

# The History of Surgery for Crohn's Disease at The Mount Sinai Hospital

ARTHUR H. AUFSES, JR., M.D.

## Abstract

Almost certainly, the physicians and surgeons of The Mount Sinai Hospital cared for patients with inflammatory bowel disease prior to 1932. However, the accepted beginning of the surgery of granulomatous inflammatory bowel disease (IBD) and Crohn's disease (CD) at our institution occurred when the landmark paper by Crohn, Ginzburg, and Oppenheimer was published in 1932.

As a major referral center for patients with both medical and surgical complications of IBD, the surgical service has had a long and abiding interest in the disease. This review highlights the major contributions of our staff to the management of this illness over the past 67 years.

Despite major innovations in both medical and surgical management of patients with Crohn's disease, individuals suffering from this condition are ideally managed by a multidisciplinary team. **Key Words:** Crohn's disease, surgery.

June 8, 1855 — THE DOORS of The Jews Hospital opened to admit patients. Patient No. 1 was Mr. L.S., a forty-two-year-old white male with a fistula-in-ano. He was operated on by Dr. Israel Moses, one of the three attending surgeons on the staff at that time. The operation was successful and the patient was discharged on June 14th (1). Seventy-seven years later, Crohn, Ginzburg, and Oppenheimer (2) noted that the disease they were reporting was "associated with the formation of multiple fistulas," and in 1934, Bissel (3) provided the first report of a perianal fistula in association with ileitis.

Did Mr. L.S. have Crohn's disease?

April 17, 1866 — The name of our institution was changed to The Mount Sinai Hospital.

April 14, 1889 — Dr. John Wyeth, who joined the surgical staff in 1880, operated on a 12-year-old male with abdominal pain of four days' duration and drained a large abscess.

Postoperatively the patient developed an enterovesical fistula which closed slowly (4). Although this young patient had had no prior history, and the history of the present illness was most suggestive of appendicitis, the development of an enterovesical fistula was certainly not in keeping with the diagnosis of appendicitis, but is a significant complication of Crohn's disease.

Did this patient have Crohn's disease?

December 30, 1899 — Dr. Howard Lilienthal (5) operated on a 21-year-old female who "had for years suffered from diarrhea, accompanied by hemorrhages and the passage of foul mucus, and finally become so weak and anemic that a left inguinal colostomy had to be performed to give rest to the lower portion of the colon and rectum. The surgeon who opened the colon at this time saw that the walls of the viscus were covered with polypoid growths which bled easily even on gentle manipulation. The patient was very much benefitted by the operation, the hemorrhages finally ceasing so that it was thought best to close the opening. No sooner had she left the hospital, however, than her old trouble returned in all its severity. . . . Dr. Lilienthal first performed a cecostomy for irrigation of the colon, then on March 6, 1900 performed an ileo-sigmoid anasto-

From the Department of Surgery, Mount Sinai School of Medicine, New York, NY.

Address correspondence to Arthur H. Aufses, Jr., M.D., Department of Health Policy, Box 1077, Mount Sinai School of Medicine, One East 100th Street, New York, NY 10029-6574.

mosis (using a Murphy button to perform the anastomosis) with exclusion of the terminal ileum and the remaining colon. Three months later, the excluded bowel was removed. After two more procedures, the patient did well and on January 14, 1901 was presented to the New York Surgical Society as a case of 'hyperplastic colitis.' At that time the patient was 'in excellent general health and has 2 movements a day. . . .' (6)

Did this patient have Crohn's disease?

February 18, 1919 — Dr. A.O. Wilensky (7) operated on a twenty-three-year-old male with a right lower quadrant mass. The past history included diarrhea of about two years' duration, weight loss and anemia, and an attack of acute suppurative appendicitis treated by appendectomy. Six months after the procedure, he developed pain in the right lower quadrant and a mass appeared. The mass was in the cecum and was resected with anastomosis. Although a postoperative fecal fistula necessitated another operation, the patient did well save for episodic diarrhea, until December 1920, when an episode of acute intestinal obstruction required a resection of about twelve inches of the ileum. He again did well for about two years, when he developed an episode of peritonitis, for which no cause was found at laparotomy. Following drainage, he recovered. Pathological study revealed a granulomatous lesion of the cecum with multiple giant cells, usually present within clumps of lymphocytes. "The entire thickness of the gut appears densely infiltrated. . . . A rather strange finding is the presence of giant cells in what seems an apparently normal lymph follicle in a portion of the contiguous colon that is otherwise entirely normal." Examination of the small bowel revealed that "the gut is extremely thickened and enlarged. The peritoneal surface is much congested and is covered with fresh fibrin. Cross-section shows an immense thickening of all the coats of the gut so that the lumen is merely a bare slit. The infiltration involves the adjacent mesentery which averages 1 cm. In thickness . . . fresh fibrin covers the surface of the mucosa. Removal of the fibrin reveals numerous superficial ulcerations." Microscopic examination was similar to the colon, but there were far more giant cells, the majority of which contained an unrecognizable foreign body.

