Current Status

WILLIAM G. SMITH, M.D., *Editor*

"Current Status" will not appear as a regular part of the Journal, but rather as a sporadic feature of special interest. Manuscripts published in this special section will be prepared by individuals who have comprehensive and special expertise concerning a particular subject, and will reflect their personal experience, knowledge, opinion, and judgment regarding that subject. The purpose of these reports will be to supply readers with precise, accurate, and current information on pertinent, but limited subjects which might reasonably be considered within the purview of the Journal's interests.

Intestinal Suturing

Review of the Experimental Foundations for Traditional Doctrines

GARTH H. BALLANTYNE, M.D.

From the Department of Surgery, St. Luke's Hospital, Cleveland, Ohio

Ballantyne GH. Intestinal suturing: review of the experimental foundations for traditional doctrines. Dis Colon Rectum 1983;26:836–843.

The doctrines of intestinal suturing have been handed down from the 19th century. It has been widely accepted that intestinal wounds heal most reliably when an inverting suture line is constructed. The serosal surfaces of the bowel should be apposed by sutures, anchored in the submucosa, forming an inverting suture line. The wound should be kept free of hematoma, necrotic tissue, or infection. Intestinal wounds heal with a pattern similar to that of wounds in other tissues. During the lag period of repair, the wound is cleansed of debris. Excessive tissue injury, foreign body, or infection incite inflammation, prolonging this period of wound healing. Cellular elements proliferate during the phase of fibroplasia. Collagen within the wound assumes its mature form only during the prolonged phase of maturation. The return of wound integrity can be quantified by measuring its tensile strength, bursting strength, or collagen content. Such measurements have shown that, during the lag period, sutures provide almost the entire strength of the wound. During the phase of fibroplasia, new collagen adds to the suture line integrity. The contribution of new collagen to wound strength soon overtakes that of sutures. It is only during the first week of wound healing, the lag period, that surgical technique plays a significant role in ensuring intestinal wound integrity. Surgical techniques developed during the 19th century provide secure closure of intestinal wounds during the lag period of wound healing. After the onset of the period of fibroplasia, newly formed collagen replaces sutures in ensuring wound integrity.

[Key words: Wound healing; Intestinal suturing, anastomoses, wounds; Experimental surgery; History of surgery]

THE MODERN AGE of intestinal suturing began in the early 19th century. The doctrines that have guided surgeons since that time were developed either in clinical practice or in limited experimental studies. Remarkably successful techniques were discovered. By the 20th century, these techniques were used throughout the world.

Although several principles were generally agreed upon, the techniques by which these goals should be accomplished were argued. Before different suturing styles could be compared by the scientific method, the general pattern of wound healing needed to be identified. During the last two centuries, many experimental studies have succeeded in defining the progression of wound healing in intestinal anastomoses.

Several experimental techniques have been useful in the study of wound healing. Measurement of tensile strength, bursting strength, and collagen content of wounds has allowed quantitative assessments of the progress of healing. Analysis of these three parameters reveals a distinct pattern of wound healing, not only in intestinal wounds, but in wounds in all tissues.

This review traces the development of the doctrines o intestinal suturing. The available experimental dat supporting these doctrines are outlined. The histologi pattern of wound healing derived from these studies i

---

Received for publication April 26, 1983.

Address correspondence to Dr. Ballantyne: 707 17th Street S.E., Rochester, Minnesota 55904.

described. The pattern of quantitative measurements is related, in terms of the histologic classification of the stages in wound healing. Review of this experimental evidence supports the veracity of the general principles upon which the doctrines of intestinal suturing are based. A subsequent paper will review experimental studies to evaluate alternative surgical techniques.

Doctrines of Intestinal Suturing

Systematic studies on intestinal suturing really began in the early nineteenth century. In 1812, Travers[1] studied the healing of hand sewn anastomoses in rabbits. He emphasized the importance of the visceral peritoneum in the healing process. He wrote that "the uniform contiguity of the peritoneal surfaces, and the ready disposition of these surfaces to assume the adhesive inflammation, are the means provided by nature for the reparation of intestinal wounds and injuries." He stressed the importance of uniform apposition of the intestinal surfaces. He stated that "the union of a divided bowel requires the contact of the cut extremities in their entire circumference." Travers believed that the technique of anastomosis was less significant. He indicated that "the species of suture employed is of secondary importance, if it secures the contact." Indeed, Travers used an everting suture, not an inverting suture. These observations laid the groundwork for the advances of intestinal surgery gained in the remainder of the 19th century.

