A Comparison of Multiple Synchronous Colorectal Cancer in Ulcerative Colitis, Familial Polyposis Coli, and *de Novo* Cancer

ADRIAN J. GREENSTEIN, M.D. TOMAS M. HEIMANN, M.D. DAVID B. SACHAR, M.D.*
GARY SLATER, M.D. ARTHUR H. AUFSES, JR., M.D.

Multiple synchronous colorectal cancer (MSCC) among 1537 patients (69 with familial polyposis coli (FPC), 780 with ulcerative colitis (UC), and 685 with *de novo* colorectal (DNC) cancers) admitted to The Mount Sinai Hospital between 1945 and 1981 was tabulated. MSCC occurred in five of 24 cancer patients with FPC (21%), in 12 of 65 cancer patients with UC (18%), but in only 17 of 685 DNC patients (2.5%). The proportions of MSCC cases with *more* than two synchronous tumors were also much greater in the former two groups (UC 6/12 = 50%, FPC 3/5 = 60%) than in DNC (0/17 = 0%). Multiplicity of cancers is thus a distinguishing feature of UC and FPC. MSCC differed from solitary cancers by association with older age and more advanced stage at diagnosis in patients with FPC and by a rightward shift in anatomic distribution in all patients, especially those with FPC and UC.

From the Departments of Surgery and Medicine, Mount Sinai School of Medicine of the City University of New York and The Mount Sinai Hospital, New York, New York*

THE SIMULTANEOUS OCCURRENCE of multiple primary malignancies was noted by Billroth in 1889.[1] Colorectal cancers are most frequently solitary, but multiple cancers occur in a small percentage of cases. The frequency of such synchronous lesions is generally recognized to be much greater with ulcerative colitis[2-4] and familial polyposis coli[5] than in the general population.[6-10] Since the reported incidences of multiple tumors are quite variable, and since there has been no direct comparison of these three groups in the same hospital population, we have studied the occurrence of multiple synchronous colorectal cancers seen at The Mount Sinai Hospital over a 35-year period.

Material and Methods

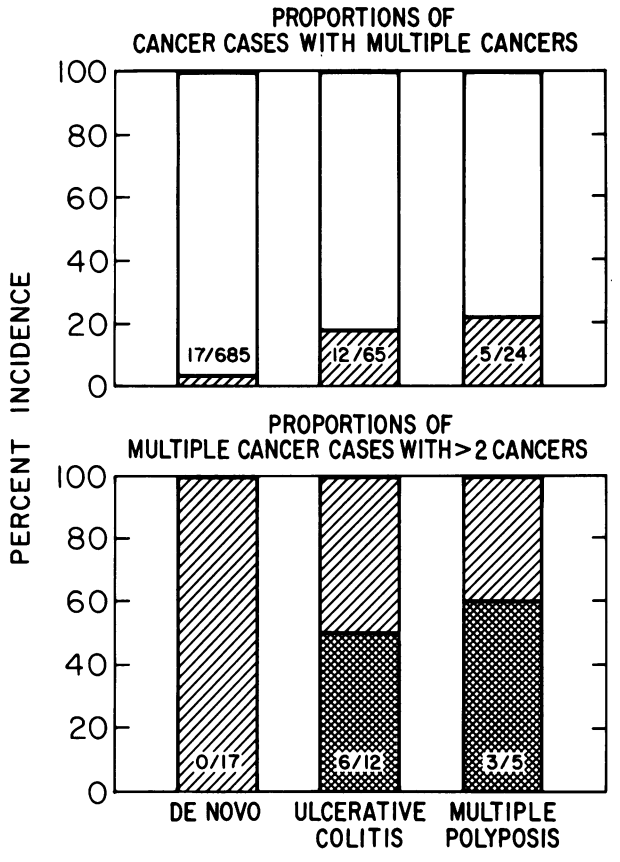
We have retrospectively examined the records of 1537 patients with multiple polyposis coli, ulcerative colitis, or *de novo* colorectal cancer, admitted to The Mount Sinai Hospital during various intervals between 1945 and 1981. Twenty-four of 69 familial polyposis coli patients (35%) admitted between 1945 and 1981 developed colorectal cancer, and five of these 24 cases (21%) had multiple synchronous cancers. Sixty-five of 780 ulcerative colitis patients (8.3%) admitted between 1960 and 1981 developed colorectal cancer, and 12 of these 65 cases (18%) had multiple synchronous cancers. Among 685 patients with *de novo* colorectal cancer admitted between 1975 and 1981, only 17 (2.5%) had multiple tumors.

