9).

Fig. 9.



Experiment No. 32.—Left common carotid. Coarse catgut. Ligatures removed 6 days after operation. Animal killed 14 days after ligation. On removing distal ligature vessel gave away. No hemorrhage. Distal end closed by a narrow cicatrix. Very minute thrombus. Thrombus in proximal end 2′ in length; firmly adherent. At point of proximal ligature narrow circular cicatrix. Intervening portion of vessel separated at one end. Not necrosed. Both ends of vessel connected by a strong bridge of connective tissue.

Double Ligation of Veins:

Experiment No. 33.—Right jugular. Catgut ligature. Animal killed six hours after operation. Minute peripheral thrombus. Increased vascularity of adventitia.

Experiment No. 34.—Left femoral vein. Catgut ligature. Animal killed after 24 hours. Filiform distal thrombus; none on the proximal side. Intervening portion completely empty, and slightly adherent to surrounding tissues.

Experiment No. 35.—Right femoral vein. Coarse catgut ligature. Animal killed after 3 days. Small distal thrombus. Intervening portion adherent to surrounding tissues, and containing in its interior a small granulation thrombus

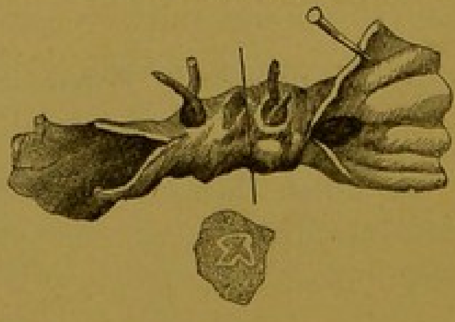
Experiment No. 36.—Right jugular vein. Coarse catgut ligature. Animal killed after 5 days. Minute distal thrombus in folds of intima. On removing proximal ligature the inner surfaces of intima were found firmly adherent, evidently by direct union.

Experiment No. 37.—Right femoral. Coarse silk ligature. 7 days. Suppuration after operation. Minute peripheral clot. Ligatures encysted. Intervening portion partially destroyed by suppuration. Ends of vessel united by a bridge of connective tissue. Vessel underneath the ligatures obliterated.

Experiment No. 38.—Right jugular vein. Silk ligature. Animal killed after 9 days. Suppuration followed the operation. Abscess communicated directly with the intervening portion of the vessel which has nearly separated. Small truncated distal thrombus, non-adherent. Ends of vessel firmly closed and united by a strong bridge of connective tissue.

Experiment No. 39.—Right jugular vein. Medium sized silk ligature. 12 days. Minute adherent distal thrombus. Ligatures encysted. Intervening portion surrounded by a capsule of connective tissue. On transverse section the star-shaped lumen of vessel is discernible, firmly closed by young connective tissue (Fig. 10).

Fig. 10.

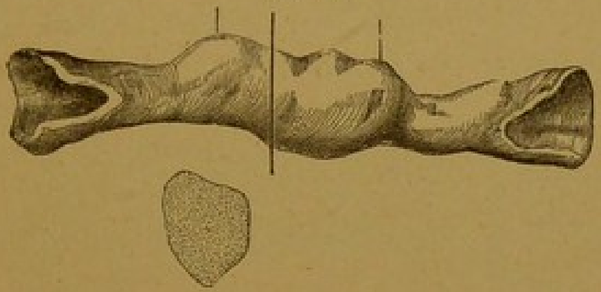


Experiment No. 40.—Left jugular vein. Silk ligature. Animal killed after 14 days. No thrombi. Ligatures encysted. In removing the proximal ligature firm adhesions between folds of intima. Intervening portion empty, and adherent to surrounding tissues.

Experiment No. 41.—Right jugular vein. Horse-hair ligatures. 21 days. No thrombi. Ligatures not encysted, loose upon the remaining parts of the intervening portion. Ends of vessel closed by very narrow cicatrix.

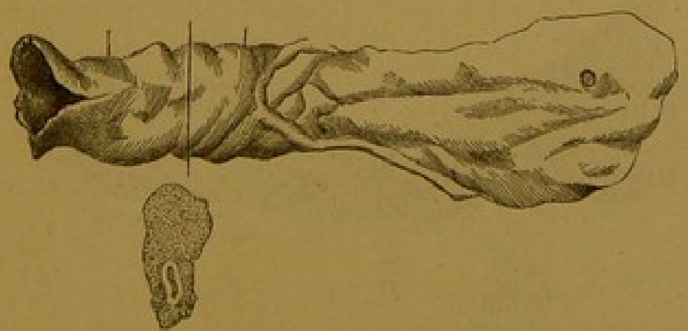
Experiment No. 42.—Right jugular vein. Catgut ligature. 37 days. Ligatures encysted. Vessel obliterated to a distance half an inch from ligatures on both sides. Intervening portion a solid string of connective tissue in which no traces of the vessel can be found (Fig. 11).

Fig. 11.



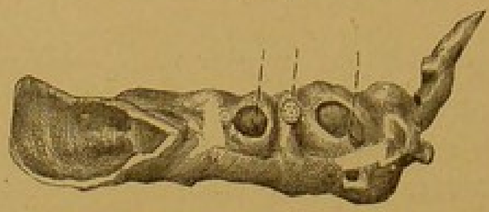
Experiment No. 43.—Right jugular vein. Coarse silk ligature. 49 days. Vessel pervious to near ligatures. Ligatures encysted. Intervening portion surrounded by a mass of connective tissue in which the obliterated vessel can be readily identified (Fig. 12).

Fig. 12.



Experiment No. 44.—Right femoral vein. Medium-sized silk ligature. 54 days. Vessel pervious to near ligatures. Ligatures evidently have cut their way through the vein and are encysted in the cicatrix. Intervening portion transformed into connective tissue (Fig. 13).

Fig. 13.



