THE LYMPHATIC AND VENOUS SPREAD OF CARCINOMA OF THE RECTUM*

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AN UNDERSTANDING of the spread of carcinoma of the rectum is essential for the treatment of the disease. Four main routes are possible: (1) By direct extension; (2) by the lymphatics; (3) by the blood stream; and (4) by transplantation through the peritoneal cavity. The second and third routes of spread are the subjects of this report.

LYMPHATIC SPREAD

The clinical observations of Miles,^{1, 2} in 1925, on the lymphatic spread of carcinoma of the rectum and injection studies by French and German anatomists have formed the basis for its present surgical treatment. Recent work by Gilchrist and David,³ and Coller, Kay, and MacIntyre⁴ has thrown further light on the subject. The present study makes use of their methods, and is based on the examination of 75 specimens of the rectum and rectosigmoid removed at operation during the past three years. Sixty-two were removed by abdominoperineal resection, ten by perineal excision, and three by anterior abdominal resection of the rectosigmoid, with either colostomy and inversion of the distal stump or end-to-end anastomosis. In these three cases the superior hemorrhoidal vessels were divided and a wide area of the mesentery was removed. All specimens were cleared by the Spalteholtz method, as used by Gilchrist and David, with some slight modifications. All lymph nodes were dissected out, sectioned, and charted on drawings to show their relationship to the tumor and the main blood vessels. By this method, many more lymph nodes were found than would have been possible by less accurate methods. As a result the number of node metastases found was also greatly increased. Metastases were frequently seen in the smallest nodes, with a diameter of only 1-2 mm. Mere size proved to be a completely unreliable guide to the presence or absence of a metastasis in a node.

In this series of 75 cleared specimens, the average number of nodes per specimen was 52. The average number found in specimens removed by abdominoperineal resection was 54, by perineal proctectomy, 31, and by anterior resection, 67. The greatest number found in any one specimen was 124. Metastases were found in 55 per cent of the cases. This incidence is somewhat less than that of 68 per cent reported by Gilchrist and David³ in 25 cleared cases, and that of 64 per cent found by Coller⁴ in 53 cases. It stands out in contrast, however, to that of 36 per cent which was found in a similar series¹⁵ of cases at this hospital, from 1916–1932, in which the clearing tech-

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nic was not used. The incidence in the present series is 19 per cent higher, and demonstrates the value of this method. This increase occurred in spite of the fact that more cases in this series were operated upon at an earlier stage, when fewer metastases might be expected. Thus, in the 1916–1932 series, 34 per cent of the specimens examined grossly were completely annular, whereas in the present series only 22 per cent were annular. That a relationship exists between the extent of bowel circumference involved and the frequency of metastasis will be shown later.

TABLE I

INCIDENCE OF NODE METASTASES REPORTED BY PREVIOUS AUTHORS

	No. of Specimens	No. of Nodes per Specimen	Per Cent with Metast.
McVay	100	6	47%
Wood and Wilkie	100	11	51%
Westhues	74 (cleared)	25	59%
Gabriel, Dukes, and Bussey	100	28	62%
Gilchrist and David	{ 22 25 (cleared)	24	68%
Onemist and David	25 (cleared)	52 ∫	00 /0
Coller. Kay, and MacIntyre	53 (cleared)	67	64%
Grinnell (1916–1932)	107		36%
Present series (1938–1941)	75 (cleared)	52	55%

THE LYMPHATICS OF THE RECTUM.—Our knowledge of the lymphatics of the rectum is based chiefly on the injection studies of Delamere, Poirier, and Cuneo,⁵ Villemin,⁶ and Rouviére.⁷ The intramural lymphatics which lie in the mucosa, submucosa, and muscle layers, are continuous with those in the rectosigmoid above and with the dermal and subcutaneous lymphatics of the anus below, and draïn into the extramural lymphatic system. This system consists of three main lymphatic trunks, the inferior, middle and superior, which correspond, in general, with the inferior, middle, and superior hemorrhoidal vessels, and constitute the three zones of spread—upward, lateral, and downward, described by Miles.^{1, 2}

The inferior trunks arise from the anal region in the lowest portion of the rectum, and drain, chiefly, to the inguinal nodes by way of the perineum and the inner side of the thigh, and probably, occasionally, directly to the iliac and sacral nodes in the pelvis. The middle trunks arise in the rectum near the level of, and just above, the insertion of the levator ani muscles and pass laterally between the peritoneum and the levator muscles to the hypogastric and sacral nodes along the middle hemorrhoidal and sacral vessels. The superior trunks arise from the entire length of the rectum from as low as the anal canal and drain into perirectal and mesocolic nodes along the superior hemorrhoidal and inferior mesenteric vessels. As these three lymphatic trunks anastomose with each other, it is possible for a cancer of the rectum to have metastases along two or even three routes of spread.

