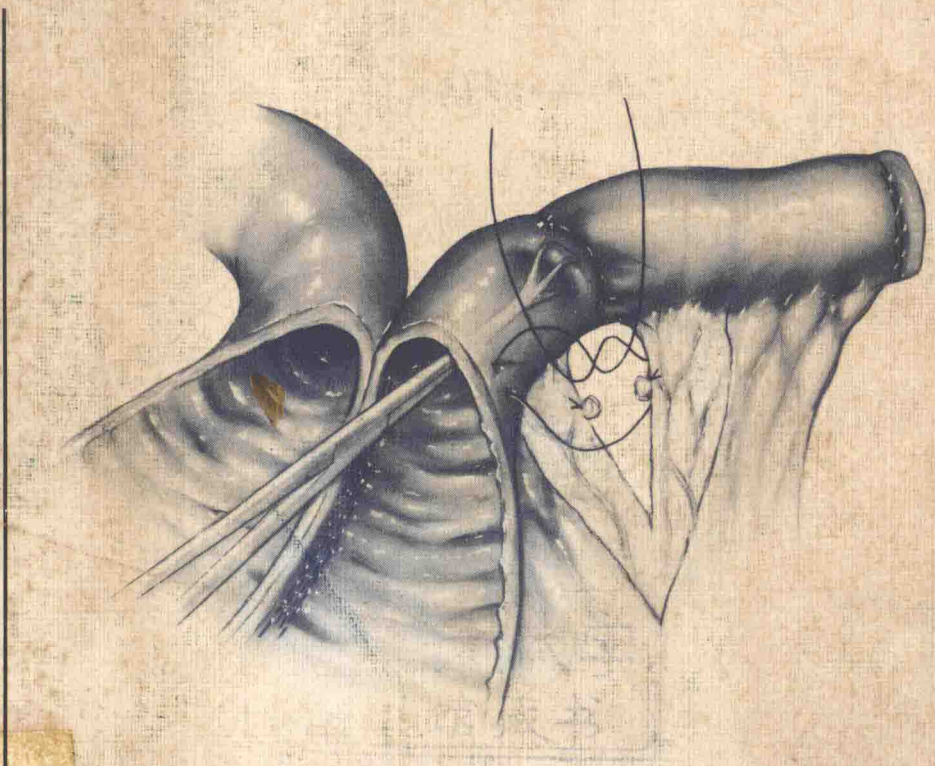
Inflammatory Bowel Disease

Experience and Controversy



Edited by

Burton I. Korelitz

Inflammatory Bowel Disease

Experience and Controversy

A Teaching Seminar on Inflammatory Bowel Disease
Sponsored by Lenox Hill Hospital (New York)
and the American College of Gastroenterology

Edited by

BURTON I. KORELITZ, MD

1982
MARTINUS NIJHOFF PUBLISHERS
THE HAGUE / BOSTON / LONDON

Library of Congress Cataloging in Publication Data
Teaching Seminar on Inflammatory Bowel Disease
(1979) : Lenox Hill Hospital)
Inflammatory bowel disease.

Bibliography: p.
Includes index.
1. Enteritis--Congresses. 2. Enteritis, Regional--Congresses. I. Korelitz, Burton I., 1926- . II. Lenox Hill Hospital. III. American College of Gastroenterology. IV. Title. (DNLM: 1. Intestinal diseases--Congresses. 2. Inflammation --Congresses. 3. Crohn disease--Congresses. WI 420 T253i 1979]
RC862.E5T42 1979 616.3'44 81-4954
ISBN: 0-88416-310-5 AACR2

Distributors for all countries outside North America

Kluwer Academic Publishers Group
Distribution Center
P.O. Box 322
3300 AH Dordrecht
The Netherlands

Joint edition published by

MARTINUS NIJHOFF PUBLISHERS
P.O. Box 566, 2501 CN The Hague, The Netherlands
and
John Wright • PSG Inc
545 Great Road
Littleton, Massachusetts 01460, U.S.A.

This volume is listed in the Library of Congress Cataloging in Publication Data

ISBN 90-247-2489-9

Printed in Great Britain by
John Wright & Sons (Printing) Ltd. at The Stonebridge Press, Bristol.