According to Senn,[2] the modern era of enteric anastomoses began in 1826. At that time, Lembert proposed many of the principles that remain today. Lembert stressed the importance of apposing serosal surfaces.[3] As Senn stated,[2] "The great principle inculcated by Lembert to rely on the serous coat in procuring early and permanent adhesions will never be rejected." The vertical mattress suture, which bears his name, apposes the serosal surfaces of the two ends of bowel. This suturing technique inverts the edges of the cut bowel. Since Lembert's papers[3,4] appeared, in the early 19th century, the necessity of an inverting anastomosis in intestinal suturing has been widely accepted.

Lembert's technique of suturing intestinal anastomoses was modified in 1881 by Czerny.[5] He advocated the addition of an inner layer of sutures, which apposes the mucosal surfaces. This layer serves to prevent the escape of intestinal contents through the outer layer of Lembert sutures. It is this two-layered inverting technique, called the Czerny-Lembert suture, that is so widely used today.

An additional modification appeared in 1892. At that time, Connell[6] introduced his continuous inverting suture line. The major advantages of this technique were the reduction of the number of knots "to two, or even one" and the "rapidity of the operation, as compared when using Czerny-Lembert or other sutures." Although Connell proposed a single-layer inverting anastomosis, many people have subsequently used his continuous suture as a second layer below Lembert sutures.

Until 1887, little concern about the technique of placing serosal stitches had been voiced. Halstead published the results of his experimental studies of enteric anastomoses. He revealed the importance of the submucosa in gastrointestinal anastomoses, "Each stitch should include a bit of the submucosa. A thread of this coat is much stronger than a shred of the entire thickness of the serosa and muscularis."[7] During the last 100 years, the veracity of Halstead's observation has been confirmed repeatedly.

Halstead also emphasized the importance of surgical technique in successful intestinal suturing. He pointed out that the surgeon must take care not to compromise the natural actions of the peritoneal cavity by leaving debris around. Halstead wrote that "it is evident that bacteria which otherwise would be readily absorbed, may take lodgement and grow, if they find in the peritoneum stagnating nutritive fluids or ulcerated and necrotic tissue." A successful anastomosis must be constructed in a clean environment, without hematoma or ischemic tissue.

Halstead did not agree with Czerny concerning the importance of a second layer of sutures. Halstead preferred a single layer of horizontal mattress (plain-quilt) stitches for his circular enteric anastomoses. The debate over using one or two layers in sewn anastomoses continued throughout this century.

By the late 19th century, the fundamental doctrines of enteric anastomoses were well established. Most agreed that serosal surfaces of the bowel should be apposed uniformly around the full circumference of the anastomosis by an inverting suture technique. The suture accomplishing this must include within its bite the submucosa. The anastomosis should be within an environment that is free of hematoma, necrotic tissue, or infection. Clinical experience soon proved the soundness of these principles.

The Pattern of Wound Healing

A great deal of effort has been spent in the last two centuries identifyi the pattern of wound healing. Once this was established, the impact of various factors upon this pattern could be studied. The general sequence followed in wound reparation has been recognized since the early 19th century.

Travers studied, in 1812, the healing process of intestinal anastomoses in rabbits. He attempted to classify the stages of wound healing that he observed:

> It commences with the agglutination of the contiguous mucous surfaces, probably by the exudation of a

> fluid similar to that which glues together the sides of a recent flesh wound, when supported in contact. The adhesive inflammation supervenes and binds down the reverted edges of the peritoneal coat, from the whole circumference of which a layer of coagulable lymph is effused, so as to envelope the wounded bowel...The sutures loosen by the process of ulcerative absorption. During this time the lymph deposited becomes organized, by which further retraction is prevented, and the original cylinder, with the threads attached to it are encompassed by the new tunic.[1]

Travers recognized a specific, reproducible pattern in wound healing. A phase of agglutination was followed by a phase of adhesive inflammation. Periods of ulcerative absorption and organization soon followed. Many sophisticated experimental studies designed since 1812, have basically confirmed the observations of Travers. These studies have clarified the histologic processes involved in the sequence of wound healing.

