INVOLVEMENT OF THE LYMPH-NODES IN CARCINOMA OF THE RECTUM*

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The rectum next to the stomach is the most common location for malignant disease in the gastro-intestinal tract. Mayo reported 561 cases of malignant disease of the gastro-intestinal tract seen in the Mayo Clinic in

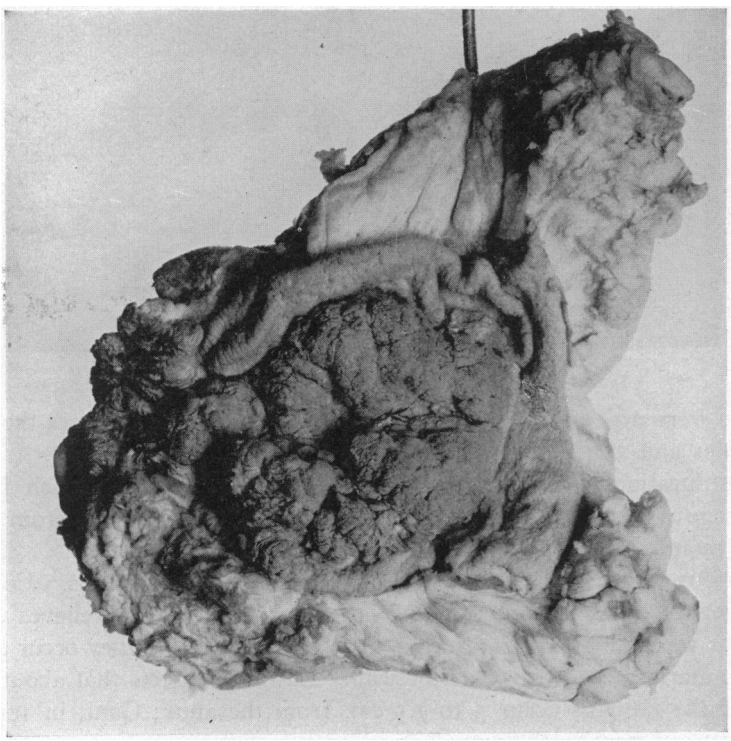

Fig. 1.—(Case A100372). Typical specimen of Group 1.

1908 and 1909. Of these growths, 387 were in the stomach, three were in the small intestine, sixty-nine were in the large intestine, and ninety-two were in the rectum. Gant, Ball, and Halsted assert that rectal cancers make up about 4 per cent. of all the cancers of the body, and that about 80 per cent. of the intestinal cancers occur in the rectum.

Patients with cancer of the rectum are usually in the sixth decade, but

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they may be any age. W. J. Mayo, in 120 operative cases, found the average age to be fifty-two years. Oehler, discussing the cases in Kraske's Clinic, says the average age is fifty-six years, slightly higher in males than in females. He quotes Kupferle in Czerney's Clinic who reported a case of rectal carcinoma in a patient aged thirteen years and the Rostocker Clinic as having two cases in patients fourteen and fifteen years, respectively.

The disease is more common in males than in females. In 25,000 cases of disease of the rectum treated for fistula, reported from St. Mark's Hospital by Edwards, 775 were malignant. Five hundred forty-two of the

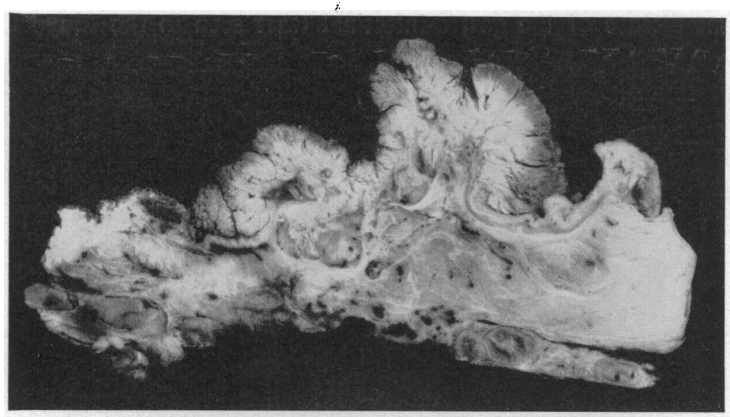

FIG. 2.—Longitudinal section of the growth shown in Figure 1.

patients were males and 233 were females. In Lynch's 491 cases there were 281 males and 210 females.

The duration of symptoms is usually under one year. Lynch found it to average eight months in 491 cases; in 20 per cent., it was from nine to twelve months.

Various writers fail to agree on the location of the growths. Cole gives the favorite site as the anterior and lateral walls; Rawling believes that the posterior wall is most often affected, and Oehler says that they occur as often on the anterior as on the posterior wall. Edwards asserts that about 80 per cent. of the growths occur 5 to 7.5 cm. from the anus; Gant, in 100 cases, found 50 per cent. in the ampulla and 15 per cent. in the upper rectum and sigmoid, while W. J. Mayo, in 100 consecutive cases, found 63 per cent. in the rectosigmoid, 30 per cent. in the rectum, and 7 per cent. in the anal canal. Mummery believes the commonest site is the rectosigmoid, and next the ampulla. He believes that those who say the growths occur at a lower level do not take into account the fact that they may descend after starting.

The usual type of growth is adenocarcinoma. In Lynch's 491 cases, 451 were adenocarcinomas. Of Gant's 100 cases, 95 per cent. were cylindric carcinomas, and in three-fourths of the cases studied by Oehler the growths were of the type which he calls adenocarcinoma simplex. In view of the various classifications which have been given to carcinomas of the rectum,

some based on clinical grounds, others on histologic grounds, and still others developed from a combination of both, it seems best not to attempt any classification other than carcinoma.