Did this patient have Crohn's disease?

May 13, 1932 — Dr. Burrill B. Crohn, as the sole author, presented a paper entitled "Terminal Ileitis" at the annual meeting of the American Medical Association in New Orleans. In the discussion that followed, Bagen stated that "several

cases of this type have come to operation annually at the Mayo Clinic." He felt that the term "terminal ileitis" was inappropriate because the disease was not a "terminal illness," and he also prophesied that the disease would be described elsewhere in the intestinal tract. Crohn's manuscript was published in the *Journal of the American Medical Association* (2) in October 1932, and the name of the syndrome was changed to "regional ileitis." Also, the names of Drs. Leon Ginzburg and Gordon S. Oppenheimer were added as co-authors, since they had accumulated a large series of cases, not otherwise categorized, of unusual conditions of the terminal ileum, which included the cases presented by Crohn. Their work was presented (also in May 1932) at the meeting of the American Gastroenterological Association and finally published in the *Annals of Surgery* (8) in January 1933. At the time, Dr. Oppenheimer, who subsequently became the Chief of Urology at The Mount Sinai Hospital, was working in the pathology laboratory and Dr. Ginzburg was the assistant to Dr. A.A. Berg, the surgeon who had operated on the 14 patients in the original series.

Although the patients described earlier may or may not have had Crohn's disease, there is little doubt that the disease had existed prior to 1932. But was it a new disease? Janowitz (9) speculated that "one cannot escape the conviction that this really is a new disease, which emerged in the early part of the century, for it is difficult to believe that the great European pathologists of the 19th century who did such careful autopsies would have missed the striking pathologic entity or confused it with tuberculosis, whose appearance they knew so well." On the other hand, cases reported more than one hundred years earlier are most suggestive, and the cases reported by Dalziel (10) in 1913 almost certainly had granulomatous disease of the bowel, affecting both small and large intestine. Six of nine were successfully operated on.

The accepted beginning of the surgery of granulomatous inflammatory bowel disease (IBD) and Crohn's disease (CD) at The Mount Sinai Hospital occurred when the landmark paper by Crohn, Ginzburg, and Oppenheimer was published in 1933 (2). The fourteen patients who made up this series of cases were all operated on by Dr. A.A. Berg, one of the leading surgeons of his day and a chief of service at The Mount Sinai Hospital. Dr. Ginzburg stated (11): "Dr. Berg was an extraordinary individual. The extent of his surgical practice was almost incredible in its day, and it would be difficult for one to believe at pre-

sent. He operated both morning and afternoon six days a week, and not infrequently on Sunday as well." Berg, as the surgeon for all of the patients, was given the opportunity to be a co-author. However, he declined (12), since it was his policy not to put his name on a paper unless he had personally written a significant portion of the manuscript. Had he accepted, and since the authors were listed alphabetically, we might now be talking about "Berg's disease" (see chapter 18).

In 1934, the first report of a patient with ileitis crossing the ileocecal valve to involve the cecum and ascending colon was reported by Dr. Ralph Colp (13). Dr. Colp was a graduate of the College of Physicians and Surgeons of Columbia University, trained at the Presbyterian Hospital, and was a senior surgeon at the Beekman-Downtown Hospital before he joined the staff of the Department of Surgery of The Mount Sinai Hospital in 1923. The patient, a twenty-two-year-old medical student, had been operated on at the Beth Israel Hospital where Dr. Colp was a consultant. Dr. Colp noted that "the microscopical pathology of both the ileum and the cecum were similar, that of a nonspecific granuloma." He went on to say that "nonspecific granulomas of the terminal ileum, the ileocecal region and the colon are probably one and the same disease." Although Hirschman of Detroit, in his discussion of Crohn's presentation, had cited the case of an 18-year-old male with "chronic ulcerative colitis" of 9 years' duration, who at operation was found to have a "large doughy thickened ileum" of about 12 inches in length, Colp's report is the first documented and published case of granulomatous ileocolitis.

