

# Colonoscopy: Its Role in Cancer of the Colon and Rectum\*

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In order to determine the feasibility, yield, and impact of routine total colonoscopy on the management of large-bowel cancer, 157 cancer patients underwent 175 colonoscopic procedures; 13.6 per cent of the cancers had been missed on double-contrast barium enema examination.

Among 92 patients undergoing perioperative colonoscopy, the lesion was reached in 89 per cent and the cecum in 60 per cent; 7.6 per cent demonstrated synchronous cancers, all curable, and all missed on barium-enema examination.

Seventy-eight patients underwent colonoscopy at an average of 3.7 years after treatment of the index cancer; 7.7 per cent demonstrated metachronous cancers, all curable, two-thirds of which were missed on barium-enema examination.

Benign polyps were noted in 62 per cent of the patients studied; 77 per cent of those polyps, 1 cm or greater in size, were missed on barium-enema examination. Polyps were found proximal to the cancer in 60 per cent of the patients with polyps. Approximately 85 per cent of those with multiple cancers demonstrated benign polyps. Preoperative total colonoscopy with periodic postoperative colonoscopy at an interval of three to five years are essential in the reliable detection of synchronous cancers and for the detection of metachronous cancers at an earlier, more favorable stage. [Key words: Cancer, colorectal; Polyps, colorectal; Cancers, multiple; Colonoscopy; Barium enema]

SINCE the first published description of multiple large-bowel cancers by Czerny one century ago,<sup>1</sup> consideration of this more intensely "cancer-prone" patient population has been limited to calculations of the incidence of synchronous or metachronous cancers in large series of patients with colorectal cancer. Thus, it is generally observed that an average of 2.0 to 6.5 per cent of patients will demonstrate additional large-bowel primaries at the time of diagnosis or treatment of the index primary.<sup>2</sup> Similarly, it is understood that roughly 1.5 to 2.5 per cent of those

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surviving after treatment of a first cancer will have one or more new primaries detected at follow-up.<sup>3,4</sup>

Beyond providing feeling for the magnitude of the problem, the literature on multiple cancers has had, until recently, little to contribute to our deeper understanding of the dynamics of colorectal cancer and its early detection or prevention. The data, vocabulary, and very concepts embodied in this literature are derived from investigative methods that are, from our present perspective, incomplete, insensitive, and inanimate. Data obtained from operative or autopsy specimens, rigid sigmoidoscopy, and conventional single-contrast barium radiography are inappropriate representations of an oncogenetic process which occurs to a varying degree over the entire large bowel, and, as implied by the "adenoma-carcinoma model," over an impressive length of time.

The advent of fiberoptic colonoscopy has permitted refined and repetitive surveillance of the entire large bowel. In its sensitivity, such a tool permits the generation of a more reliable data base. Coller *et al.*<sup>5</sup> and Penfold and Renney<sup>6</sup> have demonstrated that aggressive colonoscopy adds a significant yield of small curable cancers undetected by other modalities. Appel,<sup>7</sup> reporting in 1976, observed that in colorectal cancer, perioperative colonoscopy yielded a surprising number of otherwise undetected lesions, including adenomatous polyps with foci of invasive cancer.<sup>7</sup>

The clear message was consistent with the emerging concepts of the polyp-cancer association: the curable cancers are small lesions, and success in early detection of these lesions or their precursors requires refinement of technique of total colonic surveillance. Such is the sentiment of Heald and Bussey<sup>8</sup> in reporting the experience at St. Mark's with synchronous cancers. They note that progress in curability of multiple lesions requires "a fixed routine" of "total colorectal investigation," that leaves "nothing to chance."

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In this spirit, we were encouraged to undertake a study of the impact of aggressive colonoscopy on a group of 157 cancer patients. With an eye to practical application, we sought to refine the data and rework the concepts of multiple large-bowel cancers.

