

THE PROGNOSTIC SIGNIFICANCE OF DIRECT EXTENSION OF CARCINOMA OF THE COLON AND RECTUM*

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THE PROGNOSIS of a patient with cancer of the large bowel is dependent upon the progress made by that lesion up to the time of the operation. Very important in evaluating the outlook for the lesion is its character and extent of its spread. This spread may occur through the lymphatics, by direct extension and by the blood stream.

The adverse influence on prognosis of invasion of lymph nodes by carcinoma has been stressed repeatedly. A study of cancers of the rectum and low sigmoid made in our clinic² demonstrated that of those patients with involvement of the lymph nodes, 61 per cent survived *less* than five years, and only 29 per cent lived more than five years. Welch and Giddings⁷ reported upon 1,876 cases of carcinoma of the large bowel seen at the Massachusetts General Hospital from 1937 through 1944. On the basis of operative survival for cure, 55 per cent of those without nodal involvement lived five years, but this figure was reduced to 26 per cent if lymph nodes were involved. Coller, *et al.*,¹ and Gilchrist and David⁴ substantiate these findings. Grinnell⁵ reported a similar drop in five year survival concomitant with venous invasion, and also showed that vascular involvement was infrequent until the muscle layers of the bowel had been penetrated. The prognostic significance of direct extension by

cancer cells has been less emphasized, but the important influence of direct extension upon prognosis has been well documented.

Cuthbert E. Dukes,³ in 1932, carried out a study of direct extension of rectal carcinoma in its relation to prognosis. In this study he proposed a classification based upon his observations in 215 cases of cancer of the rectum, but he stated that the grouping might well be utilized for cancer of any part of the intestinal tract. Three categories were established. Type A cases were those in which the carcinoma was limited to the rectal wall with no extension to lymph nodes or adjacent tissues. Type B cases were those in which the lesion had spread by direct continuity to the surrounding tissues but had not involved the lymph nodes. Finally, Type C cases were those which presented, in addition to direct penetration of the wall, metastases in regional lymph nodes. This study did not attract the attention it deserved, since in many other subsequent investigations emphasis was placed upon lymphatic and/or blood-vascular involvement as major influences in prognosis.

In 1949, Kirklin, Dockerty, and Waugh⁶ suggested a modification of Dukes' classification which we consider helpful. Their criteria were as follows: Type A, lesions limited to the mucosa; Type B₁, lesions extending into the muscularis propria, but not penetrating it, with negative nodes; Type B₂, lesions penetrating the muscularis propria, with negative nodes; and, fi-

* Presented before the Southern Surgical Association, Hot Springs, Virginia, December 10, 1953.

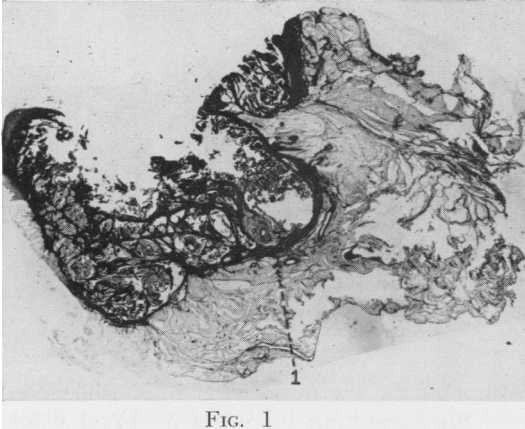


FIG. 1

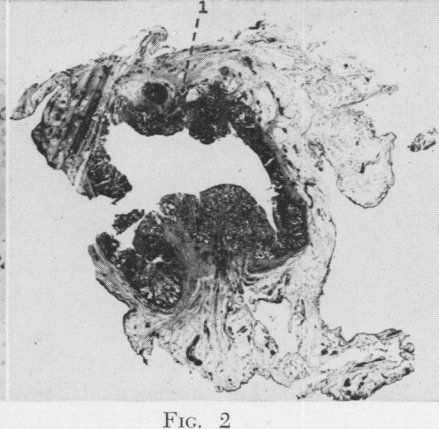


FIG. 2

FIG. 1. Complete circumferential involvement of the sigmoid colon by well differentiated papilliferous adenocarcinoma mucosum, which has invaded the adjacent mesentery by direct continuity (1). No involved lymph nodes were found (Dukes' Class B₂).

FIG. 2. Involvement of the entire circumference of the cecum by moderately well differentiated adenocarcinoma which was in part mucin forming. Invasion of the adjacent adipose tissue by direct continuity (1). No involved lymph nodes were found (Dukes' Class B₂).

nally, Type C, comprising lesions of either Type B₁ or B₂, with involvement of lymph nodes. This modified Dukes' classification has been utilized in our study, but with the additional separation of Type C into C₁ (limited to the wall with positive nodes), and C₂ (through all layers with positive nodes).