Much of the knowledge of wound healing comes from studies on skin lacerations. It has been assumed that all wounds heal in a similar manner. Reid, a student of Halstead, wrote in 1936 that "wound healing is wound healing under whatever circumstances it may occur and the reparative processes are essentially the same except in degree."[8] Thus, the observations made on one healing tissue often have been applied to other tissues. Such is the case in the study of enteric anastomoses. The terminology used in describing the pattern of wound repair in enteric anastomoses largely stems from studies of skin or abdominal wounds.

The classification of wound healing by Travers has been refined over the last two centuries. The outline of events in wound healing described by Carrel[9] has been adopted generally. In 1910, he studied the healing of surface wounds, observing two major phases of wound healing. A quiescent period of one to five days was followed by a period of cicatrization. Howes, Sooy, and Harvey[10] modified this classification. They divided their observations on wound tensile strength into three periods: lag period, phase of fibroplasia, and, finally, a phase of maturation. They noted that the period of agglutination, described by Travers, largely corresponded to their lag period. The histologic events in these stages of wound healing have been well studied.

The cellular response in all healing wounds is similar. The duration and magnitude of each stage in the sequence of wound healing differs with the type of wound. Sandbloom[11] divides the cellular response during the lag phase into two segments. During the "phase of traumatic inflammation," the wound fills with blood and lymph. These coagulate, forming a fibrin mesh between the wound edges. Neighboring vessels dilate. Intercellular fluid increases. It is during this phase that the classic signs of injury are observed: Dolar, Kalor, Rubor, and Tumor. This is followed by the "exudative or destructive phase." Neutrophils and macrophages cleanse the wound of pathogens and debris. This phase is succeeded, and partially overlapped, by the "reparative phase." Capillaries sprout, forming granulation tissue. Fibroblasts proliferate. Collagen is deposited in the wound. Mature connective tissue cells appear. Realignment of collagen fibrils evolves. This sequence is fairly uniform in all tissues. Many studies indicate that a similar sequence of cellular response occurs at healing intestinal anastomoses.[12-14]

Injury to tissue sets in motion a fairly uniform cellular response. The sequence of response following injury can be divided conveniently into three overlapping segments: a lag period (0 to 4 days), in which wounds are cleansed of debris; a phase of fibroplasia (3 to 14 days), in which cellular elements proliferate; and a phase of maturation (10 to 80 days), in which collagen assumes its mature form.[12,15]

Measurements of Wound Healing

Several techniques have been developed for quantifying wound healing. The most commonly used methods have been measurements of wound tensile strength, bursting strength, and collagen concentration. These techniques have been used more extensively in studying healing abdominal and skin wounds than enteric anastomoses. The information from these studies supplement nicely that available for anastomoses. These measurements indicate weaknesses in the natural healing process of enteric anastomoses, which must be buttressed by surgical technique.

Tensile Strength: The measurement of the distracting force necessary to disrupt a wound was the first experimental technique used for quantifying wound healing. Paget,[16] in 1853, measured the tensile strength of transected rabbit achilles tendons after repair. He demonstrated a dramatic increase in wound strength between six and ten days after repair. Chlumsky,[17] in 1899, attempted to apply this technique to intestinal anastomoses. The sensitivity of his apparatus was inadequate, causing him to switch to other methods. Thirty years passed before this technique was resurrected.

In 1929, Howes, Sooy, and Harvey[10] carefully studied the tensile strength of healing wounds in various tissues. They measured the strength in incised skin, fascia, muscle, and stomach. The return of tensile strength for all types of wounds followed a similar pattern. The tensile strength of the wounds was essentially zero for four to six days. Thus, during the lag period of healing, tensile strength of the wounds was too low to measure. After about a week, tensile strength increased rapidly at first, then more slowly, until the maximum strength of the wound was reached. The period of rapid gain in tensile strength corresponds to the histologic period of fibroplasia. The period of slowly increasing wound strength occurs during the period of maturation.

Similar measurements have been repeated, in a variety of experimental models. Levenson *et al.*[18] demonstrated a similar pattern of increasing tensile strength in rat skin wounds. The same progression was found in rabbit rectus sheaths.[19] In these studies, sutures were removed prior to measurements of the tensile strength of the wound. Adamsons *et al.*[20] attempted to quantitate the contribution of sutures to wound strength. They measured the tensile strength of guinea pig abdominal wounds, with and without sutures. By the third day after surgery, wounds with sutures in place had regained 35 per cent of their ultimate tensile strengths. Wounds with sutures removed had only regained 4.6 per cent of their ultimate tensile strength within three days. The importance of sutures of wound strength is much greater during the lag period of healing than during the periods of fibroplasia or maturation.