The diagnosis of ulcerative colitis was made on a clinical, radiological, and/or endoscopic basis in all cases and was confirmed pathologically on all biopsied or resected specimens. Cases with skipped areas, ileal disease, right-sided colitis, granulomas, fissures, or transmural inflammation suggestive of Crohn's disease were excluded from the series, as were those in which specific pathologic microorganisms were cultured. The diagnosis of familial polyposis was made by the gross appearance of more than 100 polyps, confirmed histopathologically to be adenomatous.

To establish the diagnosis of multiple synchronous carcinomas, we adapted the criteria of Warren and Gates.[11] Each cancer was diagnosed macroscopically and microscopically as a separate primary malignancy and not a metastasis, and each tumor was clearly separated from any adjacent tumor by an area of normal intact bowel wall. Although other series have accepted as "synchronous" any lesion occurring separately and resected at a second operation within 6 months of the primary excisional operation, we have included only those tumors occurring simultaneously in the same specimen; the figures

Reprint requests: Adrian J. Greenstein, M.D., Department of Surgery, The Mount Sinai Medical Center, One Gustave L. Levy Place, New York, NY 10029.

Submitted for publication: September 6, 1985.



No. of cancers:	Pts	Cancers	Pts	Cancers	Pts	Cancers
1	668	(668)	53	(53)	19	(19)
2	17	(34)	6	(12)	2	(4)
3	0	(0)	5	(15)	1	(3)
4	0	(0)	1	(4)	1	(4)
5	0	(0)	0	(0)	1	(5)
Total:	685	(702)	65	(81)	24	(35)

FIG. 1. The proportions of colorectal cancers with multiple cancers is shown. There are significantly more patients with two or more than two cancers in ulcerative colitis, and polyposis, than in *de novo* rectal cancer.

reported here may thus slightly underestimate the true incidence.

Patients were divided into two groups, according to the stage of disease. Early cancers were defined as Dukes' stages A and B, and advanced cancers as Dukes' stages C and D.[12]

Results

There was a markedly higher frequency of multiplicity in ulcerative colitis-related cancers (12/65 = 18%) and polyposis-related cancers (5/24 = 21%) than in *de novo* colorectal cancers (17/685 = 2.5%). Moreover, the proportions of multiple-cancer cases with more than two synchronous cancers were also much greater for both of these premalignant conditions (colitis 6/12 = 50%, polyposis 3/5 = 60%) than for *de novo* cancers (0/17 = 0%) (Fig. 1).

The mean age of patients with *de novo* colorectal cancer (70 years), was much higher than that of patients with colitis-related (49 years), or polyposis-associated cancers (40 years) (see Table 1 and Fig. 2). The mean age at diagnosis of cancer was virtually the same for multiple as for single cancers associated with ulcerative colitis (46 *vs.* 50 years) and *de novo* cancer (67 *vs.* 70 years). By contrast, polyposis coli patients with multiple cancer were considerably older than those with single cancer (52 *vs.* 37 years) (see Table 1). As the mean age at onset of ulcerative colitis was identical, 27 years, the duration of colitis before development of either multiple or single cancers was similar (17 *vs.* 21 years).

There were more male than female patients with *de novo* colorectal cancer, (M:F = 388:297 = 57% male) and ulcerative colitis-associated cancer (M:F = 41:24 = 63% male), and fewer with polyposis-associated cancer (M:F = 8:16 = 33% male); but in each group there was no significant difference in the male-to-female ratios for multiple *vs.* solitary cancers.