CONTRIBUTORS

Arthur H. Aufses, Jr, MD
Chairman and Franz W. Sichel Professor
Department of Surgery
Mount Sinai School of Medicine of the City University of New York
New York, New York

Theodore M. Bayless, MD
Associate Professor of Medicine
The Johns Hopkins University School of Medicine,
Physician
The Johns Hopkins Hospital
Baltimore, Maryland

Michael S. Bruno, MD
Director of Medicine
Lenox Hill Hospital, and
Professor of Medicine and Associate Dean
New York Medical College
New York, New York

Robert S. Coles, MD
Director of Ophthalmology
Lenox Hill Hospital, and
Associate Clinical Professor of Ophthalmology
Mount Sinai School of Medicine of the City University of New York
New York, New York

Richard G. Farmer, MD
Chairman, Department of Medicine
Director, Division of Gastroenterology
Cleveland Clinic
Cleveland, Ohio

Harry D. Fein, MD
Consulting Physician
Formerly Chief of Gastroenterology
Lenox Hill Hospital, and
Associate Professor of Clinical Medicine
New York University School of Medicine
New York, New York

Irwin Gelernt, MD
Associate Clinical Professor
Department of Surgery
Mount Sinai School of Medicine of the City University of New York
New York, New York

Myron D. Goldberg, MD
Assistant Adjunct Physician (Gastroenterology)
Lenox Hill Hospital
New York, New York

Mansho T. Khilnani, MD
Consulting Radiologist
Lenox Hill Hospital, and
Clinical Professor of Radiology
Mount Sinai School of Medicine of the City University of New York
New York, New York

Burton I. Korelitz, MD
Chief of Gastroenterology
Lenox Hill Hospital, and
Clinical Professor of Medicine
New York Medical College
New York, New York
President, American College of Gastroenterology

Arthur E. Lindner, MD
Associate Professor of Medicine
New York University School of Medicine
New York, New York

Jerry Nagler, MD
Assistant Adjunct Physician (Gastroenterology)
Lenox Hill Hospital
New York, New York

Daniel H. Present, MD
Associate Clinical Professor
Division of Gastroenterology
Mount Sinai School of Medicine of the City University of New York
New York, New York

Robert R. Rickert, MD
Co-Director
Department of Pathology
Saint Barnabas Medical Center
Livingston, New Jersey, and
Adjunct Associate Professor of Pathology
Columbia University College of Physicians and Surgeons
New York, New York

Richard D. Robbins, MD
Assistant Adjunct Surgeon
Lenox Hill Hospital
New York, New York

Margaret Roche, RN
Enterostomal Therapist
Lenox Hill Hospital
New York, New York

Heidi Z. Rotterdam, MD
Associate Pathologist
Lenox Hill Hospital
New York, New York

Irving A. Rubin
President
National Foundation for Ileitis and Colitis, Inc.
Detroit, Michigan

David B. Sachar, MD
Associate Professor of Medicine
Mount Sinai School of Medicine of the City University of New York
New York, New York

Michael J. Schmerin, MD
Assistant Adjunct Physician (Gastroenterology)
Lenox Hill Hospital
New York, New York

Norman Sohn, MD
Adjunct Surgeon
Lenox Hill Hospital
New York, New York

Sheldon C. Sommers, MD
Director of Laboratories
Lenox Hill Hospital, and
Clinical Professor of Pathology
Columbia University College of Physicians and Surgeons
New York, New York

Felicien M. Steichen, MD
Director of Surgery
Lenox Hill Hospital
Professor of Surgery
New York Medical College
New York, New York

Jerome D. Waye, MD
Attending Physician (Gastroenterology)
Lenox Hill Hospital, and
Associate Clinical Professor
Department of Medicine
Mount Sinai School of Medicine of the City University of New York, and
Chief, Gastrointestinal Endoscopy Unit
Mount Sinai Hospital
New York, New York

Michael A. Weinstein, MD
Adjunct Surgeon
Lenox Hill Hospital
New York, New York

Nathaniel Wisch, MD
Chief of Hematology
Lenox Hill Hospital, and
Associate Clinical Professor
Department of Medicine
Mount Sinai School of Medicine of the City University of New York
New York, New York

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required. The author and the publisher of this work have made every effort to ensure that the treatment and drug dosage schedules herein is accurate and in accord with the standards accepted at the time of publication. Readers are advised, however, to check the product information sheet included in the package of each drug they plan to administer to be certain that changes have not been made in the recommended dose or in the indications and contraindications for administration. This recommendation is of particular importance in regard to new or infrequently used drugs.