Tensile strength has been used to study healing enteric anastomoses. Herrmann, Woodward, and Pulaski[12] studied colonic anastomoses in rats. Sutures were left in place. During the lag phase, tensile strength was approximately one-fifth of the ultimate tensile strength of the wounds. Between six days and 15 days after surgery, the anastomoses regained more than 80 per cent of their ultimate strength. Jiborn, Ahonen, and Zederfeldt also studied anastomoses in rat colons[21] and found similar results. They measured tensile strengths of normal colon. The breaking strength of the rat's left colon was 65 per cent higher than that of the transverse colon. Enteric anastomoses regains tensile strength at a rate similar to that of other tissues.

During the lag period, sutures provide almost 100 per cent of the wound's tensile strength. Even with sutures, the tensile strength during the lag period of enteric anastomoses is only 35 per cent of its ultimate strength. The technique of suturing used in constructing enteric anastomoses is extremely important during the lag period, but less important during the period of fibroplasia. Sutures must compensate for the weakness of wounds during the lag period.

Bursting Pressure: Bursting pressure measurements provide a more appealing method for testing enteric anastomoses. In this technique, the bowel is distended with gas or liquids until any portion of the wound disrupts. The pressure at which disruption occurs is recorded as the bursting pressure. Chlumsky,[17] in 1899, switched to this technique, after discarding tensile strength measurements. He found a steady decrease in the pressure necessary for water to leak through the anastomoses during the first four days. This requisite pressure increased rapidly from the fourth through the tenth day. By this time the anastomoses were stronger than the surrounding intestines. Chlumsky's experiments were little noticed for the next 50 years.

Bursting strength measurements were popularized as an experimental method by Harvey,[22] in 1929, from the Yale School of Medicine. His studies also revealed a lag period, lasting about four days, before bursting pressure valves began increasing rapidly. Once this phase ended, the rate of regaining strength jumped to a maximum. Throughout the phases of fibroplasia and maturation, this rate of gaining strength drops slowly, so that the maximum level of strength is approached asymptotically.

Many researchers have adopted this technique for studying enteric anastomoses. Several groups have demonstrated a similar pattern of regaining bursting strength in colonic anastomoses in rats.[23-25] Irvin and Edwards'[26] studies on colonic anastomoses in rabbits revealed the same results. Many studies in dogs have also confirmed this general pattern in the healing of colonic anastomoses.[27-31] Anastomoses with sutures removed obtain bursting pressures of about 10 per cent of their ultimate strength during the lag period.[27] Anastomoses with sutures in place regained only 20 to 50 per cent of their ultimate strength during this time period.[27,28]

Bursting pressure can be used to measure wound healing for approximately two weeks after operation. The limitation in this technique is that the bursting pressure of the narrowed anastomosis soon exceeds that of the surrounding bowel, because of Laplace's law.[32] Consequently, after about two weeks, measurements no longer reflect the strength of the anastomoses. During the lag period and the phase of fibroplasia, bursting pressure is an extremely useful measurement of anastomotic healing.

Bursting strength, like tensile strength, is weakest during the lag period of wound healing. It is greatly dependent upon sutures during the first four days. Thus, surgical technique can affect radically the pressure needed to disrupt an enteric anastomosis. During the lag period, the integrity of the anastomosis is almost solely dependent upon surgical technique.

Fibroblasts and Collagen in Wound Healing: Bursting strength and tensile strength measurements have revealed the alterations of wound strength during the lag period and period of fibroplasia. The biochemical basis for this was discovered only when experimental studies examined more closely the fibroblasts and collagen metabolism.

The importance of the fibroblast in wound healing has been recognized since at least 1929. At that time, Howes, Sooy, and Harvey[10] stated that "it is to be assumed with reasonable safety that the increasing strength of the wound and the contraction of it as seen in surface wounds is in the major part a function of the growth of the fibroblasts." Later studies tried to distinguish the effects of cell growth from cell maturation. Burr, Harvey, and Taffel,[33] in 1939, showed that cell growth predominated up to the eighth day and that, after that point, maturation had increasing importance. Sandbloom,[11] in his exhaustive study of healing wounds, stressed that in the reparative phase "the main role is played by connective tissue cells, especially fibroblasts." Sandbloom mentioned collagen only in passing. "Subsequently, the cells will differentiate into mature connective tissue cells and the fibrin will be substituted by intercellular substance containing collagen fibrils." During the next decade, biochemical research exposed the fundamental importance of collagen in wound healing. By 1958, Edwards and Dunphy[34] were able to write in their review of wound healing that "collagen fibers principally account for the restoration of tensile integrity to a severed tissue." It was recognized that the progress of wound healing could be followed by studying the collagen content of wounds.

