Cancer of the Colon

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THE INCIDENCE of cancer of the colon varies greatly throughout the world, probably because of differences in environment, living habits and geographical conditions. The disease is particularly frequent in Scotland, Canada, the United States and Denmark, but is uncommon in Israel, Italy, Finland, Chile and Japan.

Survival rates for cancer of the colon have improved steadily, particularly in the United States, where the incidence has remained constant although the incidence of gastric cancer is decreasing. Nevertheless, an examination of overall data permits no room for complacency, as 70,000 patients, more than half of whom die, develop colonic cancer each year. In spite of the favorable prognosis of surgically treated localized cancer, three of every ten patients expected to survive will die within five years of diagnosis.[4]

Cancer of the colon is the foremost cause of death from all types of cancer in the United States. The mortality increases steadily with advancing age, especially among city dwellers. The risk for cancer of the colon seems to be conditioned by the most recent residence rather than by ecologic factors existing in the place of birth, prior to migration. Cancer of the colon seems to be unrelated to social and familial factors, with the exception of familial polyposis. Although intriguing, these and other epidemiologic factors are as yet of no practical importance in the control of cancer of the colon. Surgery is still the principal form of treatment, and until the causes of cancer of the colon are determined and more specific treatment is designed, every effort should be made to improve the results of surgical management.

The total experience in the surgical management of cancer of the colon at the University of California Hospitals between 1913 and 1965 was evaluated by computer. The Tumor Registry staff transferred this information to data-processing cards and computers were used for extensive analysis. Unfortunately, early records were not as complete as more recent ones, but certain basic information, such as age, race, sex, localization of the tumor, pathologic findings and survival data, was available in all cases.

There is no significant controversy at present concerning the surgical management of cancer of the colon. The choice of surgical procedure is based upon such factors as the presence or absence of obstruction, local extension of the disease, and distant metastases.

Correction of nutritional deficiencies, proper preoperative and postoperative care, simplified methods of bowel preparation

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and improved anesthesia have greatly decreased the risk of primary resection in carefully selected patients. Postoperative sepsis and hemorrhage are no longer a problem. There is still some controversy as to whether resection or colostomy alone should be performed for cases that are obviously not curable because of distant metastases. It has been stated that colostomy alone does very little for the patient unless it relieves intestinal obstruction and it is assumed that colostomy alone usually does not prolong life.

Resection of the lesion is desirable whenever feasible even in the presence of metastases, but excellent clinical judgment is required in the selection of patients for this procedure. One-stage operations are preferable, particularly with modern technics of bowel preparation. There is evidence to suggest that older patients may be able to tolerate one major procedure better than several lesser ones. The treatment of choice for carcinoma of the right colon, with or without obstruction, is primary resection when feasible. Primary resection has also been used to treat carcinoma of the left colon without obstruction. In this series, proximal decompressing colostomy or cecostomy followed by second-stage resection was used in patients with severe obstruction. When minor obstruction was present without significant dilatation of the colon, or edema and friability of the intestinal wall, primary resection and anastomosis were carried out with safety.

In patients with metastases and obstruction, resection should not be radical. Resection in the presence of obstruction is not always associated with increased mortality and frequently decreases morbidity.

Age and Sex Incidence. Although cancer of the colon is often thought to occur primarily in men, there were 519 women and 456 men in this series; this preponderance of women has been reported in other series.[9, 29] The median age for the entire group was 60 years (61.5 years for men and 59 years for women). The youngest man was 24 years old and the youngest woman was 14 years old. The oldest man was 93 and the oldest woman was 90. None were in the first decade of life. Three patients, all women, were in the second decade of life. Three patients were older than 90 years. The highest incidence was in the sixth decade; it was slightly lower in the fifth, and considerably lower in the seventh decade.

Most of the patients were Caucasian. The number of Oriental and Negro patients was so small that statistical analysis was unwarranted.

Site, Incidence and Histology. Carcinoma of the rectum and rectosigmoid lesions that required an abdominoperineal resection have been excluded from this series and will be reported in a later study.

The distribution of tumors of the colon is shown in Figure 1. It was similar to that of other reported series.[24] The sigmoid colon was the most common site of cancer, both in men and women (44.5%), and the cecum, transverse colon and ascending colon were the next most frequent sites. The preponderance of lesions in the sigmoid reflects the frequency with which carcinoma of the colon can be diagnosed by sigmoidoscopy.