Careful gross appraisal of operative specimens is usually neglected. The surgeon, having removed the involved organ or lesion, passes it on to the pathologist and then awaits the report wherein may lie his prognostic yardstick. A few moments spent examining the fresh, unfixed specimen affords considerable information regarding the degree of extension. Indeed, one is often able to delineate the advancing neoplastic border and thereby gain some insight into the patient's prognosis. If extension through all coats of the bowel is apparent, one must then admit the probable existence of grossly undetectable neoplastic extension into the surrounding tissue. Carcinomatous invasion of lymph nodes is likewise often undiscernible when studied in the gross, but a study of the gross specimen by the surgeon or the path-

TABLE I. Analysis of Specimens of Cancer of the Colon and Rectum Removed From 850 Patients 1940-1950, According to Modified Dukes' Classification.

Grade A.....	7 Cases	0.82%
Grade B ₁	101 Cases	11.88%
Grade B ₂	341 Cases	40.12%
Grade C.....	401 Cases	47.18%
850 Cases		

ologist frequently affords vital information, especially concerning the future.

A follow-up study² carried out in this clinic on patients with cancer of the rectum and rectosigmoid from five to 15 years after operation demonstrated that recurrence after five years following combined abdomoperineal resection for cancer of the rectum was always local. These patients developed perineal recurrence three to 12 years following operation, indicating that cancer residue might remain quiescent locally for years after operation removal of the primary lesion. It should be emphasized that these patients were not those found at operation to have hepatic involvement or technically unremovable lymph nodes. The patients with these advanced lesions died

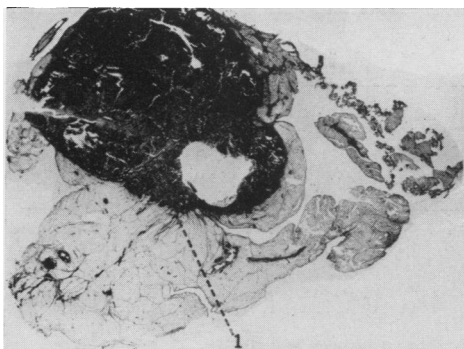


FIG. 3



FIG. 4

FIG. 3. Complete circumferential involvement of the transverse colon by a moderately well differentiated papilliferous adenocarcinoma which has infiltrated the mesentery by direct extension (1). No metastases were found in lymph nodes (Dukes' Class B₂).

FIG. 4. Moderately well differentiated papilliferous adenocarcinoma involving over one-half the circumference of the sigmoid colon and infiltrating the mesentery by direct continuity (1). The neoplasm protrudes as a fungating mass into the lumen which is reduced at this level to a narrow crescent. Lymphogenous metastases were not found in the lymph nodes, but the node nearer the colon in the figure has been involved from without by direct extension (Dukes' Class C).

of their disease with its extension before the development of late local recurrence. The former group, though small, offered interesting points for speculation. Were these locally recurrent neoplasms a product of grossly undetected lymph nodes? We thought a more plausible explanation was the occurrence of cancer cells in pericolic or perirectal fat as a result of direct extension. This theory is substantiated in two ways by this study: (1) Actual nests of cancer cells were occasionally detectable in the included "life-sized" sections. These nests were found in adipose tissue exclusive of vessels and nodes. (2) The survival curve for patients with extension through the wall without positive lymph nodes, B₂, showed a very slight but even drop from the second to the fifth years. This would suggest a small but steady mortality occurring after cases with grossly unremovable neoplasm had succumbed (Fig. 7).

MATERIAL AND METHODS

The material studied included only those specimens removed at operation and later examined by our pathologists. Such cases

TABLE II. *Distribution of Lesions According to Modified Dukes' Classification in Specimens From Patients Operated Upon in Years 1940 Through 1944.*

A.....	1 Case	0.28%
B ₁	48 Cases	13.64%
B ₂	164 Cases	46.59%
C ₁	14 Cases	3.98%
C ₂	125 Cases	35.51%
	352 Cases	100.00%

with cancer of the rectum or colon were reviewed from the years 1940 through 1950 (Table I). All of these cases were classified by Dukes' method as modified by Kirklin, Dockerty, and Waugh.⁶ Thus the pathologist completed a thorough examination or re-examination of the entire surgical specimen removed at the primary operation. This included a gross and microscopic search for extent of spread by all routes in each of the cases. In order to amplify and increase the accuracy of this re-evaluation, large sections were prepared from a series of current cases under the direction of Professor Carl V. Weller, according to a technic previously described by him.⁸ Some of these sections are reproduced here to illustrate the modes and extent of the