INTRODUCTION

Grouping ulcerative colitis with Crohn's disease (Inflammatory Bowel Disease) in a teaching seminar has historical support. The medical literature includes descriptions of both diseases in the latter half of the 19th century; they share many symptoms; in some instances, differentiating them may be very difficult; and the cause of each remains unknown. Furthermore, one member of a family may suffer with Crohn's disease while another has ulcerative colitis. And both processes are prone to the late complications of carcinoma at a site of previous involvement. Finally, the investigators and students of one disease have usually also contributed to the understanding of the other disease.

The incidence of Crohn's disease seems to be increasing rapidly. This has been suggested by reports from Sweden, the Netherlands, England, Scotland, and South Africa as well as the United States. Though methods of recording data vary, the increase is further supported by cases of greater virulence, still younger ages of onset, and more cases in the elderly. This is remarkable when we consider that fifty years ago, when the classic description from Mt. Sinai Hospital was being prepared, the disease was rare. Since the cause remains elusive, we must try to cope with this entity as skillfully as we can, with consideration of indications, and timing of drug and surgical intervention. The choice of forms of management has been controversial, even among the most experienced physicians.

The incidence of ulcerative colitis seems to be stable. Nonsurgical management has improved, however, so that surgery under urgent circumstances is not required as often. Many patients now have the opportunity to have a continent ileostomy when surgery can be performed electively. However, successful nonsurgical management has also created a greater likelihood of developing carcinoma of the rectum or colon. These considerations also introduce controversy.

The accumulated experience of the participants in this seminar is vast. It represents a background of concerted interest and study in inflammatory bowel disease at the Cleveland Clinic, The Johns Hopkins Hospital, Mount Sinai Hospital, New York University School of Medicine, St. Barnabas Medical Center, the National Foundation for Ileitis and Colitis, and Lenox Hill Hospital. Many disciplines and physicians of varied specialties are represented in these proceedings. Lenox Hill is proud to present this course on inflammatory bowel disease.

Burton I. Korelitz, MD

CONTENTS

Introduction ix
Burton I. Korelitz, MD

PART I Moderator: Burton I. Korelitz, MD

1 **The History of Crohn's Disease** 1
Harry D. Fein, MD

2 **An Internist's View of Inflammatory Bowel Disease** 5
Michael S. Bruno, MD

3 **Evidence for Crohn's Disease as an Extensive Process** 9
Burton I. Korelitz, MD

4 **Implications of Uveitis and Other Extraintestinal Manifestations of Inflammatory Bowel Disease** 15
Robert S. Coles, MD

5 **Environment vs Heredity in Inflammatory Bowel Disease** 21
Theodore M. Bayless, MD

6 **Is There an Immunological Contribution to Inflammatory Bowel Disease?** 25
Jerry Nagler, MD

7 **Is Investigation Headed in the Right Direction?** 29
David B. Sachar, MD

PART II Moderator: Harry D. Fein, MD

8 **What is Considered Good Medical Care in Crohn's Disease?** 35
Burton I. Korelitz, MD

9 **What is the Role of Immunosuppressive Therapy in Inflammatory Bowel Disease?** 43
Daniel H. Present, MD

10 **Hematologic Complications of Inflammatory Bowel Disease and Its Drug Therapy** 51
Nathaniel Wisch, MD

11 **The Role of Hyperalimentation in the Treatment of Crohn's Disease** 55
Richard D. Robbins, MD

12 **Inflammatory Bowel Disease in the Elderly 59**
Myron D. Goldberg, MD

13 **Special Problems of Adolescents with Inflammatory Bowel Disease 63**
Theodore M. Bayless, MD