**Methods**

In 1973, the flexible fiberoptic colonoscope was added to our diagnostic and therapeutic armamentarium.<sup>9</sup> Initially, colonoscopy was found most useful in the clarification of questionable radiographic findings and in the refined workup of lower gastrointestinal blood loss. A surprising yield of radio-occult polyps and cancers led us to institute a program of routine perioperative colonoscopy for our patients with large-bowel cancer.

Using the F9A, F9L, and FX-92 colonoscopes (ACMI),\* endoscopy was performed on the second day of a two-day bowel preparation for patients for whom the index primary did not represent a surgical emergency. For those few patients in whom preoperative colonoscopy was not feasible or for others in whom the cecum could not be reached because of technical reasons (chiefly an occlusive primary), colonoscopy was performed within six months after resection. If the index cancer was an adenomatous polyp with invasive cancer deemed curable by snare excision, total colonoscopy was completed either at the same time or soon after the therapeutic scoping. In this manner, 92 cancer patients underwent perioperative colonoscopy in the five-year period studied.

Total colonoscopy was then applied to the routine follow-up of 78 patients at varying intervals after curative resection of the index cancer. This application was seen as a complement to rigid sigmoidoscopy and periodic double-contrast barium-enema examination in the early diagnosis of metachronous neoplastic lesions. Following the observations of Kirsner<sup>10</sup> and Williams *et al.*<sup>11</sup> concerning the average time required for polyp-cancer transition, colonoscopy was performed at four-year intervals after perioperative clearance of polyps.

All colonoscopic procedures were performed in the hospital with fluoroscopy available, both to aid in passage of the scope and to localize otherwise undetected lesions in the event that directed resection would become necessary.

In all instances, small sessile polyps (1 to 4 mm) were fulgurated without biopsy, and their locations were noted. Larger polyps were snare-excised and retrieved for pathologic examination. All elec-

TABLE 1. Sites of 157 Index Cancers

Bowel Segment	Cancers in Segment	Per Cent
Rectum	52	33
Sigmoid colon	50	32
Descending colon	9	6
Splenic flexure	6	4
Transverse colon	10	6
Hepatic flexure	4	3
Ascending colon	19	12
Cecum	7	4

troscopy was performed with precautionary insufflation of carbon dioxide.

In the five-year period of the study, 157 patients underwent 175 colonoscopic procedures without complication.

**Results**

During the five-year period of study, 157 patients with colorectal cancer underwent 175 colonoscopic procedures to determine the place of endoscopy in the preoperative assessment and postoperative management of such patients.

Table 1 demonstrates that the 157 index cancers were distributed along the length of the large bowel in a classic fashion, with fully two-thirds of the lesions found in the rectum and sigmoid.

The spectrum of pathologic stages in the index lesions is documented in Table 2. The cancers are grouped according to the original Dukes' classification with the addition of a Dukes' "D" category to connote lesions resected for palliation in the presence of distant metastases. That only approximately 10 per cent of our study group fell in this category reflects our feeling that routine colonoscopy should generally be reserved for patients with curable lesions.

Approximately 13 per cent of our patients demonstrated foci of invasive adenocarcinoma confined to the head of a pedunculated adenomatous polyp. As such, and in the absence of lymphatic invasion and poor cellular differentiation, they have been treated with endoscopic polypectomy with apparent cure.

TABLE 2. Pathologic Stages of 157 Index Cancers

Dukes' Stage	Number	Per Cent
Focal invasion in polyp	20	12.7
Dukes' A	65	41.4
Dukes' B	35	22.3
Dukes' C	23	14.6
"Dukes' D"	14	8.9

\* American Cystoscope Makers, Inc., Stamford, Connecticut.

TABLE 3. *Diagnostic Reliability of Barium-enema Examination for Index Cancers*

Dukes' Stage	Total Number of Patients	Number Outside Range of Rigid Scope	Number Missed on Barium-enema Examination	Per Cent Missed
Focal invasion in polyp	20	10	6	60.0
Dukes' A	65	45	7	15.6
Dukes' B	35	23	1	4.3
Dukes' C	23	12	0	0
"Dukes' D"	14	13	0	0
Total	157	103	14	13.6

Table 2 is presented chiefly to indicate the more satisfying yield of curable lesions obtained with aggressive colonoscopy.