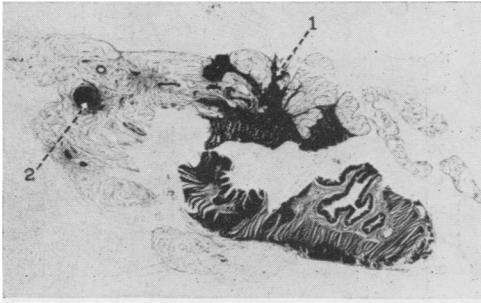


FIG. 5

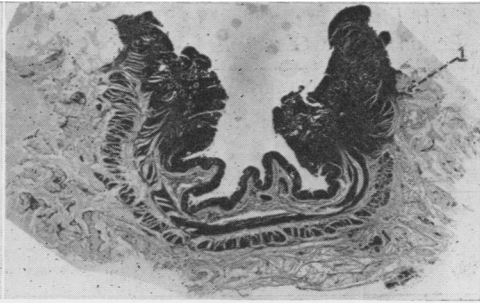


FIG. 6

FIG. 5. Well differentiated adenocarcinoma which has involved only a portion of the circumference of the sigmoid colon, but has invaded the pericolic adipose tissue by direct extension (1). The node contains carcinoma (2) (Dukes' Class C).

FIG. 6. Poorly differentiated adenocarcinoma which has involved almost half the circumference of the rectum and has invaded the perirectal adipose tissue (1). Lymph nodes were positive for metastatic carcinoma.

spread of cancer through the varying routes, including direct extension. Such preparations are suitable for either lantern projection or microscopic study, and we were enthusiastic about the state and progress of the disease demonstrated by them. Large sections were not prepared on all cases included in the series, but it is a pity that such preparation cannot be made routinely. As can be seen, the great majority of the lesions were far advanced, either passing through the wall without involved lymph nodes, or passing through the wall with involved lymph nodes. Cases of the last five years of this study were suitable only for classification of direct extension, since a five-year follow-up is not possible at this time.

RESULTS OF STUDY

As seen in Table II, we were able to trace 352 resected cases of carcinoma of the colon and rectum (both palliative and curative procedures) seen in this clinic from the year 1940 through 1944. Four cases were untraced, giving a 98.8 per cent five-year follow-up. From this table it is obvious that cancers of the colon are seen rather late in this hospital, judging from the frequency of direct extension. Approximately 82 per cent of the total group had

penetrated all layers of the large bowel at the time of operation. Also, 40 per cent showed positive lymph nodes by this time. These facts re-emphasize earlier diagnosis as the chief field of endeavor if more persons are to be cured of this disease.

Table III shows the graphic year-by-year survival of each of these classes, with the ultimate five-year survival shown in the last column. The lesions limited to the mucous membrane (Class A) were so rare in this study as to make the figure statistically unsound. Classes B₁ and B₂ warrant special observation. Neither of these classes included by definition patients with positive lymph nodes. In spite of this, the five-year survival is seen to diminish about 11 per cent by the occurrence of extension through the muscle coats (B₂) in comparison with cases limited to the muscularis propria (B₁). The most significant delineation of classification occurred between the B₁ plus B₂ groups (negative nodes) as compared to the C₁ plus C₂ groups (positive nodes). The Chi Square test revealed a phenomenal $P = 34.25$. The small C₁ class (14 cases) was interpreted as being statistically insignificant. This representation of survival (Fig. 7) for the patients with lymph node involvement (C groups) shows an abrupt fall in survival from oper-

TABLE III. Five-Year Survival of Patients Whose Lesions Were Classified in Table II.

A—100.0%	
B ₁ — 66.6%	
B ₂ — 53.9%	
C ₁ — 42.8%	
C ₂ — 22.4%	
Total Group —5 Year Salvage —44.1%	
60%—Negative nodes	
40%—Positive nodes	
82%—Through all layers wall	

ation to two years. This decline levels out after two years, indicating an early death for significant numbers of those patients showing positive lymph nodes. The Chi Square values, between the adjacent classifications, B₁ and B₂ and C₁, both approach significance. The addition of more cases to these classes would doubtless lead to significance.

The average age of this entire group of patients was 58.0 years. Males comprised 59.1 per cent and females 40.9 per cent of the group. The sex variation in this cancer of the colon population is significant at the P .01 level. There is evidence from this study that cancer of the colon occurs more frequently in males than in females.