In none of our cases was extensive intramural lymphatic spread in the submucosa or muscularis found. No attempt was made, however, to study this point by serial sections. We are inclined to agree with Miles,¹ Wood and Wilkie,⁸ Westhues,⁹ Cole,¹⁰ and Monsarrat¹¹ that this type of spread is

rare. $^{\lambda}$ As far as intramural extension is concerned it is probably safe to divide the bowel within a few centimeters of the tumor.

UPWARD SPREAD.—The extramural lymphatic spread in the 41 cases with lymph node metastases in our series of 75 rectal and rectosigmoid carcinomata, was studied carefully. The main lymphatic path is upward along the superior hemorrhoidal vessels. In over one-half of the cases with node Imetastases only three nodes or less were involved. The largest number of

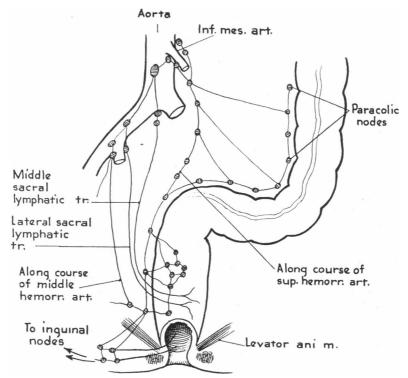


FIG. 1.—Schematic drawing of the extramural lymphatic system of the rectum and pelvic colon (after Miles and Villemin).

metastases in any one specimen was 13. In over one-half of these cases all the involved nodes lay within 3 cm. of the tumor. If cases without metastases are included, 73 per cent of all cases in this series were found to have either no metastases or very localized ones. In the remaining 20 cases, or in nearly one-half of those with metastases, some of the involved nodes were at a considerable distance from the tumor. One can conclude that the disease tends to remain localized and usually spreads slowly through the lymphatics but that exceptions to this rule are frequent.

In nine, or 22 per cent, of the 41 cases with metastases the most proximal nodes near the point of division of the superior hemorrhoidal vessels showed metastases. This group would be expected to have a particularly unfavorable prognosis. Gabriel, Dukes, and Bussey¹² found that 30 per cent of their

cases with metastases were in this group. Five of our nine cases with the most proximal node involved, had had an abdominoperineal resection, and

TABLE II

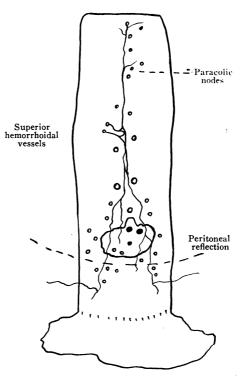
NODE INVOLVEMENT IN 41 CASES WITH METASTASES

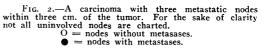
Cases with 1 node involved Cases with 2 nodes involved Cases with 3 nodes involved	2
Cases with 4 or more nodes involved	23 18

four had had a perineal excision. Thus, only 8 per cent of 62 cases having an abdominoperineal resection fell into this unfavorable group, whereas 40 per

cent of our ten cases having a perineal excision were so classified. This emphasizes, strikingly, the inadequate removal of lymph node-bearing tissue obtained by the perineal operation.

In most of our cases the lymphatic spread of the disease progressed upward along the superior hemorrhoidal vessels in a fairly orderly manner. In seven of our 41 cases with metastases, however, the spread was definitely discontinuous, with a considerable gap of uninvolved nodes between the tumor and the more proximal involved ones. Figure 5 shows such a specimen. Gabriel. Dukes, and Bussey¹² had only one such case in 62 cases with metastases, whereas Wood and Wilkie⁸ reported six in 51 cases. This discontinuity of spread is undoubtedly explained by the fact that there





are a variety of upward lymphatic pathways. In injection studies, Villemin, Montagné, and Huard⁶ describe three lymphatic routes passing upward with the superior hemorrhoidal vessels. The short paths are the most numerous and drain into a group of nodes near the bifurcation of these vessels. The middle paths pass upward without stopping at intermediate nodes to enter nodes

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near the junction of the superior hemorrhoidal and lowest sigmoid vessels. The long paths pass upward without any intermediate stops to enter nodes near the junction of the left colic and the inferior mesenteric vessels. In six of our cases one or more nodes at the bifurcation of the superior hemorrhoidal vessels were involved, and in four cases nodes at the junction of the superior hemorrhoidal and lowest sigmoid arteries showed metastases. Two of these

