Few experienced surgeons have escaped the frustration of having a technically excellent low colonic anastomosis leak for no obvious reason. Traditionally, we have explained this misfortune by assuming that a technical error was committed. There is now reason to believe that we must take into account other factors which previously have been ignored.

During the past few years, a number of investigators have studied healing in the colon, and a powerful new concept of a dynamic healing process in the intestine has emerged. We now know that significant lysis of collagen occurs in the anastomotic area and for distances of at least several centimeters to each side as a consequence of injury. The process of healing, that is, connective tissue synthesis and restoration of circulation across the injured area, therefore, must not only bridge the surgical discontinuity but must produce a net positive collagen gain in the face of active collagen lysis. Healing then becomes the net tissue accumulation, or the difference between tissue lysis and tissue synthesis. This added complexity may dismay some. On the other hand, it should arouse surgeons to take into account, in their surgical judgment, all factors which affect collagen degradation and collagen synthesis. It should lead to more careful and accurate appraisal of operative risk. It should expand the rational basis of surgical judgment in the performance of anastomotic surgery.

The mechanical properties of the colonic suture line follow a predictable pattern which differs in some ways from that of skin or fascia. In the first two or three days after operation, the colonic anastomosis has such a low bursting strength (to internal pressure) that accurate measurements are difficult to make. After three days, the strength of the anastomosis increases rapidly, and usually by the end of the first week it is not the anastomosis but the "normal bowel" on either side which ruptures first when the segment is distended.
Indirect measurements indicate that at some time between the first and fourth day the "normal" bowel wall near the anastomosis is weakened.

Recently, Cronin, Jackson, and Dunphy\(^2\)\(^,\)\(^3\) have added a new dimension to research in colonic healing by studying the turnover of collagen in the anastomotic area and in the surrounding colon. Radioactive proline was administered to rats at various times after anastomotic surgery and the fraction of radioactive hydroxyproline subsequently found in bowel collagen was measured. This technic depends on the fact that proline is incorporated into the new collagen molecule and then is converted to hydroxyproline. The quantity of radioactive proline incorporated into collagen and changed to hydroxyproline is, of course, proportional to the rate of synthesis of collagen at the time of radioproline administration. With modification, this method will also measure the rate of collagen degradation. Cronin and his associates found that the total collagen in the bowel in the area of the anastomosis fell to approximately half the normal value by the third postoperative day. They also found that collagen synthesis was already active by the second day after wounding. Since total collagen had halved by the third day, and since synthesis is already active by that day, one can assume that if collagen synthesis were delayed or slowed for any reason, the total collagen content of the bowel would decrease even further. After such a profound loss of strength, the bowel would be torn easily.

The concept of collagen lysis is well substantiated by the work of Gross, Lapierre and Tanzer,\(^5\) who isolated a collagenolytic enzyme active at extracellular pH. Grillo and Gross\(^7\) later demonstrated that healing wounds contain large amounts of collagenase. Since that time, other investigators have demonstrated collagenolytic enzymes in leukocytes.

From the information already available, it is obvious that the collagenolytic mechanism plays a major part in the healing of colonic wounds. Any physiologic event which tends to increase the lysis of collagen, or any situation which tends to decrease the rate or delay the onset of collagen synthesis, is likely to lead to an unusually weak suture line and can be expected to produce anastomotic complications. Several such physiologic events are already well known. Although none has yet been specifically demonstrated as important in colonic healing, they are known to affect other healing tissues.

The following conditions increase collagen lysis:

A. Starvation

It is well known that collagen participates in the catabolic process which occurs during severe starvation. As bone or muscle mass is lost, the corresponding collagen content is lost as well. The loose atrophic skin seen in severe starvation is graphic evidence that dermal collagen is catabolized and lost. Lysis, therefore, would seem to have been exaggerated over the normal range in patients who have lost large amounts of weight very quickly.

B. Steroids

Houck\(^9\) has shown that when cortisone is administered to animals, collagen in skin is lysed. Stress followed by the production of cortisone liberates collagen from pre-existing stores, thus weakening collagenous structures which might be wounded in the process of curing the stressful illness. Fragile skin and osteoporotic bone are characteristic of Cushing's disease. This suggests that collagen is lysed in a nonspecific response to stress and implies that patients who have received large doses of steroids preoperatively face increased risk of anastomotic failures.