The superiority of colonoscopy over barium-enema examination in the early diagnosis of colonic cancer is outlined in Table 3. One hundred three of the 157 index cancers were outside the range of conventional rigid sigmoidoscopy. Review of barium enema examinations performed reveals that 14 (13.6 per cent) of these lesions were missed on barium-enema examination. A significant proportion of surgically curable lesions was missed (15.6 per cent Dukes' A and 4.3 per cent Dukes' B), and the majority (60 per cent) of endoscopically curable lesions were missed.

Table 4 demonstrates that approximately half (79) of the 157 patients underwent preoperative colonoscopy alone. An additional 13 underwent preoperative as well as one or more postoperative procedures. Table 5 makes the observation that in the overall group of 92 preoperative procedures, the lesion could be reached approximately 90 per cent of the time. It was often difficult to pass the scope beyond the interposed cancer to the cecum. Total colonoscopy was achieved preoperatively in only 60 per cent of the patients. Correlation with the stage of the cancer demonstrates that greater success in reaching the cecum is achieved in the less advanced Dukes' lesions (approximately 75 per cent) than in the more advanced tumors (approximately 40 per cent).

TABLE 4. *Timing of Colonoscopy*

Timing	Number of Patients	Total Procedures
Preoperative only	79	79
Preoperative and postoperative	13	31
Postoperative only*	65	65
Total	157	175

\* First colonoscopy at average of 3.7 years after treatment of index cancer.

Table 4 also notes that 65 patients underwent their first colonoscopy in the postoperative period, at an average of 3.7 years after treatment of the index cancer (range six months to 22 years). The additional 13 patients who underwent preoperative and postoperative endoscopy make a total of 78 undergoing "metachronous" colonoscopy.

Table 6 tabulates the colonoscopic yield of multiple cancers. In 92 preoperative procedures, seven patients (7.6 per cent) were found to have an additional, synchronous, cancer. In 78 postoperative procedures, six patients (7.7 per cent) demonstrated a total of seven metachronous cancers.

As demonstrated in Table 7, of 14 additional cancers, 13 were out of range of the rigid sigmoidoscope. Eleven of these (85 per cent) were missed on barium-enema examination, requiring colonoscopy for their diagnosis.

Tables 8 and 9 characterize the seven synchronous and seven metachronous cancers, respectively, comparing their sites and pathologic stages with those of the corresponding index cancers. It is noted (Table 8) that four of the seven synchronous cancers were out of range of standard cancer resection planned for the index primary. All of these were eminently curable, and all were missed on barium-enema examination.

Of the seven metachronous cancers (Table 10), all were curable, and the vast majority (86 per cent) appeared in a segment adjacent to that previously resected. Two-thirds of the six extrarectal metachronous cancers were missed on barium-enema examination.

Table 10 demonstrates that 62 per cent of patients with cancer had associated polyps, approximately one-third of which were 1 cm or more in size; 77 per cent of these large polyps were missed on barium-enema examination.

For the 13 patients with multiple cancers, the overall polyp association was approximately 85 per cent; 86 per cent of patients with synchronous cancers and 83 per cent with metachronous cancers had polyps.

TABLE 5. Extent of Colonoscopy in 92 Patients Studied Preoperatively

Dukes' Stage	Total Number of Patients	Colonoscopy to Cancer		Colonoscopy to Cecum	
		Number	Per Cent	Number	Per Cent
Focal invasion in polyp	16	14	88	12	75
Dukes' A	34	33	97	27	79
Dukes' B	17	14	82	7	41
Dukes' C	11	8	73	4	36
"Dukes' D"	14	13	93	5	36
TOTAL	92	82	89	55	60

In order to elucidate polyp-cancer relationships along the length of the large bowel, we scrutinized the 55 patients who underwent preoperative colonoscopy in which the cecum was reached. Thirty (55 per cent) of the patients in this group had associated polyps (Table 11). In relation to the cancer, 40 per cent had polyps in the distal segment alone, and 23 per cent had polyps in the proximal segment alone. Thirty-seven per cent demonstrated polyps both proximal and distal to the lesion. Thus, a total of 60 per cent of cancer patients had polyps proximal or, from the endoscopist's viewpoint, "beyond" the index lesion.

