26

Planting Seeds of Knowledge about Inflammatory Bowel Disease:

Half a Century of Science, Prescience, and Prophecy in the Pages of Mount Sinai's Journal

DAVID B. SACHAR, M.D.

Abstract

This is a review of those clinical observations, innovative concepts, and predictions concerning inflammatory bowel disease that were first published in *The Journal of the Mount Sinai Hospital*, renamed in 1970 *The Mount Sinai Journal of Medicine*. The review was based on a hand search of every volume of *The Journal* from its inception in 1934 to the present day.

Key Words: Crohn's disease, ulcerative colitis, inflammatory bowel disease, The Journal of The Mount Sinai Hospital, The Mount Sinai Journal of Medicine.

THIS IS SURELY THE AGE OF "Evidence-Based Medicine." In the courtrooms of academia, the only "admissible evidence" these days seems to be fully-powered randomized clinical trials. By this restrictive criterion, though, we pay attention only to the final product — the harvested fruit. But what about the seeds? What about the original observations and seminal ideas that bore fruit only after many years of cultivation?

In March of 1997, the distinguished physician and editor, Frank Davidoff, lectured at Medical Grand Rounds at The Mount Sinai Hospital. His talk, entitled "In the teeth of the evidence: The curious case of evidence-based medicine," included the following statement (1): "All good science begins with good observations, but observations serve largely to generate hypotheses rather than confirm them." The speaker clearly intended to emphasize the importance of "confirmation," harvesting the fruit. In this essay, by contrast, I intend to emphasize the "generation," the planting of the seeds.

A pair of "Theme Issues" in this journal last year has already surveyed the many contributions of Mount Sinai doctors to the field of inflammatory bowel disease (IBD). I have, however, set myself a rather different agenda.

David B. Sachar, M.D., Clinical Professor of Medicine, Director Emeritus of the Dr. Henry D. Janowitz, Division of Gastroenterology, Mount Sinai School of Medicine, New York, NY.

Address correspondence to David B. Sachar, M.D., Division of Gastroenterology, Mount Sinai School of Medicine, Box 1069, One East 100th Street, New York, NY 10029-6574.

Specifically, I shall review those "good observations," innovative concepts, and predictions concerning IBD that were first published in *The Journal of The Mount Sinai Hospital*, renamed in 1970 as *The Mount Sinai Journal of Medicine*. This review is based on a hand search of every volume of *The Journal* from its inception in 1934 to the present day.

Anatomic Distribution

Although "regional ileitis" had been thoroughly described in two nearly simultaneous presentations in May 1932 by Crohn, Ginzburg, and Oppenheimer (2, 3), it took more than 20 years before the same pathologic process in the colon was firmly classified as part of the same disease (4). Nonetheless, Ginzburg and Oppenheimer's initial compilation of cases of "non-specific granulomata of the intestine" (2) meticulously described "localized hypertrophic colitis" associated with peri-anal fistula, an observation repeated by Crohn, Garlock, and Yarnis 15 years later and further emphasized in a *Journal of the Mount Sinai Hospital* abstract (5) regarding the entity of "segmental right-sided colitis": "Peri-anal and peri-rectal fistulas are very common."

While it was the team of a British surgeon, H.E. Lockhart-Mummery, and pathologist, Basil Morson, who argued most strongly for classifying granulomatous colitis as an integral part of Crohn's disease (6), this concept received its major impetus in the United States from the work of Mount Sinai radiologists, particularly

B.S. Wolf and especially R.H. Marshak (7). Indeed, the classic, most exhaustive description of the features and differential diagnosis of ulcerative and granulomatous colitis appeared in a 59-page article in *The Journal of the Mount Sinai Hospital* by Marshak and Lindner in 1966 (8). This radiologic magnum opus was often reproduced and modified by its authors — as in a *Mount Sinai Journal of Medicine* paper (9) that prefigured a chapter in their classic W.B. Saunders textbook, *Radiology of the Colon* — but the clarity and thoroughness of the 1966 publication was never surpassed. Indeed, as Henry Janowitz foretold in his introduction to the 1966 paper (10): "This exhaustive study and detailed illustration of the radiographic features of the major inflammatory disorders of the colon by Drs. Marshak and Lindner will, I believe, contribute enormously to our sorting out of this baffling group of diseases."

A different view of ulcerative and granulomatous colitis, however, from a colonoscopic perspective, was outlined in 1975, in a paper by Jerome Waye (11), comprising "an in-depth review based on a personal experience of several thousand colonoscopies." This whole topic of recognizing Crohn's disease of the colon has also been reviewed in *The Mount Sinai Journal of Medicine* by one of the pioneering investigators of this disorder, Arthur Lindner, a former fellow in gastroenterology at The Mount Sinai Hospital (12).