Studies of collagen in healing wounds began appearing in the early 1960's. Peacock[35] studied collagen content in rat skin wounds. He found that saline-extractable collagen (tropocollagen) decreases during the lag period of wound healing. Normal amounts were not found in the wound before the seventh postoperative day. Maximum levels were found three weeks after injury. Subsequently, other studies utilizing a unique quality of collagen have better outlined collagen metabolism during wound healing.

The biochemical structure of collagen has facilitated its study. Each collagen molecule is formed of three alpha chains (polypeptide chains) wrapped together, forming a triple helix. After synthesis of the alpha chains by ribosomes, they enter the cisternae of the rough endoplastic reticulum. There, they undergo several biochemical modifications, before forming the triple helix. The proline in the alpha chains is hydroxylated, giving this polypeptide the unique characteristic of containing the amino acid hydroxyproline. This step is dependent upon ascorbic acid (vitamin C).[36,37] The presence of this unique amino acid has provided an important tool for studying collagen metabolism. Assays of hydroxyproline reflect wound collagen content.

Hydroxyproline metabolism in sutured wounds was first examined in 1962 by Rosenthal *et al.*[38] Hydroxyproline content of rat abdominal incisions increased progressively from day zero to day eight. This curve followed closely that of wound tensile strength. Adamsons, Musco, and Enquist[39] uncovered a similar pattern in guinea pig abdominal wounds. The rise of wound collagen paralleled rising wound tensile strength during the first 15 days after wounding. Madden and Peacock,[40,41] using tritiated proline for measuring hydroxyproline content in rat dorsal skin wounds, found about the same changes. Studies of collagen synthesis in granulating wounds in rat skin showed similar values.[42] During the early period of wound healing, tensile strength correlates well with collagen concentration in the wound.

The collagen content of a wound is a function of breakdown of mature collagen and the synthesis of new collagen. In the bowel, this catabolism is mediated by collagenase, which is present in the bowel wall.[43] Collagen content of a wound drops initially following injury, due to destruction of old collagen.[39] As the wound heals, new collagen is synthesized. Eventually, collagen synthesis exceeds collagenase-mediated catabolism, and wound collagen content increases. Only this new collagen forms the bond between the two wound edges. Consequently, for two weeks, wound tensile strength is dependent upon the rate of new collagen synthesis. Wound strength continues to increase for long periods after total collagen content has stabilized.[18,41] Studies by Peacock,[44] in 1966, attributed this continued gain in tensile strength to intermolecular and intramolecular bonding in the collagen. Alterations of the type of collagen in the wound may also contribute to wound strength. Type III collagen is deposited early in granulating tissue. During maturation of the wound, Type III collagen is replaced by Adult Type I collagen.[36] Thus , measurements of collagen synthesis or content reliably reflect wound strength for only two weeks, during the lag period and period of fibroplasia.

Collagen metabolism in enteric wounds follows a pattern similar to that of other tissues. Cronin, Jackson, and Dumphy[23,45] showed a 40 per cent drop in collagen concentration during the first three days of healing in colonic anastomoses in the rat. According to this group, collagen concentration remains low in the healing anastomoses until the fifth day. By the tenth day, the collagen concentration is only slightly below normal, though bursting strength has surpassed that of the surrounding bowel. Studies by Jiborn, Ahonen, and Zederfeldt[25] support these findings. Alterations in collagen concentration in enteric anastomoses follow a similar pattern. Hawley and Faulk[46] showed a 27 per cent reduction of collagen at the anastomotic site in rabbit colons by the third postoperative day. In this study, collagen concentration returned to near normal by the seventh day. Changes in bursting strength were much like those found in the rat colon. Experiments in rabbits by Irvin and Edwards[26] supported the findings of Hawley's group. Yamakawa *et al.*[47] and Morgenstern *et al.*[48] studied colonic anastomoses in mongrel dogs. Three weeks were required before normal levels of collagen were reached. Wise[31] *et al.* also demonstrated a similar drop in collagen concentration in colonic anastomoses in the dog. Bursting strength dropped to a low at three days; the same time that collagen levels reached their low point Bursting strength measurements increased from the fifth to the 19th day, keeping pace with collagen concentration. These studies have all shown a similar pattern of colonic healing in mammals. Bursting strength and collagen concentration at the anastomoses drop to a low at about three days following surgery. Both return toward normal levels within two weeks of operation.

