REGIONAL LYMPHATIC METASTASES OF CARCINOMA OF THE COLON

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A KNOWLEDGE of the incidence and the location of the regional lymphatic metastases from carcinoma primary in the large intestine is essential in the treatment of this disease.

This study, similar to one made by us on the regional lymphatic metastases of the rectum,[1] and the stomach,[2] is based upon the dissection and examination of all the lymph nodes from 46 cases of carcinoma of the large intestine. This included the following distribution:

TABLE I

Site of Tumor	No. of Cases
Cecum	4
Ascending colon	4
Hepatic flexure	3
Transverse colon	9
Splenic flexure	3
Descending colon	3
Sigmoid colon	20
Total	46

The lymph nodes were dissected from each specimen after they had been visualized (Fig. 1) with clearing by the Spalteholtz method, as modified by Gilchrist and David.[3] All nodes were examined microscopically and the results charted on a diagram, upon which every node was indicated. The presence or absence of regional lymph node metastases were then correlated with: (1) The age of the patient; (2) sex; (3) duration of symptoms; (4) gross type of neoplasm; (5) size; (6) circumferential extent; (7) depth of infiltration; (8) microscopic type; and (9) the degree of cellular differentiation.

Lymph nodes may be isolated by this method which, because of their smallness, go unnoticed by the usual method of dissection. Many large nodes were found to be inflammatory and many small impalpable nodes were found to contain metastatic carcinoma. Unless a lymph node was definitely replaced by carcinoma, it was impossible to determine without microscopic section whether it was involved. These facts of observation demonstrate clearly that the operative procedure should not be minimized because of the absence of palpable lymph nodes. It is in these cases that cure may be obtained if the operation be radical.

As a result of this special method of investigation, 28 of the 46 cases studied, or 60.87 per cent, showed evidence of regional lymph node metastases. An average of 52.07 nodes was isolated per specimen. There was an average of 59.4 nodes isolated per specimen in cases having nodal involvement and 41.4 nodes in those without metastases. Of the carcinomata of the right colon, 62.5 per cent showed metastases in comparison to 60 per cent of those of the left colon.

The superiority of this method of determining the presence of regional lymph node metastases is realized when these findings are compared to those of other workers. Craig and MacCarty,[4] in 1923, studied the incidence of regional lymph node metastases from 100 cases of carcinoma of the cecum by the usual method of dissection. They were able to isolate only 10.25 nodes per specimen, with an incidence of nodal involvement of 32 per cent. Hayes,[5] in 1921, found an incidence of 37 per cent nodal metastases in carcinoma of the large intestine, excluding the cecum, in which only 14.06 lymph nodes per specimen were isolated. Rankin and Olson,[6] in 1933, reported an incidence of 34 per cent regional lymph node metastases in 187 cases of carcinoma of the right colon, and only 31 per cent in 260 cases of carcinoma of the left colon.

In 1939, Simpson and Mayo[7] reported an incidence of 41.4 per cent nodal metastases in 120 patients with carcinoma of the colon. These were distributed as follows:

TABLE II

Site of Tumor	No. of Cases	No. of Cases with Metastases	Percentage
Right colon	28	14	50.0%
Transverse colon	15	6	40.0%
Descending colon	26	12	46.2%
Sigmoid colon	51	15	29.4%
Totals	120	47	Avg. 41.4%

The incidence of nodal metastases and the anatomic distribution of our cases are:

TABLE III

Site of Tumor	No. of Cases	No. of Cases with Metastases	Percentage
Cecum	4	3	75 %
Ascending colon	4	2	50 %
Hepatic flexure	3	1	33.3%
Transverse colon	9	7	77.7%
Splenic flexure	3	2	66.6%
Descending colon	3	2	66.6%
Sigmoid colon	20	11	55.0%
Totals	46	28	Avg. 60.87%

It is interesting to note that there were three patients with well-differentiated papilliferous adenocarcinomata of only Grade II malignancy, who had small hepatic metastases without demonstrable local regional lymph node involvement.