Meanwhile, as Crohn's disease was being increasingly recognized in the colon, other *Journal of the Mount Sinai Hospital* publications and abstracts throughout the 1950s were calling attention to involvement of the stomach, duodenum, and jejunum (13–15). (It is interesting that the lure of studying IBD at Mount Sinai was so strong that the principal review of Crohn's gastroduodenitis (14) was written by Alexander Richman, chief of the Liver Clinic who was primarily a specialist in hepatic and pancreatic diseases). Further classic descriptions of gastric and duodenal Crohn's disease, accompanied by magnificent radiographs, appeared subsequently in the "Radiologic Notes" section of *The Mount Sinai Journal of Medicine* edited by C. Bloch and H.M. Peck (16, 17).

Natural History and Epidemiology

Throughout the 1960s, even before establishing himself as the pioneer of immunosuppressive therapy for IBD in the United States, Burton Korelitz, then a young gastroenterologist at The Mount Sinai Hospital, was a leading chronicler of the natural history of ulcerative colitis and Crohn's disease. As early as 1962, he had begun to publish, together with a pediatrician, Donald Gribetz, their observations on the course of ulcerative colitis in children. In 1968, *The Journal of the Mount Sinai Hospital* carried Korelitz's seminal paper on the prognosis of granulomatous colitis in childhood (18). By 1979, Korelitz had accumulated experience with more than 350 patients with Crohn's disease. His report in *The Mount Sinai Journal of Medicine* that year (19) was a landmark in establishing the scientific value of clinical experience garnered by scholarly specialists in private practice.

From a broader perspective of global epidemiology, Mount Sinai's chairman of surgery, Arthur Aufses, Jr., made a remarkably accurate prediction at an IBD symposium in 1982 marking 50 years' experience with IBD and celebrating 25 years of Henry Janowitz's directorship of Mount Sinai's Division of Gastroenterology. On that occasion, Dr. Aufses said (20): "If I had to venture a guess, I would say that granulomatous [Crohn's] disease, which has been on a marked increase in the northern parts of the world, will slowly plateau and then begin to decline. That will be followed by increases in its incidence in other parts of the world, where they don't see very much of it now." As usual, Aufses's crystal ball proved reliable.

Complications

Although Mount Sinai physicians in 1987 were most strongly emphasizing the external origins of upper gastrointesinal (GI) fistulas in Crohn's disease (21), *The Journal of the Mount Sinai Hospital*, as early as 1948, carried a paper recognizing duodenal fistula as colonic in origin, and describing its surgical correction by simple closure of the duodenal hole and definitive resection of the diseased colon (22). Similarly, an early paper on "gastrocolic fistula" clearly identified this complication as arising from "transmural colitis" and at one point in its text used the more accurate term, "cologastric fistula" (23). A much rarer complication involving the upper GI tract is pancreatitis supposedly associated with primary Crohn's disease of the duodenum. One of the earliest reports (actually only the third paper) describing this association appeared in *The Mount Sinai Journal of Medicine* in 1987 (24).

Important observations concerning the much more common complication of lower GI tract fistulization were reported by Korelitz in

The Mount Sinai Journal of Medicine in 1984 (25). His review of 22 patients with ileosigmoid and ileorectal fistulae called early attention to two cardinal principles, both insufficiently appreciated even today. The first point was that "the entero-enteric fistula does not require surgical intervention for its own sake," since it was often asymptomatic and even in cases requiring treatment might well respond to medical therapy. The second key concept was his emphasis on identifying "the segment of origin" — in other words, carefully distinguishing the perpetrator (site of origin) from the innocent bystander victim (the site of re-entry).

Another set of Crohn's disease manifestations largely clarified by Mount Sinai investigators comprised urologic complications. Although a number of Mount Sinai papers from the 1960s are often cited as the earliest publications on this topic, the urologic complications of regional ileitis were first described by Ginzburg and Oppenheimer in the *Journal of Urology* in 1948 and abstracted shortly after in *The Journal of the Mount Sinai Hospital* (26). It should be noted that this same Gordon Oppenheimer of "Crohn, Ginzburg, and Oppenheimer" fame was in fact an eminent urologist. In this article, patients were reported as presenting with retroperitoneal abscesses; but their characteristic symptom of lower extremity pain and limp — prominently described in 1969 by Daniel Present et al., one of IBD's most productive investigators (27) — had actually been emphasized some years before in a radiological vignette in *The Journal of the Mount Sinai Hospital* (28). In this brief report, a patient was described with "severe pain in the lumbosacral region radiating to both legs, associated with difficulty in walking." The paper called attention to the complication of presacral abscess presenting as hip pain and being confused with an orthopedic problem. The correct diagnosis was revealed by a plain film of the spine showing air in the presacral space!