Some authors have pointed out problems with the experimental techniques used in the above papers.[44,49,50] Water content of anastomoses increases because of swelling. Consequently, collagen concentration also drops,[51] thus, the drop in collagen content of the anastomoses is not as dramatic as suggested by the above studies. Pulse labeling studies using radiosotopes may not reflect collagen metabolism adequately. Experiments, in which animals were given repeated dosages of radioisotopes from early life, showed somewhat different results.[51] Lysis of polymerized collagen content of the anastomoses increased dramatically between the third and seventh days. Irvin and Hunt concluded that mature collagen is lysed during the healing of enteric anastomoses, but the drop in collagen content is not as great as previous studies indicated.

The Pattern of Wound Healing

Tensile strength, bursting strength, and collagen measurements follow a similar pattern during the healing of wounds in all tissues. During the lag period of wound healing, each drops to a low point by about three days following injury. In the phase of fibroplasia, each increases rapidly in colons; bursting strength of anastomoses exceeds that of the surrounding bowel within two weeks. Similarly, collagen content approaches that of the normal colon within two weeks. During the period of maturation, wound tensile strength continues to increase as the new collagen assumes mature forms. The collagen content remains stable during this phase. Bursting strength, since it exceeds that of the surrounding bowel, cannot be measured for enteric anastomoses during this period.

These experimental techniques have exposed the inherent weakness of enteric anastomoses during the lag period. The surgical techniques, which were developed during the 19th century for constructing anastomoses, succeed in maintaining the integrity of the anastomosis during this vulnerable period. Inverting stitches, anchored in the collagen-rich submucosa, provide a watertight seal during the dangerous lag period. Newly formed collagen assumes this duty during the period of fibroplasia. The doctrines of intestinal suturing were arrived at largely empirically. Experimental studies support the soundness of the principles upon which they are based.

Summary

The modern age of intestinal suturing began in 1812, with the publication of Travers' studies on the healing of intestinal anastomoses. The doctrines of intestinal suturing date to 1826, when Lembert described his inverting anastomosis. During the remainder of the 19th century, several modifications of Lembert's technique were described. These methods all shared several principles. It was deemed essential that the serosal surfaces of the two cut ends of bowel should be apposed uniformly around the full circumference of the anastomosis. The sutures that accomplished this must be anchored in the submucosa because of its holding strength. In order for an anastomosis to heal reliably, it should be constructed in an environment free of hematoma, necrotic tissue, or infection. These doctrines remain generally accepted today.

Before surgeons could examine experimentally the merits of these doctrines, it was necessary to establish the general pattern of wound healing. Experimental studies over the last two centuries have attempted to classify the progression of wound healing into histologically recognizable stages. During the lag period, the wound first fills with blood and lymph. After several days, neutrophils and macrophages cleanse the wounds of pathogens and necrotic tissue. Within the period of fibroplasia, sprouting capillaries form granulation tissue, and fibroblasts proliferate. Immature collagen appears in the wound. During the period of maturation, collagen assumes a mature form. This classification provides a framework around which the study of healing wounds can be organized.

The return of strength in the healing wound follows a pattern that can also be divided into three periods with the same time sequence. Whether measured by tensile strength or bursting strength, healing anastomoses have very little intrinsic integrity during the lag period. After approximately four to six days, wound strength begins to rise rapidly. By two weeks, the bursting strength of intestinal anastomoses exceeds that of the surrounding bowel. Tensile strength initially rises rapidly in the period of fibroplasia, but asymptotically approaches preoperative levels only during the prolonged period of maturation. It is during the lag period that surgical technique plays such a crucial role in the healing of the intestinal anastomosis. During this period, the suture line accounts for essentially all the measurable strength in the anastomosis.

Measurements of wound collagen content have elucidated the relationship between observable histologic events and measurable changes in wound strength. During the lag period, collagen content drops, because of increased collagenase activity. The wound edges are adhered only by fibrin. The holding strength of suture lines is dependent upon the collagen content of the submucosa. As this content drops, the strength of the anastomosis decreases. During the period of fibroplasia, new collagen fibrils are formed. Collagen bridges the anastomosis. Rising wound strength follows the rising wound collagen content. The strength of the wound approaches preoperative levels only during the phase of maturation, as the collagen assumes mature forms.