Regional lymph node metastases is only one factor in determining the operability and prognosis of carcinoma of the large intestine. Inoperability or poor prognosis may result from extensive local infiltration, hematogenous metastases or peritoneal implants. Ten per cent of the neoplasms (five of 46 cases) showed microscopic evidence of infiltration into blood vessels. This figure is slightly less than the incidence of 15 per cent microscopic infiltration of blood vessels noted by us in both carcinomata of the rectum and stomach. These were, in early cases, suitable for operation prior to *demonstrable* gross hematogenous metastases. As to local infiltration, 93.1 per cent had completely infiltrated through the bowel wall. This is a constant source of free peritoneal implantation.

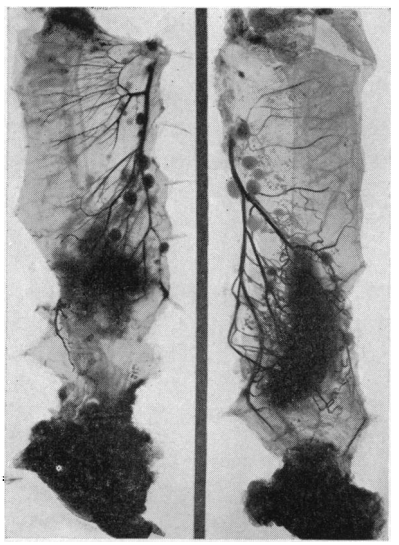
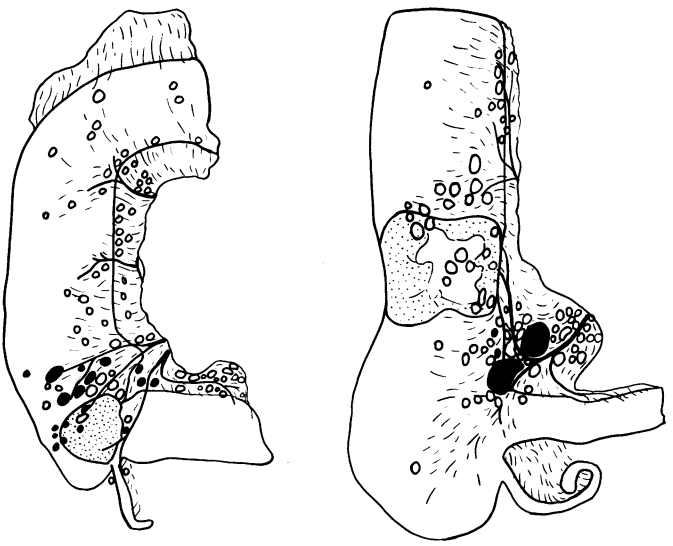


FIG. 1.—Photographs of cleared specimens of carcinoma of the rectum.

Lymphatic Drainage of the Large Intestine.—Delamere, Poirier and Cuneo,[8] and Jamieson and Dobson[9] were the first thoroughly to investigate the lymphatic drainage of the large intestine. This consists of three systems: The intramural; intermediary; and extramural lymphatic networks.

The intramural system consists of the submucosal, intermuscular and subserosal networks. Where the large intestine is devoid of a continuous longitudinal muscle layer, the intermuscular and subserosal networks are the same. The lymph channels begin about the mucosal glands of Lieberkühn and drain to the submucosal network. This network communicates freely with similar channels above and below the site of the lesion, but lymph tends to flow toward the deeper intermuscular and subserosal networks. Since lymph channels follow the course of the radial blood vessels around the circumference of the bowel, carcinomata of the large intestine, as well as the rectum tend to be annular. The lymph then flows from the intramuscular system through the intermediary lymph channels to the extramural lymphatic system. This consists of a group of nodes and lymph channels anatomically arranged about the blood vessels and are described by Jamieson and Dobson[9] as corresponding to these vessels. Thus, there is the ileocolic chain; the right colic chain; the middle colic chain; the left colic chain; and the inferior mesenteric chain. Along each chain, there are aggregations of nodes that are designated as the epicolic, paracolic, intermediate, and the main group of nodes.