Two other rarely recognized associations or complications of IBD that received some of their earliest attention in *The Journal* were the presentation of regional ileitis as gross rectal bleeding (29) and the co-existence of ulcerative colitis with hemophilia A (30). Yet the tradition of "good observations" in *The Journal* is not restricted to papers from long ago. A very recent issue of *The Mount Sinai Journal of Medicine* carried only the second published case report of a preoperative diagnosis of gallstone ileus in Crohn's disease, and the only one without biliary-enteric fistula (31).

Extraintestinal Manifestations

Few Mount Sinai papers on IBD, at least since the landmark *JAMA* article of 1932 on regional ileitis (2), have been cited as frequently in the medical literature as the 1976 review of extraintestinal manifestations in *Medicine* by Greenstein et al. (32). This analysis of 700 cases of IBD distinguished between "colitis-associated" conditions and those attributable to "small bowel pathophysiology." Yet it is noteworthy that this attempt at classification was foreshadowed more than 20 years earlier in the pages of *The Journal of the Mount Sinai Hospital* by Albert Cornell, then chief of the Gastro-Intestinal Clinic of The Mount Sinai Hospital (33). Moreover, one of the early efforts at treating an extraintestinal complication on the basis of a pathophysiologic rationale was described in *The Mount Sinai Journal of Medicine* when Gelernt and Kreel reported on the use of cyproheptadine, a platelet deaggregrator, in the management of pyoderma gangrenosum (34).

Cancer

It is already well known that Burrill Crohn was an author of the first report of colon cancer in ulcerative colitis (35), and that Leon Ginzburg co-authored the first report of small bowel cancer in regional enteritis (36). It is less widely appreciated, however, that half a dozen key observations about the relationships between cancer and IBD were first published in *The Journal*.

1. Pathology. In 1952, the redoutable Mount Sinai pathologist, Sadao Otani, and the legendary Mount Sinai clinician, Isidore Snapper, teamed up to clarify the relationships among adenomatous polyps, inflammatory polyps, and cancer associated with ulcerative colitis (37). A generation later, Mount Sinai's most prolific surgical author on IBD, Adrian Greenstein, spearheaded a study of the clinical and pathologic features distinguishing colitis-associated from sporadic colorectal cancer (38).

2. Small bowel cancer. Although, as we have seen, Ginzburg et al. first reported jejunal carcinoma complicating Crohn's disease in 1956 in the journal, *Surgery* (36), B.S. Wolf in that same year described the radiologic findings in detail in *The Journal of the Mount Sinai Hospital* (39).

3. Cancer in bypassed loops of bowel. The first American report of ileal cancer in a bypassed bowel segment with Crohn's disease appeared in *The Journal of the Mount Sinai Hospital* in 1970 (40). This paper did not speculate heavily on the pathogenesis of such neoplasms, but it stressed two of the most important clinical implications: first, that these cancers were clinically silent ("...the presence of a clinically silent neoplasm in a bypassed or excluded loop of intestine is extremely difficult to diagnose radiologically...."); and second, that bypass surgery, while efficacious in the short term ("...bypass usually leads to quiescence of the inflammatory process..."), could be detrimental in the long term ("[We] emphasize the possible long-term dangers inherent in this type of surgery."). While many subsequent investigators proposed a variety of biological mechanisms for the occurrence of cancer in excluded loops of bowel, my analysis published in *The Mount Sinai Journal of Medicine* in 1983 (41) indicated that the apparently high frequency of this phenomenon was simply a statistical artefact of the confounding factor of disease duration: "...it is not the bypassed loop itself that puts the patient at risk for cancer; it is the long duration of the disease."

4. Left-sided ulcerative colitis. While conventional wisdom had held that only patients with ulcerative pancolitis were at significantly increased risk for colorectal cancer, our 1979 study in *The Mount Sinai Journal of Medicine* pointedly called attention to the risk in less-than- universal colitis (38): "It is important to recognize that after a sufficiently long interval, cancer may develop in left-sided as well as in universal colitis."

5. Mortality. Another prevalent concept dispelled in this same 1979 paper was that the case-fatality rate in colitis-associated colorectal cancer was much higher than in sporadic cancer (38): "The long-term mortality from colitis-associated cancer did not appear to be worse than that from colorectal cancer in the general population."

6. Cancer in Crohn's colitis. Perhaps the most tenacious myth concerning colorectal cancer in IBD has been that the risk is much greater in ulcerative colitis than in Crohn's disease of the colon. Although the final nails were not driven into the coffin of this widespread misconception until 1994 (42, 43), the strongest prediction of the actuality had appeared in *The Mount Sinai Journal of Medicine* as early as 1983 (41): "When cases of ulcerative and Crohn's colitis of similar anatomical extent are followed for similar durations of time, the two diseases may ultimately prove to have similar increases in risk for colorectal cancer." Subsequent studies indicated that the risks were not only similar, but virtually identical (42).