The clinical behavior of tumors in these various sites and the problems in surgical technic justify the division of these lesions into three large classes in order to facilitate analytical and statistical study of end results: *right colon* included appendix, cecum, ascending colon and hepatic flexure; *middle colon* included the transverse colon and splenic flexure; *left colon* included the descending colon and sigmoid. The rectosigmoid lesions that were high enough for primary anterior resection and anastomosis were included in the left colon group (Fig. 1). The more numerous low-lying rectosigmoid lesions treated by abdominoperineal resection were included in the group of rectal lesions that will be reported later.

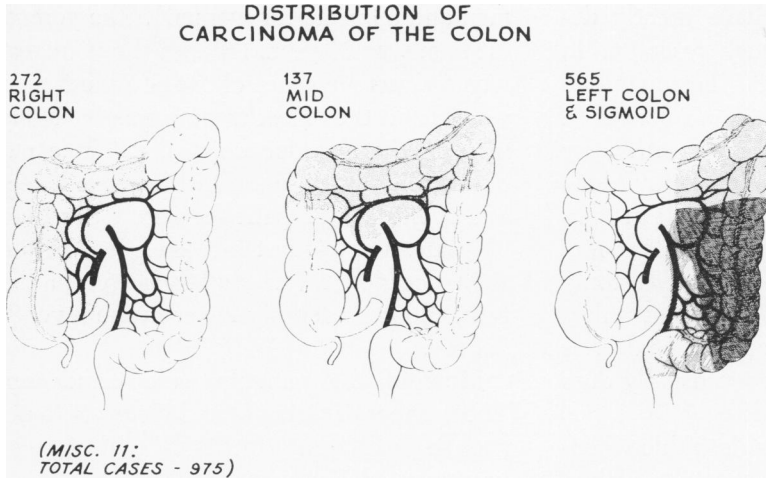

FIGURE 1.

The predominant histologic type was adenocarcinoma. "Polypoid carcinoma" was so designated in 37 patients. Colloid or mucoid carcinoma was found in 34 cases.

The growth was "localized" to the superficial layers of the bowel wall in 466 specimens (48%); it invaded the muscular layers to a varying extent ("transmural") in 382 specimens (38%). The regional lymph nodes were free of metastases in 315 of 466 patients with localized disease, but were positive for metastases in 172 patients with transmural disease (Table 1). The influence of the basic biological propensity of the tumor is evidenced by the 196 instances in which nodes were negative despite transmural spread. Thus, the lymph nodes were negative in 511 cases and positive in 323. In 76 cases the histological status of the lymph nodes could not be determined with acceptable accuracy from the records.

Surgical Management. A better understanding of the role of proximal decompressing colostomy in bowel obstruction, the improvement of anastomotic technics and preoperative bowel preparation with antibiotics have made it possible to abandon the exteriorization operation practiced until the late 1930's. Instead a primary resection was performed in which removal of regional lymphatics and lymph nodes was an integral part of the operation.

TABLE 1. *Extent of Spread of the Disease*

All Cases	Nodes Positive	Nodes Negative	Undetermined	Total
Localized	151	315	0	466
Transmural	172	196	14	382
Undetermined	26	39	62	127
Total	349	550	76	975

The preferred surgical procedure at present is wide radical resection of the primary tumor, with sufficient proximal and distal bowel and of the regional lymphatics *en bloc* as indicated in Figure 1. The extent of resection was of course modified when performed as a palliative operation in the presence of metastases.

Therapeutic resections were performed in 712 patients, an operability rate "for cure" of 73%. In 172 patients a more limited resection was done or colostomy alone was performed for palliation as gross disease was noted beyond the field of operation (17.5%). Laparotomy was performed in 91 patients in whom neither resection nor colostomy appeared to offer any chance of palliation (Table 2). There has been a progressive increase in the number of therapeutic resections for each decade, reaching 82.6% in the last decade (Table 3).

