Inflammatory Bowel Diseases – Basic Research and Clinical Implications

EDITED BY

H. Goebell
Department of Internal Medicine and Gastroenterology
University of Essen
Federal Republic of Germany

B. M. Peskar
Department of Experimental Clinical Medicine
Ruhr University of Bochum
Federal Republic of Germany

H. Malchow
Division of Gastroenterology
Department of Medicine
Municipal Hospital, Leverkusen
Federal Republic of Germany

Proceedings of Falk Symposium 46 held during Gastroenterology Week, Titisee, Federal Republic of Germany, June 7–9, 1987

MTP PRESS LIMITED
a member of the KLWGER ACADEMIC PUBLISHERS GROUP
LANCASTER / BOSTON / THE HAGUE / DORDRECHT
Contents

List of Contributors xiii

SECTION 1 PATHOLOGY AND PATHOGENESIS

1 Ultrastructural pathology of Crohn's disease
   A. M. Dvorak 3
2 Dysplasia in ulcerative colitis
   R. H. Riddell 43
3 Colonic glycoproteins in ulcerative colitis: potential meaning in heterogeneity
   D. K. Podolsky 49
4 Absorption and secretion in relation to inflammatory bowel disease
   K. Ewe 57
5 The role of colonic mucosal metabolism in the pathogenesis of ulcerative colitis
   W. E. M. Roediger 69

SECTION 2 VIROLOGY—BACTERIOLOGY

6 Viral and other transmissible agents in inflammatory bowel disease
   W. L. Beeken 81
7 Mycobacteria in inflammatory bowel disease
   W. R. Thayer, R. Chiodini, H. van Kruiningen and J. Coutu 89
SECTION 3 IMMUNOLOGY

8 Activation and regulatory function of lamina propria T cells: implications for inflammatory bowel disease
S. P. James, M. Zeitz, M. E. Kanof, C. Fiocchi and W. Strober

9 Altered secretion patterns of IgA and IgG subclasses by IBD intestinal mononuclear cells
R. P. MacDermott

10 Immunocytotoxicity and lymphokines in inflammatory bowel disease
C. Fiocchi, K. Kusugami, J. Trudel, B. Y. Lieberman, Q. Ouyang and M. El-Youssef

11 Autoimmunity in chronic inflammatory bowel disease
I. O. Auer

12 Neutrophils and macrophages in inflammatory bowel disease
D. P. Jewell

SECTION 4 EICOSANOIDS

13 Prostaglandins in inflammatory bowel disease
D. Rachmilewitz

14 Leucotriene B4 in inflammatory bowel disease
W. F. Stenson

15 Effect of anti-inflammatory drugs on human colonic leucotriene formation
B. M. Peskar and Ch. Coersmeier

16 Effect of therapy on eicosanoid formation in inflammatory bowel disease
K. Lauritsen, L. S. Laursen, K. Bukhave and J. Rask-Madsen

17 The role of eicosanoids in animal models of inflammatory bowel disease
N. K. Boughton-Smith and B. J. R. Whittle

SECTION 5 EPIDEMIOLOGY AND GENETICS

18 Genetic aspects of inflammatory bowel disease
J. Purrmann

19 Smoking and inflammatory bowel disease
R. F. A. Logan
CONTENTS

20 Sugar intake and Crohn's disease
   K. W. Heaton 225

21 Genetic studies in Crohn's disease
   S. W. Bender and Paediatric Crohn’s Disease Study Group 233

SECTION 6 ROUNDTABLE: TRENDS IN EPIDEMIOLOGY OF IBD

22 Trends in epidemiology of inflammatory bowel disease in Denmark/Scandinavia
   V. Binder 237

23 Epidemiology of IBD in Central Israel 1970–1980
   T. Gilat 239

24 Prospective analysis of the frequency of chronic inflammatory bowel disease in an urban population (Ruhr)
   H. Goebell, E. Dirks and S. Förster 241

25 Inflammatory bowel disease epidemiology in the United States
   A. I. Mendeloff 243

26 Epidemiology of inflammatory bowel disease in regio Leiden, the Netherlands
   S. Shivananda, M. L. Hordijk, A. S. Peña and E. J. Ruitenberg 245