Medical Therapy

The many contributions of Mount Sinai doctors to the medical therapy of IBD have been amply recounted in previous issues of this journal (44 – 46) and do not need to be repeated here. Yet it is worth noting how often the most seminal therapeutic principles found early and forceful expression in the pages of *The Mount Sinai Journal of Medicine*. Two symposia in particular provided occasion for giants in the field, from both home and abroad, to demonstrate their prescient vision in the area of medical treatment.

First was the celebratory Anniversary Symposium of 1982 already mentioned in the section on Natural History and Epidemiology above. It was ambitiously entitled, "Inflammatory Bowel Disease: The Next Fifty Years," and even then five of the most vital current trends in therapy were foreseen. First, Korelitz predicted the modern movement toward earlier introduction of 6-mercaptopurine (6-MP) in the management of Crohn's disease (47): "Perhaps when we feel more comfortable with its use it might be justified even earlier in the course, when the disease is still considered mild." In the same presentation, he also accurately foretold two more guiding principles in present-day immunosuppressive treatment: its indefinite continuation for long-term maintenance of remission, and its efficacy in ulcerative colitis as well as in Crohn's disease: "The results have been impressive and suggest that the response rate in ulcerative colitis is similar to that in Crohn's disease.... There is no longer justification for the belief that predisposition to carcinoma in long-standing ulcerative colitis warrants postponing double blind trials of 6-MP similar to those conducted in Crohn's disease."

A fourth "new wave" of therapy was predicted by both Henry Janowitz and John Lennard-Jones at that symposium nearly 20 years ago, namely, the ascendancy of antibiotics in the treatment of Crohn's disease (48, 49). Lennard-Jones — to this day still unsurpassed in his genius as a clinical investigator in IBD — foresaw the 21st century's emphasis on designing biological agents to target specific points in the pathogenetic pathway of the diseases (48): "I think we'll find out how the treatments affect...pathogenetic mechanisms.... I suspect that

ileostomy associations in the United States, Lyons focused on the central importance of patients' psychosocial adjustment to ileostomy, in a 1983 article in *The Mount Sinai Journal of Medicine* (58), only shortly after Mount Sinai's first paper on the subject (59) and long before surgical "quality of life" studies in IBD had become academically fashionable. More recently, *The Mount Sinai Journal of Medicine* again provided the forum for a ground-breaking study bringing quantitative science to bear on such elusive but critical issues as individual coping mechanisms and family dynamics in the course of IBD (60).

Postoperative Recurrence of Crohn's Disease

It has often been said that the inexorable tendency of Crohn's disease to recur following surgical resection is still the thorniest single problem in present-day management of inflammatory bowel disease (61). The medical and surgical literature of the past 20 years is replete with studies of this phenomenon, its natural history, and attempts at its prevention. But as early as the 1950s, papers in *The Journal of the Mount Sinai Hospital* were already focusing this troublesome issue. An interdisciplinary conference of ten Mount Sinai clinicians in January 1952 devoted the great bulk of its attention to detailed discussions by Burrill Crohn and the surgeon, Ralph Colp, concerning cases of postoperative recurrence of ileitis and ileocolitis (62). In this context, it is noteworthy that even at this early date, Mount Sinai surgeons and gastroenterologists were prefiguring the surgical conservatism of today; in Colp's words, "In the present state of our knowledge, we are operating on these patients only when our hand is forced by intestinal obstruction, fistulae, and abscess formation."

Fully forty-five years ago, in a *Journal of the Mount Sinai Hospital* Symposium edited by Dr. Crohn, Henry Janowitz provided an overview of "Problems of Regional Enteritis" that has scarcely been improved upon to the present day (63). His review included several pathophysiologic insights (e.g., the suggestion that "the noxious agent is present in the intestinal stream") that are currently being validated (64). With particular regard to the problem of postoperative recurrence, Dr. Janowitz drew both pathophysiologic and therapeutic conclusions: regarding the former, "The hypothesis of widespread initial lesions...might explain the high incidence of recurrence following operation even though biopsy at the site of resection or by-pass may be entirely negative"; and regarding the latter, "With the increasing recognition that the rate of recurrence is a function of the length of follow-up, and with increasing numbers of recurrences, the [surgical] approach to therapy is now in a disillusioned phase." It must be noted that what Janowitz so confidently alluded to in *The Journal of the Mount Sinai Hospital* as "increasing recognition" in 1955 was validated by "admissible evidence" in the *New England Journal of Medicine* only 20 years later (65)!

History

This essay was not undertaken to replicate last year's historical review of Mount Sinai's contributions to the study of IBD (66), but it has instead tried to assess the unique role of *The Mount Sinai Journal* over the last half century as a seedbed and sounding board for innovative and forward-looking thoughts about the nature and management of these disorders. Yet this assessment would not be complete without some mention of several remarkable historical reviews that have appeared in these pages in years past, especially since these historical perspectives have looked not only backward but also forward.