In patients with distant metastases, in

TABLE 2. *Management of Carcinoma of the Colon*

Management	Number of Cases	Males	Females
Inoperable	87	45	42
Therapeutic	712	323	389
Palliative	172	85	87
Total*	975	456	519
* Undetermined	4	3	1

our experience, morbidity is less when the lesion is resected rather than when a colostomy alone is performed. Diffuse peritoneal seeding has been the principal contraindication to any palliative procedure. This parallels the experience of others.[11]

End Results (Survival). End results were measured in terms of five-year survival rates calculated from the time of operation by the actuarial method. This permits calculation of survival rates for intermediate periods. In evaluating the results of surgical therapy it is important to distinguish between procedures undertaken for *cure* and the more limited operations performed only for *palliation* because of residual tumor.

It would be of value to give survival rates for patients free of recurrence for certain determinate periods, but accurate accumulation of such information proved to be difficult and occasionally impossible. Of necessity, survival figures refer only to patients still alive after a certain period, regardless of whether clinically detectable recurrence was present.

Survival According to Treatment. Contrary to surveys that report lower survival rates,[9, 20] 67.4% of patients were alive a year after operation, 50.7% lived for three

TABLE 3. *Therapeutic Resections*

1913–1924	37.9%
1925–1934	41.4%
1935–1944	71.9%
1945–1954	74.0%
1955–1965	82.6%

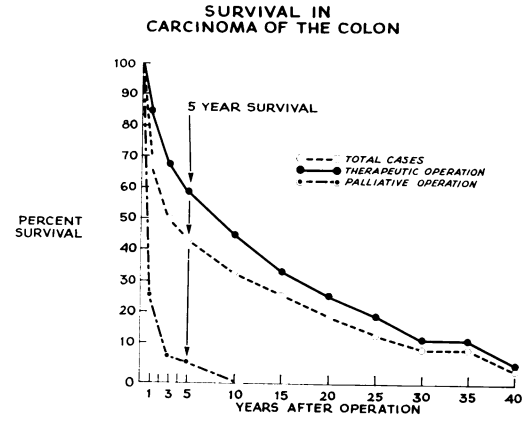

FIGURE 2.

years and 43.5% for five years, regardless of age, sex or scope of therapy (Fig. 2). Regardless of the extent of the disease, the five-year survival for patients who underwent therapeutic resections was 58.8%, which is in sharp contrast to the survival rate of 3.1% for patients who had palliative operations. A significant proportion of patients died of carcinoma of the colon even after the five-year period.

Our experience indicates that although the morbidity is significantly decreased when patients with "incurable" disease undergo palliative resections instead of colostomy alone, the length of survival is not significantly better than in the group of patients undergoing laparotomy alone in which the five-year-survival rate is only 2.2%. The patients may not live longer, but they may live better (Table 4).

Age and Sex. The prognosis for cancer of the colon in young patients is generally considered poor, presumably because of the more rapid growth and greater aggressiveness of the tumor.

In this series the number of patients under 40 years of age was relatively small,

TABLE 4. *Survival According to Procedure*

	1 Year	3 Years	5 Years
Palliative procedures	92.5%	6.2%	3.0%
Laparotomy only	11.4%	3.4%	2.2%

but the five-year over-all survival rate was 35.2% for men and 51.1% for women.

It is generally assumed that the survival rate for cancer of the colon is highest in patients in the fifth and sixth decades of life.[27] In our series, however, there appeared to be no significant correlation between age and survival if men between the ages of 40 and 49 were excluded. This group had the lowest survival rate, 27%. Survival rates were otherwise uniformly distributed throughout the various age groups, particularly among women (Fig. 3). The over-all five-year survival was 39.1% for men and 47.3% for women, regardless of age, surgical procedure, or extent of disease. Women of all ages uniformly had higher survival rates. Only 19 women were in the eighth and ninth decades of life, a number which is too small to be statistically significant.

Relation between Location of the Tumor and Survival. Lesions of the cecum and ascending colon frequently produce few symptoms which often lead to delay in diagnosis and treatment. Yet survival rates after therapeutic resection of the right colon are uniformly highest (61.7%) regardless of the extent of local involvement by tumor. The next highest survival rates are among patients with lesions in the left colon (58.6%) and transverse colon (52.8%) (Fig. 4). The high survival rate

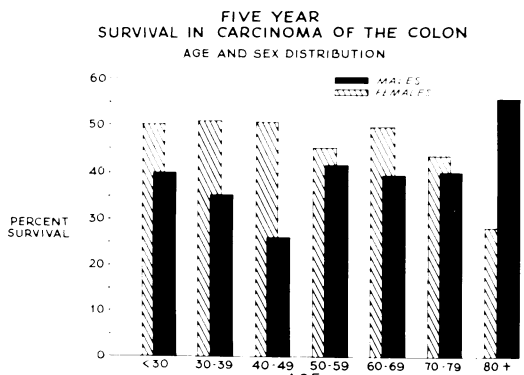

FIGURE 3.