The epicolic nodes lie anterior or posterior to the intestinal wall. The paracolic nodes are located upon the medial aspect of the intestine along the vascular arcades and the short terminal vessels leading from the arcades. The intermediate nodes are situated about midway between the arcades and



A B

FIG. 2.—(A) Line drawing illustrating the regional lymphatic metastases along the ileocolic chain from carcinoma of the cecum. (B) Line drawing illustrating the downward spread of lymphatic metastases to the ileocolic chain from carcinoma of the ascending colon.

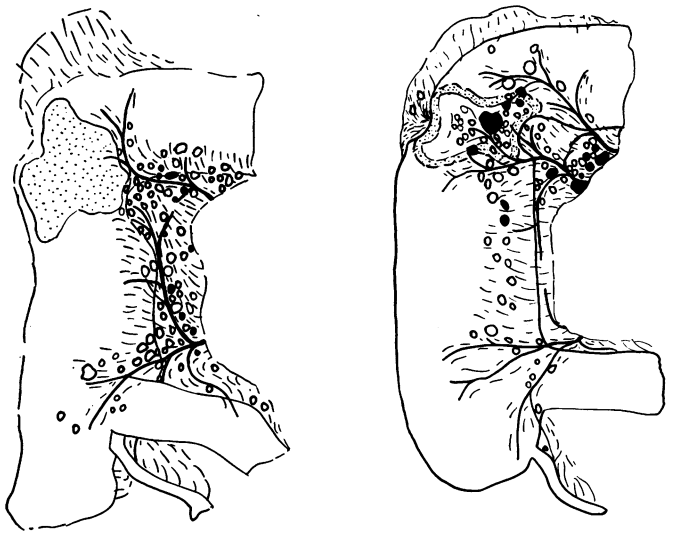


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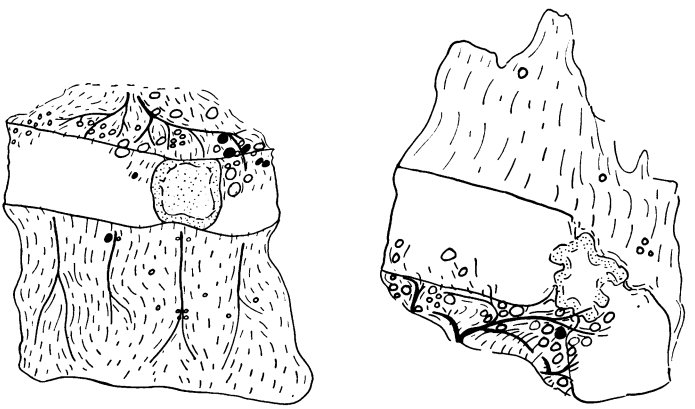
FIG. 3.—(A) Line drawing illustrating two routes of lymphatic metastases from carcinoma of the hepatic flexure; one downward along the ileocolic chain, the other along the middle colic chain. (B) Line drawing illustrating two routes of lymphatic metastases from carcinoma of the hepatic flexure; one along the right colic chain, the other along the middle colic chain.

the origins of the ileocolic, colic, or sigmoidal branches, whereas the main group surrounds the stems of the vessels at their origins.

The ileocolic route of spread drains the terminal ileum, cecum, appendix and the greater part of the ascending colon. Figure 2 A aptly demonstrates this route of lymph node metastases from carcinoma of the cecum. In Figure 2 B, a carcinoma of the ascending colon, the downward metastases toward the ileocecal junction is well shown.