Before the current set of three theme issues edited by Jeremy Hugh Baron and Henry D. Janowitz, there were at least seven other historical surveys published in this journal between 1945 and 1993 that deserve citation:

1. 1945. In a retrospective of "Gastroenterology at The Mount Sinai Hospital" prepared for the Moschowitz Anniversary Issue of *The Journal of the Mount Sinai Hospital* (67), Burrill Crohn was especially gracious in his discussion of the disease that ultimately came to bear his name:

> ...in 1932, dated from The Mount Sinai Hospital, appeared the first paper or papers [note the plural!] on a new clinical entity "regional ileitis." The earlier pathological and clinical studies on intestinal granulomata had been laid down by Drs. Eli Moschowitz [whom this issue of *The Journal* was honoring] and A.O. Wilensky as early as 1923. The pathological studies of these granulomata had been re-begun by Drs. Leon Ginzberg [*sic*] and Gordon Oppenheimer. The combination of these studies with the clinical and surgical observa-

> tions of myself and Dr. A.A. Berg led in 1932 to the formulation of the entity of "ileitis." With practically no hesitation, with little scientific criticism, but with many constructive additions, the medical profession has accepted ileitis, or regional enteritis, as an established clinical concept.... The Attending Staff of this hospital have thus been given proper credit for the recognition of a disease, which knows no limited geographical incidence and which provides an ample and new arena for extensive surgical operative skill and original initiative.

2. 1951. In the Albert A. Berg Memorial Issue of *The Journal of the Mount Sinai Hospital*, Crohn once again downplayed his own role and lavished primary credit upon Dr. Berg, Mount Sinai's late chief of surgery, for developing the concepts of regional ileitis and "right-sided or segmental ulcerative colitis," as well as for advancing the "increasing utility of ileostomy for severe ulcerative colitis and the feasibility of subsequent total colectomy for otherwise incurable forms of universal colitis...." (68).

3. 1955. Under the editorship of Dr. Lester R. Tuchman, *The Journal of the Mount Sinai Hospital* in 1955 published the first in a series of symposia to "cover areas in which workers at The Mount Sinai Hospital are at the present time engaged on a broad front, or fields to which they have made significant contributions." The topic was "Regional Ileitis." In an even-handed bow to two men who were both colleagues and rivals, Dr. Tuchman concluded his editorial introduction (69): "Since the seminal paper on Regional Ileitis was by Drs. Crohn, Ginzburg and Oppenheimer, it is fitting that the first be Guest Editor and the second the author of the article on its surgical management." In his "Reminiscences," Crohn paid tribute yet again to the contributions of Berg, Ginzburg, and Oppenheimer to the recognition of regional ileitis as a clinical and pathologic entity (70). Remarkably, both in the closing paragraphs of this article, as well as in a 1949 paper (13), Crohn prefigured a designation of inflammatory bowel diseases that has only very recently taken shape as the "Rome" (71) and "Vienna" (72) Classifications of Crohn's disease!

4. 1966. The first section of this paper, "Anatomic Distribution," opened with a review of *The Journal*'s contributions to an understanding of involvement of the colon by Crohn's disease. For those interested in a more detailed review of the evolution of the history of this concept, an historical gem is nestled in the pages of a 1966 issue of *The Journal of the Mount Sinai Hospital* (73). Entitled, "Granulomatous colitis: An attempt at clarification," and authored by Crohn and Yarnis, this article provides a fascinating, step-by-step chronicle of what Lindner (12) much later referred to as "Recognizing Crohn's disease of the colon." In their historical retrospective, Crohn and Yarnis credit British workers of the 1950s for first recognizing the connections between "segmental" or "right-sided" colitis and the granulomatous disease, regional ileitis. They go on to acknowledge frankly, "Many of us, myself [presumably Crohn] in particular, altered opinion slowly, hesitating to admit that the segmental [cases of colitis] were truly granulomatous in nature. But over the course of years and with more extensive study on the part of the pathologist, it would seem that not only because of fact, but also in the interest of simplification one must accept as truly granulomatous disease all cases of so-called right-sided colitis." These two giants in the field of IBD also called attention to the phenomenon we now call "rectal sparing," and they confessed ignorance concerning its cause: "The most interesting fact here is that even when observed for years, this process [of granulomatous disease involving the entire colon] will not pass the rectosigmoid. It would almost appear that the rectosigmoid area constitutes a barrier to the progression of the pathological process *provided no surgery is performed* [italics added to emphasize yet another of their seminal observations!]. Why the lesion halts at this nodal point is difficult to understand." Thirty-five years later, we are none the wiser on this question.