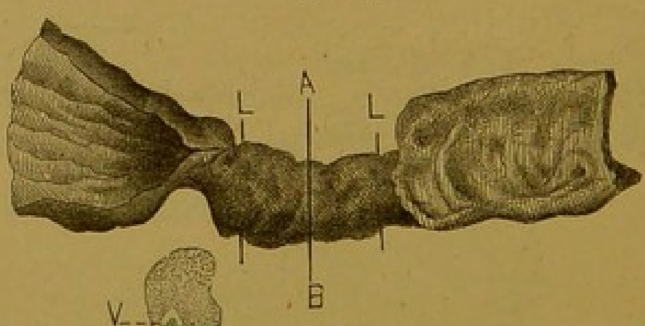
Experiment No. 45.—Right jugular. Medium-sized catgut. 80 days. Ligatures absorbed. Intervening portion transformed into connective tissue.

Experiments with the Double Temporary Ligature on Veins.

Experiment No. 46.—Right jugular of goat. Silk ligature, removed 24 hours after operation. Animal killed 10 days after operation. Circulation on removing ligatures not arrested. Intervening portion contracted by a mass of intramural and para-vascular cicatricial tissue, but patent. Intima normal in appearance An abscess communicates with the seat of the operation, only the coats of the vein intervening between it and the lumen of the vessél.

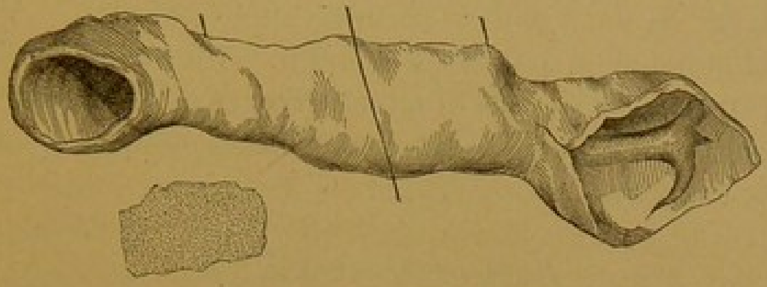
Experiment No. 47.—Left jugular vein. Silk ligature, removed 48 hours after operation. Animal killed 34 days after ligation. Circulation arrested. No thrombi. Intervening portion of vessel transformed into a firm string of connective tissue, in which no trace of the original structure can be recognized (Fig. 14).

Fig. 14.



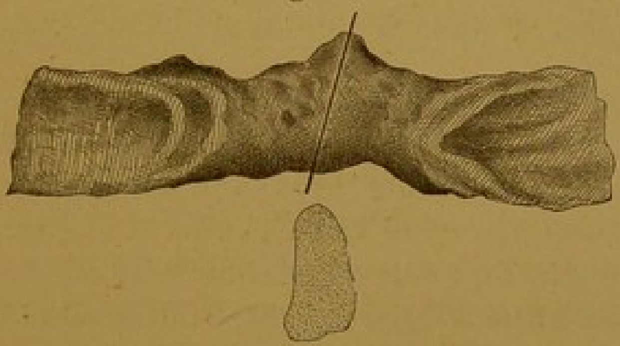
Experiment No. 48.—Right jugular. Silk ligature, removed 3 days after operation. Animal killed 27 days after ligation. Circulation arrested at seat of ligatures. Peripheral clot narrow, partially adherent, one inch in length At the seat of operation about 2′ of the vessel converted into a solid string of connective tissue (Fig. 15).

Fig. 15.



Experiment No. 49.—Left jugular. Coarse silk ligature, removed 3 days after operation. Animal killed 40 days after ligation. Circulation interrupted. No thrombi. Intervening portion converted into a massive string of connective tissue (Fig. 16).

Fig. 16.



Experiment No. 50.—Left jugular. Coarse silk ligature removed 4 days after operation. Animal killed 35 days after ligation. Circulation interrupted. A short truncated peripheral clot adherent at its base. Constricted portion of vessel almost but not completely obliterated. Folds of intima filled with recent connective tissue, bridges of same material spanning the lumen of the vessel. The surface of the intima corresponding to the wound covered by a copious plastic exudation.

Experiment No. 51.—Right jugular. Coarse catgut ligature, removed after 6 days. Animal killed 15 days after the operation. Suppuration followed the operation. Circulation arrested. An immense white peripheral thrombus adherent at its base. Vessel at seat of distal ligature obliterated by a narrow cicatrix. Intervening portion contracted, walls thickened, circumscribed patches of exudation underneath the proximal ligature.

Experiment No. 52.—Right jugular. Coarse catgut, removed after 6 days. Animal killed 14 days after operation. Vein completely obliterated at points of ligation. Intervening portion surrounded by a dense capsule of connective tissue, a transverse section of which shows the lumen of the vessel almost completely obliterated by plastic exudation.

Experiments on a Horse.

Experiment No. 53.—Right carotid. Silk ligatures. Animal died 8 days after operation, death being caused by chloroform during the second experiment. Proximal clot extending to near subclavian, partly adherent, distal clot 8′ in length, extending beyond nearest collateral branch. Ligatures encysted. Intervening portion surrounded by a capsule of connective tissue. Walls thickened. Beginning cicatrization under peripheral ligature.

Experiment No. 54 —Right jugular vein of same animal. Coarse silk ligature. 8 days. Large distal thrombus completely distending the vein, and extending beyond bifurcation. Ligatures encysted. Proximal portion of vein diminished in size. Intervening portion surrounded by a capsule of connective tissue. Underneath proximal ligature firm adhesions between folds of intima.

XXIII. *Remarks.*

A. *Effect of Suppuration.*—The deleterious influence of suppuration on the process of cicatrization is well illustrated by these experiments. In all cases where the wound healed by primary union, the isolated portion of the vessel became adherent as early as the second day to the adjacent tissues, and, after a few days more, the interrupted vascular connections were restored. In all cases, with the exception of Experiments Nos. 9, 21, 37, 38, where the wound was not reopened for the purpose of removing the ligatures, the wound healed by primary union, and cicatrization in the vessel progressed in a favorable manner. In using the temporary ligatures suppuration was a more frequent concomitant on account of the necessary interference with the reparative process in the wound, and the increased difficulties encountered in preventing infection. Suppuration supervened in Experiments Nos. 26, 29, 30, 50, with the temporary ligature, so that this event occurred 8 times out of 55, the whole number of experiments. In all cases where suppuration followed the operation the vitality of the intervening portion of the vessel was destroyed in part or in its entirety, and if a sufficient length of time had elapsed, this portion of the vessel was usually found completely separated and within the abscess cavity. Secondary hemorrhage, however, was never observed as the result of suppuration, or sloughing of the intervening portion, as the narrow intra-vascular cicatrix in both ends of the vessel was usually supported by a strong para-vascular ring of connective tissue which formed a part of the thick walls of the abscess. In all these cases the vessels had invariably suffered a loss of continuity by the ligature. These facts force upon us the following conclusions:—

1. All surgical operations on bloodvessels should be performed under strict antiseptic precautions for the purpose of preventing suppuration.