The techniques of intestinal suturing, developed during the 19th century, compensate for the intrinsic weakness of the anastomosis during the lag period. This is accomplished by constructing a water-tight suture line, in which the serosal surfaces are apposed. The holding strength of the sutures, and thus the anastomosis, is dependent almost solely on the collagen content of the submucosa. As the collagen content of the submucosa drops during the lag period, the strength of the anastomosis drops to a low. Providing the anastomosis has been constructed in an advantageous environment, new collagen produced during the phase of hyperplasia restores rapidly the strength of the suture line. Application of these few sound principles in clinical settings has produced the remarkable success of intestinal surgery achieved over the last century. A subsequent review will describe the merits of other surgical techniques in constructing intestinal anastomoses.

References

1. Travers B. An inquiry into the process of nature in repairing injuries of the intestines: illustrating the treatment of penetrating wounds, and strangulated hernia. London: Longman, Hurst, Rees, Orme, and Brown, 1812.
2. Senn N. Enterorrhaphy; its history, technique, and present status. JAMA 1893;21:215-35.
3. Lembert A. Nouveau procede d'enterorraphie. Repertoire General d'Anatome et de Physiologie Pathologique 1826;2:3.
4. Lembert A. Nouveau procede d'enterorraphie. Arch Gen Med 1827;13:234.
5. Czerny. Quoted by Jaffee K. Uber darmresection bei gangranosen hernien. Sammlung Klinischer Vorträge 1883;201:1689-1702.
6. Connell ME. An experimental contribution looking to an improved technique in entorrhaphy, whereby the number of knots is reduced to two, or even one. Med Rec 1892;42:335-7.
7. Halstead WS. Circular suture of the intestine - an experimental study. Am J Med Sci 1887;94:436-61.
8. Reid MR. Some considerations of the problems of wound healing. N Engl J Med 1936;215:753.
9. Carrel A. The treatment of wounds. JAMA 1910;55:2148-50.
10. Howes EL, Sooy JW, Harvey SC. The healing of wounds as determined by their tensile strength. JAMA 1929;92:42-5.
11. Sandbloom P. The tensile strength of healing wounds: an experimental study. Acta Chir Scand 1944;90 (Suppl 89):1-108.
12. Herrmann JB, Woodward MD, Pulaski J. Healing of colonic anastomoses in the rat. Surg Gynecol Obstet 1964;119:269-75.
13. Weilbaecher DA, Mathieu FJ, Cohn I Jr. Nonsuture intestinal anastomosis. Am J Surg 1964;107:353-60.
14. Getzen LC. Intestinal suturing: II. Inverting and everting intestinal sutures. Curr Probl Surg 1969;Sept:1-36.
15. Van Winkle W Jr. The tensile strength of wounds and factors that influence it. Surg Gynecol Obstet 1969;129:819-42.
16. Paget J. Lectures on surgical pathology. Philadelphia: Lindsay and Blakiston, 1853;1:271.
17. Chlumsky V. Experimentelle untersuchungenuber die verschiedenen method der darmvereinigung. Beiträge zur Klinisch Chirurgie 1899;25:539-600.
18. Levenson SM, Geever EF, Crowley LV, Oates JF, Berard CW, Rosen H. The healing of rat skin wounds. Ann Surg 1965;161:293-308.
19. Lichtenstein IL, Herz S, Koff S, et al. The dynamics of wound healing. Surg Gynecol Obstet 1970;130:685-90.
20. Adamsons RJ, Musco F, Enquist IF. The relationship of collagen content to wound strength in normal and scorbutic animals. Surg Gynecol Obstet 1964;119:323-5.
21. Jiborn H, Ahonen J, Zederfeldt B. Healing of experimental colonic anastomoses: II. Breaking strength of the colon after left colon resection and anastomosis. Am J Surg 1978;136:595-9.
22. Harvey SC. The velocity of the growth of fibroblasts in the healing wound. Arch Surg 1929;18:1227-40.
23. Cronin K, Jackson DS, Dunphy JE. Changing bursting strength and collagen content of the healing colon. Surg Gynecol Obstet 1968;126:747-53.
24. Trueblood HW, Nelsen TS, Kohatsu S, Oberhelman HA. Wound healing in the colon: comparison of inverted and everted closures. Surgery 1969;65:919-30.
25. Jiborn H, Ahonen J, Zederfeldt B. Healing of experimental colonic anastomoses: I. Bursting strength of the colon after left colon resection and anastomosis. Am J Surg 1978;136:587-94.
26. Irvin TT, Edwards JP. Comparison of single-layer inverting, two-layer inverting, and everting anastomoses in the rabbit colon. Br J Surg 1973;60:453-7.
27. Fellows NM, Burge J, Hatch CS, Price PB. Suture strength and healing strength of end-to-end intestinal anastomoses. Surg Forum 1951;2:111-7.
28. Getzen LC, Roe RD, Holloway CK. Comparative study of intestinal anastomotic healing in inverted and everted closures. Surg Gynecol Obstet 1966;123:1219-27.
29. Hamilton JE. Reappraisal of open intestinal anastomoses. Ann Surg 1967;165:917-24.
30. McAdams AJ, Meikle AG, Taylor JO. One layer or two layer colonic anastomoses. Am J Surg 1970;120:546-50.
31. Wise L, McAlister W, Stein T, Schuck P. Studies on the healing of anastomoses of small and large intestines. Surg Gynecol Obstet 1975;141:190-4.
32. Nelsen TS, Anders CJ. Dynamic aspects of small intestinal rupture with special consideration of anastomotic strength. Arch Surg 1966;93:309-14.
33. Burr HS, Harvey SC, Taffel M. Bio-electric correlates of wound healing. Yale J Biol Med 1938;11:103-7.
34. Edwards LC, Dunphy JE. Wound healing; I. Injury and normal repair. N Engl J Med 1958;259:224-33.
35. Peacock EE Jr. Some aspects of fibrogenesis during the healing of primary and secondary wounds. Surg Gynecol Obstet 1962;115:408-14.
36. Robbins SL, Cotran RS. Inflammation and repair. In: Pathologic basis of disease. Philaldelphia: WB Saunders, 1979.
37. Van Winkle W Jr. The fibroblast in wound healing. Surg Gynecol Obstet 1967;124:369-86.
38. Rosenthal S, Lerner B, Dibiase F, Enquist IF. Relation of strength to composition in diabetic wounds. Surg Gynecol Obstet 1962;115:437-42.
39. Adamsons RI, Musco F, Enquist IF. The comparative effects of silk and catgut on collagen lysis during the lag phase of primary healing. Surg Gynecol Obstet 1965;121:1028-34.
40. Madden JW, Peacock EE Jr. Measurement of the rate of collagen synthesis in sutured rat wounds. Surg Forum 1967;18:58-9.
41. Madden JW, Peacock EE Jr. Studies on the biology of collagen during wound healing: I. Rate of collagen synthesis and deposition in cutaneous wounds of the rat. Surgery 1968;64:288-94.
42. Stein HD, Keiser HR, Sjoerdsma A. Collagen synthesis in granulating wounds of rats and man. Surg Forum 1969;20:63-5.
43. Hawley PR, Faulk P, Hunt TK, Dunphy JE. Collagenase activity in the gastro-intestinal tract. Br J Surg 1970;57:896-900.

