*Summary and Conclusions*

A study was undertaken to evaluate the effects of a programme of early presumptive antibacterial therapy of serious infections in surgical patients with intestinal disease. During the eight-month period of this study, 46 patients were evaluated and classified into one of five clinical groups according to the nature of the illness and requirements for antibacterial therapy. In 29 of these, serious infections were encountered, including bacteriæmia, peritonitis, intra-abdominal or pelvic abscesses, urinary tract infections, and pneumonia. When infection was recognized, antibacterial therapy was initiated, or changed promptly on the basis of a presumptive etiological diagnosis after appropriate bacteriological cultures were obtained, but before the causative organisms had been identified, or their *in vitro* susceptibility determined. Definitive antibacterial therapy was subsequently determined on the basis of the patient's clinical response and the results of *in vitro* susceptibility studies. Septic shock developed in 3 patients, and only one died. However, 4 other patients having serious infections without clinical shock died; the presence of potentially lethal underlying noninfectious diseases probably precluded recovery.

Bacteriæmia was detected in about one-fourth of the patients with serious infections. The practice of routinely obtaining blood cultures before initiating or changing systemic antibacterial therapy in such patients may result in a precise bacteriologic diagnosis and provide a useful guide for antibacterial therapy. The practice of obtaining materials from abscesses, exudates, and infected body tissues at laparotomy and immediately inoculating them into appropriate media in the operating room may also be of inestimable value in diagnosis and treatment of infections in surgical patients.

Gram-stained smears of materials obtained from significant sites of infection should be examined more frequently because they may provide valuable immediate information before the results of cultures become available.

We believe that constant awareness of the possibility of infection, an orderly diagnostic approach, and prompt appropriate antibacterial therapy may often prevent irreversible septic shock in surgical patients with intestinal disease.

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## Etiology of Colonic Anastomotic Leaks

Colonic and rectal anastomoses are more subject to leakage than anastomoses in other parts of the gastrointestinal tract. The incidence depends upon the criteria accepted for what constitutes a leak, but is always greater in extraperitoneal anastomoses. Herter & Slanetz (1967) reported that 8% of patients who had anterior resection and whose colons were prepared with antibiotics developed leaks, and 25% of those not so prepared developed leaks, while 5% of patients prepared prior to intraperitoneal colonic anastomosis had anastomotic leaks. Whitaker (1968) mentions a rate of 12·5–28·5% from three hospitals for anterior resections, but some of his criteria for leakage, such as leukocytosis, would not be generally accepted. The rate of overt leakage from anterior resections at St Mark's Hospital, London is approximately 5%. In view of the frequency of colon and rectal resection today this represents a significant complication.

The integrity of an anastomosis will depend upon the technique of the surgeon. Sutures should be correctly placed, the anastomosis should be under no tension and an adequate blood supply to the cut ends is essential. However, breakdown can still occur when the anastomosis is technically correct. The incidence of breakdown of closed colotomy incisions is as great as that in anastomoses at a similar site. There must be additional factors, as yet not widely appreciated, which play a role, and probably the dominant one in leakage.

### *Anastomotic Integrity*

Little new knowledge has been added to the technique of suturing alimentary tract anasto-

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moses since the turn of the century. Sutures are held in the cut edge of the bowel wall by the connective tissue or collagen; the muscle layers, mucosa and serosa contribute very little to the strength. It was first appreciated by Halsted (1887) that most of the collagen was situated in a dense submucous layer. Any changes in the quantity or quality of this collagen will have a profound effect upon the integrity of the anastomosis.

Previous experimental studies of the strength of anastomoses of the intestine as measured by the bursting pressure show that strength is gradually lost until the third or fourth post-operative day. There is then a rapid gain which will equal that of the original uninjured bowel at seven days and will be considerably stronger at ten days (Herrmann *et al.* 1964). Cronin *et al*, (1968) have shown a correspondingly rapid turnover of collagen around an anastomosis in the first week after injury.