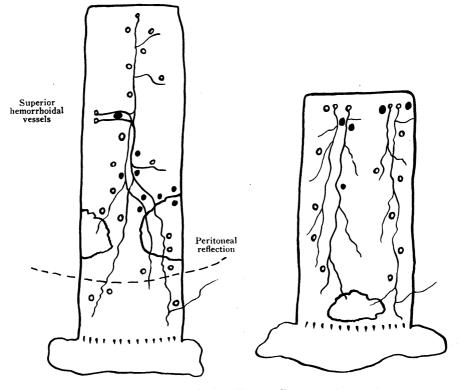


FIG. 3.—A carcinoma removed by abdominoperineal resection with a metastasis in one of the most proximal nodes near the point of ligation of the superior hemorrhoidal vessels.

FIG. 4.—A low rectal tumor removed by perineal excision with metastases in the most proximal nodes near the divided branches of the superior hemorrhoidal vessels.

four cases, apparently, represent examples of direct spread along the middle route. The other two showed metastases at both these sites, and may either represent spread by both the short and middle routes or a secondary relay from the short route which ends at the bifurcation. We had no cases illustrating metastasis by the long route, as the usual abdominoperineal resection does not extend as high as the origin of the left colic vessels.

The cases with lymph node metastases were also studied to compare the adequacy of simple perineal excision with that of abdominoperineal resection. The average limit of adequate removal of mesentery in the perineal operation was taken to be 3 to 4 cm. above the peritoneal reflection. Only cases with tumors lying completely beneath the peritoneal reflection were taken. Some

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cases with tumors partly above and partly below the peritoneum could probably have been included, but it was decided to limit the group only to cases best suited to the perineal operation. There were 17 cases with node metastases in this group. Only four of the 17 cases, or 24 per cent, appeared to be curable by perineal excision. In the remaining 13 cases, the involved nodes could not have been reached by such a limited operation. The inadequacy of this operation is obvious.

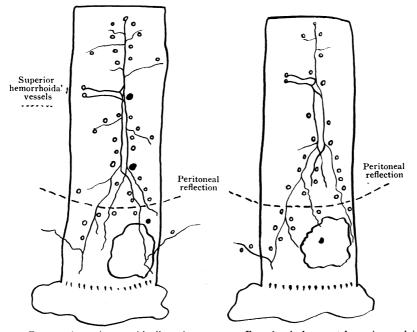


FIG. 5.—A carcinoma with discontinuous lymphatic spread. One involved node lies at the bifurcation of the superior hemorrhoidal vessels and another at their junction with the last sigmoid vessels.

FIG. 6.—A low rectal carcinoma lying below the pelvic peritoneum. It has only one nearby metastasis and is suitable for the perineal excision operation.

LATERAL SPREAD.—The lateral spread of the disease along the lymphatics accompanying the middle hemorrhoidal vessels has been an alternate route, emphasized especially by Miles^{1, 2} for carcinomata arising in the lower rectum near the level of the levator ani muscle insertion. Gilchrist and David had four cases, and Coller six, in their series. Wood and Wilkie had no instance of it. Our study showed only one case (Fig. 8), which demonstrates upward, downward, and lateral spread from a tumor situated 6 cm. above the pectinate line. It seems probable that lateral spread is most apt to occur in a low-lying tumor, where the main upward channels have been blocked by extensive metastases in the nodes. This was true in our case, and in Coller's six cases. As the middle hemorrhoidal vessels are sometimes hard to identify in cleared specimens it is possible that in one or two instances lymph nodes along this route may have been incorrectly charted along superior hemorrhoidal branches. We agree with Gilchrist that section of the levator ani muscles should be made as widely as possible in order to reach nodes along this pathway. It seems probable, however, that this route of spread is of secondary importance, and occurs chiefly in advanced cases when the main upward path has been blocked.

DOWNWARD SPREAD.—Downward lymphatic spread has also been emphasized, chiefly by Miles.^{1, 2} All writers on the subject agree that it occurs only when extensive metastases have occurred, blocking the other routes and causing retrograde lymph flow downward. Miles' observations were based mainly on cases with recurrent tumor nodules following inadequate perineal operations. We had only one case (Fig. 8) which has already been cited as illustrating upward, lateral, and downward spread. In this case the tumor lay

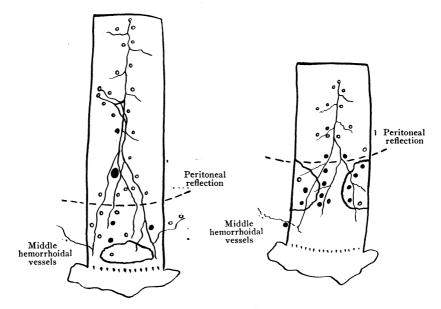


FIG. 7.—A low tumor with high node metastases unsuitable for the perineal excision operation.