27 The incidence of inflammatory bowel disease at the tip of Africa
   J. P. Wright 249

SECTION 7 ACTIVITY AND PROGNOSIS

28 Different activity indices in Crohn’s disease and their possible role
   H. Goebell 253

29 Prognostic indices on Crohn’s disease
   G. Lanfranchi, C. Brignola, A. Tragnone and P. Farruggia 259

SECTION 8 NATURAL COURSE OF IBD

30 Natural course of Crohn’s disease
   R. G. Farmer 267

31 The course of Crohn’s disease after surgery: factors affecting recurrence
   R. N. Allan 275
32 Ileal pouch-anal anastomosis for benign colonic diseases: critical analysis of the Cleveland Clinic Foundation experience
V. W. Fazio and M. H. McCafferty

33 Cancer in inflammatory bowel disease
D. B. Sacher

SECTION 9 THERAPY OF IBD (I)

34 Treatment of ulcerative colitis: state of the art
G. Watkinson

35 Absorption and utilization of nitrogen during enteral feeding of whole versus hydrolyzed protein in active Crohn’s disease
H. J. Steinhardt, E. Payr, B. Henn, K. Ewe and S. Biederlack

36 Nutritional treatment of inflammatory bowel disease including EPA
C. A. Ó’Morán

SECTION 10 THERAPY OF IBD (II)

37 Results of the European Cooperative Crohn’s Disease Study IV
H. Lochs, H. J. Steinhardt, B. Klaus-Wentz and H. Malchow

38 Anal lesions in Crohn’s disease—a surgical view
G. Hellers

39 The evolution of the new salicylates
S. C. Truelove

40 Pharmacokinetic properties of 5-aminosalicylic acid (mesalazine)
U. Klötz

41 5-ASA for the prevention of relapse in ulcerative colitis
M. J. Dew

42 Osalazine—clinical studies and relapse prevention in ulcerative colitis
H. Sandberg-Gertzen

43 Topical treatment with 5-aminosalicylic acid as rectal enemas
M. Campieri, P. Gionchetti, A. Belluzzi, G. M. Tabanelli, C. Brignola, M. Migaldi, M. Mignoli and L. Barbara

44 Cyclosporin A—still experimental or a new drug in IBD
J. Brynskov
CONTENTS

POSTER ABSTRACTS

1 Electron microscopic studies in acute and chronic ulcerative colitis I. Alterations of the mucosa
M. Balázs, T. Kertész and A. Kovács, János Hospital, Budapest 369

2 Erythrocyte-associated laminin in normal mucosa and in Crohn’s disease
A. Stallmach, U. Hahn, E. G. Hahn and E. O. Riecken, Free University of West Berlin 370

3 Induction of experimental ulcerative colitis in mice, with special reference to the change of intestinal microflora
I. Okuyasu, G.-F. Kao, S. Hatakeyama, M. Yamada, T. Okhusa, Y. Inagaki, C. Ekañsin, T. Chida and R. Nakaya, Tokyo Medical School and Dental University, Tokyo 371

4 Collegenous colitis. Retrospective study
P. Egerszegi and G. Vadász, János Hospital, Budapest 372

5 Interaction of human monocytes and mycobacteria: preliminary studies comparing Crohn’s patients with controls
D. Y. Graham and D. C. Markesich, VA Medical Center and Baylor College of Medicine, Houston 373

6 Mucosal T lymphocytes and HLA-DR expression in grossly involved and uninvolved ileum of patients with Crohn’s disease
F. Tavarela Veloso and J. V. Saleiro, University Hospital S. Joao, Porto, Portugal 374

7 Peripheral blood lymphocyte subpopulations in inflammatory bowel diseases
K. Pecze and X. Balogh, University Medical School, Debrecen, Hungary 375

8 Neutrophil activation in inflammatory bowel disease
T. McCaill and C. A. O’Morain, Trinity College Medical School, Dublin 376

9 T cell and OKM1-positive monocyte populations in the intestinal lamina propria mucosae and in the peripheral venous blood in Crohn’s disease: a quantitative immunohistochemical analysis
G. Schürmann, R. Decker, M. Betzler, P. Möller, A. V. Herbay and K. Koretz, University of Heidelberg 378