PART III Moderator: Burton I. Korelitz, MD

14 **What is the Role of Sigmoidoscopy and Rectal Biopsy in Inflammatory Bowel Disease? 77**
Sheldon C. Sommers, MD

15 **Where Has Colonoscopy Had Its Greatest Value in the Management of Inflammatory Bowel Disease? 87**
Jerome D. Waye, MD

16 **The Significance of Microgranulomas in Crohn's Disease 91**
Heidi Z. Rotterdam, MD

17 **Scanning Electronmicroscopic Appearance of "Early" Lesions in Crohn's Disease 97**
Robert R. Rickert, MD

18 **Has There Been Any Progress in the X-ray Diagnosis and Differential Diagnosis of Inflammatory Bowel Disease? 107**
Mansho T. Khilnani, MD

19 **When in the Course of Crohn's Disease Should X-ray Studies be Performed? 117**
Arthur E. Lindner, MD

PART IV Moderator: Felicien M. Steichen, MD

20 **Recurrence Rates After Surgery for Crohn's Disease and Their Implications Regarding Indications for Surgery (As Seen by the Gastroenterologist) 125**
Burton I. Korelitz, MD

21 **Indications for Surgery in Crohn's Disease (As Seen by the Colon and Rectal Surgeon) 133**
Norman Sohn, MD

22 **What is the Best Management of Perirectal Abscess and Fistula in Crohn's Disease? 137**
Michael A. Weinstein, MD

23 **An Appraisal of Surgical Procedures for Crohn's Disease** 141
Arthur H. Aufses, Jr, MD

PART V Moderator: Jerome D. Waye, MD

24 **What is the Best Medical Management for Ulcerative Colitis?** 149
Richard G. Farmer, MD

25 **Why Do Results of Management of Toxic Megacolon Differ?** 153
Michael J. Schmerin, MD

26 **An Appraisal of the Cancer Problem in Ulcerative Colitis** 157
Richard G. Farmer, MD

27 **The Problems Arising in Diagnosis of Dysplasia as a Premalignant Lesion in Ulcerative Colitis** 161
Sheldon C. Sommers, MD

28 **A Program for Management of Ulcerative Colitis With Respect to Cancer** 175
Burton I. Korelitz, MD

SPECIAL PRESENTATION

29 **Why Is There a Foundation for Patients with Inflammatory Bowel Disease?** 185
Irving A. Rubin

PART VI Moderator: Norman Sohn, MD

30 **What Problems Lie Ahead for a Patient With an Ileostomy?** 189
Margaret M. Roche, RN, ET

31 **The Continent (Kock) Ileal Reservoir: Technique and Indications** 197
Felicien M. Steichen, MD

32 **Experience and Late Results with the Continent Ileostomy** 207
Irwin M. Gelernt, MD

33 **An Appraisal of the Results of the Continent Ileostomy (As Seen by the Gastroenterologist)** 221
Daniel H. Present, MD

PART I

Moderator: Burton I. Korelitz, MD

1 The History of Crohn's Disease

Harry D. Fein, MD

It is probable that Morgagni, as early as 1769 in *De Sedibus et Causis Morborum,* ("The Seats and Causes of Diseases"), gave the first clinical description of a case of Crohn's disease. In 1865, probably the first clinical and pathological description of ulcerative colitis was recorded in the annals of the Union Army Medical Corps. It was not until 1909 that Braun described several cases of inflammatory disease masses involving the small intestine. Dalziel in 1913 reported, in detail, six cases similar to those of Braun, in which tuberculosis (though suspected) was excluded by careful bacteriological studies. This evoked some acceptance that a benign, chronic, granulomatous condition of the small intestine existed which was not tuberculosis.