FIG. 8.—A low rectal carcinoma illustrating upward, lateral, and downward lymphatic spread. One involved node lies along the middle hemorrhoidal vessels two centimeters distal to the tumor. Thirteen of 46 nodes showed metastases.

6 cm. above the pectinate line and had metastasized to 13 nodes, 12 involved nodes blocking the upward spread and one lying along the middle hemorrhoidal vessels, about 2 cm. distal to the tumor. Westhues⁸ had only one case in 74 operative resections which lay I cm. below the tumor and was associated with other metastases in the nodes above. Gilchrist reported one case with a metastasis 4 cm. below the tumor, and Coller another, with the involved node lying I cm. distal to the growth. It seems evident that downward lymphatic spread is of little importance except in advanced cases, which are probably already inoperable because of extension along the main lymphatic route upward. The very rare occurrence of downward extension in our Volume 116 Number 2

cases, and in those of others, suggests that the operation of anterior resection with ligation of the superior hemorrhoidal vessels may have a greater usefulness for tumors just above the rectosigmoid junction. There were three of these cases in our series with metastases, and none showed evidence of retrograde extension.

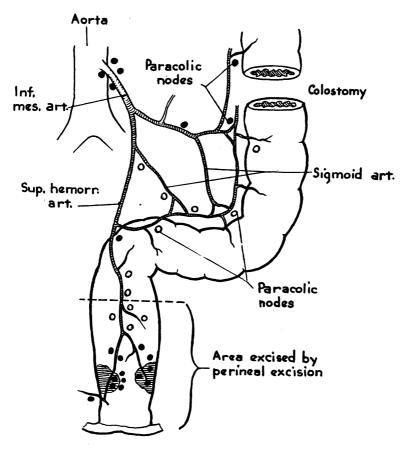


FIG. 9.—A drawing of a tumor with late retrograde extension to the paracolic nodes following perineal excision and the probable node metastases present. This is the same case as that shown in Figure 8.

Metastases to the paracolic nodes are rarely found in operative specimens. There is, apparently, little tendency for retrograde flow to take place at this stage from the inferior mesenteric-superior hemorrhoidal chain laterally to the paracolic nodes along the pelvic colon. We found no instance of it in any of our 62 specimens removed by radical abdominoperineal resection. Miles^{1, 2} has stated that the paracolic nodes frequently show metastases by retrograde involvement. Wood and Wilkie⁸ had no cases of it. Gabriel, Dukes, and Bussey¹² had only one such case, and this was an advanced growth with extensive involvement of the higher nodes. We had one clinical example of it, very similar to one reported in detail by Miles. This case has already been

described (Fig. 8). The patient, a female, age 55, with a low rectal tumor, had had a colostomy and a perineal excision performed in two stages. At the first operation no liver or intraperitoneal metastases were found. The tumor lay well below the peritoneal reflection. One month later the perineal excision was performed, with removal of the lower 27 cm. of the rectum. Metastases were found in 13 of the 46 lymph nodes. All the involved nodes were fairly close to the tumor. Five months later, two recurrent tumor nodules were removed from both the proximal and distal limbs of the colostomy, and showed a histologic picture similar to that of the original tumor. The nodules evidently represented retrograde spread from metastatic paracolic nodes. It seems probable that involvement of the paracolic nodes occurs late, when radical surgery can offer little hope of cure.

No relationship could be demonstrated between the size of the tumor and the frequency of metastases. In fact the square area of bowel involvement was very slightly greater in the tumors without metastases than in those with them. There was some correlation, however, between the amount of bowel circumference involved and the frequency of metastasis. Thus, the incidence of node metastases was 53 per cent when the tumor was not completely annular, and 71 per cent when it was.