A comparison of the anatomical sites of cancer in the three groups of patients is shown in Table 1 and Figure 3. In all groups of patients, solitary cancers were found more frequently in the left side (*i.e.*, distal to the splenic flexure): 62% for ulcerative colitis-related cancer, 84% for polyposis-related cancer, and 68% for *de novo* cancer. Figure 3 shows that the distribution of multiple cancers remained predominantly left-sided in *de novo* cases but was significantly shifted to the right side in both ulcerative colitis and polyposis-related cases ($p < 0.01$).

Multiple polyps were by definition present in all the multiple polyposis cancers, but true adenomatous polyps, as distinct from pseudopolyps, were not found in the ulcerative colitis patients, in whom premalignant changes are not necessarily associated with polyp formation. However, nine of the 17 patients with multiple *de novo* cancers (53%) had additional polyps in the resected segment.

The stages of the cancers at the time of surgery are shown in Table 2 and Figure 4. Multiple cancers proved to be no more advanced than single cancers, except in the polyposis patients in whom the finding of multiple cancers was associated with a 15-year old mean age. In *de novo* colorectal cancer, all the advanced cancers were in the index group. The second cancers were found incidentally at pathology in almost all *de novo* cancer cases and were all in categories A and B of the Dukes classification. Thus the C and D lesions actually comprise 48% of the index cancers (Fig. 4).

TABLE 1. *Comparison of Multiple and Solitary Colorectal Cancers in Ulcerative Colitis, Familial Polyposis, and the Normal Population*

	De Novo Cancers		Ulcerative Colitis Cancer		Familial Polyposis	
	Single	Multiple	Single	Multiple	Single	Multiple
Total number of patients in series	685		780		69	
Number of patients with cancer (mean age)	685 (70 yrs.)		65 (49 yrs.)		24 (40 yrs.)	
	668 (70)	17 (67)	53 (50)	12 (46)	19 (37)	5 (52)
Male:Female	(377:291)	(11:6)	(32:21)	(9.3)	(7:12)	(1:4)
Total cancers	668	34	53	31	19	16
	(%)	(%)	(%)	(%)	(%)	(%)
Cecum	104 (16)	4 (12)	6 (11)	5 (17)	2 (11)	3 (19)
Asc. colon	23 (4)	5 (15)	6 (11)	10 (33)	0 (0)	3 (19)
Hepatic flexure	30 (5)	3 (9)	2 (4)	0 (0)	1 (5)	1 (6)
Transverse colon	27 (4)	4 (12)	4 (8)	6 (17)	0 (0)	2 (13)
Splenic flexure	29 (4)	0 (0)	2 (4)	0 (0)	0 (0)	1 (6)
Descending colon	30 (5)	2 (6)	2 (4)	5 (17)	1 (5)	0 (5)
Sigmoid colon	255 (38)	11 (32)	18 (34)	2 (7)	9 (47)	0 (0)
Rectum	170 (25)	5 (15)	13 (25)	3 (10)	6 (32)	2 (13)
Right side (colon + ascending colon)	127 (19)	9 (27)	12 (23)	15 (48)	2 (11)	6 (50)
Tv. colon + flexures	86 (13)	7 (21)	8 (15)	6 (19)	1 (5)	4 (17)
Left side	455 (68)	18 (53)	33 (62)	10 (33)	16 (84)	2 (33)
	*		†		†	

* Chi square right side *vs.* left side in multiple *vs.* single groups, $\chi^2 = 0.29$, N.S.

† Chi square right side *vs.* left side in multiple *vs.* single groups, $p < 0.005$ and $p < 0.01$, respectively.

Discussion

In this series, the proportions of multiple synchronous cancers (2.5% for *de novo* colorectal cancer, 18% for ulcerative colitis-related cancer, and 21% for polyposis-related cancer) are comparable to those published in other reports. Table 3 shows the proportions of synchronous and metachronous cancers found in a survey of the literature. The proportions range from 2.8–5.4%, 8–43%, and 25–44% for *de novo,* colitis-related, and polyposis-related cancers, respectively. Multiplicity of cancers thus appears to be a feature of the two conditions, ulcerative colitis and familial polyposis coli, with recognized premalignant potential.