A B

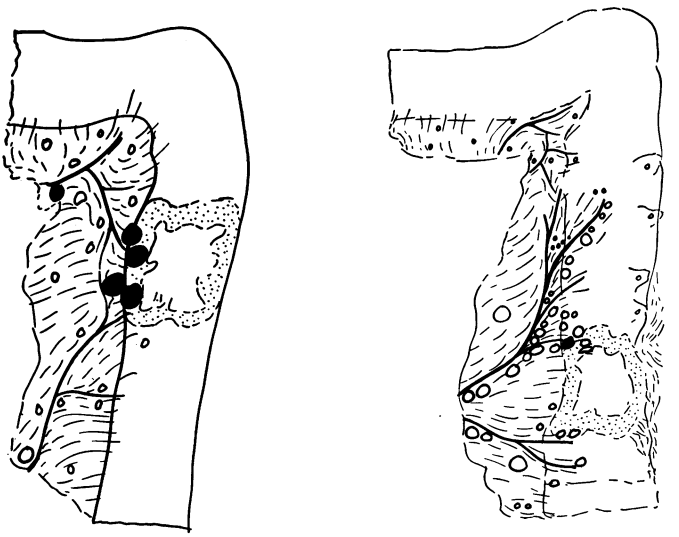
FIG. 4.—(A) Line drawing illustrating the regional lymphatic spread along the middle colic chain from carcinoma of the transverse colon and, also, the metastases of carcinoma of the transverse colon to lymph nodes in the omentum. (B) Line drawing illustrating the regional lymphatic metastases from carcinoma of the splenic flexure.

The right colic chain drains the area supplied by the right colic artery. These nodes are not constant, in that the right colic artery is not constant. They may drain downward into the ileocolic chain, may go medially toward the superior mesenteric nodes, or may drain upward into the middle colic chain. Figure 3 A, demonstrating the lymph node metastases of a carcinoma of the hepatic flexure, illustrates two routes of spread, one downward along the ileocolic chain, and the other passing more medially along the middle colic chain. Whereas, in Figure 3 B the carcinoma of the hepatic flexure appears to be metastasizing by the right colic chain, as well as the middle colic chain, to a lesser extent.

Similarly, the middle colic chain drains the area of distribution of the middle colic artery; that is, the upper part of the ascending colon, hepatic flexure and the proximal two-thirds of the transverse colon. Since the direction of the middle colic artery is to the right, toward the head of the pancreas, in the base of the mesocolon, the spread of metastases is downward and then toward the right. Furthermore, there is a communication between the lymphatics of the transverse colon and those of the omentum, which drain into the nodes along the greater curvature of the stomach. Figure 4 A illustrates this point.

The left colic chain drains the area of distribution of the left colic artery (Fig. 4 B). Neoplasms of the distal one-third to one-half of the transverse

colon would tend to drain toward the left, whereas neoplasms of the upper descending colon might drain either upward toward the splenic flexure (Fig. 5 A), or downward toward the sigmoidal vessels (Figs. 5 and 6). Lesions of the splenic flexure may spread through lymphatics of the omentum and eventually drain to the splenic lymph nodes.