VENOUS SPREAD

The occurrence of blood-borne metastases from carcinoma of the rectum has long been recognized, but the relative importance of this route of spread is still largely a matter of conjecture. It is apparent from the frequency of five-year postoperative survivals in early cases without lymph node metastases, that venous metastasis does not usually precede lymphatic involvement. Many surgeons, however, are familiar with the occasional small, early tumor, without node involvement, which is found to have liver metastases at operation. Brown and Warren¹³ have recently thrown further light on this subject. They studied a series of 165 cases of carcinoma of the rectum in which complete postmortem findings were available. These were cases of patients dying immediately after resection or colostomy, survivals following operation, and cases dying of the disease without operation. These cases were studied particularly for local blood vessel invasion in the tumor and for visceral and lymph node metastasis. We have made a similar study in our series of 75 cases. The search for vessel invasion by tumor cells was carried out as recommended by Brown and Warren. At least three sections of the tumor were taken in each case and stained with Masson's aniline blue trichrome stain to emphasize the smooth muscle wall of the small veins. The chief difficulty encountered was in differentiating tumor cells in veins from those in lymphatics. The main point in differentiation was the presence of smooth muscle cells in the vessel wall not usually seen except in the largest lymphatics. The finding of red blood cells in the lumen, especially if in considerable numbers, was also helpful. Vessel invasion was found most frequently in the fat and connective tissue outside the muscle wall of the rectum along the deep edge of the tumor. The next most common site was in the submucosa. Nearly every case was checked by Dr. A. P. Stout. Where there was any doubt of blood vessel invasion, it was not accepted.

BLOOD VESSEL INVASION.—In the 75 specimens of carcinoma of the rectum in this series, in which blood vessel invasion was studied, definite invasion was found in 36 per cent. If 84 colon carcinomata, which were also studied, are added to this group, the incidence of vessel invasion rises to 41 per cent. Brown and Warren¹³ found it in 61 per cent, but the majority of their specimens were from autopsies of advanced cases in which

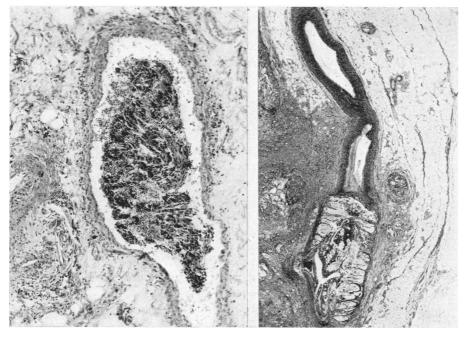


FIG. 10.—Tumor cells in a small vein. Note the FIG. 11.—A tumor thrombus adherent to the accompanying artery. (x125) wall of a vein. (x28)

no operation had been attempted. A higher frequency of vessel invasion might be expected in these cases. They probably represent a less differentiated and more invasive group of tumors, and one in which vessel invasion has had more opportunity to occur in the late stages of the disease.

TABLE	III
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INCIDENCE OF LOCAL BLOOD VESSEL INVASION

	rotal Cases	Vessel Invasion	
		Cases	Per Cent
Present series:			
Rectum (operative specimens)	75	27	36%
Colon (operative specimens)	84	39	46%
Brown and Warren:			
Rectum (operative and nonoperative specimens)	165	100	61%
209			

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The frequency of vessel invasion was found to vary with the degree of differentiation of the tumor. The growths were classified into three grades -I, II, and III; using as criteria the degree of invasive tendency, glandular arrangement, nuclear polarity, and the frequency of mitoses. This classification has been described previously.¹⁵ Our series of 75 cleared specimens was increased by 15 other rectal carcinomata from a 1916-1932 group, which were also searched for tumor invasion in the veins. These additional cases had little effect on the result, but contributed to a larger series of Twenty-five per cent of the Grade I cases had vessel invasion, 34 cases. per cent of the Grade II cases, and all of the Grade III cases. That such a relationship should exist is not surprising. Just as poorly differentiated tumors frequently invade nerve sheaths, so do they often penetrate into the lumen of vessels. We have already shown previously¹⁵ the close relationship between the grade of the tumor, the frequency of node metastasis, and the five-year results. The value of grading is further demonstrated here. It influences prognosis, whether the disease spreads by the lymphatics or by the blood stream.

TABLE IV		
SION AND HIST	OLOGIC GRADE	
Grade I	Grade II	Grade III
12	38	0
75%	66%	
4	20	16
25%	34%	100%
	SION AND HIST Grade I 12 75% 4	SION AND HISTOLOGIC GRADE Grade I Grade II 12 38 75% 66% 4 20

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It was also found that the frequency of vessel invasion increased with the depth of penetration of the bowel wall by the tumor. The cases were grouped according to Dukes'¹⁴ classification. A-cases are those in which the growth is confined to the wall of the rectum, B-cases those which have penetrated to the extrarectal tissues but have not reached the lymph nodes,

TABLE	V		
VESSEL INVASION AND DUI	KES' CLASS	SIFICATION	
	Α	В	с
Vessel Invasion:			
Absent:			
Cases	II	20	19
Per cent	84%	69%	40%
Present:			
Cases	2	9	29
Per cent	16%	31%	60%

and C-cases those which have metastasized to the regional nodes. Vessel invasion was found to be nearly four times as frequent in C-cases as in the A-cases, of which there were two. Presumably, the tumors which have penetrated farthest are usually the least differentiated and the most invasive.