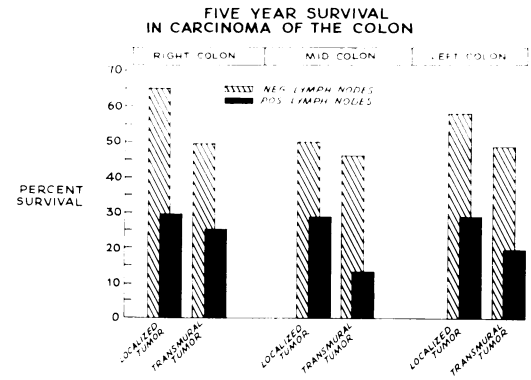

FIGURE 4.

after right-colon operations is similar to that reported in a much smaller series by Botsford[2] from the Peter Bent Brigham Hospital. It is interesting that over-all survival in that study was 43.3%, and in the present study was 43.5%. It would appear that variations in histologic aspects of the lesion may be more significant than its precise location in the colon.

Microscopic Involvement and Lymph Nodes. It is impossible to evaluate the role of early diagnosis in the management of colonic carcinoma by determining the time between onset of symptoms and operation because of the unavoidable inaccuracies in reporting clinical symptomatology. Yet until the various factors affecting the host-tumor relationship are well understood, earlier diagnosis and adequate operation offer the most hope for improving survival.

The most important single factor influencing survival was the presence or absence of metastases to the lymph nodes. This factor was particularly important in the period of 3 to 15 years following operation regardless of the extent of involvement of the intestinal wall. The second most important factor in survival was the extent of involvement of the musculature of the bowel and its peritoneal covering (Fig. 5, 6).

Multiple Primary Malignancies. The gastrointestinal tract is frequently the site of multiple cancers and the colon is the

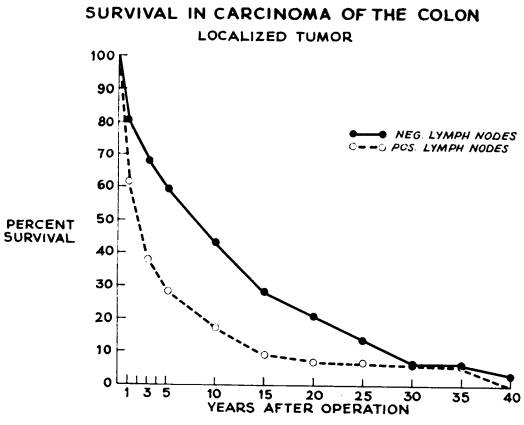

FIGURE 5.

most commonly affected segment. It is still undecided whether a patient who has developed one cancer has a certain degree of immunity against the development of another,[6, 14] whether he is more apt to develop another cancer,[13, 15] or whether the risk of developing a second cancer is neither increased nor decreased.[16]

Synchronous carcinomas occur more frequently than metachronous malignant growths in the colon. A patient with six distinct synchronous lesions has been reported.[18]

Metachronous cancers may appear from 1 to 25 years following removal of the first cancer. Although 60% of multiple carcinomas appear in the same or adjacent segment of colon, they may occur in disparate portions of the colon with different lymph-bearing areas, necessitating subtotal colectomy and ileoproctostomy when the rectum is free of disease.[17]

In our series of 975 patients, the rate of synchronous and metachronous carcinomas was 11% (113 patients), which is among the highest reported (Table 5).