5. 1973. In a memoir written for *The Mount Sinai Journal of Medicine* (74), Leon Ginzburg pulled off an extraordinary feat. He published a four-page article chronicling the history of regional enteritis without once mentioning the name of Burrill Crohn — except in a dismissive six-word footnote in very small type, appended to his description of the twelve cases that he and Oppenheimer had so laboriously collected and meticulously studied: "*Dr. Crohn later added two more." The insertion of this footnote seems reminiscent of the practice of bequeathing one dollar to a particularly unfavored relative, just to prove the point that the disinheritance was not the result of an innocent oversight. By the time of a subsequent memoir ten years later (75), Ginzburg's rhetoric may have

softened somewhat, but not his heart, in the judgment of those of us privy to his uninhibited correspondence and conversations.

6. 1983. In a more objective vein, Dr. Janowitz provided an overview of "The road to Crohn's disease" that emphasized three cardinal points (76): (a) that the disease was relatively new in appearance and increasing in incidence; (b) that it affected the entire GI tract as well as "overflowing" into surrounding tissues; and (c) that it had systemic effects ("an impact on the organism") beyond the gastrointestinal tract and its immediately adjacent organs.

7. 1993. At the dedication of the Dr. Henry D. Janowitz Division of Gastroenterology at Mount Sinai on December 8, 1992, Dr. Daniel Present delivered a review of "Advances in knowledge of inflammatory bowel disease at Mount Sinai Medical Center" (77). In so doing, he paid homage to our teacher and mentor, Dr. Janowitz; modestly understated his own many contributions; and paid tribute to all those who have played, are playing, and will play important roles in the continuing study, elucidation, and amelioration of these cruel and baffling diseases.

Acknowledgments

I am indebted, first, to Jeremy Hugh Baron, D.M., FRCP, FRCS, Visiting Lecturer in Medicine, and to Henry D. Janowitz, M.D., Clinical Professor Emeritus of Medicine, for their gentle but unyielding insistence that I write about some historical aspect of IBD. Next, I owe a vote of thanks to the most unexpected of sources — the restaurant of the Sheraton Hotel in Halifax, Nova Scotia, which for some unaccountable reason was decorated with bound volumes of *The Journal of the Mount Sinai Hospital*, the browsing of which last year suddenly inspired me with the idea of focusing this review on the role of our distinguished journal. Third, I must acknowledge the support and encouragment of Sherman Kupfer, M.D., *The Journal*'s current editor-in-chief. Finally, I am most grateful to all those colleagues and predecessors who have actually made the history that I have merely recorded.

References

1. Davidoff F. In the teeth of the evidence: The curious case of evidence-based medicine. Mt Sinai J Med 1999; 66:75–83.
2. Ginzburg L, Oppenheimer GD. Non-specific granulomata of the intestines (inflammatory tumors and strictures of the bowel). Trans Am Gastro-Enterol Assoc 1932; 35:241–283. [Reprinted in Mt Sinai J Med 2000; 67:246–262.]
3. Crohn BB, Ginzburg L, Oppenheimer GD. Regional ileitis: A pathologic and clinical entity. JAMA 1932; 99:1323–1328. [Reprinted in Mt Sinai J Med 2000; 67:263–268.]
4. Wells C. Ulcerative colitis and Crohn's disease. Ann R Coll Surg Engl 1952; 11:105–120.
5. Crohn BB, Garlock J, Yarnis H. Right-sided (regional) colitis. JAMA 1947; 134:334. [Abstracted in J Mt Sinai Hosp 1949; 16:206.]
6. 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.
7. Wolf BS, Marshak RH. Granulomatous colitis (Crohn's disease of the colon): Roentgen features. AJR Am J Roentgenol 1962; 88:662–670.
8. Marshak RH, Lindner AE. Ulcerative and granulomatous colitis. J Mt Sinai Hosp 1966; 33:444–502.
9. Marshak RH, Lindner AE, Maklansky D. Granulomatous colitis. Mt Sinai J Med 1979; 46:431–454.
10. Janowitz HD. Ulcerative and granulomatous colitis: A foreword. J Mt Sinai Hosp 1966; 33:441–442.
11. Waye JD. Colonoscopy: A clinical view. Mt Sinai J Med 1975; 42:1–34.
12. Lindner AE. Recognizing Crohn's disease of the colon. Mt Sinai J Med 1983; 50:105–107.
13. Crohn BB. Ileojejunitis. NY State J Med 1949; 49:1808, abstracted in J Mt Sinai Hosp 1952; 18:370–371.
14. Richman A. Non-specific granulomatous disease of the stomach and duodenum. J Mt Sinai Hosp 1955; 22:175–183.
15. Wolf BS (editor). Granulomatous terminal ileitis; segmental granulomatous colitis, gastritis and duodenitis, granulomatous? [radiological notes]. J Mt Sinai Hosp 1959; 26:78–84.
16. Bloch C, Peck HM (editors). Crohn's disease of the stomach [radiologic notes]. Mt Sinai J Med 1974; 41:699–703.
17. Bloch C, Peck HM (editors). Crohn's disease of the duodenum [radiologic notes]. Mt Sinai J Med 1974; 41:703–710.
18. Korelitz BI. Prognosis of granulomatous colitis with onset in childhood. J Mt Sinai Hosp 1968; 35:1–13.
19. Korelitz BI. From Crohn to Crohn's disease: 1979. An epidemiologic study in New York City. Mt Sinai J Med 1979; 46:533–540.
20. Aufses AH, Jr. The next fifty years [panel discussion]. Mt Sinai J Med 1983; 50:193–200.
21. Klein S, Greenstein AJ, Sachar DB. Duodenal fistulae in Crohn's disease. J Clin Gastroenterol 1987; 9:46–49.
22. Masters H. Duodenal-colic fistula as a complication of regional ileitis. J Mt Sinai Hosp 1948; 15:264–265.
23. Wilk PJ, Moqtaderi FF. Gastrocolic fistula complicating transmural colitis. Mt Sinai J Med 1976; 43:525–529.
24. Newman LH, Wellinger JR, Present DH, Aufses AH, Jr. Crohn's disease of the duodenum associated with pancreatitis. Mt Sinai J Med 1987; 54:429–432.
25. Korelitz BI. The ileorectal and ileosigmoidal fistula in Crohn's disease: A clinical-radiological correlation. Mt Sinai J Med 1984; 51:341–346.
26. Ginzburg L, Oppenheimer GD. Urological complications of regional ileitis. J Urol 1948; 59:948 [abstracted in J Mt Sinai Hosp 1950; 17:146.].
27. Present DH, Rabinowitz JG, Banks PA, Janowitz HD. Obstructive hydronephrosis: A frequent but seldom recognized complication of granulomatous disease of the bowel. N Engl J Med 1969; 280:523–528.
28. Bloch C, Peck HM (editors). Presacral pelvic abscess secondary to regional ileitis [radiological notes]. J Mt Sinai Hosp 1963; 30:456–458.