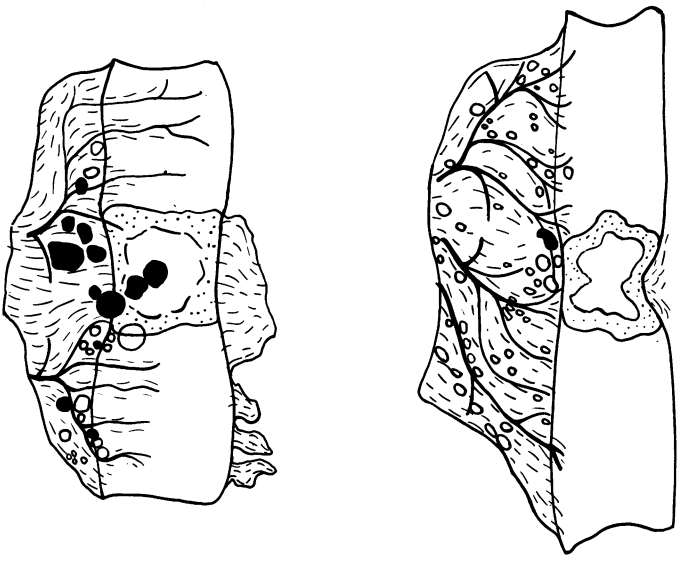
A B

FIG. 5.—(A) Line drawing illustrating the upward lymphatic metastasis of carcinoma of the descending colon along the left colic chain. (B) Line drawing illustrating the regional lymphatic metastasis of carcinoma of the desending colon along the sigmoidal chain.

The inferior mesenteric chain, and specifically the sigmoidal division, drains the area of distribution of the sigmoid vessels. Here, the intermediate nodes lie along the sigmoidal vessels, while the main nodes lie along the course of the inferior mesenteric vessels. Figures 6 A and 7 show, diagrammatically, the lymph spread of carcinoma of the sigmoid colon, demonstrating metastases to the epicolic, paracolic, and intermediate lymph nodes whlie a single paracolic metastasis is seen in Figure 6 B.

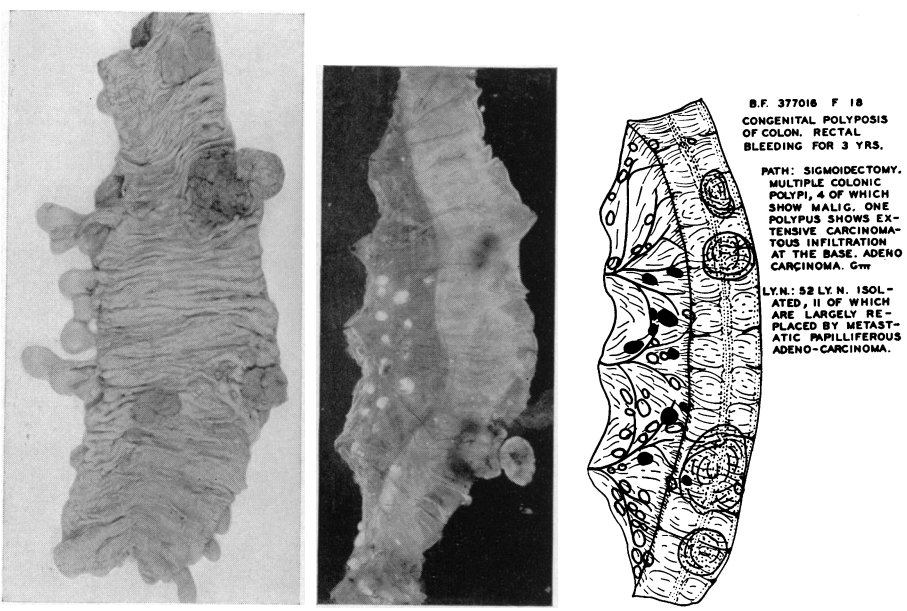
Since it is impossible to determine the presence or absence of regional lymph node metastasis by manual palpation, and since this study has shown that 60.87 per cent of the neoplasms of the large intestine have metastasized to lymph nodes, the surgeon must recognize the necessity of including these areas within the confines of the operative resection, even in the absence of palpable nodes.

Lymphatic vessels differ from blood vessels in that instead of one or two channels draining the same area, the lymph is returned by a number of channels which tend to form a plexus about the blood vessels. There may also be a number of efferent vessels to any one node, thus explaining the observation that contiguous lymph nodes may not be involved. As a rule, the epicolic nodes are the first to be involved by metastatic neoplastic emboli. However,



A B

FIG. 6.—(A) Line drawing illustrating regional lymph node metastases to the epicolic, paracolic and intermediate lymph nodes of the sigmoidal chain from carcinoma of the sigmoid colon. (B) Line drawing illustrating the singular regional paracolic metastasis from carcinoma of the sigmoid colon.