10 Immunoreactive cells in tissues of Crohn’s disease by the monoclonal antibody to measles virus
H. Miyamoto, T. Tanaka and S. Nishioka, Wakayama Medical School, Japan 379

11 Evidence of contrasuppression mediated by Vicia villosa agglutinin (VVA) binding T cells in patients with Crohn’s disease

12 The metabolism and function of peripheral blood neutrophils (PBN) in patients with ulcerative colitis (UC)
A. Stadnicki, A. Hurcek and H. Stasiura, Silesian School of Medicine, Katowice, Poland 381

13 Significance of autoimmune reactions to pancreatic juice in Crohn’s disease
W. Stöcker, M. Otte and P. C. Scriba, Medical University of Lübeck 382

14 Characterization and immunologic manipulation of the progression of chronic inflammatory bowel disease of the colon in a rat model
P. L. Beck, G. P. Morris and J. L. Wallace, Queen’s University, Kingston, Ontario 384

15 Tumor-necrosis-factor (TNF) production by peripheral monocytes in inflammatory bowel disease (IBD) patients
T. Morita, K. Nara, H. Odagiri, M. Yokoyama, D. Seito, M. Sasaki, M. Kono and K. Ono, Hirohaki University School of Medicine, Japan 385

16 Studies on interleukin-2 in patients with ulcerative colitis
K. Kuroe, A. Nikai, Y. Murata, M. Akiyama and Y. Yoshida, Hirohaki University School of Medicine, Japan 386

17 Deficient spontaneous and interferon-induced natural killer cell activity and antibody-dependent cellular cytoxicity in Crohn’s disease
P. Knoll, Ch. Mueller and C. C. Zellinsuki, University of Vienna 387
18 Experimental immune complex-mediated intestinal disease leading to protein-losing enteropathy
P. Knoflach, B. Albini and M. M. Weiser, University of Vienna

19 Effect of 16,16-dimethyl prostaglandin E2 (dmPGE2) and sulfasalazine (SASP) on arachidonic acid (AA) metabolism by colonic tissue from guinea pigs with an immune colitis
L. Da Costa and P. Dinda, Queen’s University, Kingston, Ontario

20 Development of the epidemiology of chronic inflammatory bowel disease (IBD) in the county of Tübingen from 1970 to 1984
W. Daiss, M. Scheurlen and H. Malchow, University Medical Clinic, Tübingen

21 Regional differences in the distribution of inflammatory bowel disease (IBD) in the county of Tübingen
M. Scheurlen, W. Daiss and H. Malchow, University Medical Clinic, Tübingen

22 Bowel permeability to 51Cr-EDTA in patients with Crohn’s disease
R. T. Jenkins, J. K. Ramage, R. L. Goodacre, R. H. Hunt and J. Bienenstock, McMaster University, Hamilton, Ontario

23 99mTc-HMPAO and 111In-oxine labeled granulocyte scans in chronic inflammatory bowel diseases; clinical experience in 120 patients
W. Becker, W. Fischbach, M. Jenett and W. Börner, University Medical Clinic, Würzburg

24 99mTc-HMPAO labeling of leukocytes in the assessment of patients with Crohn’s disease (CD)
J. Schölmerich, C. Schümichen, E. Schmidt and W. Gerok, University of Freiburg

25 75SeHCAT-test for characterization of ileal involvement in Crohn’s disease
K. Balzer, E. Dirks, N. Breuer and H. Goebell, University of Essen

26 Fecal blood loss in inflammatory bowel disease
O. P. van der Ven, L. K. Ko, J. W. O. van der Berg and E. A. R. Knot, Erasmus University, Rotterdam

27 Determination of the small bowel transit time using barley groats
R. J. Vonk, C. H. P. Collin, J. J. de Vries and C. M. A. Bijleveld, University Hospital, Groningen

28 Study on colonic transit in man using colonoscopy
K. Murakami, H. Nakano, N. Inatsugi, H. Fujii, T. Hashimoto and T. Shiratori, Nara Medical University, Japan