The survival rates for patients with multiple cancers of the colon paralleled those of patients with single colonic growths (Fig. 7). Thus, the five-year survival was 43.5% and 39.0%, respectively, for the two groups of patients, which supports the belief that survival is a factor of individual lesions rather than of multiplicity of growths. Peltokallio[20] reports a five-year survival rate of 40.0% in his group of patients with multiple carcinomas of the colon. The rate of incidence of multiple colonic lesions (3 to 11%) should not be used as an argument for radical subtotal colectomy *for all colonic lesions,* particularly because more than half the cancers occurring after segmental colectomy are found in the rectum. Moreover, the risk of the second carcinoma is no greater than that of the first. Nevertheless, the frequency with which synchronous and metachronous lesions occur and their favorable prognosis necessitate a thorough diagnosis, meticulous palpation of the entire colon at the time of operation, and a long period of follow up including sigmoidoscopic and

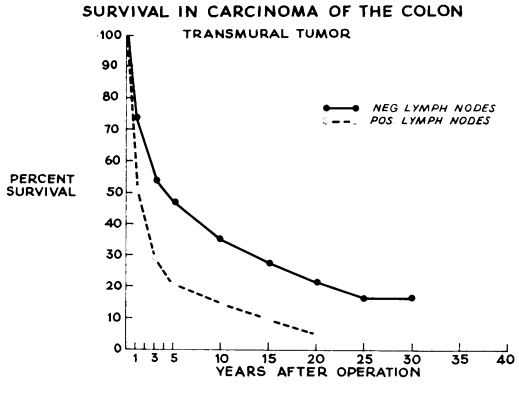

FIGURE 6.

TABLE 5. *Incidence of Multiple Colonic and Rectal Cancers*

Reported by	% of Cases
Peltokallio	3.0
Glenn and McSherry	5.8
Bacon and Tavenner	7.5
dePeyster and Gilchrist	5.5
Sokol and Smith	11.0
C. Naunton-Morgan	3.6
Ginzburg and Dreiling	8.3
Brindley and Rice	4.7
Welch and Giddings	2.5
Mider	3.0

radiologic examinations, particularly in patients with adenomatous polyps.

"Polypoid" and Mucoid Carcinoma. Although the histologic nature and degree of malignancy are repeatedly reported as important for the prognosis of carcinoma of the colon, they were not considered in this series because the degree of anaplasia for each tumor was not uniformly reported. Nevertheless, two histologic types of colonic carcinoma deserve special mention.

"Polypoid" carcinoma was reported in 37 patients. Figure 8 illustrates the over-all survival rates for various intervals compared with survival for the group at large. The five-year survival rate was 81.5%, irrespective of sex, stage of the disease, or age. These lesions had the most favorable prognosis of the entire group. Conversely, mucoid growths generally have a poor prognosis. In this group of 34 patients the five-year survival was 23.0%, similar to that in other reported series (Fig. 8).

Hepatic Involvement. Hepatic involvement does not always mean a hopeless situation. Our experience suggests that palliative resections are justifiable in patients with metastases to the liver, provided there are no other contraindications to resection, such as massive hepatic involvement, diffuse peritoneal carcinomatosis, or extreme debilitation. The three-year survival rate was 11.5% and the five-year survival rate

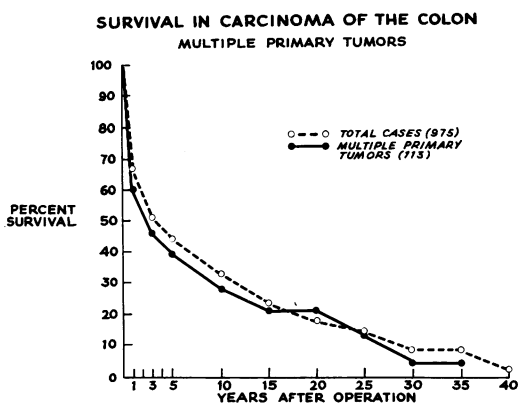

FIGURE 7.

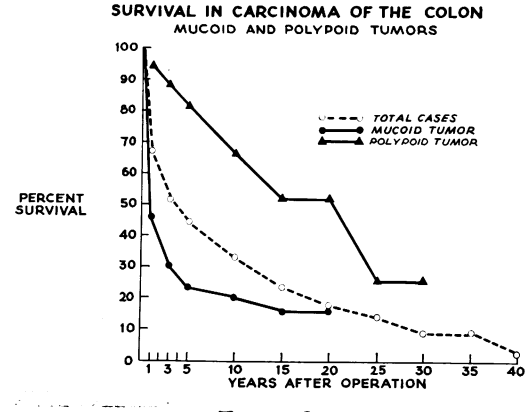

FIGURE 8.

was 5% in this group of 74 patients. As stated before, in carefully selected patients with metastatic disease extending beyond the field of operation, judicious palliative resection of the primary growth reduces the morbidity associated with the advanced stages of the disease. Survivals for five, seven, and even ten years or more have been reported after colostomy alone.