The years between 1932 and 1960 were punctuated by tremendous advances in our understanding of this newly described entity. Numerous reports documented that granulomatous inflammatory bowel disease was truly panenteric, and the distinction between granulomatous and ulcerative colitis was firmly established by Lockhart-Mummery and Morson (14) in 1960. Until that time (and even after, in some quarters), granulomatous colitis had been considered to be a variant of ulcerative colitis. What in retrospect was clearly granulomatous ileocolitis had then been considered by most gastroenterologists and surgeons to be ulcerative colitis or a variant thereof, in association with regional or granulomatous disease of the small bowel.

It must be remembered that, in the years that these early patients were operated on (1925–1935), antibiotics were nonexistent, fluid and

electrolyte management was in its infancy, and blood transfusions were a tour de force. As a result, one-stage ileocolic resection, the preferred operation today and the operation performed by Berg and others of his day, then had a significant mortality rate, as high as 25%. As a consequence, many surgeons performed the procedure in two stages. In the first procedure, the ileum proximal to the diseased segment was divided, the distal end closed and the neoterminal ileum anastomosed to either the transverse or sigmoid colon. At a later date, the excluded segment was resected.

Two years after Colp's 1934 report, Berg (15), who had performed primary resections on all of the early cases, reported on "an operative procedure for right-sided ulcerative colitis." This was an ileo-sigmoidostomy with exclusion of the most distal ileum. In addition, however, the sigmoid proximal to the ileal anastomosis was divided, and the distal end closed. A stoma was created with the proximal end. This effectively isolated the colon, and allowed for drainage of colonic mucus and for irrigation of the colon via the stoma. Not all of these patients did well and several, therefore, had resection of the excluded bowel. The article (15) contains an artist's rendition of the specimens. One of them depicts a terminal ileum and colon with deep punched-out ulcers and significant thickening of the affected areas, almost certainly granulomatous disease rather than ulcerative colitis.

In 1938, Richard Lewisohn (16), best known as the individual responsible for the development of citrate solution for blood preservation, summarized the then current thinking of The Mount Sinai Hospital surgical staff. His conclusions are worth noting, as many are still relevant today:

- 1) Segmental or regional enteritis is not a rare disease.
- 2) Opinions differ widely not only as to the pathogenesis of these interesting lesions, but also as to the best method of surgical treatment.
- 3) The lesion is encountered most frequently in the terminal ileum. However, it may occur in any part of the gastro-intestinal tract.
- 4) It is doubtful whether segmental colitis and ileocolitis are clinical entities. They may represent an attenuated form of acute ulcerative colitis and ileitis.
- 5) Perianal fistulas are frequently encountered.
- 6) Ileocolostomy with division of the ileum may effect a complete cure.
- 7) In the presence of fistulous communications with other parts of the intestinal tract primary resection becomes mandatory.

Ileotransverse colostomy with exclusion became the procedure of choice at Mount Sinai, and in 1939 Ginzburg, Colp, and Sussman (17) presented 32 cases of “ileostomy with exclusion,” at the meeting of the American Surgical Association. Nineteen of the procedures were performed as definitive surgery for inflammatory disease, and in 13 patients the operation was performed as a first-stage procedure in the management of carcinoma of the right or transverse colon. The development of this procedure was later eloquently described by Ginzburg in 1955 (18):

Originally, localized ileitis was treated by ileocolic resection. Before the present era of antibiotics, blood banks, intestinal intubation and improved anesthesia, this procedure was accompanied by a mortality rate rarely under twenty per cent and at times considerably greater. In order to reduce the mortality, recourse was had to a two stage operation, the primary one consisting of an ileocolostomy with exclusion. Secondary operation revealed that recession of the active inflammatory process was present in the excluded loop in almost all cases. The routine second stage procedure was therefore abandoned and performed only on those few occasions where there was evidence that healing had not taken place in the excluded loop. The results following ileocolostomy with exclusion proved to be as good as that obtained following resection and were achieved with a negligible mortality.