29 Neopterin serum levels in Crohn’s disease
E. F. Strange, W. E. Fleig and H. Ditschuneit, University Clinic, Ulm

30 Ultrasound in Crohn’s disease
P. P. Michielsen, T. J. Hartoko, P. A. Pelckmans, J. H. Pen and Y. M. van Maercke, University Hospital of Antwerp

31 Prospective endoscopic follow-up of the evolution of Crohn’s recurrence at the ileocolonic anastomosis after surgery
P. Rutgeerts, K. Geboes, G. Vantrappen, J. Belys, G. Coremans and R. Kerremans, University Hospital Gasthuisberg, Leuven

32 Prospective endoscopic and histologic study in patients with ulcerative proctitis
G. Geboes, P. Rutgeerts, N. Ectors and G. Vantrappen, University Hospital Gasthuisberg, Leuven

33 Early recurrence of Crohn’s disease (CD) after curative resection. First results of a prospective study using colonoscopy
C. C. Singe, S. Biederlack and K. Ewe, Medical University, Mainz

34 Recurrence of Crohn’s disease in patients with curative resection as compared to conservatively treated patients
E. Dirks, K. Schaarschmidt, H. Goebell and F. W. Eigler, University of Essen

35 A classification of small bowel strictures in Crohn’s disease
P. McDonald, R. Petras, V. Fazio and S. Galandiuk, Cleveland Clinic Foundation, Cleveland, Ohio

36 Antithrombin III levels and thromboembolic complications in inflammatory bowel disease
D. Hüpke, U. Kamp, R. Tönissen and H. D. Kuntz, University Clinic, Bochum
CONTENTS

37 Crohn’s disease and pregnancy
H. Jenss, H. Elser and P. Weber, University of Tübingen 414

38 Serum retinol levels in inflammatory bowel disease
I. Janeczewska, W. Bartnik, J. Ostrowski and E. Bultuk, Medical Center of Post-graduate Education, Warsaw 415

39 Vitamin D and calcium regulation in patients with Crohn’s disease (CD)
H. Vogelsang, P. Ferenci, R. Schilling, W. Wolszczuk, F. Haschke, H. Lochs and A. Gang, University of Vienna 416

40 Changes of the calcium metabolism in inflammatory bowel disease
J. Kocián and J. Kociánová, Faculty Hospital Bulovka, Prague 417

41 Impaired cholesterol metabolism in Crohn’s disease
M. Malavolti, G. Borghi, E. Roda, B. Grigolo, A. M. Morselli Labate, P. Simon and L. Barbara, University of Bologna 418

42 Parenteral nutrition (PN) in inflammatory bowel disease (IBD)
M. Cravo, M. L. Tavares, M. T. Tavares, M. E. Camilo and J. Pinto Correia, University of Santa Maria, Lisbon 419

43 Therapeutic efficacy of sliding scale based cyclic home enteral alimentation in Crohn’s disease

44 The adjuvant therapy of colitis ulcerosa with loperamide
I. Altaparmakov, R. Trapp and P. Czygan, Lucas Academic Hospital, Neuss 421

45 A controlled randomized trial of budesonide versus prednisolone retention enema in active distal ulcerative colitis

46 Protective effect of metronidazole in ulcerative colitis experimentally induced by dextran sulfate sodium
T. Ohkusa, M. Yamada, N. Yamamoto, M. Sasabe, I. Takashimuzu, H. Fujimoto, Y. Kuyama, N. Aoki, T. Chida, M. Higaki, N. Okamura, R. Nakaya, I. Okayasu and S. Hatakeyama, Soka City Hospital, Saitama and Tokyo Medical and Dental University 424

47 Results and significance of thymectomy in patients with ulcerative colitis
H. Yoshimatsu and K. Ando, University of Occupational Health, Japan, Kitakyushu and Shizuoka Red Cross Hospital, Shizuoka, Japan 425

48 Strictureplasty in Crohn’s disease
S. Galandiuk, V. W. Fazio and P. McDonald, Cleveland Clinic Foundation, Cleveland, Ohio 426