2. In aseptic wounds the complete isolation of a vessel from its sheath for a distance of one inch is not followed by any serious disturbance of nutrition in the vessel-walls.

3. Suppuration invariably produces a loss of continuity of the vessel at the seat of ligature.

4. Inflammation beyond the limits of the reparative process interferes with the typical formation of the intra-vascular cicatrix.

B. *Thrombus.*—For nearly fifty years the idea has prevailed, and to a great extent is still prevalent, that in applying a ligature to an artery a thrombus forms on the proximal side which extends to the nearest collateral branch, and that by organization of the clot the vessel is obliterated to the same extent. All authors who attribute definitive vessel closure to organization of a thrombus assert that the latter always precedes cicatrization, and when thrombus formation fails to take place, permanent obliteration of the ligated vessel is an impossible occurrence. I have shown elsewhere that thrombosis by no means necessarily follows every case of ligation, in fact that it very often fails to take place, and yet definitive closure takes place as promptly as though a thrombus had formed. Coagulation of the blood means necrosis or death of the morphological elements of the clot, and as such an occurrence it is more likely to result from conditions unfavorable to the process of cicatrization. Severe traumatic injuries of the vessel and, more particularly, an infectious inflammation of the seat of operation, are conditions which favor the formation of a thrombus. In my experiments on arteries I find that in 34 cases the presence of a proximal thrombus is mentioned 13 times to 10 in the distal portion of the artery. In four of the experiments it is noted that only a peripheral thrombus formed in seven cases in which the thrombus was only found on the proximal side of the ligature. In most of the cases the thrombus was quite minute, only seldom filling the entire lumen of the vessel, and never adherent to the entire inner surface of the vessel. A notable exception was furnished by the experiment on a horse, where an immense proximal and distal thrombus formed, filling the entire lumen of the vessel, extending on the proximal side near to the subclavian artery, and on the peripheral to beyond the bifurcation of the vessel.

In the specimens derived from 21 experiments on veins I was never able to find even a trace of a thrombus on the proximal side of the ligature, while the presence of a distal thrombus is noted eleven times or a little more than fifty per cent. of all the cases. The vein experiments furnished the most favorable opportunities to study the process of cicatrization underneath the proximal ligature independently of a thrombus, as the presence of a clot was excluded in every instance. With the exception of the specimen obtained from the horse, the thrombi in veins were also usually small in size, and seldom adherent over any considerable surface. Only in exceptional cases, both in arteries and veins, did the thrombus reach as far as the nearest collateral branch. The results of these experiments render it obvious that the time-worn rule laid down in most of our text-books on surgery, which directs the operator to apply the ligature in such a manner as to leave a space of one inch or more between the ligature and the nearest proximal collateral branch for the purpose of insuring the formation of a thrombus, is wrong, both in theory and in practice, and should no longer be followed as a guide in deciding upon the seat of ligature.

C. *Ligature.*—All ligatures were made strictly aseptic, and in all instances where suppuration did not follow the operation they were encysted irrespective of the material used. Silk, silkwormgut, and horsehair were not affected by the granulating process, but were always found unchanged in the cyst. In all aseptic wounds the loop of the ligature was found covered completely by the swollen adventitia after the first forty-eight hours. A great contrast was observed between the catgut ligature and ligatures made of material not susceptible to absorption as far as their effect on the vessel-walls was concerned. Catgut applied itself easily and smoothly to the exterior of the vessel-walls, and by becoming softened and infiltrated with cells, it appeared to constitute a part and parcel of vessel-tissues until it was replaced by substitution by a ring of organized tissue, which served as a material support to the vessel until cicatrization was completed, thus preserving the continuity of the vessel. All the remaining kinds of ligatures appeared to act as foreign bodies as far as the vessel tunics were concerned, and invariably produced a solution of continuity after a sufficient length of time had elapsed. They were usually found encysted in the mass of connective tissue between, and some distance from, the ends of the vessel. Catgut, on the other hand, did not manifest this tendency. It became encysted, and underwent absorption *in situ*. The earliest time in which the catgut ligature was found absorbed was twenty-one days, in Experiment No. 14, where only the knot remained. In Experiment No. 19, where fifty-two days had elapsed after the operation, no trace of the ligature could be found. For the following obvious reasons, catgut recommended itself as the most desirable and efficient material:—

1. If catgut is well prepared it will resist absorption until definitive obliteration of the vessel has taken place.

2. It does not act as a foreign body, and does not destroy the continuity of the vessel.

3. It is completely absorbed and replaced by organized tissue, which furnishes an additional support to the vessel-walls at the seat of cicatrization.

D. *Extra-vascular Cicatrix.*—The first attempt at obliteration of a bloodvessel after ligature is manifested in the connective tissue of the adventitia and the para-vascular connective tissue. As early as twenty-four hours after ligation, the isolated portion of the vessel has become adherent to the surrounding tissues, and the swollen adventitia overlaps and covers the loop of the ligature. The connective tissue becomes very vascular, and undergoes rapid embryonal transformation, being converted in a few days into granulation tissue which completely surrounds and embraces the ligatures, the intervening portion, and the vessel ends in a similar manner as the provisional callus incloses the ends of a fractured bone. This capsule of connective tissue was always found present in every specimen, and in many instances was of remarkable size and strength. The thickest portion of the capsule always corresponded to the locality which had been subjected to the greatest amount of traumatism, that is, the side of the vessel towards the operation wound. As soon as definitive closure of the vessel has taken place, the capsule diminishes in size, until after a period of three months it did not exceed the original diameter of the ligatured vessel. The contraction incident to all cicatricial tissue manifests itself also in the spindle-shaped mass of connective tissue which forms around vessels after ligation, and renders material assistance in the process of obliteration by compressing the vessel, thus diminishing its lumen. In all of our experiments where union of the operation wound occurred without suppuration, the intervening portion of the vessel was found covered by granulation tissue as early as the third day, and the fibrous capsule was always firmly adherent to it. Through the medium of this connective-tissue capsule the ligated ends of the vessel always form firm adhesions with the surrounding structures, the artery, vein, and nerve often being enveloped by one common capsule, as may be seen well illustrated by Fig. 4.