Our observation that polyposis patients with multiple cancer tended to be 15 years older than their counterparts with single cancers probably reflects the simple fact that the risk of colorectal cancer in polyposis coli increases steadily with age.[5] In other words, the older the patient by the time of surgery, the more likely that additional cancers will have developed. It is interesting that while cancer risk in ulcerative colitis also increases with disease duration[14,15] and hence secondarily with age, other premalignant factors besides time alone must be operative in this group, since multiplicity in our colitis-related cancer cases was associated with a slightly younger age group (46 *vs.* 50 years). Perhaps anatomical extent of colitis, another important determinant of age-related risk,[14] played a role that we have not analyzed in this study.

Although other authors have described cases of more than two, and up to five, multiple synchronous *de novo* colorectal cancers,[8,16,21,30] we did not find any such cases in our series. On the other hand, multiplicity beyond two cancers occurred in over half the multiple-cancer cases

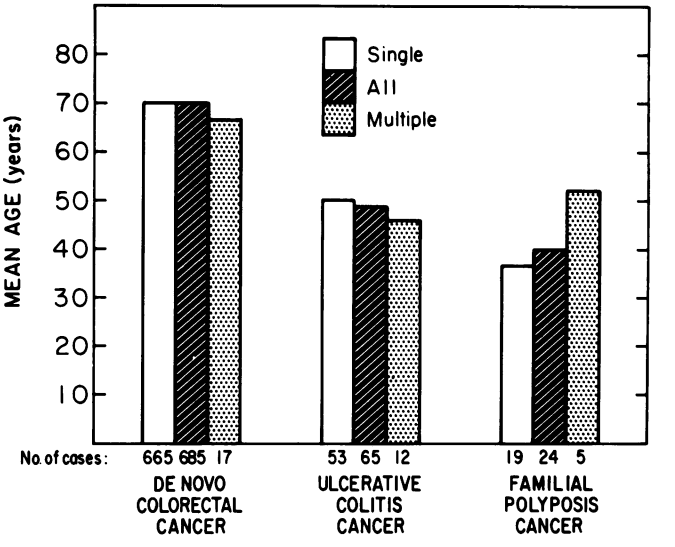
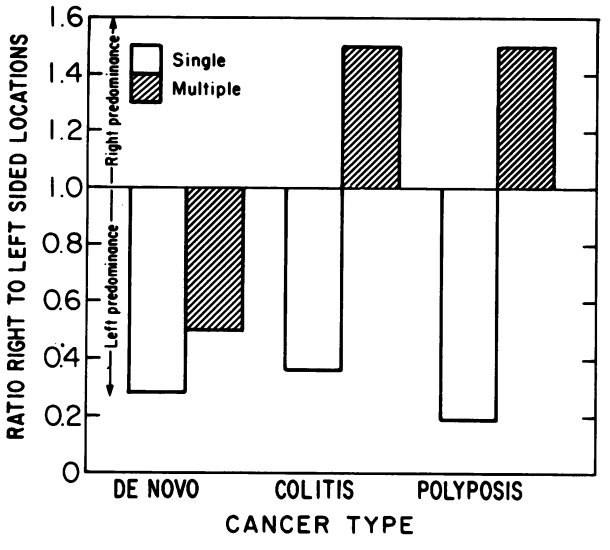
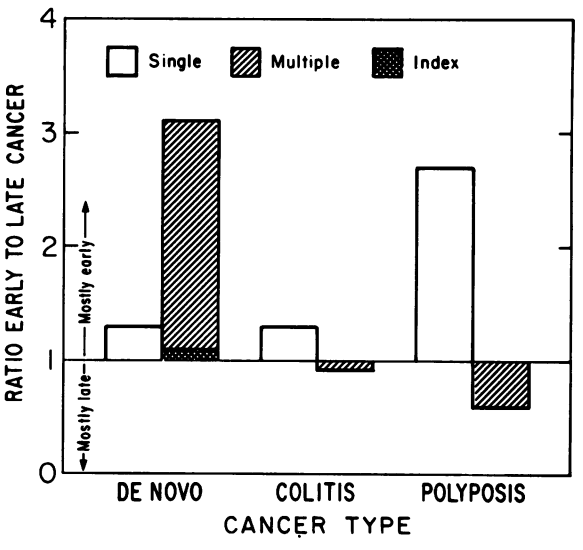