This operation became known as “The Mount Sinai Operation.” That it was a wise decision at the time was evident in the 1945 report by Garlock and Crohn (19) reporting the series of patients personally operated on by Dr. Garlock. For these 145 patients, the mortality rate was 16% for a one-stage resection (9/55), 12% (3/25) for a two-stage resection, and 0% in 65 patients treated with ileotransverse colostomy with exclusion. In 1980, 35 years later, we were able to report 100 consecutive ileocolic resections for CD without mortality (20). Today almost all major medical centers report large series of one-stage resection with minimal mortality. Unquestionably, the advances noted by Ginzburg have had a great impact on the improved results.

Ileotransverse colostomy with exclusion as a definitive procedure fell into disfavor when it became apparent that the procedure had deficiencies. The inflammatory process in the excluded loop did not always subside, and the right colon

was unnecessarily sacrificed, thereby losing its water-absorbing capacity. The report of Greenstein and his colleagues (21), showing that the excluded loop was a major risk for the development of small bowel cancer, was probably the final nail in the coffin for this procedure. On the other hand, there will always be a role for this procedure in the rare instance of massive inflammatory reaction, where the surgeon feels that resection may prove fatal. In this situation, ileocolostomy with exclusion as the preliminary step in a staged procedure may prove to be lifesaving.

In the 66 years (1932–1998) since the first description of Crohn's disease, the surgeons and surgical specialists of the staff of Mount Sinai have contributed significantly to present-day understanding of the state of the art management of the disease and its complications. As The Mount Sinai Hospital has been a major referral center for IBD, its surgeons have amassed a broad experience in the management of the surgical issues confronting this group of patients and have shared their experiences via literally hundreds of papers. In the past thirty years, approximately 5000 patients with Crohn's disease and ulcerative colitis have been treated. In 1968, Dr. Allan Kark, the then chairman of the Department of Surgery, recruited Dr. Adrian Greenstein to the staff. Dr. Greenstein became the “keeper of the records” of our inflammatory bowel disease population. His publications on the extraintestinal manifestations of IBD (22) and the nature and magnitude of reoperation and recurrence (23), written in collaboration with our colleagues in Gastroenterology, are classics. His bibliography of more than 135 papers, 30 book chapters and innumerable abstracts has catalogued the gamut of IBD.

For more than twenty years, the Department of Surgery has encouraged medical students to participate in research. There have also been a number of outstanding fellows. Many of the surgical faculty have an uncanny knack of stimulating and encouraging the students and fellows to be academically productive. Utilizing electron microscopic techniques, Michael Marin, then a student and now a member of the faculty in vascular surgery, made significant contributions to our understanding of the earliest pathological abnormalities in CD (24–26). Anthony Pucillo did yeoman work on the papers relating to the development of cancer in bypassed loops (21) and was a co-author of papers on cancer in ulcerative colitis (27, 28). Among the fellows, Yamazaki and Ribeiro deserve special recognition for their contributions to the papers dealing with carci-

noma of the small bowel in CD (29), the management of intra-abdominal abscess in CD (30), and a review of colorectal strictures in CD (31). One of Adrian Greenstein's many contributions related to the concept of two types of CD, i.e., obstructive and fistulizing (32). Originally criticized by many in the field, this concept is now generally accepted. Recent laboratory work by Dr. Robert Greenstein and colleagues (33) may provide the molecular basis underlying the concept.

Almost all of the abdominal surgeons in the department have contributed their knowledge and specific expertise in papers, monographs, book chapters, and reviews. Dr. Tomas Heimann has focused his efforts on the immunological aspects of CD, and their effect on the postoperative course and recurrence (34–40). His paper on the factors responsible for early symptomatic recurrence (41) was presented at the 1993 meeting of the American Surgical Association. Dr. Paul Tarter, one of the first to document the effects of blood transfusion on the immune system, has studied the effects of transfusion in CD patients undergoing surgery (42, 43). Dr. Isidore Kreel has had extensive surgical experience in the management of CD. In association with Dr. Arthur Aufses and then Dr. Gary Slater, he was one of the first to point out the value of ileostomy in CD (44, 45). Slater and Aufses have also been major contributors to what has been an important cooperative venture on the part of all of the surgeons of the department. A partial listing of other papers appears in the reference list (20, 46–66).