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They also have a greater opportunity for vessel invasion and a larger area available for its search. In addition to the two A-cases mentioned, vessel invasion was also found in a third case, a small, early carcinoma developing on a polyp. This was a very undifferentiated Grade III tumor, which was only excised locally, and was not included in this series of cleared specimens. This patient is still well, two years after operation.

VISCERAL METASTASES .- Except in a few instances, it was not possible in this series to correlate the finding of blood vessel invasion with the later development of blood-borne metastases, because a sufficient follow-up period has not yet elapsed. Brown and Warren¹³ have shown in their cases that 67 per cent of those with local intravascular invasion had visceral metastases. They emphasize the fact that many tumor cells that enter the venous circulation fail to survive and grow in distant foci. The size of the vein involved is also an important factor, as Willis¹⁶ has pointed out. Large veins containing tumor cells are far more likely to have distant metastases than microscopic ones. In only seven of our cases had visceral metastases occurred at the time this report was made. However, 25 other cases of rectal carcinoma were found in an older series of cases,15 from 1916-1932, which had had definite visceral metastases, and whose specimens could be sectioned and searched for vessel invasion. All but three cases had liver metastases, with occasional lung and bone involvement as well. The presence of liver metastases was determined by autopsy findings, obvious metastases seen at operation, or clinical evidence of a rapidly enlarging nodular liver.

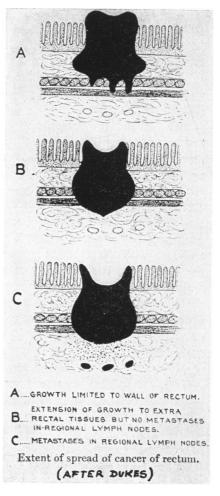


FIG. 12.—Dukes' classification of carcinoma of the rectum (after Dukes).

There were 32 cases with visceral metastases in this combined group. When the distribution of these cases into three histologic grades was studied, and compared to that of our recent cleared cases, a much larger percentage of Grade III cases was found in the former group. As we have already shown that vessel invasion is more frequent in Grade III cases, it is not surprising to find that visceral metastases are also more frequent.

TABLE VI

DISTRIBUTION OF CASES BY HISTOLOGIC GRADE IN 32 CASES WITH VISCERAL METASTASES AND IN PRESENT SERIES

	Grade I	Grade II	Grade III	
Cases with visceral metastases selected from present and 1916-1932 series:				
Cases	4	15	13	
Per cent	13%	47%	40%	
Present series (all cases):				
Cases	15	52	13	
Per cent	19%	65%	16%	

If this combined group with visceral metastases is analyzed as to bowel wall and node involvement, as measured by Dukes' classification, several striking facts appear. In the first place, no A-cases were found in this group. Evidently venous metastasis did not occur until after the tumor had completely penetrated the muscle wall of the rectum. Secondly, the percentage of B-cases, *i.e.*, cases with complete tumor penetration of the muscle wall, but without node involvement, with visceral metastases was surprisingly high and will be discussed further in the next paragraph. Finally, the proportion of C-cases, *i.e.*, cases with complete tumor penetration of muscle wall and node metastases, was found to be large, as might be expected. The comparison of this group with our recent cleared cases, and also with the 1916-1932 series, emphasizes these points. The farther the tumor penetrates the bowel wall the more frequent is vessel invasion and the chance of blood-borne metastasis. We have previously shown¹⁵ the close relationship between this classification and the five-year postoperative results. Here is another demonstration of its relation to prognosis.