FIG. 2. The mean ages of patients with *de novo* colorectal cancer, ulcerative colitis cancer, and familial polyposis cancer are shown for single, multiple, and all cancers. Patients with *de novo* cancer are the oldest, those with familial polyposis the youngest, and ulcerative cancer patients intermediate in age at the time of diagnosis of the cancer.



Percentage right:	19	27	23	48	16	50
Percentage left:	65	53	62	32	84	33
Ratio:	0.28	0.50	0.36	1.5	0.19	1.5

FIG. 3. Proportion of right-sided to left-sided locations of solitary *vs.* multiple colorectal cancers. Right side is defined as cecum and ascending colon, and left side as descending colon and rectosigmoid; transverse colon cases are omitted. In *de novo* cases, there is no difference in the predominantly left-sided distribution between single *vs.* multiple cancers, whereas, in the colitis and polyposis groups, multiplicity is associated with a marked rightward shift.



		(Index)				
Percentage early:	56	46 (52)	57	48	73	38
Percentage late:	44	24 (48)	43	52	27	62
Ratio:	1.3	3.1 (1.1)	1.3	0.9	2.7	0.6

FIG. 4. Proportions of early (Dukes' A and B) to late (Dukes' C and D) stagings of solitary *vs.* multiple colorectal cancers. There is no difference in staging of single *vs.* multiple colitis-related cancers. In polyposis-related cases, multiple cancers are farther advanced than solitary tumors, but the patients are also an average of 15 years older. In the *de novo* group, multiple cancers are less advanced than single ones, but this is an artifact of the secondary tumors being incidentally discovered in early stages; in cases of multiple cancers in this group the *index* cancers are no different from the solitary ones.

among our ulcerative colitis and polyposis patients. Indeed, a considerable proportion of ulcerative colitis cancer are not only multiple, but often diffuse or extensively infiltrating.[3] Two of our patients had multiple areas of dysplasia or of diffuse superficial carcinoma or carcinoma-*in situ,* in addition to the three described cancers. One of these patients, listed as having three cancers, had what appeared macroscopically to be seven separate cancers. Unfortunately, sections of the additional four areas were not available for review. Four of our first 26 cases had extensive infiltration into adjacent areas.[3] Similar diffuse or multiple cancers have been described in Crohn's disease,[26–28] indicating the diffuse multifocal nature of the premalignant epithelial changes in both of these forms of inflammatory bowel disease.

Patients with multiple *de novo* cancers seemed to have a lower proportion of advanced stage cancers than their counterparts with solitary tumors (24% *vs.* 44%). Other series have also suggested lower proportions of advanced lesions (7–40%) among multiple cancers[21,30,33] than among solitary cancers (42–47%).[17,31,32] This observation, however, is merely an artifact of the relatively early staging of second cancers found incidentally upon colonoscopy[33] or upon pathological review of resected specimens.[21,30] In the *de novo* group, all the second cancers were stage A and B, so that the 48% proportion of advanced stages among the index cancers was similar to the 44% for solitary cancers.

In ulcerative colitis, Lavery et al.[34] found 59% of invasive cancers to be Dukes' C or D cancers,[11] and Johnson et al.[35] found 57% to be advanced. At St. Mark's, 41% fell into the C category.[2] The figures in our colitis group of 43% for single cancers and 52% for multiple cancers are in the same general range.