29. Horwitz F, Baronofsky ID. Regional enteritis presenting as gross rectal bleeding. J Mt Sinai Hosp 1960; 27:19–22.
30. Radensky PW, Sorett E, Schoenbaum EE, Aledort LM. Ulcerative colitis and hemophilia A. Mt Sinai J Med 1983; 50:268–269.
31. Almogy G, Bauer JJ, Ventrurero M, Present DH. Gallstone ileus and Crohn's disease without biliary-enteric fistula: Report of a unique case. Mt Sinai J Med 2000; 67:159–162.
32. Greenstein AJ, Janowitz HD, Sachar DB. The extraintestinal manifestations of ulcerative colitis and Crohn's disease: A study of 700 patients. Medicine 1976; 55:401–412.
33. Cornell A. The extra-intestinal manifestations of regional ileitis: Some comparisons with chronic ulcerative colitis. J Mt Sinai Hosp 1955; 22:170–174.
34. Gelernt IM, Kreel I. Pyoderma gangrenosum in ulcerative colitis: Prevention of the gangrenous component. Mt Sinai J Med 1976; 43:467–470.
35. Crohn BB, Rosenberg H. The sigmoidoscopic picture of chronic ulcerative colitis (non-specific). Am J Med Sci 1925; 170:220–227.
36. Ginzburg L, Schneider KM, Dreizin DH, Levinson C. Carcinoma of the jejunum occurring in a case of regional enteritis. Surgery 1956; 39:347–351.
37. Otani S, Snapper I. On the incidence of carcinoma in chronic ulcerative colitis. J Mt Sinai Hosp 1952; 19:275–288.
38. 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.
39. Wolf BS. Case of ileojejunitis with jejunal carcinoma. J Mt Sinai Hosp 1956; 23:844–847.
40. Brown N, Weinstein V, Janowitz HD. Carcinoma of the ileum 25 years after bypass for regional enteritis: A case report. Mt Sinai J Med 1970; 37:675–678.
41. Sachar DB. New concepts of cancer. Mt Sinai J Med 1983; 50:133–137.
42. Gillen CD, Andrews HA, Prior P, Allan RN. Crohn's disease and colorectal cancer. Gut 1994; 35:651–656.
43. Sachar DB. Cancer in Crohn's disease: Dispelling the myths. Gut 1994; 35:1507–1508.
44. Janowitz HD. Inflammatory bowel disease after 1932. Mt Sinai J Med 2000; 67:190–197.
45. Korelitz BI, Present DH. A history of immunosuppressive drugs in the treatment of inflammatory bowel disease. Mt Sinai J Med 1996; 63:191–201.
46. Korelitz BI, Present DH. A history of immunosuppressive drugs in the treatment of inflammatory bowel disease: Origins at The Mount Sinai Hospital. Mt Sinai J Med 2000; 67:214–226.
47. Korelitz BI. The role of immunosuppressives. Mt Sinai J Med 1983; 50:144–147.
48. Lennard-Jones JE. The next fifty years [Panel Discussion]. Mt Sinai J Med 1983; 50:193–200.
49. Janowitz HD. The next fifty years [Panel Discussion]. Mt Sinai J Med 1983; 50:193–200.
50. Sachar DB (editor). Inflammatory bowel disease therapies for the 1990s: Scientific basis and clinical experience. Mt Sinai J Med 1990; 57:271–332.
51. Lichtiger S. Cyclosporine therapy in inflammatory bowel disease: Open-label experience. Mt Sinai J Med 1990; 57:315–319.
52. Korelitz BI. Antimetabolites in inflammatory bowel disease: Long-term experience. Mt Sinai J Med 1990; 57:297–304.
53. Janowitz HD. Assessing therapeutic efficacy: How well does anything work? Mt Sinai J Med 1990; 57:329–332.