TABLE	VII
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DISTRIBUTION OF CASES BY DUKES' CLASSIFICATION IN 32 CASES WITH VISCERAL METASTASES PRESENT SERIES AND 1916-1932 SERIES

	Α	В	с
Cases with visceral metastases selected from present and 1916–1932 series:			
Cases	0	8	24
Per cent		25%	75%
Present series (all cases)			
Cases	13	24	41
Per cent	17%	31%	52%
1916-1932 series:15			
Cases	20	49	40
Per cent	18%	45%	37%

Eight, or 25 per cent, of the 32 cases with visceral metastases were B-cases, and failed to show metastases in the regional nodes. Apparently blood-borne metastasis, before the nodes are involved, is not as rare as has been believed. In our 1916–1932 series the incidence of five-year Volume 116 METASTASES OF CANCER OF RECTUM

survivors after operation in the A-, B-, and C-cases was 100, 59, and 23 per cent, respectively. These results applied only to cases surviving operation five years and those dying of the disease. The fact that 100 per cent of the A-cases survived five years without disease, agrees with our findings that visceral metastases have not been found in the A-group. As for lymph node metastases, Dukes¹⁴ and Grinnell¹⁵ have shown that they almost never occur in the A-cases until the muscle layer of the bowel has been penetrated and the case can no longer be classed as an A-case. The difference between the survival rate of 100 and 59 per cent in the A- and B-cases can be largely explained by the greater liability of venous spread in B-cases, for as far as lymphatic spread is concerned all the A- and B-cases should have survived. It is possible, also, that some of the B-cases would have been classed as C-cases had the clearing technic been used in the search for node metastases. This would have raised the five-year survival rate of the B-cases somewhat nearer that of the A-cases.

TABLE VIII

FOLLOW-UP RESULTS ACCORDING TO				
Cases Surviving Operation Five Yea	ars and	Those Dying of	Cancer in T	hat Period
		Α	В	С
Cases	63	10	27	26
Five-year survivors:				
Cases	32	10	16	6
Per cent	51%	100%	59%	23%

When the cases with visceral metastases were studied for the presence of local vessel invasion, it was found to be present in nearly everyone. Out of the 30^{*} specimens of rectal carcinoma removed at operation, vessel invasion was found microscopically in all but three, or 90 per cent. Brown and Warren were able to find it in all but one of their 70 cases with visceral metastases. In other words, the absence of vessel invasion after careful search in the sections from the primary growth will nearly always rule out the possibility of visceral metastases. Unfortunately, because of lack of sufficient follow-up period in our series, so far, the prognostic value of a positive finding of vessel invasion as regards visceral metastasis could not be determined. A negative finding, however, is probably far more important.

SUMMARY

(1) A series of <u>75 specimens</u> of the rectum and rectosigmoid were cleared by the modified Spalteholtz technic, and studied for lymph node metastasis and blood vessel invasion.

(2) The average number of nodes per specimen was 52.

(3) Node metastases were found in 41 cases, or in 55 per cent. This incidence is 19 per cent higher than that found in a similar series of cases at this hospital, from 1916-1932, in which the clearing technic was not used.

(4) No intramural lymphatic spread of any significance was seen in any case.

^{*} Two cases were omitted because sections were inadequate for vessel invasion study.

(5) The main extramural lymphatic spread is upward along the superior hemorrhoidal vessels. In over one-half of the cases with metastases, only three nodes or less were involved, and in over one-half of the cases the involved nodes lay within 3 cm. of the tumor. In nine, or 22 per cent, of the cases with metastases the most proximal nodes, near the point of ligation of the superior hemorrhoidal vessels, were involved. Thus, 40 per cent of the ten cases having perineal excision, and only 8 per cent of the 62 cases having abdominoperineal resection, fell into this unfavorable group, with a probably inadequate operation.

(6) In most cases with node metastases the upward spread was relatively progressive and orderly. In 17 per cent, however, it was definitely discontinuous.

(7) Only four, or 24 per cent, of the 17 cases with node metastases, having tumors below the peritoneal reflection, could have had adequate node removal by perineal excision.

(8) There was only one proven case of lateral lymphatic spread along the middle hemorrhoidal vessels, and only one instance of downward spread found in our series.

(9) Metastasis to the paracolic nodes was not found in any of the specimens. One case showed clinical evidence of extension along this route following operation.

(10) The incidence of node metastasis was 18 per cent higher when the tumor was completely annular than when it was not. No relationship could be demonstrated between the square area of the tumor and the frequency of metastasis.

(11) Blood vessel invasion was found in 36 per cent of 75 specimens of carcinoma of the rectum, and in 41 per cent of a combined group of 162 colon and rectal tumors.

(12) The incidence of blood vessel invasion was four times as great in the Grade III cases as in the Grade I. It was present in all the Grade III cases. Cases with visceral metastases showed a higher incidence in Grade III than unselected cases.

(13) The incidence of visceral metastasis and its relation to local blood vessel invasion could not be determined because of the insufficient follow-up period.

(14) There were no A-cases with visceral metastases. Eight, or 25 per cent, of the 32 cases with visceral metastases were B-cases, without node involvement.