Mount Sinai Medical Center was one of the first academic medical centers to create a separate division of endoscopic surgery (1992) to promote the use of these new surgical techniques. The experiences of these laparoscopists with respect to resection for CD were reported shortly thereafter (67–69).

In conclusion, starting from the first description of the disease now known throughout the world as Crohn's disease, the surgeons of The Mount Sinai Medical Center have worked in close collaboration with colleagues in gastroenterology to the benefit of many grateful patients. This collaboration will continue to promote not only superior patient care, but also the future training of physicians and other health care workers in the ever-changing aspects of the treatment of Crohn's disease.

#### References

1. Case records of the Jews Hospital — Book 1, Case #1. 1855; Archives of the Mount Sinai Medical Center.
2. Crohn BB, Ginzburg L, Oppenheimer GD. Regional ileitis. A pathologic and clinical entity. *J Am Med Ass* 1932; 99:1323–1329.
3. Bissell AD. Localized chronic ulcerative ileitis. *Ann Surg* 1934; 99:957–966.
4. Wyeth, JA. Some recent surgical cases. *Intl J Surg* April, 1890.
5. Lilienthal H. Hyperplastic colitis: Extirpation of the entire colon, the upper portion of the sigmoid flexure and four inches of the ileum. *Am Med* 1901; 1:164–165.
6. Lilienthal H. Extirpation of the entire colon, the upper portion of the sigmoid flexure, and four inches of the ileum for hyperplastic colitis. *Ann Surg* 1903; 37:616–617.
7. Moschowitz E, Wilensky AO. Non-specific granulomata of the intestine. *Am J Med Sci* 1923; 166:48–66.
8. Ginzburg L, Oppenheimer GD. Non-specific granulomata of the intestines (inflammatory tumors and strictures of the intestines). *Ann Surg* 1933; 98:1046–1062.
9. Janowitz HD. Crohn's disease — 50 years later. *N Engl J Med* 1981; 304:1600–1602.
10. Dalziel TK. Chronic interstitial enteritis. *Br Med J* 1913; 2:1068–1070.
11. Ginzburg L. The road to regional enteritis. *Mt Sinai J Med* 1974; 41:272–275.
12. Crohn BB. The early days of regional ileitis at the Mount Sinai Hospital — reminiscences. *J Mt Sinai Hosp N Y* 1955; 22:143–146.
13. Colp R. A case of nonspecific granuloma of the terminal ileum and cecum. *Surg Clin North Am* 1934; 14:443–449.
14. Lockhart-Mummery HE, Morson BC. Crohn's disease (regional enteritis) of the large intestine and its distinction from ulcerative colitis. *Gut* 1960; 1:87–105.
15. Berg AA. An operative procedure for right-sided ulcerative colitis. *Ann Surg* 1936; 10:1019–1023.
16. Lewisohn R. Segmental enteritis. *Surg Gynecol Obstet* 1938; 66:215–222.
17. Ginzburg L, Colp R, Sussman M. Ileocolostomy with exclusion. *Ann Surg* 1939; 110:648–658.
18. Ginzburg L. The surgical treatment of regional enteritis. *J Mt Sinai Hosp N Y* 1955; 22:215–222.
19. Garlock JH, Crohn BB. Appraisal of results of surgery in the treatment of regional enteritis. *J Am Med Ass* 1945; 127:205–208.
20. Slater G, Greenstein AJ, Aufses AH, Jr. Postoperative complications after right colonic resections for inflammatory bowel disease and carcinoma. *Am J Gastroenterol* 1980; 74:516–518.
21. Greenstein AJ, Sachar D, Pucillo A, et al. Cancer in Crohn's disease after diversionary surgery. A report of seven carcinomas occurring in excluded bowel. *Am J Surg* 1978; 135:86–90.
22. Greenstein AJ, Janowitz HD, Sachar DB. The extra-intestinal complications of Crohn's disease and ulcerative colitis: A study of 700 patients. *Medicine* 1976; 55:401–412.
23. Greenstein AJ, Sachar DB, Pasternack BS, et al. Reoperation and recurrence in Crohn's colitis and ileocolitis: Crude and cumulative rates. *N Engl J Med* 1975; 293:685–690.
24. Marin ML, Greenstein AJ, Geller SA, et al. A freeze fracture study of Crohn's disease of the terminal ileum: Changes in epithelial tight junction organization. *Am J Gastroenterol* 1983; 78:537–547.
25. Marin ML, Geller SA, Greenstein AJ, et al. Ultrastructural pathology of Crohn's disease: Correlated transmission electron microscopy, scanning electron microscopy, and freeze fracture studies. *Am J Gastroenterol* 1983; 78:355–364.
26. Marin ML, Greenstein AJ, Geller SA, et al. Freeze-fracture analysis of epithelial cell lysosomal inclusions in Crohn's disease. *Ultrastruct Pathol* 1984; 6:39–44.