E. *Intra-vascular Cicatrix.*—By continuity the inflammatory tissue production proceeds from the adventitia in a central direction towards the lumen of the vessel until the connective-tissue proliferation perforates the endothelial lining of the intima, an event which initiates the formation of the intra-vascular cicatrix. Simultaneous with the appearance of the granulation process in the intima and the appearance of new vessels from the adventitia the endothelial cells assume an active part in the process of cicatrization, the new tissue elements mingling with the connective-tissue product and assisting the same in the formation of the internal or definitive cicatrix. Cicatrization begins always underneath and in the immediate vicinity of the ligature. This fact receives a satisfactory explanation by assuming that the greatest amount of traumatism is inflicted at this point, and that by interrupting the circulation in the vasa vasorum by the ligature an active engorgement is produced which accelerates tissue changes and the formation of new vessels, at the same time the inner surfaces of the intima are here brought into accurate and uninterrupted contact. In my experiments on arteries three days was the shortest period of time in which a narrow firm cicatrix formed underneath the proximal ligature (Exp. No. 3). In the experiments on veins the condition of the vessel was always examined underneath the proximal ligature, inasmuch as any changes in the tunics and lumen of the vessel at this point had to be attributed to the tissues themselves independently of a bloodclot, as the intervening portion was always made bloodless and a thrombus was never found on the proximal side of the ligature. In the specimen derived from Experiment No. 36 I found a firm circular cicatrix underneath the ligature on the fifth day. The intervening portion of the vessel was carefully examined at times ranging from six hours to ninety days after the operation. This portion of the vessel, although deprived of all vascular supply, never necrosed unless suppuration followed the operation. Nutrition was sustained by plasma derived from para-vascular tissues until the interrupted circulation in the vasa vasorum was established, when the vessel tunics were again brought into a condition capable of entering into active tissue proliferation. In many of the specimens it is noted that the walls of the intervening portion were found thickened, which would certainly indicate that the tissues did not remain in a passive condition but were actively engaged in the work of tissue proliferation. The earliest time at which granulation tissue was found upon the free surface of the intima was seven days in the case of arteries (Experiment No. 4), and three days in the case of veins (Experiment No. 35). The formation of the cicatrix in the lumen of the vessel always began near the ligatures, the material filling the folds of the intima often forming distinct bridges connecting the highest points of adjacent ridges. In several instances I observed the greatest amount of exudative tissue on that surface of the vessel which was directed towards the wound. The amount of granulation material in the lumen of the vessel appeared to vary; in some specimens the lumen presents a stellate shape, the surfaces of the intima adherent with a minimum amount of material between them (Fig. 10), while in other specimens a cylindrical mass of embryonal connective tissue occupies the interior of the vessel (Fig. 5). Complete obliteration of the intervening portion took place in the femoral artery 35 days after operation (Experiment No. 15½), in 39 days in the carotid (Experiment No. 16), and in 12 days in the jugular vein (Experiment No. 39). As cicatrization advances the original structures of the tunics disappear, the endothelia are transformed into connective tissue, and between the para-vascular and intra-vascular cicatrix the elastic and muscular tissues undergo degeneration and are removed by absorption. The ultimate effects of the ligature are obliteration of the lumen and conversion of all the tunics of the vessel into a solid string of connective tissue which is again destined to undergo various degrees of atrophy.

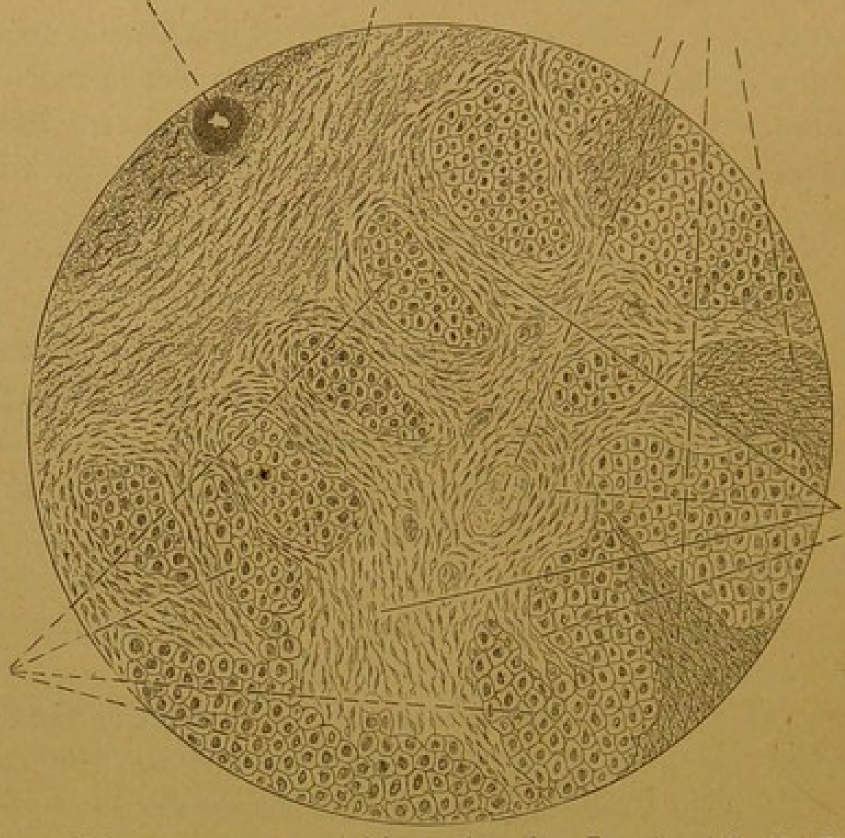
F. *Temporary Ligature.*—The experiments with the temporary ligature were made with a view to ascertain *intra vitam*, the time required for definitive closure to take place after ligation. In arteries where the ligatures were removed 24 and 25 hours after ligation, and the animals killed on the 10th and 9th days, no definitive closure had taken place, but the specimens presented evidences of arteritis and endarteritis. In Experiment No. 29 the carotid artery was ligated and the ligatures were removed 72 hours after operation, when the circulation was found completely interrupted; and the specimen obtained 35 days after operation showed that the vessel had been completely divided by one of the ligatures, but both ends were permanently obliterated. In Experiment No. 31 (carotid artery) the ligatures were removed after 6 days, and the specimen obtained 16 days after operation showed that the intervening portion was undergoing definitive obliteration, its contracted lumen being filled with a small granular thrombus (Fig. 9).