44. Peacock EE Jr. Inter- and intramolecular bonding in collagen of healing wounds by insertion of methylene and amide cross-links into scar tissue: tensile strength and thermal shrinkage in rats. Ann Surg 1966;163:1–9.
45. Cronin K, Jackson DS, Dunphy JE. Specific activity of hydroxyproline-tritium in the healing colon. Surg Gynecol Obstet 1968;126:1061–5.
46. Hawley PR, Faulk WP. A circulatory collagenase inhibitor. Br J Surg 1970;57:900–4.
47. Yamakawa T, Patin CS, Sobel S, Morgenstern L. Healing of colonic anastomoses following resection for experimental "diverticulitis." Arch Surg 1971;103:17–20.
48. Morgenstern L, Yamakawa T, Ben-Shoshan M, Lippman H. Anastomotic leakage after low colonic anastomosis: clinical and experimental aspects. Am J Surg 1972;123:104–9.
49. Klein L, Rudolph R. H-collagen turnover in skin grafts. Surg Gynecol Obstet 1972;135:49–57.
50. Klein L, Lewis JA. Simultaneous quantification of 3H-collagen loss and 1H-collagen replacement during healing of rat tendon grafts. J Bone Joint Surg 1972;54:137–46.
51. Irvin TT, Hunt TK. The effect of trauma on colonic healing. Br J Surg 1974;61:430–6.