DISCUSSION

The utilization of a modified Dukes' classification is not suggested as a substitute for Broder's histologic classification. We feel from our small experience with it that it does afford real additional help in determining prognosis to the surgeon. In this respect it possesses certain obvious advantages over any grouping based upon histologic criteria alone because: (1) Grading varies between individual pathologists; (2) different areas of a tumor may vary histologically; (3) this classification is based upon gross inspection of the operative specimen, which, as Dukes pointed out, correlates rather accurately with subsequent microscopic examination. This same accuracy by gross inspection does not hold

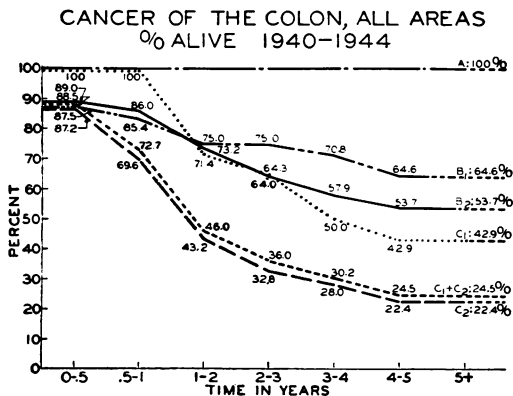


FIG. 7. Graphic year by year survival of all cases of carcinoma of the colon and rectum seen at University Hospital 1940 through 1944 (5 years). These cases are grouped according to Dukes' modified classification.

for the presence or absence of nodal involvement.

The direct spread of carcinoma of the colon and rectum appears to follow a logical pattern. Lesions originate in the mucous membrane. Invasion proceeds through the submucous tissues and muscularis mucosae. Next the *muscularis propria* is progressively involved following a variable period of delay. Finally extension through the muscle coats occurs. In lesions below the peritoneal reflection, the neoplasm is now anatomically without barrier and may extend readily throughout the perirectal fat. Intraperitoneal lesions must penetrate the additional serosal layer before dissemination may proceed. These factors, in addition to anatomical peculiarities with regard to lymphatic drainage, may explain the poorer prognosis of extraperitoneal lesions reported by some authors.

The figures of Gilchrist and David⁴ show a five-ten year survival of 51 per cent for extraperitoneal cases, and 65 per cent for intraperitoneal lesions. There were practically identical figures (61 per cent and 63 per cent) showing carcinomatous lymph node involvement. In addition, 74 per cent of cases below the peritoneal reflection without nodal involvement lived five or more years as compared to 90 per cent

above the reflection without nodes. Extraperitoneal incidence of local recurrence was 23 per cent, as compared to 3.6 per cent in those cases situated above the peritoneal reflection. These figures suggest unfavorable factors other than lymphatic spread in respect to the extraperitoneal lesions. We believe they are related, in part, to direct extension. The extraperitoneal perirectal investment of adipose tissue affords a semi-liquid circumferential diffusion medium which has no analogous counterpart in the colonic mesentery. Confirmatory evidence is added by study of the "life-sized" sections.

These factors re-emphasize the need for radical extirpation of perirectal tissues if delayed local recurrence is to be conquered.

SUMMARY AND CONCLUSION

1. A study was made of 850 specimens of carcinoma of the rectum and colon removed at operation between 1940 and 1950. These were classified according to Dukes' classification, as modified by Kirklin, Dockerty and Waugh.

2. Three hundred fifty-six of these specimens were from patients with carcinoma of the colon and rectum who underwent removal of their lesion in the period from 1940 through 1944. A follow-up was made for five years, which included 352 of these cases, or 98.8 per cent.

3. Eighty-two per cent of this group showed penetration of all coats of the bowel at the time of resection, and 40 per cent revealed involved lymph nodes. These figures indicate obvious delay in diagnosis.

4. Of this total group, 44.1 per cent survived five years. This included palliative and curative resections. This figure represents a true appraisal, and could obviously

be elevated by deleting operative and post-operative deaths and truly palliative resections, such as those on patients with widespread peritoneal or hepatic involvement.

5. The occurrence of spread by direct extension was studied by means of the "life-size" sections.

Graphic representation of the yearly survival of patients grouped according to the degree of direct extension reveals a progressive decline proportional to the depth of penetration of the colonic wall. Lymph node involvement lessens five-year survival even more drastically. Examination of the gross specimen is urged as a complement to the microscopic study.

ACKNOWLEDGMENTS

We wish to thank Professor C. V. Weller, of the Pathology Department, for his aid in preparing the large tissue sections and constructive criticism, and Mrs. Lin Wong for her help in preparing the statistical data.

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