In the veins the temporary ligature appeared to produce its effects in a shorter time and with a greater degree of certainty. In two experiments on the jugular vein (Experiments Nos. 47 and 48) the ligatures were removed after 48 hours, and in both cases the circulation was completely and permanently arrested; and the specimens obtained 34 and 27 days after operation showed that the intervening portions had been converted into strings of connective tissue (Figs. 14 and 15).

From these experiments it appears that in arteries the size of the carotid at least three days are required for the cicatrix underneath the ligature to become sufficiently firm to resist the intra-arterial pressure independently of the ligature, while in the jugular vein the same object is accomplished in two days.

G. *Microscopical Appearances of the Recent Intra-vascular Cicatrix.*—I shall not attempt to give a detailed account of the microscopical appearances of the different tunics at different and successive stages during the process of cicatrization, but I shall limit my remarks to a short description of the embryonal tissues which are found within the lumen of the intervening portion of the vessel and its immediate boundaries. These observations were made on transverse sections through the intervening portion equidistant from the ligatures. Figure 17 represents the inner border of the wall of the femoral artery and a portion of its lumen in a transverse section of the specimen obtained from Experiment No. 19, 52 days after operation. The open lumen of a small vessel can be seen in the intima near its inner border. From the intima projections of connective-tissue proliferation

Fig. 17.

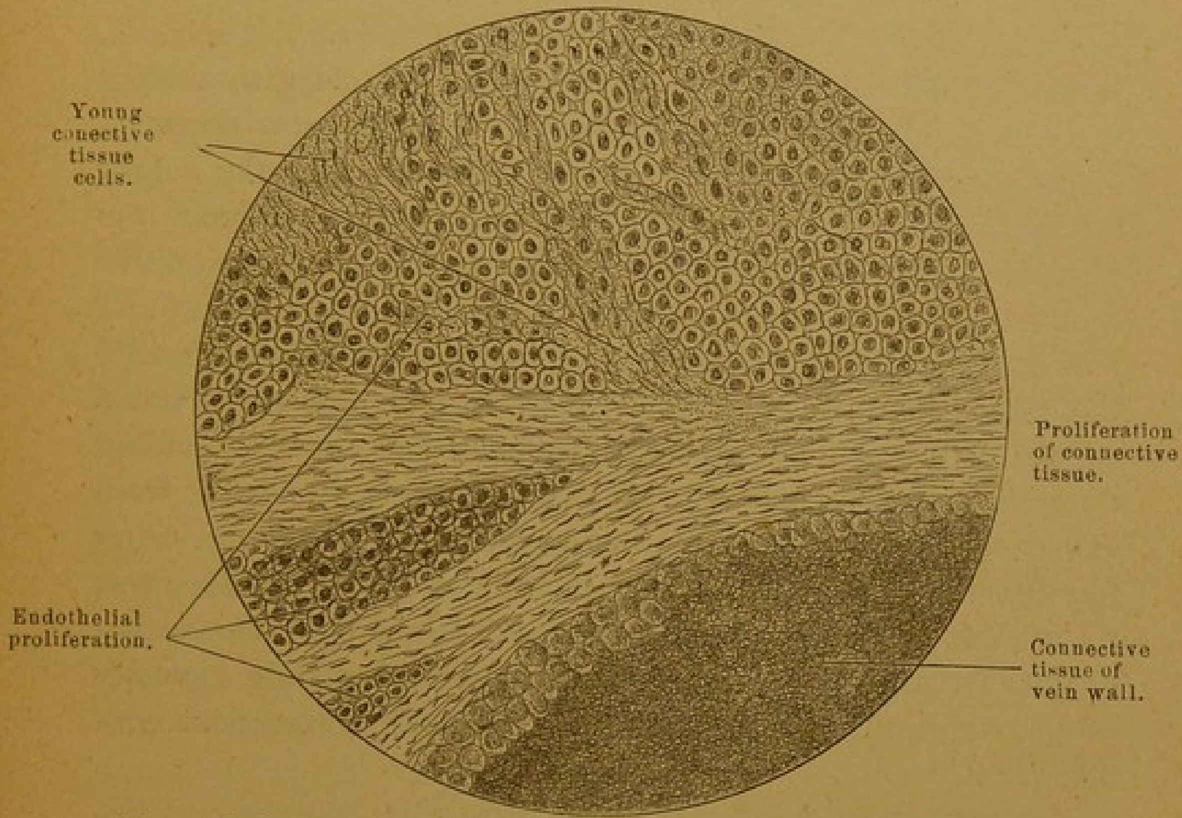


Microscopical appearances presented by specimen from Experiment No. 19. Fig. 7. Transverse section through border, artery. × 240.

are seen to penetrate into the lumen of the vessel, pushing before them the endothelial lining, and perforating it at different points, forming subsequently a network of connective tissue in the interior of the vessel, in the meshes of which are seen masses or nests of new endothelial cells, also products of the pre-existing endothelial elements. At certain places the endothelial cells assume an oval and spindle-shaped form prior to their being transformed into connective tissue. Bloodvessels from the intima accompany the projections of connective tissue into the lumen of the vessel.