**Discussion**

Although a recognized phenomenon since 1880, the problem of multiple large-bowel cancers had, for a considerable time, been relegated to the status of clinical rarity. Greater attention to the significance of the second cancer is evident in a number of reports appearing in the last decade.

In the early 1970s, Heald and associates<sup>4,8</sup> reviewed the considerable experience at St. Mark's Hospital with multiple cancers of the large bowel. In a comprehensive study of 4884 patients operated upon for colorectal cancer, the authors tabulated 157 cases of synchronous cancer and 83 cases of metachronous cancer, demonstrating at the outset that second cancers are, "by no means, extreme rarities."<sup>8</sup> They observed that, while often "eminently curable," second growths were "astonishingly easy to miss" with the usual modalities of rigid sigmoidoscopy, single-contrast barium radiography, and operative palpation.<sup>8</sup> It was also noted that periodic postoperative surveillance, despite the absence of symptoms, resulted in the detection of metachronous cancers at an earlier, more favorable, stage.<sup>4</sup> The foundation for a rational approach to the diagnosis of multiple cancers was suggested by their advocacy of a "fixed routine" of "total colorectal investigation" that left "nothing to chance."<sup>8</sup>

The past decade has witnessed revolutionary advances both in the understanding of the biology of colorectal cancer and in the sensitivity of methods of investigation.

We have lately seen a convergence of various lines of investigation which have substantiated and led to general acceptance of the "adenoma-carcinoma" model for large-bowel cancer.<sup>12</sup> Striking in this model is the implication that virtually all colorectal cancer develops gradually and progressively from a benign adenomatous precursor with a generous period, often spanning more than a decade, of clinical silence. The model implies that cancer prevention should be defined more practically as the early detection and ablation of benign precursor polyps at some time in the preclinical latent period and periodically thereafter. Technical advances of the past decade have provided the tools for refined large-bowel examination. Aggressive application of double-contrast barium radiography and, particularly, of fiberoptic colonoscopy improves dramatically the ability to demonstrate and intervene in the polyp-cancer progression at an earlier, more favorable stage.

The Malmo technique is a truly refined radiographic modality, as evidenced by a reported sensitivity approaching that of direct inspection at autopsy.<sup>13</sup> It is, for instance, generally claimed that this technique will detect up to 98 per cent of polyps greater than 1 cm (polyps considered to be of significant malignant potential), and 78 per cent of those 1 cm or smaller.<sup>11</sup> In other settings, however, the perform-

TABLE 6. Colonoscopic Yield of Multiple Cancers

Timing	Number of Patients	Number with Second Cancer(s)	Per Cent
Preoperative	92	7	7.6
Postoperative	78	6	7.7

TABLE 7. *Diagnostic Reliability of Barium-enema Examination for Synchronous/Metachronous Cancers*

Dukes' Stage	Total Cancers	Outside Range of Rigid Scope	Cancers Missed on Barium-enema Examination	Per Cent Missed
Focal invasion in polyp	6	5	5	100
Dukes' A	7	7	5	71
Dukes' B	1	1	1	100
TOTAL	14	13	11	85

ance of the double-contrast barium-enema examination has been less encouraging; one of us (FJT) has previously reported only 46 per cent of polyps 1 cm or larger detected radiographically.<sup>14</sup> When associated with colorectal cancers, as our study shows, fully 77 per cent of polyps 1 cm or more in size are missed.

Such statistics may reflect, to some degree, inadequate patient preparation, inattention to technical detail, or simple observer error. Nevertheless, the implication is that, under average circumstances, the barium-enema examination is inadequate in the reliable detection of colonic polyps.