In Bussey's series of multiple polyposis patients at St. Mark's Hospital,[5] the proportions of advanced cancers for both single and multiple cancers were almost identical with our figures. Among 124 cases, Bussey found a 36% proportion of advanced stages among solitary cancers, compared to 64% of advanced stages among multiple

TABLE 2. *Stage of Disease According to Dukes Classification at Surgery for Solitary and Multiple Colorectal Cancers*

	De Novo Cancer		Colitis Cancer		Polyposis Cancer	
Stage	Single	Multiple	Single	Multiple	Single	Multiple
A	7%	12%	11%	19%	21%	19%
B	49%	64%	46%	29%	52%	19%
C	28%	21%	13%	52%	11%	62%
D	16%	3%	30%	0%	16%	0%

TABLE 3. *Multiple Colorectal Carcinomas*

Author	Year	Total Number Cancers	Number with Multiple Cancers	% Incidence
De Novo				
Moertel et al.[10]	1958	6012	261	4.3*
Glenn et al.[6]	1966	1026	59 (S + M)	5.8
Bussey et al.[7]	1967	6309	164 (S)	2.6
			82 (M)	1.3
Devitt et al.[16]	1969	1140	25 (S)	2.2
McSherry et al.[9]	1969	1625	46 (S)	2.8
			76 (M)	4.7
Franklin et al.[38]	1970	314	17 (S)	5.4
			9 (M)	2.9
Travieso et al.[39]	1972	2230	34 (S)	1.5
			13 (M)	0.6
Mzabi et al.[40]	1976	656	19 (S)	2.8
Heald et al.[8]	1975	4884	83 (M)†	1.6
			157 (S)	3.2†
Hancock[22]	1975	831	46 (S)	5.5
Lasser et al.[21]	1978	1002	62 (S)	6.2
Lee et al.[41]	1982	308	10 (S)	3.2
			3 (M)	0.97
	1982	30275‡	1407	4.6
Enker et al.[30]	1978	3842	68 (S)	1.8§
			53 (M)	1.4
			13 (M)	1.1
Langevin et al.[33]	1984	166	8 (S)	4.8
Present series	1984	685	17 (S)	2.5
(With Perioperative or Postoperative Colonoscopy)				
Appel[42]	1976	14	1 (S)	7.0
Reilly et al.[43]	1982	92	7 (S)	7.6
		78	6 (M)	7.7
Maxfield[44]	1984	90	4 (S)	4.4
Ulcerative colitis				
Bargen[45]	1928	14	6	43
Goldgraber et al.[3]	1964	33	14	42
Edwards et al.[46]	1964	22	5	23
Welch et al.[47]	1965	25	2	8.0
Hinton[48]	1966	32	7	22
Kewenter et al.[13]	1978	17	2	12
Greenstein et al.[3]	1979	26	3	12
Nugent et al.[49]	1979	23	6	21
Ritchie et al.[2]	1981	67	15	22
Ohman[50]	1982	29	5	17
Present series	1984	65	12	18
Familial Polyposis				
Bussey[5]	1975	151	67 (S)	44
Present series	1984	24	5 (S)	21
			4 (M)	17

S = single; M = multiple.

* Autopsy and surgical series including ulcerative colitis and familial polyposis.

† Among metachronous 18 missed synchronous cancers.

‡ Collected series.

§ Including four with ulcerative colitis and familial polyposis and three with multiple adenomas.

cancers. Our figures were 37% and 62%, respectively (see Table 2). Once again, this apparently worse prognosis for multiple cancers in polyposis coli, like the 15-year older mean age for the patients, is probably just a reflection of delayed diagnosis and later surgical intervention.

Acknowledgments

The authors wish to thank Mrs. Jean DiCarlo for her excellent assistance in the preparation of this manuscript, Mrs. Karen Bolnick, R.R.N., and Mrs. Eileen Montgomery for assistance in organizing the data, and Devaprasad Reuben, R.R.A., of our Medical Records Department for obtaining the medical records from the computer files of the hospital and assisting in the organization and analysis of the data for this research project.