Figure 18 represents a transverse section through the intervening portion of the jugular vein obtained 49 days after operation from Experiment No. 43, and illustrated by Fig. 12. It shows the intima and a portion of the granulation thrombus

Fig. 18.



Microscopical appearances presented by specimen from Experiment No. 43. Fig. 12.
Transverse section of part of vein in ligated portion. × 240.

which has permanently closed the lumen of the vessel. The microscopical appearances are almost identical with the arterial specimen. Both of these illustrations furnish the best possible demonstration of the manner in which the intra-vascular cicatrix is formed from the connective tissue and endothelia. The macroscopical and microscopical examination of the specimens are alike confirmatory of the assertion that the intra-vascular cicatrix is the exclusive product of connective tissue and endothelial proliferation.

XXIV. *Practical Suggestions.*

The results of my own experiments, as well as the literature on the subject, tend to prove that all kinds of ligatures, provided they have been made aseptic, always become encysted in aseptic wounds. All ligatures, however, which permanently resist absorption destroy the continuity of the vessel, and on this account, instead of adding strength to the para-vascular cicatrix, weaken the vessel-walls at the seat of ligation. I have never observed a single case in hospital or private practice where the catgut ligature failed to fulfil in the most satisfactory manner the purposes of a provisional hæmostatic agent until the definitive cicatrix had become sufficiently firm to resist the intra-arterial pressure. In place of severing the tunics of the ligated vessel the catgut ligature is gradually displaced by organized tissue which increases the resisting capacity of the vessel, providing an additional safeguard against secondary hemorrhage if from any cause definitive obliteration is retarded. In enumerating the superior advantages of the catgut ligature, Nussbaum says: "The most careful microscopical examinations have shown that catgut increases to a considerable extent the resisting capacity of an artery in forming firm connective-tissue connections with the vessel."[1]

The aseptic animal ligature possesses two distinct and important advantages over all permanent ligatures. 1. It does not necessarily destroy the continuity of the vessel. 2. It adds additional strength to the extra-vascular cicatrix. These advantages recommend the animal ligature more particularly for the purpose of tying a vessel in its continuity. I am firmly convinced that in many of my experiments the internal tunics of the arteries remained intact after ligation, and yet cicatrization progressed in a satisfactory manner. Hence it is no longer necessary to tie the ligature so firmly as to crush the tunics of the vessel. All that is necessary is to tie with sufficient force to approximate the inner surfaces of the intima with a view to insure effective

[1] Op. cit.

provisional obliteration of the vessel when cicatrization will follow as a necessary result, provided the vessel tunics are in a healthy condition. If cicatrization in a vessel takes place from the fixed cells of its tunics without the formation of a thrombus, it will be seen that in many instances a vessel can be ligated with safety in its continuity close to a collateral branch when existing circumstances dictate such a course.

One of the constant rules usually given by all authors in vessel surgery was to make a small opening in the sheath of the vessel, only of sufficient size to permit of passing the ligature needle around it. It was feared that a more free opening in the sheath, and a more extensive isolation of the vessel would lead to necrosis of its tunics on account of the cutting off of the vascular supply. That this idea still prevails is evident from one of the most recent text-books on surgery. Lidell calls special attention to this point in the following language: "The risk of sloughing, however, arises mainly from isolating the artery too much, or from separating it too extensively from its sheath, while dissecting to expose it, or while preparing to pass a thread around it whereby the minute vessels which nourish its coats are too extensively destroyed; hence the dangerousness of passing a spatula or the handle of a scalpel under the artery, and of dragging it out of its bed when tying it."[1]

All of these fears are unfounded when operating under antiseptic precautions. In all of my experiments I did all what is here cautioned against: I isolated the arteries and veins from their sheaths for an inch or more, and dragged the vessel near to the surface of the wound in applying the second ligature, and yet I never observed any sloughing except in the cases where the operation was followed by suppuration. I am strongly in favor of opening the sheath freely, so that the operator can not only feel but *see* what he is doing, and I am convinced by pursuing this course there is less harm done than by operating in the dark. My experiments on the veins have taught me

[1] Injuries of Bloodvessels. The International Encyclop. of Surgery, vol. iii. p. 90.

another important and practical lesson, viz., their tolerance to traumatic insults. In not one of the cases was death produced by the operation, although in a few of the animals both the jugular and femoral veins were tied at different times. I never observed progressive phlebitis, embolism, or pyæmia. Veins, like those of the peritoneum, may be contused, torn, lacerated, cut, punctured, burned, and ligated with immunity, if infection is avoided. Veins are exceedingly prone to infection, but if infection can be prevented their injuries are repaired with wonderful rapidity. As regards the time required for definitive obliteration to take place, the results of the experiments would indicate that in the case of arteries of the size of the carotid or femoral from four to seven days are necessary, while in the jugular vein the same object is accomplished in three to four days.

The double catgut ligature may be resorted to with advantage in the human subject in ligating large vessels in their continuity, more especially if the operation is done near a collateral branch as it approximates the inner surfaces over a larger area and thus furnishes a more extensive surface for cicatrization. The practicability and utility of the double ligature is, however, rendered most apparent in the treatment of varicose veins. For many years I have successfully used the subcutaneous double catgut ligature in the treatment of varicocele. In operating on varicose veins of the lower extremity, the intervening portion can readily be rendered bloodless by applying an Esmarch's bandage before tying the ligatures. The entrance of blood into the vessel between the ligatures through small collateral branches can be prevented, and the process of cicatrization materially assisted by applying an antiseptic compress over the seat of the operation before removing the elastic bandage.

A careful examination of the literature on the subject of this paper, as well as the results of my own investigations, warrant me in submitting for your further consideration and discussion the following conclusions:—

I. All operations on bloodvessels should be done under antiseptic precautions.

II. The aseptic catgut ligature is the safest and most reliable agent in securing provisional and definitive closure of blood-vessels.

III. A thrombus after ligature is an accidental formation which never undergoes organization and takes no active part in the obliteration of a vessel.

IV. The intra-vascular or definitive cicatrix is the exclusive product of connective tissue and endothelial proliferation.