However, for most of us, the history of this disease really started in 1932. On May 13, 1932, in New Orleans, a paper by Crohn, Ginzburg and Oppenheimer was read before the Section of Gastroenterology and Proctology at the 83rd Session of the American Medical Association. It was entitled "Regional Enteritis, a Pathological and Clinical Entity." The authors proposed to describe in its pathological and clinical details, "a disease of the terminal ileum affecting mainly young adults, characterized by a

subacute or chronic, necrotizing and cicatrizing inflammation." They stated that "the ulceration of the mucosa is accompanied by a disproportionate connective tissue reaction of the remaining walls of the involved intestine, a process which frequently leads to stenosis of the lumen of the intestine and is associated with multiple fistulas." To further quote, "The disease is clinically featured by symptoms that resemble those of ulcerative colitis; namely, fever, diarrhea, and emaciation leading eventually to an obstruction of the small intestine. The constant occurrence of a mass in the right iliac fossa usually requires surgical intervention, that is, resection. The terminal ileum alone is involved." The process begins abruptly at and involves the ileocecal valve in its maximum intensity, tapering off gradually as it ascends the ileum proximally for 20 to 30 cm. The familiar fistulas usually lead to segments of the colon forming small tracts communicating with the lumen of the large intestine. Occasionally the anterior abdominal wall is the site of one or more of these fistulous tracts. Continuing quotes of that paper, "The etiology of the process is unknown" and perhaps we have not advanced too far in that direction. "It belongs in none of the categories of recognized granulomatous or accepted inflammatory groups, the course is relatively benign, all the patients who survive operations being alive and well." Such, in essence, is the definition of a disease. The description is based on a study of 14 cases up to 1932.

We then made some progress when in 1949 Dr Crohn, in a monograph, indicated that regional ileitis was a better term than terminal ileitis, as the first 14 cases were named. It denotes a much more widespread distribution. Ileocolitis was introduced to denote the frequent involvement of the colon. Then ileojejunitis came about to include anatomically all the jejunum continuously or sequentially, and finally coloileitis.

It should be mentioned, however, that as early as 1923, and again in 1927 Drs Moschowitz and Wilensky described four cases of benign intestinal granuloma, detailing one case involving the terminal ileum which closely resembled that in Crohn's original description.

More recently, a monograph entitled "Crohn's Disease," by Brook, Cave, Gurry and King, published in 1977, indicated that in a review of the history of the subject, 16 different eponymous terms had been listed, reflecting the protean manifestations and interpretations of the disease.

In the absence of any known etiology, definition is of necessity based on a synthesis of clinical, radiological, and pathological criteria. Such a definition provides a framework for discussion and distinguishes Crohn's disease from ulcerative colitis. There is some overlap, although their interrelationship remains obscure. Crohn's disease is a chronic, progressive, granulomatous disorder which can affect the gastrointestinal tract from mouth to anus. Secondary lesions may involve regional lymph nodes, liver, skin, eyes and joints. The cellular reaction in the intestine is transmural and consists of hyperplasia of histiocytic cells associated with acute and chronic inflammatory cells and lymphoid aggregates. The histiocytes may coalesce to form Langhans type giant cells and noncaseating granulomas. Ulceration of the mucosa and deep fissures which lead to fistula formation are present. Microscopically, its anatomical discontinuity, skip lesions, a tendency to fistula formation, and a very high incidence of recurrence after surgery are the hallmarks of the disease. The radiologic changes reflect the macroscopic changes, and although they are of some value diagnostically, they may not be of definitive help.

Since the theme of this symposium is experience and controversy, I would like to introduce a little element of controversy, even in the historical background. Actually, Dr Crohn had observed only two cases of the original 14 cases reported. Most of the cases

had been carefully studied by Dr Ginzburg, whose interest was aroused in this subject as early as 1925. He was a house surgeon, then an adjunct, and then Dr A. A. Berg's assistant in private practice. Those who knew Dr Berg as the Chief of Surgery, or knew of him, knew that aside from his tremendous skill as a surgeon with an enormous private practice, he was also quite an autocrat. It was his idea that Dr Crohn's name be listed among the authors of the paper. It was also his feeling that the names should be in alphabetical order. Thus, Crohn came first, and Crohn's disease was born. Dr Berg declined to have his own name on the paper, or we might be talking about Berg's disease. However, it became Crohn's disease.

BIBLIOGRAPHY

Braun H: Veber entzunollische Geschwultse, am Darm. *Dtsch Z Chin* 100:1, 1909.

Brooke BN, Cave DR, Gurry JF, et al: *Crohn's Disease.* New York, Oxford University Press, 1977.