49 Placebo controlled trial of 4-amino salicylic acid enemas in left sided ulcerative colitis
A. L. Ginsberg, L. S. Beck, T. M. McIntosh and L. E. Nochomovitz, George Washington University School of Medicine, Washington D.C. 427

50 Prospective, randomized, double-blind comparison of salazobenzoic acid (SAB) and sulfasalazine (SASP) in the treatment of active ulcerative colitis
W. E. Fleig, G. Laudage, E. F. Stange and J. Riemann, University Medical Clinics of Ulm and Erlangen 428

51 In vitro screening of alternative salicylate derivatives for therapeutic use in ulcerative colitis
W. E. W. Roediger, E. J. Deakin, M. J. Lawson and S. H. Nance, University of Adelaide at the Queen Elizabeth Hospital, Adelaide 430

52 Crohn’s disease and ulcerative colitis: treatment with 7S-immunoglobulin
INFLAMMATORY BOWEL DISEASES

53 Flow cytometric DNA analysis in longstanding ulcerative colitis—a possible complement in cancer surveillance
   R. Löfberg, O. Broström, H. Reichard, B. Tribukait and A. Öst 433

54 Increased frequency of HLA-B27/44 in patients with Crohn’s disease and ankylosing spondylitis
   J. Purmann and J. Bertrams, University of Düsseldorf and Elisabeth-Krankenhaus, Essen 434

55 Dietary management in idiopathic inflammatory bowel disease (IBD)
   H. Steinhardt 436

Index 439
Autoantibodies to exocrine pancreas (Pab) have been detected by indirect immunofluorescence in sera of patients with Crohn’s disease (CD). High titres were frequent in CD, but could neither be recorded in ulcerative colitis nor in healthy subjects. Pab in CD were as conspicuous as autoantibodies to intestinal goblet cells (Gab) in ulcerative colitis (UC) and other autoantibodies in proven autoimmune diseases. The possible implication of pancreatic immunity in the pathogenesis of CD was discussed. Results of additional studies enhance the significance of these observations.

The association of Pab with CD could be verified by examination of new, larger collectives consisting of 150 patients with CD, 164 patients with UC and 100 healthy control persons (Co). Pab were predominant in CD (CD 35%, UC 2%, Co 0%). High Pab-titres were only detectable in CD (1:100 or higher in 30% of 150 patients). On the contrary, Gab were confirmed to be an exclusive marker for UC (CD 0%, UC 26%, Co 0%).

The prevalence of Pab and Gab was determined in the sera of the patients’ family members who are assumed to carry an elevated risk for developing chronic inflammatory bowel disease. Since none of 185 healthy appearing first degree family members exhibited Pab or Gab, these antibodies seem to be disease-specific and do not yet indicate a disposition for CD or UC.

It was possible to isolate the CD-related autoantigen from pancreatic juice. The antigen was shown to be a macromolecule different from functionally active trypsin, chymotrypsin, amylase and lipase, and it could neutralize Pab of each positive CD-serum.

The autoimmune reactions in CD differed fundamentally from those observed in disorders of the pancreas: Pab were rare in chronic (2 of 51) and acute (3 of 26) pancreatitis, their titres were low and did not exceed 1:32, they consisted only of IgA (CD: IgG or IgG + IgA) and could not be neutralized by the CD-related autoantigen. A number of sera contained Pab or Gab with only one type of light chains, kappa or lambda. This uneven distribution speaks in favour of an oligoclonal
POSTER ABSTRACTS

antibody response and possibly indicates that the corresponding autoimmune reactions are phenomena of primary significance—a secondary immunization against pancreatic or goblet cell antigens in the course of CD or UC seems to be excluded.

In Crohn's disease, the bowel may have developed a state of hypersensitivity against a physiologically occurring component of pancreatic juice. Pancreatitis is not predominant in CD since the bulk of autoantigens comes into contact with the immune system only outside the pancreas. As with other autoimmune diseases, the cause of sensibilization cannot yet be explained, and further investigations are required to completely reveal the etiology of CD.

Determination of Pab is of great diagnostic value. In combination with Gab, they permit the diagnosis of CD or UC in one third of patients with chronic inflammatory bowel disease.

References