(15) Twenty-seven, or 90 per cent, of the 30 cases with visceral metastases showed blood vessel invasion. Only three cases, or 10 per cent, failed to show it.

CONCLUSIONS

(1) The use of the modified Spalteholtz method for finding and charting lymph nodes will greatly increase the number of node metastases found, and will so aid in more accurate prognosis. (2) The main extramural lymphatic spread is upward along the superior hemorrhoidal vessels. It tends to remain localized and to extend slowly in most cases. More distant spread, often discontinuous and unpredictable, is not uncommon, however.

(3) Lateral lymphatic spread along the middle hemorrhoidal vessels is probably infrequent and of secondary importance, occurring chiefly when the higher nodes are blocked by metastases.

(4) Downward lymphatic spread is exceedingly rare in operative specimens, and only occurs by retrograde flow when the high nodes are blocked.

(5) The rare occurrence of downward extension suggests that the operation of anterior abdominal resection, with ligation of the superior hemorrhoidal vessels, may have a wider field of usefulness for tumors near the rectosigmoid junction.

(6) Metastasis to the paracolic nodes is rare except in cases that are probably beyond operative cure.

(7) Perineal excision is a completely inadequate operation, even for carcinomata lying below the pelvic peritoneum.

(8) The tendency of rectal carcinoma to metastasize by way of the blood stream varies, in general, with the degree of differentiation of the tumor, and with the extent of local spread, as outlined by Dukes.

(9) Blood stream metastasis before the muscle wall of the rectum has been completely penetrated by the tumor is probably rare.

(10) Blood-borne metastasis after complete penetration of the muscle wall, but before the regional nodes are involved, is not as rare as has been believed.

(11) The value for prognosis of both the grading of tumors and their classification according to local spread has been further demonstrated.

(12) Failure to find local blood vessel invasion in the tumor after careful search is strong evidence that no visceral metastases exist.

REFERENCES

¹ Miles, W. E.: Cancer of Rectum. London, Harrison and Sons, 1926.

- ² Idem: The Spread of Cancer of the Rectum. Lancet, 208, 1218, 1925.
- ³ Gilchrist, R. K., and David, V. C.: Lymphatic Spread of Carcinoma of the Rectum. ANNALS OF SURGERY, 108, 621, 1938.
- ⁴ Coller, F. A., Kay, E. B., and MacIntyre, R. S.: Regional Lymphatic Metastasis of Carcinoma of the Rectum. Surgery, **8**, 294, 1940.
- ⁵ Delamere, G., Poirier, P., and Cuneo, B.: The Lymphatics. Chicago, W. J. Keener and Co., 1904.

⁶ Villemin, F., Huard, P., and Montagné, M.: Recherches anatomiques sur les lymphatiques du Rectum et de l'Anus. Rev. de Chir., **63**, 39, 1925.

- ⁷ Rouviére, H.: Anatomy of the Human Lymphatic System. Paris, Masson et Cie, 1932.
- Translated by Tobias, M. J., Ann Arbor, Michigan, Edwards Brothers, Inc., 1938. ⁸ Wood, W. Q., and Wilkie, D. P. D.: Carcinoma of the Rectum: An Anatomico-Pathological Study. Edinburgh Med. Jour., 40, 321, 1933.
- ⁹ Westhues, H.: Die pathologisch-anatomischen Grundlagen der Chirurgie des Rektumkarzinoms. Leipzig, Georg Thieme, 1934.

- ¹⁰ Cole, P. P.: The Intramural Spread of Rectal Carcinoma. Brit. Med. Jour., 1, 431, 1913.
- ¹¹ Monsarrat, K. W., and Williams, I. J.: Intramural Extension in Rectal Carcinoma. Brit. Jour. Surg., 1, 173, 1913-1914.
- ¹² Gabriel, W. B., Dukes, C., and Bussey, N. J. R.: Lymphatic Spread in Cancer of the Rectum. Brit. Jour. Surg., 23, 395, 1935.
- ¹³ Brown, C. E., and Warren, S.: Visceral Metastasis from Rectal Carcinoma. Surg., Gynec., and Obstet., 66, 611, 1938.
- ¹⁴ Dukes, C.: The Classification of Cancer of the Rectum. Jour. Path. and Bacteriol., **35**, 323, 1932.
- ¹⁵ Grinnell, R. S.: The Grading and Prognosis of Carcinoma of the Colon and Rectum. ANNALS OF SURGERY, 109, 500, 1939.
- ¹⁶ Willis, R. A.: The Spread of Tumours in the Human Body. London, J. and A. Churchill, 1934.