Three factors, hæmorrhage, distant trauma and infection, were investigated to see if they had an effect on a standard colonic anastomosis in rabbits. At the time of surgery one group of rabbits had a quarter of its blood volume removed, one had the thigh muscles traumatized, and another had infection introduced into the peritoneal cavity around the anastomosis. Results in a preliminary study of bursting pressures showed that anastomoses which were infected were weaker than those with associated hæmorrhage or trauma.

*Infected Anastomoses*

It was difficult to produce a constant infection around an anastomosis since organisms in the peritoneal cavity will cause little inflammatory reaction. In the absence of foreign material, 1 ml *E. coli* and *S. fæcalis* in a mixed culture of $10^9$ bacteria failed to produce abscesses even of sterile autoclaved fæcal matter was added to the inoculum, abscesses could be consistently produced.

Measurements of bursting pressure of infected anastomoses showed a statistically significant weakness at seven days compared with the normal control (Fig 1).

The peritoneum plays a most important part in the protection of an anastomosis. Contamination by bacteria released from the lumen of the bowel will normally be dispersed throughout the peritoneal cavity in a very short time and phagocytosed. However, if organisms are prevented from reaching the general peritoneal cavity and are confined around the anastomosis, inflammatory changes and abscess formation take place which can lead to disruption.

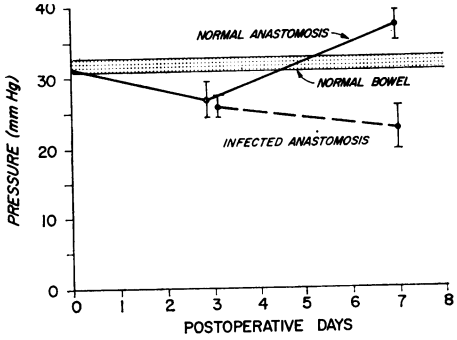


Fig 1 *Effect of infection on the bursting pressure of a rabbit colonic anastomosis. Each point represents the mean of at least 15 recordings and the bar is twice the standard error.* t=3·43

A series of experiments was done to exclude a normal anastomosis from the peritoneal cavity by carefully placing a piece of autoclaved latex around it, ensuring that the blood supply was undisturbed. A significant increase in the incidence of spontaneous breakdown occurred in these anastomoses (Table 1). Anastomoses constructed with a cyanoacrylate tissue adhesive (BBP-tri-fluoroisopropyl cyanoacrylate) frequently broke down for the same reason. Similar results have been suggested by Ravitch *et al.* (1967).

*Table 1*

**Effect of isolating anastomoses from the general peritoneal cavity with a covering of sterilized latex sheet or cyanoacrylate tissue adhesive**

| | *No. of animals* | *Anastomotic leak* | |
|---|---|---|---|
| Normal anastomosis | 23 | 0 | |
| Latex wrap anastomosis | 9 | 2 complete<br>2 sealed | (44%) |
| Cyanoacrylate tissue adhesive | 19 | 8 complete<br>5 sealed | (68%) |

Contamination of the peritoneal cavity could be the result of bacteria spilt during the operation or from seepage of organisms through the suture line for some time afterwards. That the former is more important has been shown in the following way. A catheter was inserted through the rabbit's anus at the completion of surgery and manœuvred to just above the anastomosis. Through the catheter 1 ml of a culture containing serratia $10^6$ was injected, and swabs were taken from the surface of the anastomosis and the surrounding peritoneum. If a continuous atraumatic suture was used in one layer, there was no leakage of organisms from the moment the anastomosis was complete. If a single interrupted layer of sutures was used there was complete sealing of the anastomosis after approximately one hour.