V. Permanent obliteration in arteries takes place in from four to seven days, in veins in from three to four days.

VI. In ligating vessels in aseptic wounds the vessel sheath can be opened freely without compromising the integrity of the vessel tunics, and such procedure renders the operation safer and easier of execution.

VII. The double aseptic catgut ligature should be preferred to the single ligature in ligating large arteries in their continuity near a collateral branch, and should always be employed in all operations of tying varicose veins in their continuity as the safest and most effective measure in producing definitive obliteration.

DISCUSSION.

Dr. Donald Maclean, of Detroit, Michigan.

It appears to me that it would be unjust for this Association to pass over Dr. Senn's paper without some observations. I certainly should not like to see it go without some comments. It is a long paper, and a pretty heavy task to listen to the whole of it at one time. But I am sure that I voice the opinion of every member of the Association, when I say that we feel proud of our brother after having listened to his production. It is an able, an ingenious, and a well-presented one in every respect, giving a number of most interesting and instructive experiments, with some very just deductions from them. The fact of the matter is, it is a paper of a somewhat revolutionary character.

One point that struck me forcibly was the manner in which the author took the various very profound and apparently widely different subjects of surgery, and led them all converging into one practical point. He speaks of ligature of the common femoral artery, a subject which was before us on the first day. The ligature of this artery for aneurism has been almost always condemned on account of the danger of secondary hemorrhage. The danger was, we believed, on account of the inability of the blood to coagulate in the collateral branches. There was not space enough for a good solid clot to form between the ligature and the collateral branches. Then, as far as aneurism is concerned, we can use the ligature if his reasoning is correct. But in wounds of the common femoral, what shall we do? I have myself not met with a wound of the common femoral. To tie the common femoral for injury would be almost sure to stop the collateral circulation. But if Dr. Senn's conclusions are correct, and his deductions just, then we can lay that danger aside. If the aseptic ligature is used, and antiseptic principles are carried out, it cannot be necessary for a clot to form; the artery is closed without the intervention of a clot.

The paper is too vast and the subject too vast to admit of discussion here. I only wish for my own part to express my gratitude to Dr. Senn for having presented so able and remarkable a contribution to the Association.

Dr. Henry F. Campbell, of Augusta, Georgia.

I arise to join Dr. Maclean in the hearty commendation he gives for the labor, the ingenuity, the deep research, and the very great importance of Dr. Senn's investigations. At the same time, I do not know that the American Surgical Association is prepared to let pass unchallenged in any manner some of his statements. I will not refer to the fact that a day or two ago we were discussing the question of ligation of the common femoral, and my own experience, as then stated, was that the danger was not from hemorrhage from the want of the formation of a clot, but that if you tie it for hemorrhage in a healthy man, with the collateral vessels undilated as by an aneurism or inflammation, you certainly kill the man by the universal stasis of the venous and arterial systems throughout the entire limb. That is my experience in three cases. But his experiments appear to rescue from neglect, from the apprehension, from the condemnation we have heretofore put upon it, the animal ligature for arresting an arterial current. It appears that the buckskin ligature was tried and abandoned for fear that it would not hold long enough. The deer-tendon ligature was suggested and tried. My predecessor in the Medical College of Georgia tried it, and had to abandon it because it did not hold the parts together long enough to form a well-organized clot. But since the days of Guthrie in the Crimea we have known that the coats of an artery unite like skin by adhesions. Therefore I am not willing to allow the utter condemnation of the silk ligature. I have been using it for forty years, and I have had secondary hemorrhage only once. I sometimes think it well to violate Guthrie's rule and put on a double ligature; one above and one below the lesion. I have had hemorrhage—recurrent hemorrhage—from the lower end, and have been obliged to apply another silk ligature, but I have never had a hemorrhage from the brachial, the femoral, the carotid, or the posterior or anterior tibial arteries, that came from the application of any kind of ligature. I have never had an accumulation of pus surrounding the point of application of my ligature. I never carbolize my silk. I wax it, and make it draw well into a knot, and I have never had any bad results in the ligation of any artery whatever. That there is sometimes retention of the knot, its slow coming away beyond the appointed time, according to the size of the artery, I must admit. You know, according to the class of the artery, many set a certain time for its closure, say ten days for the radial, twelve or fifteen for the brachial, fifteen or twenty for the carotid. I have had my ligature retained somewhat beyond this time. I have, however, never put a weight on it, but it has always come away after awhile. I know what retained it, it was the too active vitality in the part. The granulations crowded around my knot and my loop, and prevented it from coming away. Now if there was an accumulation of pus, I would have hesitated to apply that kind of a ligature; but it was the perfect ease, the perfectly fortunate results, that came from it.

I rise merely to express my admiration for a gentleman who could make such research, and who has combined with his research a philosophical inductive study. He is able to concentrate and collate the principles of fact which make a perfect induction; but even the most perfect induction possible should never deny or obliterate from our memory the teachings of experience; and it is simply that I may save the Association from giving itself without consideration to a new teaching that I have spoken.

Dr. E. H. GREGORY, of St. Louis, Missouri.

I am perhaps an old fogy, for I am not prepared to abandon the silk ligature. I should put a ligature on the common femoral artery to-day with the same anxiety as I would have applied it yesterday; and whenever an opportunity offers to avoid a merely collateral branch in the ligation of an artery, I shall certainly do it. I would not subject my conscience to the discomfort it would occasion if I were to apply a ligature to an artery close to a collateral branch, unless I were obliged to do it, notwithstanding all that has been said on the subject. In other words, whilst I agree with the previous speaker, that Dr. Senn has done much, and that the paper which he has presented is worthy of the American Surgical Association, and will, perhaps, add reputation to it, yet it is very hard for a man to change his practice. Within the last six weeks I tied at least six inches of the omentum with silk ligature, cut it off close, and returned the ends into the abdomen. And for my part I cannot see that there is any disadvantage attached to the use of the silk ligature. Now, my friend Dr. Campbell says that he finds that the growth of new tissue crowds and actually clamps his ligature; and I would add, that if it were permitted to remain there a few months it would disappear. This may seem strange to some of the Fellows, but I know that the silk ligature does disappear. I have removed it when the loop was half destroyed. Again, the author says that in a little while this ligature is infiltrated with a plasmic material. Now we know that this plasmic material is corroding, it is consuming, it assimilates every structure with which it comes into contact. I am afraid that this animal ligature will not be capable of doing its duty.