A B C

FIG. 7.—(A) Photograph of gross specimen of sigmoid colon illustrating polyposis of the colon in which four of the polyps had undergone malignant proliferation. (B) Photograph of cleared specimen shown in Figure 7 A. (C) Line drawing illustrating the regional lymph node metastases from carcinoma of sigmoid colon demonstrated in Figure 7 A.

often the neoplastic embolus is contained within a lymph channel that drains directly to either the paracolic or intermediate nodes without primary epicolic lymph node involvement. Lymph nodes act as barriers to filter out neoplastic emboli. A neoplastic embolus enters a lymph node by its peri- and subcapsular lymph channels. If the metastasis remains viable, it sets up a new neoplastic focus, tending to block the lymph channel, which then becomes dilated and

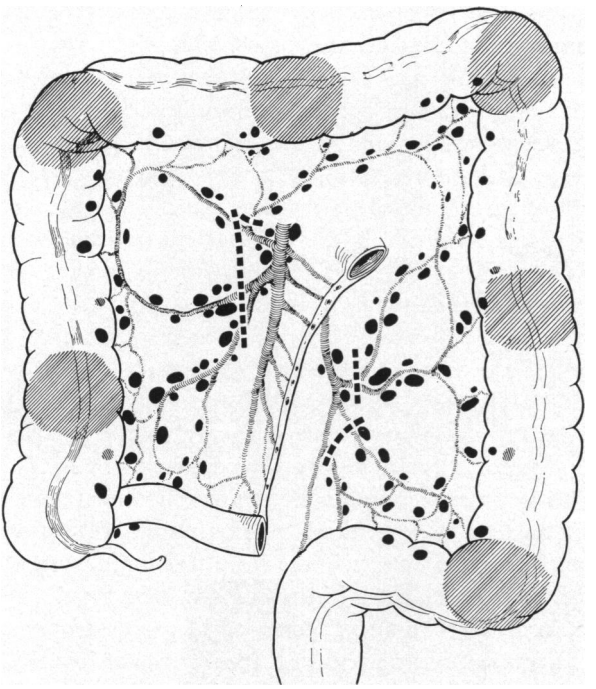


FIG. 8.—Diagrammatic drawing illustrating the lymphatic metastases from carcinoma of the colon. The dotted lines represent the ideal lines of section of the mesocolon to include the possible epicolic, paracolic, and intermediate lymph node metastases.

distended with lymphocytes. Lymph flow becomes static and other neoplastic foci are often established along the course of the lymph channels. The direction of lymph flow determines the direction of lymphatic metastases. If the lymph channels become plugged with neoplastic emboli, then the lymph will find unobstructed channels and neoplastic emboli may metastasize along other zones of spread.

Figure 8 summarizes, diagrammatically, the lymphatic drainage of the large intestine. The surgeon should include within the confines of the resection not only the primary growth but also its epicolic, paracolic and intermediate nodes of lymph drainage. If the carcinoma has metastasized to the main group of lymph nodes at the origins of the various vessels, then generalized metastases, undoubtedly, have already occurred, and any operative procedure would only be palliative in character. In Figure 8, the dotted lines represent the ideal

lines of section of the mesocolon for the various sites of carcinoma of the large intestine and simply restate the original suggestions of Jamieson and Dobson.[9]

Age and Metastases.—The average age of patients with metastases was 50.9 years, in comparison to 59.1 years in those without. There were two cases 18 years of age, a brother and sister, both of whom had polyposis of the colon, with multiple areas of carcinomatous proliferation (Fig. 7). Although these carcinomata were graded II and III, there was evidence of early hepatic metastases at the time of operation. Since both patients were obstructed, resections were performed, and the bowel continuity restored. The third youngest patient, a male, age 27, also had lymph node metastases. There were eight patients 67 years of age or over, five of whom (62.5 per cent) had metastases. Seventy-five per cent of the patients (nine of 12 cases), 50 years of age or below, had metastasized, in comparison to 55.8 per cent of the patients (19 of 34 cases) above 50 years of age. This substantiates the view that prognosis is less favorable in the younger age-groups than the older.