References

1. Moertel CG, Dockerty MB, Baggenstoss AH. Multiple primary malignant neoplasms. Cancer 1961; 14:221–230.
2. Ritchie JK, Hawley PR, Lennard-Jones JE. Prognosis of carcinoma in ulcerative colitis. Gut 1981; 22:752–755.
3. Greenstein AJ, Sachar DB, Pucillo A, et al. Cancer in universal and left-sided ulcerative colitis: clinical and pathological features. Mt Sinai J Med 1979; 45:25–32.
4. Goldgraber MB, Kirsner JB. Carcinoma of the colon in ulcerative colitis. Cancer 1964; 17:657–665.
5. Bussey HJR. Familial Polyposis Coli. Baltimore: The Johns Hopkins University Press, 1975.
6. Glenn F, McSherry CK. Carcinoma of the distal large bowel. Ann Surg 1966; 163:838–849.
7. Bussey HJ, Wallace MH, Morson BC. Metachronous carcinoma of the large intestine and intestinal polyps. Proc R Soc Med 1967; 60:208–210.
8. Heald RJ, Bussey HJR. Clinical experiences at St. Mark's Hospital with multiple synchronous cancers of the colon and rectum. Dis Colon Rectum 1975; 18:6–10.
9. McSherry CK, Cornell GJ, Glenn F. Carcinoma of the colon and rectum. Ann Surg 1969; 169:502–509.
10. Moertel CG, Bargen JA, Dockerty MB. Multiple carcinomas of the large intestine: a review of the literature and a study of 261 cases. Gastroenterology 1958; 34:85–98.
11. Warren S, Gates O. Multiple primary malignant tumors: survey of the literature and statistical study. American Journal of Cancer 1932; 16:1358–1414.
12. Dukes CE. The classification of cancer of the rectum. J Pathol Bacteriol 1932; 35:322–332.
13. Kewenter J, Ahlman H, Hulten L. Cancer risk in extensive ulcerative colitis. Ann Surg 1978; 188:824–828.
14. Greenstein AJ, Sachar DB, Smith H, et al. Cancer in universal and left-sided ulcerative colitis: factors determining risk. Gastroenterology 1979; 77:290–294.
15. Devroede GJ, Taylor WF, Sauer WG, et al. Cancer risk and life expectancy of children with ulcerative colitis. N Engl J Med 1971; 285:17–21.
16. Devitt JE, Roth-Moyo JA, Brown FN. The significance of multiple adenocarcinomas of the colon and rectum. Ann Surg 1969; 169: 364–367.
17. Slater G, Papatestas AE, Tartter PI, et al. Age distribution of right-and-left sided colorectal cancer. Am J Gastroenterol 1982; 77: 63–66.
18. Howard EW, Corallo C, Hovey LM, et al. Colon and rectal cancer in the young adult. Am Surg 1975; 41:260–265.
19. Johnson JW, Judd EJ, Dahlin DC. Malignant neoplasms of the colon and rectum in young persons. Arch Surg 1975; 79:365–372.
20. Simstein NL, Kovalcik PJ, Cross GH. Colorectal carcinoma in patients less than 40 years old. Dis Colon Rectum 1978; 21:169–171.
21. Lasser A. Synchronous primary adenocarcinomas of the colon and rectum. Dis Colon Rectum 1978; 21:20–22.
22. Hancock RJ. Synchronous carcinoma of the colon and rectum. Am Surg 1975; 41:560–563.
23. Lynch HT, Harris RE, Bardawil WA, et al. Management of hereditary site-specific colon cancer. Arch Surg 1977; 112:170–174.
24. Lynch PM, Lynch HT, Harris RE. Hereditary proximal colonic cancer. Dis Colon Rectum 1977; 20:661–668.