27. Greenstein AJ, Sachar DB, Pucillo A, et al. Cancer in universal and left-sided ulcerative colitis: Clinical and pathologic features. *Mt Sinai J Med* 1979; 46:25–32.
28. Greenstein AJ, Sachar DB, Smith H, et al. Cancer in universal and left-sided ulcerative colitis: Factors determining risk. *Gastroenterology* 1979; 77:290–294.
29. Ribeiro MB, Greenstein AJ, Heimann TM, et al. Adenocarcinoma of the small intestine in Crohn's disease. *Surg Gynecol Obstet* 1991; 173:343–349.
30. Ribeiro MB, Greenstein AJ, Yamazaki Y, Aufses AH, Jr. Intra-abdominal abscess in regional enteritis. *Ann Surg* 1991; 213:32–36.
31. Yamazaki Y, Ribeiro MB, Sachar DB, et al. Malignant colorectal strictures in Crohn's disease. *Am J Gastroenterol* 1991; 86:882–885.
32. Greenstein AJ, Lachman P, Sachar DB, et al. Perforating and non-perforating indications for repeated operations in Crohn's disease: Evidence for two clinical forms. *Gut* 1988; 29:588–592.
33. Gilberts EC, Greenstein AJ, Katsel P, et al. Molecular evidence for two forms of Crohn's disease. *Proc Natl Acad Sci U S A* 1994; 91:12721–12724.
34. Heimann T, Panvelliwalla D, Greenstein A, et al. Tissue immunoglobulins and early recurrence in Crohn's disease. *Surg Gynecol Obstet* 1982; 154:541–544.
35. Heimann T, Gelernt I, Schanzer H, et al. Surgical treatment, skin test reactivity, and lymphocytes in inflammatory bowel disease. *Am J Surg* 1983; 145:199–201.
36. Heimann TM, Aufses AH, Jr. Surgical complications and skin test reactivity in patients with inflammatory bowel disease. *Arch Surg* 1984; 119:885–887.
37. Heimann TM, Aufses AH, Jr. The role of peripheral lymphocytes in the prediction of recurrence in Crohn's disease. *Surg Gynecol Obstet* 1985; 160:295–298.
38. Heimann TM, Greenstein AJ, Mechanic L, Aufses AH, Jr. Early complications following surgical treatment for Crohn's disease. *Ann Surg* 1985; 201:494–498.
39. Heimann TM, Bolnick K, Aufses AH, Jr. Prognostic significance of severe preoperative lymphopenia in patients with Crohn's disease. *Ann Surg* 1986; 203:13–135.
40. Heimann TM, Miller F, Martinelli G, et al. Correlation of presence of granulomas with clinical and immunologic variables in Crohn's disease. *Arch Surg* 1988; 123:46–48.
41. Heimann TM, Greenstein AJ, Lewis B, et al. Prediction of early symptomatic recurrence after intestinal resection in Crohn's disease. *Ann Surg* 1993; 218:294–298.
42. Tartter PI, Heimann TM, Aufses AH, Jr. Blood transfusion, skin test reactivity, and lymphocytes in inflammatory bowel disease. *Am J Surg* 1986; 151:358–361.
43. Tartter PI, Driefuss RM, Malon AM, et al. Relationship of post-operative septic complications and blood transfusions in patients with Crohn's disease. *Am J Surg* 1988; 155:43–48.
44. Aufses AH, Jr., KreeI I. Ileostomy for granulomatous ileocolitis. *Ann Surg* 1971; 173:91–96.
45. Slater G, KreeI I, Aufses AH, Jr. Temporary loop ileostomy in the treatment of Crohn's disease. *Ann Surg* 1978; 188:706–709.
46. Slater G, Greenstein A, Aufses AH, Jr. Anal carcinoma in patients with Crohn's disease. *Ann Surg* 1984; 199:348–350.
47. Greenstein AJ, Meyers S, Szporn A, et al. Colorectal cancer in regional ileitis. *Q J Med* 1987; 62:33–40.