New Approaches in Surgery of Cancer of the Colon and Rectum

Preoperative Irradiation. The advent of supervoltage irradiation has changed many traditional concepts of cancer therapy. Only a few years ago it was generally accepted that radiation had little to offer in the treatment of colonic and rectal cancer. The retrospective studies of Stearns[26] and Ruff[23] first called attention to the probability that adjuvant irradiation might increase survival in carcinomas of the colon and rectum. In 1959, Dunphy, Patterson and Legg[7] called attention to the occasional dramatic resolution of inoperable carcinomas of the rectum following limited irradiation. On the basis of these observations an ongoing study was initiated in the Department of Surgery at the University of Oregon Medical School and a preliminary experience was reported in 1964.[8]

At the present time, more than 50 patients have been placed in the study and

the following facts have emerged: 1) in all but one instance, there was a marked reduction in the size of the tumor. This reduction began under therapy and continued for several weeks following completion of therapy. In 10% of cases, there has been complete disappearance of the tumor at the time of surgical resection; 2) in about an equal number of cases what appeared to be completely inoperable tumors were converted to an operable state; 3) despite dosages as high as 5,000 to 6,000 r, in all there were no serious reactions to irradiation. Skin reaction was a minimal erythema, and in only one patient was diarrhea a problem. This was directly related to partial obstruction which was present prior to irradiation. Mucosal reaction to the irradiation has been much more intense than that of skin, and the stoma of a colostomy should be placed outside this field of irradiation; 4) many patients received such marked amelioration of symptoms that it was difficult to persuade them to undergo operation; 5) with properly delivered irradiation no technical difficulties were encountered at operation, and in many instances the dissection seemed to be facilitated; 6) although it is too early to discuss long-term survival, it is of significance that there have been only two instances of local recurrence in the 50 cases, although "all comers," including those regarded as totally inoperable, were included.

There are several randomized studies of the place of preoperative irradiation in progress and it would appear that the findings of Quan,[21] Ruff [23] and their coworkers will be confirmed. Nevertheless, it is too early to make recommendations regarding general adoption of preoperative irradiation.

One fact stands out clearly, however, and that is that large, bulky tumors that appear to be either locally inoperable or of borderline operability should be subjected to preoperative irradiation. In selected cases at the University of California Medical Center at San Francisco we have also found that large, unfavorable rectal tumors regress considerably after irradiation, and in one of our cases disappeared completely.

Adjuvant Chemotherapy. Although the use of adjuvant chemotherapy at the time of operation to destroy innervascular tumor cells was an attractive hypothesis, it has not turned out to be fruitful in practice. To date, no agent has been sufficiently effective to alter survival rates in carcinoma of the colon and rectum. The most recent experience with intraluminal visceral perfusion of colonic carcinoma as recommended by Rousselot [22] may alter this opinion, but sufficient data are not yet available for general adoption.

Summary

The total experience with 975 patients treated for carcinoma of the colon at the University of California Medical Center between 1913 and 1965 has been reported.

In this group of patients, 712 (73%) underwent curative resections. Palliative operations were performed in 172 (17.5%) and 91 patients (9.3%) had laparotomy alone.

The five-year survival rate was 43.5% for all patients; 58.7% for patients undergoing therapeutic resections, and 3.1% for patients who had palliative procedures only.

The role of age, sex, location of the tumor, extent of invasion, lymph node involvement, multiplicity of cancers, histologic pattern and liver metastases is reported.

Our experience with 50 cases of carcinoma of the colon and rectum treated with preoperative irradiation at the University of Oregon Medical School Hospitals is summarized.

Acknowledgment

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Discussion

Dr. Benjamin F. Byrd, Jr. (Nashville): Dr. Mahorner, I rise principally to speak about the most interesting presentation of the Drs. Donald. But maybe you will also get a little insight into where Dr. Herrington got his figures when I tell you that while I was interested in looking over Dr. Donald's manuscript, I thought its subject was well known to all of us; and surely with the increasing diagnostic acumen of our radiologists, this does not present an immediate problem today.

In the 30 days prior to the 25th of November, there were five patients admitted to the 150-bed surgical service of St. Thomas Hospital who had had one or more negative barium enemas with a carcinoma of the colon present; five patients in 30 days. This accounts for some of the unplanned