*Table 2*

**Effect of distrant trauma on intraperitoneal infection: rabbits infected with 1 ml of culture containing enterococcus 10⁹ injected around anastomoses prior to closure of abdomen; blunt trauma inflicted on thigh muscles**

| | *No. of animals* | *No. with abscesses* |
|---|---|---|
| Control anastomosis | 23 | 0 |
| Anastomosis and trauma | 15 | 1 (7%) |
| Anastomosis and infection | 10 | 0 |
| Anastomosis and infection and trauma | 5 | 5 (100%) |

Recent studies by Conolly *et al.* (1969) have shown that when contaminated by a constant number of bacteria, infection of skin wounds was increased by distant trauma. It has been shown that there is a similar adverse effect upon the decontaminating processes of the peritoneum. When a constant number of organisms was introduced into the peritoneum around the anastomosis there was a significantly greater rate of abscess formation in animals subjected to distant trauma at the same time (Table 2).

*Mechanism of Collagen Breakdown*

The total amount of collagen in the submucous layer around an anastomosis at a given moment will be the sum of the mature collagen which is being broken down and that which is newly synthesized. Measurements of collagen in these studies suggested that in the infected anastomosis there is increased breakdown of mature collagen and no diminution and even some increase in the amount of new collagen formation. This new collagen has initially little tensile strength.

Collagen at body temperature, pH and ionic concentration is only broken down by an enzyme called collagenase. Collagenase activity of different parts of the alimentary tract has been measured by a tissue culture method (Gross & Lapiere 1962). The enzyme is present in considerably larger amounts in the mucosa of the colon and rectum than elsewhere in the gastrointestinal tract. It has been shown that there is an increased production of collagenase after operation, not only locally but throughout the gastrointestinal tract (Fig 2). There is increased collagenase activity at, and immediately adjacent to, an infected anastomosis compared with the noninfected (Fig 3).

A circulating inhibitor which keeps the activity of this enzyme under control has been isolated (Hawley & Faulk 1970).

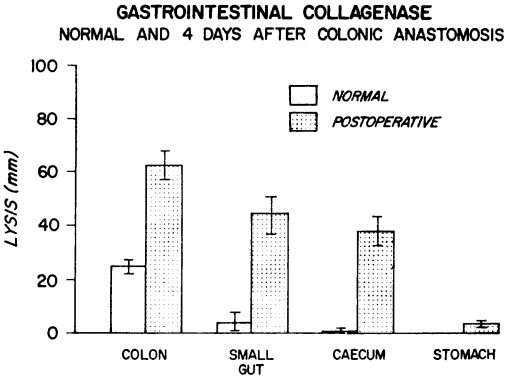


Fig 2 *Gastrointestinal collagenase activity measured as the area of lysis produced when a 2 mm explant of viable mucosa was cultured on a bovine native collagen gel*

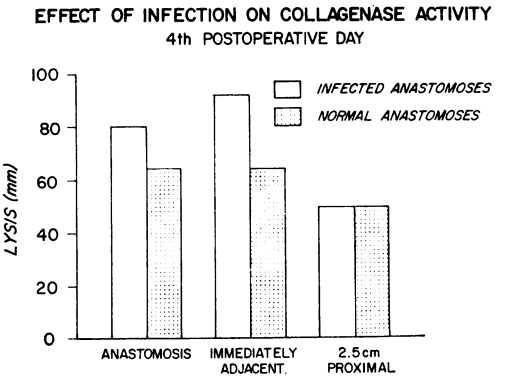


Fig 3 *Collagenase activity around a colon anastamosis four days after operation*

*Summary*

Colonic anastomotic leaks are not an uncommon complication and occur even when surgical technique and the blood supply of the cut ends of the bowel are faultless. The strength of an anastomosis depends upon the connective tissue or collagen in the submucous layer of the intestinal wall. Breakdown results from excessive lysis of mature collagen. Two factors are responsible. The first is the production of more collagenase from the injured colon and rectum than from other parts of the gastrointestinal tract. Abscess formation adjacent to the anastomosis as a result of fæcal contamination at the time of surgery results in an even more increased collagenolytic activity. These metabolic changes are considered to be the dominant factors in leakage from a well-constructed anastomosis.

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