48. Greenstein AJ, Present DH, Sachar DB, et al. Gastric fistulas in Crohn's disease. Report of cases. *Dis Colon Rectum* 1989; 32:888–892.
49. Slater G, Aufses AH, Jr. Small bowel length in Crohn's disease. *Am J Gastroenterol* 1991; 86:1037–1040.
50. Slater G, Greenstein AJ. Mesenteric fibromatosis in Crohn's disease. *J Clin Gastroenterol* 1996; 22:147–149.
51. Kim U, Aufses AH, Jr., KreeI I. Malignant tumors associated with granulomatous enterocolitis. *Am J Gastroenterol* 1975; 63:66–70.
52. Kim U, Klein M, Baek SM, et al. Carcinoma of the small intestine in Crohn's disease — occurrence in a bypassed loop. *Mt Sinai J Med* 1976; 43:461–466.
53. Heimann T, Greenstein AJ, Aufses AH, Jr. Surgical management of ileosigmoid fistula in Crohn's disease. *Am J Gastroenterol* 1979; 72:21–24.
54. Greenstein AJ, Sachar DB, Smith H, et al. A comparison of cancer risk in Crohn's disease and ulcerative colitis. *Cancer* 1981; 48:2742–2745.
55. Greenstein AJ, Meyers S, Sher L, et al. Surgery and its sequelae in Crohn's colitis and ileocolitis. *Arch Surg* 1981; 116:285–288.
56. Greenstein AJ, Panvelliwalla DK, Katz LB, et al. Tissue carcinoembryonic antigen, dysplasia, and disease duration in colonic inflammatory bowel disease. *Am J Gastroenterol* 1982; 77:212–215.
57. Greenstein AJ, Dicker A, Meyers S, Aufses AH, Jr. Perileostomy fistulae in Crohn's disease. *Ann Surg* 1983; 197:179–182.
58. Greenstein AJ, Sachar DB, Tzakis A, et al. Course of enterovesical fistulas in Crohn's disease. *Am J Surg* 1984; 147:788–792.
59. Greenstein AJ, Mann D, Sachar DB, et al. Free perforation in Crohn's disease: I. A survey of 99 cases. *Am J Gastroenterol* 1985; 80:682–689.
60. Greenstein AJ, Aufses AH, Jr. Differences in pathogenesis, incidence and outcome of perforation in inflammatory bowel disease. *Surg Gynecol Obstet* 1985; 160:63–69.
61. Greenstein AJ, Gennuso R, Sachar DB, et al. Extraintestinal cancers in inflammatory bowel disease. *Cancer* 1985; 56:2914–2921.
62. Greenstein AJ, Sachar DB, Gibas A, et al. Outcome of toxic dilatation in ulcerative and Crohn's colitis. *J Clin Gastroenterol* 1985; 7:137–143.
63. Shafir M, Martinelli G, Bekesi JG, et al. Immunoglobulins (Ig) in circulating immune complexes (CIC) in cancer and inflammatory bowel disease (IBD). *Eur J Surg Oncol* 1986; 12:351–357.
64. Newman LH, Wellinger JR, Present DH, et al. Crohn's disease of the duodenum associated with pancreatitis: A case report and review of the literature. *Mt Sinai J Med* 1987; 54:429–432.
65. Greenstein AJ, Sachar DB, Shafir M, et al. Malignant melanoma in inflammatory bowel disease [published erratum appears in *Am J Gastroenterol* 1992 Sep; 87:1237]. *Am J Gastroenterol* 1992; 87:317–320.
66. Greenstein AJ, Mullin GE, Strauchen JA, et al. Lymphoma in inflammatory bowel disease. *Cancer* 1992; 69:1119–1123.
67. Bauer JJ, Harris MT, Grumbach NM, et al. Laparoscopic-assisted intestinal resection for Crohn's disease. Which patients are good candidates? *J Clin Gastroenterol* 1996; 23:44–46.
68. Reissman P, Salky BA, Edey M, et al. Laparoscopic surgery in Crohn's disease. Indications and results. *Surg Endosc* 1996; 10:1201–1203.
69. Reissman P, Salky BA, Pfeifer J, et al. Laparoscopic surgery in the management of inflammatory bowel disease. *Am J Surg* 1996; 171:47–50.