Crohn B, Ginzburg L, Oppenheimer GD: Regional ileitis. *JAMA* 99:1323, 1932.

Dalziel TK: Chronic interstitial enteritis. *Br Med J* 2:1068, 1913.

Morgagni GB: *De Sedibus et Causis Morborum (The Seats and Causes of Disease).* London, Millar and Cadwell, 1769. Facsimile of the 1769 edition. New York, Hafner, 1960.

Moschowitz E, Wilensky A: Nonspecific granulomata of the intestine. *Am J Med Sci* 166:48, 1923.

Moschowitz E, Wilensky A: Nonspecific granulomata of the intestine. *Am J Med Sci* 178:374, 1927.

Union Army Medical Corps: *Medical and Surgical History of the Rebellion, USA:* Washington, Circular No. 6, 1865, p 139.

2 An Internist's View of Inflammatory Bowel Disease

Michael S. Bruno, MD

My premise has always been that an internist should have a broad view of the spectrum of diseases which he sees, and a comprehensive knowledge of the more common conditions. Inflammatory bowel disease is an important disease in medicine, with an incidence that appears to be increasing tremendously. This has been our experience at Lenox Hill Hospital, no doubt because we have so many physicians who are interested in the problem. The most crucial role for the internist when faced with the problem of inflammatory bowel disease is proper identification. Since patients often see internists as their primary physician, it is the internist who has the responsibility of first making the correct diagnosis. It is hoped that he will make that diagnosis as early as possible, in spite of the protean nature of these diseases and the way they can present at any given point in time. Among the conditions that often have to be considered in the group classified as the chronic diarrheas, ulcerative colitis and Crohn's disease are two of the most important. In addition, we often have to consider enterocolitis of specific infectious etiology, including amebiasis, which we see frequently. If overlooked or confused with one or the other of the two conditions we are discussing, and left untreated, amebiasis may be potentially catastrophic.

The bacillary dysenteries and giardiasis are also being seen with increasing frequency, particularly in New York City. Also to be considered in the differential diagnosis of the chronic diarrheal states is ischemic colitis, with its characteristic radiographic features seen in certain elderly groups. Its clinical picture is similar to that of certain types of Crohn's disease and perhaps even ulcerative colitis. Lastly, we must consider enterocolitis associated with administering some of our newer antibiotics, especially lincomycin and clindamycin.

As an introduction to the problems of ulcerative colitis and Crohn's disease, I shall briefly present a clinical overview of both these conditions, considering the basic pathology and pathophysiology, while emphasizing the variability of these diseases and their more important intestinal and the extraintestinal manifestations. As I see it, the role of the internist should be to identify these diseases when first seen, to sequester them from the other conditions mentioned, and to treat the majority of them appropriately if it is within his ability to do so. The extent of his role in the management of cases of inflammatory bowel disease comes down to interest and to experience.

Ulcerative colitis is a confluent, erosive, inflammatory process which is symmetrical and specifically involves the mucosal surfaces of the colon. It may occasionally extend beyond the mucosa to involve the submucosa, but it is basically a mucosal disease. It most commonly involves the rectum, rectosigmoid and left colon. In many of the cases, the distribution of the disease process stops abruptly at the mid-transverse colon for reasons that are not apparent. Approximately 30% of these patients have total involvement of the colon; half of this group also have involvement of the terminal ileum. When that is the case, radiographic differentiation from Crohn's disease may be difficult. The most common distribution of ulcerative colitis, of course, is ulcerative proctitis. Some physicians separate these two conditions, but most feel that they are the same disease process. While ulcerative proctitis can be very invasive and destructive, for reasons that we do not entirely understand, the condition usually remains localized, rarely extending beyond this segment of the bowel. While the process is quite invasive and destructive locally, these patients can do quite well, can continue to work and be fully productive, being seen as office patients almost exclusively. Patients with this disease are rarely brought into the hospital except perhaps to establish the diagnosis. The true incidence, therefore, is not too well known. While local therapy often suffices, these cases can be very resistant to therapy.