25. Lynch HT, Harris RE, Lynch PM, et al. The role of heredity in multiple primary cancer. Cancer 1977; 40:1849–1854.
26. Bersack SR, Howe JS, Rehak EM. A unique case with roentgenologic evidence of regional enteritis of long duration and histologic evidence of diffuse adenocarcinoma. Gastroenterology 1958; 34: 703–710.
27. Clemmensen T, Johansen A. A case of Crohn's disease of the colon associated with adenocarcinoma extending from cardia to the anus. Acta Pathol Microbiol Scand 1972; 80:5–8.
28. Keighley MRB, Thompson H, Alexander-Williams J. Multifocal colonic carcinoma and Crohn's disease. Surgery 1975; 78:534–537.
29. Deschner EE. Early proliferative changes in gastrointestinal neoplasia. Am J Gastroenterol 1982; 77:207–211.
30. Enker WE, Dragacevic S. Multiple carcinomas of the large bowel: a natural experiment in etiology and pathogenesis. Ann Surg 1978; 187:8–11.
31. Slanetz CA, Herter FP, Grinnell RS. Anterior resection versus abdominoperineal resection for cancer of the rectum and rectosigmoid. Am J Surg 1972; 123:110–117.
32. Lockhart-Mummery HE, Ritchie JK, Hawley PR. The results of surgical treatment for carcinoma of the rectum at St. Mark's Hospital from 1948 to 1972. Br J Surg 1976; 63:673–677.
33. Langevin JM, Nivatvongs S. The true incidence of synchronous cancer of the large bowel. Am J Surg 1984; 147:330–333.
34. Lavery IC, Chiulli RA, Jagelman DG, et al. Survival with carcinoma arising in mucosal ulcerative colitis. Ann Surg 1982; 195:508–512.
35. Johnson WR, McDermott FT, Hughes ESR, et al. Carcinoma of the colon and rectum in inflammatory disease of the intestine. Surg Gynecol Obstet 1983; 156:193–197.
36. Hughes RG, Hall TJ, Block GE, et al. The prognosis of carcinoma of the colon and rectum complicating ulcerative colitis. Surg Gynecol Obstet 1978; 146:46–48.
37. Van Heerden JA, Beart RW. Carcinoma of the colon and rectum complicating chronic ulcerative colitis. Dis Colon Rectum 1980; 23:155–159.
38. Franklin R, McSwain B. Carcinoma of the colon, rectum, and anus. Ann Surg 1970; 171:811–818.
39. Travieso CR, Knoepp LF, Hanley PH. Multiple adenocarcinomas of the colon and rectum. Dis Colon Rectum 1972; 15:1–6.
40. Mzabi R, Himal HS, Demers R, MacLean LD. A multiparametric computer analysis of carcinoma of the colon. Surg Gynecol Obstet 1976; 143:959–964.
41. Lee T-K, Barringer M, Myers RT, Sterchi JM. Multiple primary carcinoma of the colon and associated extracolonic primary malignant tumors. Ann Surg 1982; 95:501–506.
42. Appel MF. Preoperative and postoperative colonoscopy for colorectal carcinoma. Dis Colon Rectum 1976; 19:664–666.
43. Reilly JC, Rusin LC, Theuerkauf FJ. Colonoscopy: its role in cancer of the colon and rectum. Dis Colon Rectum 1982; 25:532–538.
44. Maxfield RG. Colonoscopy as a routine preoperative procedure for carcinoma of the colon. Am J Surg 1984; 147:477–480.
45. Bargen JA. Chronic ulcerative colitis associated with malignant disease. Arch Surg 1928; 17:561–576.
46. Edwards FC, Truelove SC. The course and prognosis of ulcerative colitis. IV. Carcinoma of the colon. Gut 1964; 5:15–22.
47. Welch CE, Hedberg SE. Colonic cancer in ulcerative colitis and idiopathic colonic cancer. JAMA 1965; 191:815–818.
48. Hinton JM. Risk of malignant change in ulcerative colitis. Gut 1966; 7:427–432.
49. Nugent FW, Haggitt RC, Colcher H, Kutteruf GC. Malignant potential of chronic ulcerative colitis. Preliminary report. Gastroenterology 1979; 76:1–5.
50. Ohman U. Colorectal carcinoma in patients with ulcerative colitis. Am J Surg 1982; 144:344–349.