Perhaps I was too old when Listerism came into existence; certainly I have not become enthusiastic on the subject, and I do not know why I have not taken the contagion, because it has prevailed pretty generally. I have made operations with all these precautions, because I have an assistant who makes my preparations for me, and he attaches great importance to them. But I cannot attach the same importance to it that some men seem to attach to it. So that while I am willing to praise the paper of Dr. Senn, I feel like Sir Astley Cooper felt fifty years ago, when he put an animal ligature on an artery and had to put a silk one on afterwards. It is to-day just what it was then.

Dr. J. S. Billings, United States Army.

I wish to call the attention of the Association, as this subject of Listerism has come up, to the fact that it is to be judged not by individual experience, or what may have taken place in single instances, and, more still, not by the occurrences that take place in private practice. You must judge it by the results that follow its use in the old, badly ventilated, badly arranged, and unclean hospitals of Europe, and I think the best results may be seen in the hospitals of St. Petersburg, where, before the introduction of Listerism, the amputation of even a finger was a serious question, and the surgeons were in despair. Now the sanitary condition of these hospitals has not changed. They are still filled with the same filthy, miserable class of patients, but they perform the surgical operations without any fear of erysipelas or other complication. This also is the case I might remark of all the hospitals of Germany.

It is not at all a fair thing to contrast a silk ligature with an animal ligature, for the silk is an animal ligature. It is only a little better kind of animal ligature. I am satisfied that you can get a good catgut ligature. Not everything that is called catgut is good; but there is a catgut that is as satisfactory as the silk, and the facts stated about the absorption of silk ligature, the fact that it can be returned into the abdomen, I interpret to mean that it is an aseptic ligature.

Dr. B. A. Watson, of Jersey City, New Jersey.

I desire to commend this most excellent paper. It is one of the most valuable productions I think that has ever been brought before this Association. As a scientific production alone it is worthy of our admiration. Then when we consider that the author experimented upon fifty-five animals, ligating arteries, and that in no single instance did he have septic trouble or secondary hemorrhage, and that in every instance where he used what he called the permanent ligature, he cut short the ends, placed the arteries back in their position, and even hermetically sealed and closed up the wound, the good results seem to me laudable.

I have been in the habit of using catgut ligatures for the last ten years, and feel as much confidence in them as Dr. Gregory does in silk. I feel that one of the greatest dangers in ligation is from secondary hemorrhage; and in the majority of cases it comes on from suppuration. If you can avoid suppuration in a wound, I think you will generally avoid secondary hemorrhage. With the carbolized ligature properly applied you avoid it; and I have not seen a case in which the catgut ligature, so applied, did not hold a sufficiently long time for the artery to be united and to give satisfactory results.

Dr. C. B. NANCREDE, of Philadelphia, Pennsylvania.

I would like to call attention to one fact. I have been much interested in experiments on animals, yet I think that we should be careful about applying the results obtained from experiments on animals to similar cases in the human subject. You can open a dog's abdomen and sew it up again with no bad effects, but you cannot do the same in a man and not have bad results follow.

Now, as to catgut ligature, I think surely men like Billroth, Sir James Paget, and many other foreign surgeons know as much as we do. Now, the best result obtained from animal ligature was 39 per cent., while that from silk ligature was only 4½ per cent. As to catgut ligature, if you get the right kind, I cannot conceive of the slightest danger in using it. I think we must have used it in hundreds of amputations in Philadelphia, and we seldom heard of hemorrhage following its application. I have made between sixty and seventy amputations, and I have never used anything but catgut, unless at night, when the material gave out. I cannot conceive why American surgeons believe in placing experience in a few cases against the best experiences abroad. Certainly, if you take the best results under certain circumstances, you eliminate the great cause of danger in others. The last volume of *Transactions* of our Society was treated with something very much like ridicule by foreign surgeons, inasmuch as American surgeons, they said, instead of relying on the experiences of the best men of the world, have relied on their own.

Dr. SENN. In the first place, I desire to thank most sincerely the Fellows for listening so patiently to my paper; also, for the evidences they have given of interest in it.

In reply to Dr. Campbell and Dr. Gregory, I wish to state that the ligature of to-day is not the ligature of twenty-five years ago. I put the greatest stress on the rendering of every kind of ligature aseptic; consequently we avoid the necessity of suppuration. It is possible and necessary in using animal ligatures to render them aseptic. I placed, also, stress on the behavior of ligatures, not capable of being absorbed, on the tunics of the vessels. I claimed for the animal ligature that it answers all the purposes of a temporary ligature, that is, it answers the purpose of a hæmostatic until closure of the vessel can take place; and to be that, a ligature which is found perfectly reliable and is substituted by healthy tissue possesses qualities which cannot be possessed by all. Catgut ligature is an effective ligature in every sense of the word. The other materials, more particularly that form which is not amenable to absorption, invariably produce division of the tunics of the vessel. They destroy the continuity of the vessel, and on that account are not desirable materials to be used in ligating arteries, more particularly near a large collateral branch.

I placed stress, also, on the importance of ligating an artery near a collateral branch by making the space between the two ligatures bloodless, inasmuch as you afford more space for union; and I have no doubt that in the future we shall be able to ligate large arteries in the vicinity of large branches without the dangers of secondary hemorrhage.

In regard to the remarks of Dr. Nancrede, of experiments on animals, I would say that experiments in the lower animals answer just the same results as in the human subject; consequently I believe that we are warranted in asserting that the experiments are simply a repetition of the phenomena which occur in the ligation of an artery in the human subject.

I have also placed stress upon the importance of antiseptic precautions in ligating any vessels, but more particularly in operating upon veins. Secondary hemorrhage is almost always the result of inflammatory changes at the seat of operation. Anything which will avoid an undue amount of inflammation or prevent suppuration will secure primary union of the wound and closure of the vessel.