Sex and Metastases.—There was no essential difference between sex and the presence of lymph node metastases. Sixty-one point nine per cent of the male patients (13 of 21 cases) had nodal involvement, in comparison to 60 per cent (15 of 25 cases) of the female patients.

Duration and Metastases.—It was noted that the patient with a short duration of symptoms did not always have as favorable a prognosis as the patient who had had symptoms for a longer period of time. In the groups, as a whole, there was an average duration of 10.4 months in patients having regional lymph node metastases, as compared to an average of 11.5 months in those without. In analyzing the data further, there was an incidence of only 40 per cent metastases (four of ten cases) in patients who had had symptoms for two years or more, in contrast to an incidence of 73 per cent metastases (eight of 11 cases) in patients with symptoms of three months or less. This emphasizes the fact that many patients with symptoms of long duration and who are still operable often have the best prognosis, in that the neoplasm is slowly growing and of low malignancy. These apparent discrepancies are explained by the fact that only lesions that were resected could be studied and all inoperable lesions are thus, automatically, excluded from the study.

Gross Types and Metastases.—The carcinomata of the large intestine were classified into two groups, the polypoid and the sessile. The classification was based entirely upon whether the neoplasms tended to be bulky and to grow out into the lumen (polypoid) or whether they were plaque-like and tended to infiltrate—to be invasive (sessile). The other gross characteristics, such as stenosing, annular, constricting, and ulcerating, we did not feel to be of any clinical value in determining prognosis or likelihood of metastases. It is frequently stated that carcinomata of the right half of the colon are large, ulcerating, fungating, polypoid carcinomata and that those of the left colon are small, annular, stenosing, scirrhous carcinomata. Differences in the gross characteristics of these neoplasms are not the result of any inherent factor within the neoplasm itself to assume these forms, but rather are the result of

the location in which they are found. The caliber of the right colon is considerably larger than that of the left colon, consequently a neoplasm will have acquired a larger size in the right colon than the left before symptoms referable to its presence are made known. There were as many polypoid carcinomata of the left colon as of the right colon, and in all cases there was evidence of ulceration. Twenty of the 13 carcinomata of the sigmoid flexure were stenosing in character—one in the ascending colon, two in the hepatic flexure, four in the transverse colon, three in the splenic flexure, and three in the descending colon. None of these carcinomata was shown, microscopically, to be scirrhous in character. As to the correlation between gross type and regional lymph node metastases, 57.5 per cent of the polypoid neoplasms (23 of 40 cases) had metastasized, in comparison to 83.3 per cent of the sessile neoplasms (five of six cases), demonstrating the more benign character of the polypoid growths.

Size and Metastases.—It has been mentioned that the group with metastases had given symptoms a shorter time that those without. It is of interest to note that the incidence of metastases is higher in the smaller lesions than in the larger. In order to arrive at a more accurate figure as to the size of the neoplasm, its area rather than any one diameter was used. The average size of carcinomata of the right colon with metastases was 32.75 sq. cm., in comparison to those without metastases, in which the neoplasms averaged 39.5 sq. cm. Similarly, the average size of neoplasms of the left colon with metastases was 22.11 sq. cm., in comparison to 31.73 sq. cm. in those without metastases. Thus, we see that the neoplasms in which nodal involvement occurred were definitely smaller than those in which there were none, indicating that the smaller neoplasms giving rise to symptoms were more malignant in character and metastasized sooner. Furthermore, it is noted that the neoplasms of the right colon are considerably larger than those of the left. The largest neoplasms of the entire group were those located in the cecum; these averaged 46.56 sq. cm. in size—accountable by the fact that the caliber of the lumen of the cecum is the largest in size.