When we turn from polyps to cancers, our current series reinforces our lack of confidence in the barium-enema examination. While detecting all Dukes' C and "D" primaries, large-bowel radiography was less sensitive for the more curable lesions, missing 4.3 per cent of Dukes' B and 15.6 per cent of Dukes' A cancers. Most importantly, 60 per cent of cancers presenting as foci of invasion in polyps, measuring 1 to 3 cm in size, would have been missed without colonoscopy. More significant than the overall failure rate of 13.6 per cent is the observation that the double-contrast barium-enema examination is inadequate in the reliable detection of curable cancer.

TABLE 8. *Characteristics of Synchronous Cancers*

Index Cancer		Second Cancer	
Site	Dukes' Stage	Site	Dukes' Stage
Sigmoid	Focal invasion in polyp	Descending	Focal invasion in polyp
Sigmoid	A	Sigmoid	A
Rectum	A	Ascending	A
Sigmoid	A	Transverse	A
Hepatic	B	Ascending	Focal invasion in polyp
Ascending	B	Ascending	Focal invasion in polyp
Sigmoid	"D"	Transverse	B

Coller and associates,<sup>5</sup> in 1975, reported similar dissatisfaction with the barium-enema examination as a tool for early intervention in the polyp-cancer progression. In that series, 110 patients with a barium-enema diagnosis of a solitary polyp underwent total colonoscopy; 56 per cent of these patients demonstrated a total of 128 additional, radio-occult lesions. Six missed lesions were cancers ranging in size from 0.6 to 3.5 cm.

Fortunately, colonoscopy has made highly refined colonic inspection readily available in most communities. When applied to the problem of the particular "cancer-proneness" of the multiple-cancer patient, the endoscope holds a similar edge over the barium enema. Appel,<sup>7</sup> reporting in 1976, reviewed the barium-enema findings of 14 patients undergoing resection for colorectal cancer. None showed synchronous lesions radiographically, but four of seven examined with the colonoscope preoperatively demonstrated benign polyps. Additionally, one of these four patients demonstrated a missed synchronous cancer. All 14 patients underwent one or more colonoscopic procedures at an average of 1.8 years after surgery. Ten revealed a total of 19 polyps (one, a villoglandular lesion with carcinoma *in situ*). With 85 per cent of our second cancers missed on barium-enema examination, we find ourselves in agreement with Appel, who commented that "questions concerning the multiple nature of colonic neoplasms" are "better answered with the aid of colonoscopy."<sup>7</sup>

**I. Colonoscopic Yield of Synchronous Cancers:** More than half of our patients underwent colonoscopy preoperatively, at which time the lesion was reached in 89 per cent and the cecum in from 36 to 79 per cent, depending on the pathologic stage of the cancer; 7.6 per cent of these patients had synchronous cancers. In no instance was the second cancer of a more advanced stage than the index cancer. All second lesions were curable, but all were missed on the preoperative barium-enema examination. It is interesting that 71 per cent of these lesions were out of typical range of the 65-cm flexible fiberoptic sigmoidoscope; 57 per cent were out of range of the

TABLE 9. Characteristics of Metachronous Cancers

Index Cancer		Second Cancer		Interval (Years)
Site	Dukes' Stage	Site	Dukes' Stage	
Sigmoid	Focal invasion in polyp	Descending	Focal invasion in polyp	7
Rectum	Focal invasion in polyp	Sigmoid	A	8
Sigmoid	Focal invasion in polyp*	Descending	A	4
Sigmoid	A	Rectum	Focal invasion in polyp	2
Sigmoid	C*	Descending	Focal invasion in polyp	1
Cecum	C	Transverse	A	4
		Sigmoid	A	

\* Had additional focal cancer in polyp.

standard resection for the index cancer. Without preoperative colonoscopy, three of seven synchronous cancers would have gone undetected, and a synchronous rate of 4/92 or 4.4 per cent would have been calculated. Colonoscopy added an additional 3/92 or 3.2 per cent to the synchronous rate and certainly required alteration of the surgical approach.