54. Aufses AH, Jr. The history of surgery for Crohn's disease at The Mount Sinai Hospital. Mt Sinai J Med 2000; 67:198–203.
55. Farkas AM, Gingold BS. Repair of rectovaginal fistula in Crohn's disease by rectal mucosal advancement flap. Mt Sinai J Med 1983; 50:420–423.
56. Gelernt IM. Experience with the continent ileostomy. Mt Sinai J Med 1983; 50:156–165.
57. Kern F, Jr., Alexander-Williams J, Aufses AH, Jr., et al. The next fifty years [panel discussion]. Mt Sinai J Med 1983; 50:193–200.
58. Lyons AS. Adjustment to ileostomy. Mt Sinai J Med 1983; 50:60–63.
59. Meyers S, Sachar DB, Walfish JS, et al. Quality of life after surgery for Crohn's disease: A psychosocial survey. Gastroenterology 1980; 78:1–6.
60. Gerson M-J, Schonholtz J, Grega CH, Barr DR. The importance of the family context in inflammatory bowel disease. Mt Sinai J Med 1998; 65:398–403.
61. Sachar DB. The problem of postoperative recurrence of Crohn's disease. Med Clin North Am 1990; 74:183–188.
62. King FH, Bernheim AI, Sternstein M, et al. Inflammatory diseases of the gastrointestinal tract [clinical conference]. J Mt Sinai Hosp 1953; 20:58–71.
63. Janowitz HD. Problems of regional enteritis. J Mt Sinai Hosp 1955; 22:223–228.
64. Janowitz HD, Croen EC, Sachar DB. The role of the fecal stream in Crohn's disease: An analytical and historical review. Inflamm Bowel Dis 1998; 4:29–39.
65. Greenstein AJ, Sachar DB, Pasternack BD, Janowitz HD. Reoperation and recurrence in Crohn's colitis and ileocolitis: Crude and culmulative rates. N Engl J Med 1975; 293:685–690.
66. Baron JH, Janowitz HD (editors). Gastroenterology and hepatology at The Mount Sinai Hospital 1852–2000 [Theme Issue] — Part 2. Mt Sinai J Med 2000; 67:174–268.
67. Crohn BB. Gastro-enterology at The Mount Sinai Hospital. J Mt Sinai Hosp 1945; 12:129–136.
68. Crohn BB. Gastroenterology as a surgical specialty at The Mount Sinai Hospital. J Mt Sinai Hosp 1951;17:843–847.
69. Tuchman LR. Symposium on regional ileitis [editor's note]. J Mt Sinai Hosp 1955; 22:142.
70. Crohn BB. The early days of regional ileitis at The Mount Sinai Hospital. J Mt Sinai Hosp 1955; 22:143–146.
71. Sachar DB, Andrews HA, Farmer RG, et al. Proposed classification of patient subgroups in Crohn's disease. Gastroenterol Internat 1992; 5:141–154.
72. Gasché C, Schölmerich J, Brynskov J, et al. A simple classification of Crohn's disease: Report of the Working Party for the World Congresses of Gastroenterology, Vienna 1998. Inflamm Bowel Dis 2000; 6:8–15.
73. Crohn BB, Yarnis H. Granulomatous colitis: An attempt at clarification. J Mt Sinai Hosp 1966; 33:503–513.
74. Ginzburg L. The road to regional enteritis. Mt Sinai J Med 1973; 41:272–275.
75. Ginzburg L. Remarks: A historical perspective. Mt Sinai J Med 1983; 50:101–102.
76. Janowitz HD. Overview: The road to Crohn's disease. Mt Sinai J Med 1983; 50:103–107.
77. Present DH. Advances in knowledge of inflammatory bowel disease at Mount Sinai Medical Center. Mt Sinai J Med 1993; 60:187–191.