Circumference Involved and Metastases.—In no case was there less than 25 per cent of the circumference involved. The majority of the neoplasms (37 of 46) were completely annular. In only three instances had the carcinomata involved less than 50 per cent of the lumen and, in three cases, had involved less than 75 per cent of the lumen. The remaining three cases were included in the group having from 75 to 100 per cent circumferential involvement. Because of the large incidence of completely annular carcinomata, the correlation between circumferential involvement and metastases is not striking. It is noted, however, that of the three cases in which between 25 to 50 per cent of the circumference was involved, only one had metastasized.

Depth of Infiltration and Metastases.—As might be expected from these observations, in which 40 of the 46 carcinomata were either completely annular or found to involve over 75 per cent of the bowel circumference, and had also attained large size before symptoms were produced, in all but three cases the neoplasm had completely infiltrated through the bowel wall. Of the three

infiltrating only partially through the musculature, two had already metastasized. Consequently, any attempt at correlation of depth of infiltration and the presence of lymph node metastases is futile.

Degree of Cellular Differentiation and Metastases.—The preponderance of the carcinomata were graded II as to cellular differentiation. This included 36 of the 46 patients. There were nine neoplasms graded III, and only one graded IV. There were no Grade I carcinomata in our series. As shown in Table IV, the incidence of lymph node metastases was directly proportional to the degree of cellular differentiation.

TABLE IV

DEGREE OF CELLULAR DIFFERENTIATION AND METASTASES

Grade	No. of Cases	No. with Metastases	Percentage
II	36	21	58.3%
III	9	6	66.6%
IV	1	1	100 %
Totals	46	28	

Microscopic Type and Metastases.—The majority of the carcinomata were found, histologically, to be simple adenocarcinomata. These composed 29 of the 46 cases. The papilliferous adenocarcinomata had the smallest incidence of nodal involvement. These metastasized in only 37 per cent of the cases. The medullary adenocarcinomata had the highest incidence of metastases, and metastasized in 80 per cent of the cases. The second highest incidence was noted in the adenocarcinoma mucosum. Table V designates the number and incidence of the various histologic types with metastases.

TABLE V

HISTOLOGIC TYPE AND METASTASES

Histologic Type	No. of Cases	No. with Metastases	Percentage
Papilliferous adenocarcinoma	8	3	37.5%
Adenocarcinoma (simplex)	29	18	62.07%
Adenocarcinoma mucosum	4	3	75.0%
Medullary adenocarcinoma	5	4	80.0%
Totals	46	28	

SUMMARY AND CONCLUSIONS

A study of the lymph nodes in 46 specimens of carcinoma of the colon was made by David and Gilchrist's modification of the method of Spalteholtz. An average of 52 nodes were isolated per specimen. These were examined microscopically and charted on diagrams. Sixty point eighty-seven per cent of the specimens showed evidence of involvement of the lymph nodes by metastases. There was an average of 59.4 nodes isolated per specimen in those showing nodal involvement, and 41.4 nodes isolated in specimens showing no metastases. Sixty-two point five per cent of carcinomata of the right colon showed metastases, in comparison to 60 per cent of those of the left colon.

The routes of spread of carcinoma by the lymph channels are discussed.

Size of nodes is not an index of metastatic involvement. Duration of disease and size of tumor are not correlative with extent of nodal involvement.

Operation for removal of carcinoma of the colon should be planned on an anatomic basis, so as to include lymph node-bearing areas rather than on palpability of lymph nodes. The presence of metastases in lymph nodes from carcinoma of the colon is more frequent than indicated by previous studies based on isolation of lymph nodes by gross methods of dissection.

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