The data demonstrate that perioperative colonoscopy is feasible and necessary to avoid the tragedy of the "missed synchronous lesion" which, as noted by Heald and associates,<sup>8</sup> will frequently surface, years later, in the metachronous column.

**II. Colonoscopic Yield of Metachronous Cancers:** Slightly less than half of our patients underwent follow-up colonoscopy an average of 3.7 years after initial treatment; 7.7 per cent had one or more metachronous cancers. All were curable, and two-thirds were missed by barium-enema examination.

In all instances, a second lesion appeared in a colonic segment adjacent to that removed in treating the index cancer. Eighty-three per cent of the metachronous cancers followed resection of a rectal or sigmoid primary and, therefore, appeared in the sigmoid or descending colon in range of the flexible fibersigmoidoscope. These findings are at odds with those of Spratt<sup>15</sup> and Copeland *et al.*,<sup>3</sup> who noted a more even distribution of metachronous lesions along the large bowel, despite a distribution of index primaries similar to our own. If, however, the distal large bowel is a site of particularly intense carcinogenesis, it seems reasonable that a later cancer would favor the distal bowel as well.

In the context of the polyp-cancer model, a metachronous cancer may be viewed as the end stage of evolution from a benign polyp which occupied the same site for a considerable period of time. Reliable detection and ablation of this silent antecedent should eliminate the tragedy of the patient who, having survived a first cancer, succumbs to a second lesion a

decade later. Colonoscopy performed postoperatively at an interval of three to five years should result in extinction of the metachronous cancer.

**III. Polyp-Cancer Relationships in Multiple Cancers:** One of the earliest observations suggesting a polyp-cancer sequence was the finding, in autopsy and operative specimens, of benign polyps in association with colorectal cancers. Specimens containing multiple cancers demonstrated a subgroup in which a more intense neoplastic process was at work. As an example, Copeland and associates<sup>3</sup> noted that 23 per cent of 1084 cancer patients had associated polyps, while in the multiple cancer group, the association rose to 60 per cent. Heald and associates<sup>8,16</sup> demonstrated polyps in 75 per cent of patients with synchronous cancers and 60 per cent of those with metachronous cancers. Our finding of polyps in 62 per cent of the overall cancer group and approximately 85 per cent of the multiple cancer groups demonstrates that colonoscopy confirms and extends the polyp-cancer association.

TABLE 10. Polyp-Cancer Associations

	Number of Patients	Per Cent
I. 157 index patients		
Patients with polyps over 1 cm	30	19
Patients with polyps over 4 mm	81	52
Overall patients with polyps	97	62
II. 7 patients with synchronous cancer		
Overall patients with polyps	6	86
III. 6 patients with metachronous cancer		
Overall patients with polyps	5	83

TABLE 11. *Polyp-Cancer Relationships\**

	Number	Per Cent
Distal to cancer only	12	40
Proximal and distal to cancer	11	37
Proximal to cancer only	7	23

\* Among 55 patients undergoing preoperative colonoscopy to cecum, 30 (55 per cent) with associated polyps.

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### IV. The Need for Total Colonoscopy in Cancer:

If, as we believe, the prevention of metachronous cancers requires the detection and ablation of synchronous or metachronous polyps, it is important to note that 60 per cent of cancer patients with polyps harbor these lesions proximal to the cancer. This is the case even if colonoscopy to the cancer is negative for polyps in the distal segment.

The polyp-cancer relationships observed support the concept of colorectal cancer as a dynamic, evolutionary process, occurring, with variable intensity, along the entire length of the large bowel. Our experience with multiple cancers seems to define a subgroup that is more profoundly "neoplasia-prone."

We conclude, as noted by Wolff *et al.*,<sup>17</sup> that experience with endoscopy makes "radiologic guessing games passé." The reliability and yield of aggressive total colonoscopy permit a refined diagnostic, therapeutic, and, perhaps, prophylactic approach to single and multiple colorectal cancers and their benign precursors—an approach leaving nothing to chance. The dividend is a better understanding of the evolutionary nature of colorectal cancer.