I am not going to discuss the etiology of ulcerative colitis in any detail; it will be discussed by others. Certainly ethnic, emotional, environmental, and autoimmune factors are to be considered. We still do not know the cause of ulcerative colitis. Some of these patients have elevated circulating immunoglobulins, others may have high antibody titers against colonic epithelium. What role autoimmunity, environment, stress and ethnic background play in the etiology of these diseases will be discussed further by others.

Pathologically, ulcerative colitis is also a mucosal process. The mucosa is confluently ulcerated with residual mucosal bridges; sometimes there is complete effacement of the mucosa. Pseudopolyps are an important pathologic feature of this disease, due to hypertrophy of some of the residual islets of colonic mucosa. While the submucosa is involved in some instances, ulcerative colitis is basically a symmetrical confluent mucosal disease. Crypt abscesses are prominent and the exudative process is primarily due to a leukocytic infiltration; there is a decrease in the mucous goblet cells and an increase in the numbers of mass cells. Rectal biopsy is extremely important in differentiating ulcerative colitis from Crohn's disease, but may not always be definitive. These patients usually

have a history of bloody diarrhea. The physical examination can vary from the mild case where there are no physical findings, to the severe forms of the disease, where the patient may be overwhelmed with prominent intestinal and extraintestinal manifestations. The internist continually has to be aware of the widespread nature of this disease process and the variable presenting complaints and physical findings. Sigmoidoscopy and biopsy are extremely important; barium enema has obvious indications. Stool cultures should be done in every case and stools should be repeatedly examined for ova and parasites. Identifying the occasional case of amebiasis or other parasitic infestation which can mimic this disease can spare lives. Complement fixation and hemagglutination tests for amebiasis should always be done. I won't dwell on the local complications of ulcerative colitis, but I would like to comment on some of the systemic manifestations. These are often the complaints that bring the patient to the internist, to the ophthalmologist, or to the rheumatologist. These patients may have a polyarthritis or polyarthralgia that is prominent, severe and debilitating, suggesting the diagnosis of rheumatoid arthritis. The intestinal symptoms at any one time may be subtle, if at all present, and an incorrect diagnosis of a rheumatoid-like state can be made. These patients often have a prominent erythema nodosum. Uveitis is a very important feature of this disease and may precede the development of all intestinal complaints, first bringing the patient to the ophthalmologist. Since uveitis can persist even after total colectomy and the successful removal of the disease process, one has to wonder about the persistence of circulating antibodies. Pyoderma gangrenosa, nephrolithiasis, and pericholangitis are other features of this disease when seen in its more severe form.

The systemic manifestations of ulcerative colitis usually parallel the severity of the disease, may precede bowel symptoms by years (uveitis), and may persist after successful total colectomy (uveitis and pericholangitis).

Granulomatous colitis, or Crohn's disease, was originally described as an inflammatory process involving only the terminal ileum. It is now recognized as a disease which involves any segment of the gastrointestinal tract from the mouth to the anus, with or without involvement of the terminal ileum. Ileocolitis is the most common form of the disease, and it is much more common than disease restricted to the terminal ileum.

It is important to emphasize that anal symptoms are often the presenting problem, and that the true incidence of anorectal Crohn's disease is something that has only recently been documented.

Pathologically, Crohn's disease is an inflammatory process which involves the submucosa rather than the mucosa. Granuloma or microgranuloma are found in approximately 50% of all cases. Transverse fissuring and lymphoid hyperplasia and lymphangiectasia, and crypt abscesses containing eosinophils and macrophages are not uncommon. Fistulous tract formation is not only common, but is one of the most devastating features of this process. Skip areas of involvement are very common, as well as stricture formation and obstruction. There are many clinical similarities between Crohn's disease and ulcerative colitis, including the development of massive gastrointestinal hemorrhage and toxic megacolon.

The disease process may be very protean in its presentation. Afflicted patients often present with developmental defects, symptoms of malabsorption syndrome, and nutritional deficiencies. Anorexia, weight loss, and fever of unknown origin are often presenting complaints in these patients. Patients usually have persistent, nonbloody diarrhea, abdominal cramps, low grade fever, anorexia, malaise, or a combination of these. Patients afflicted with Crohn's disease may also have erythema nodosum, iritis, polyarthritis, pyoderma gangrenosum, fistulae, and intraabdominal abscess, especially pelvic