Carcinoma of the rectum develops from the crypts or glands of Lieberkuhn which, when they take on their migratory activities, break through the tunica propria of the mucosa into the submucosa, invade the circular muscular coat and, on reaching the intermuscular lymphatic network, tend, according

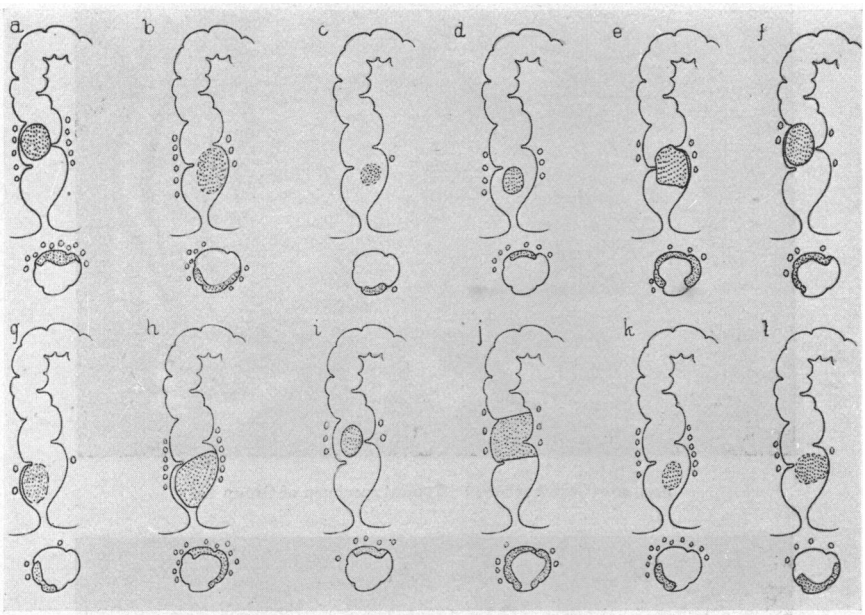

FIG. 3.—Diagram of relative position of glands and growth in twelve cases of Group 1. Glands not involved are shown as clear circles; glands involved are shown in solid black. *a* (Case A47322). Growth measuring 50 by 50 mm.; 10 cm. from anus. *b* (Case A57201). Growth on anterior wall measuring 50 by 70 mm.; 5 cm. from anus. *c* (Case A68756). Growth on anterior wall measuring 15 by 20 mm.; 5 cm. from anus. *d* (Case A70580). Growth on posterior wall measuring 25 by 33 mm.; 3 cm. from anus. *e* (Case A70730). Growth on posterior wall measuring 45 by 45 mm.; 6 cm. from anus. *f* (Case A81871). Growth on left and posterior wall measuring 40 by 50 mm.; 10 cm. from anus. *g* (Case A97023). Growth on anterior and left wall measuring 30 by 35 mm.; 3 cm. from anus. *h* (Case A100372). Growth on posterior and right wall measuring 50 by 70 mm.; 2 cm. from anus. *i* (Case A102528). Growth on posterior wall measuring 30 by 35 mm.; 10 cm. from anus. *j* (Case A103155). Encircling growth measuring 70 by 70 mm.; 10 cm. from anus. *k* (Case A104886). Growth on left and anterior wall measuring 20 by 25 mm.; 4 cm. from anus. *l* (Case 107782). Growth on anterior wall measuring 60 by 35 mm.; 4 cm. from anus.

to Cole, to progress around the bowel in the direction of these vessels. This accounts for the encircling tendency of rectal carcinoma. From here the cells invade the longitudinal muscle layer and on reaching the outer muscle wall their extension is restricted by the rectal fascia. The invasion of the lymph-nodes through the lymphatics may occur at any time after the disease reaches the submucosa, but such invasion is usually late. W. J. Mayo says that more cases are inoperable because of local extension than because of metastasis. Three methods of extension are described by Miles: Downward into the wall of the bowel below the growth, into the rectal sphincter, and ischiorectal fossa; lateralward into the fascia propria, levator ani muscles, capsule of the prostate, seminal vesicles, and base of the bladder in the male, and the vaginal

wall and genital organs in the female, and upward into the bowel above the growth, and the pelvic peritoneum and mesocolon. Handley has described a marked dissemination in the submucosa occurring early. This he claimed

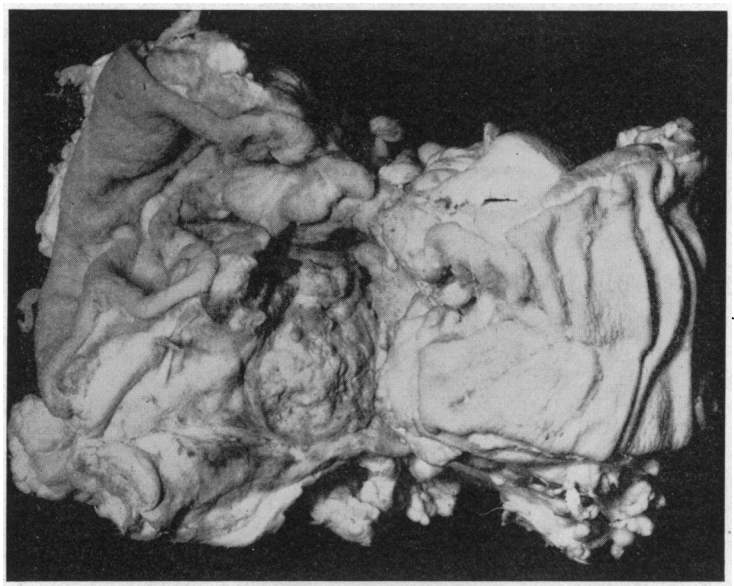

FIG. 4.—(Case A176669.) Typical specimen of Group 2.

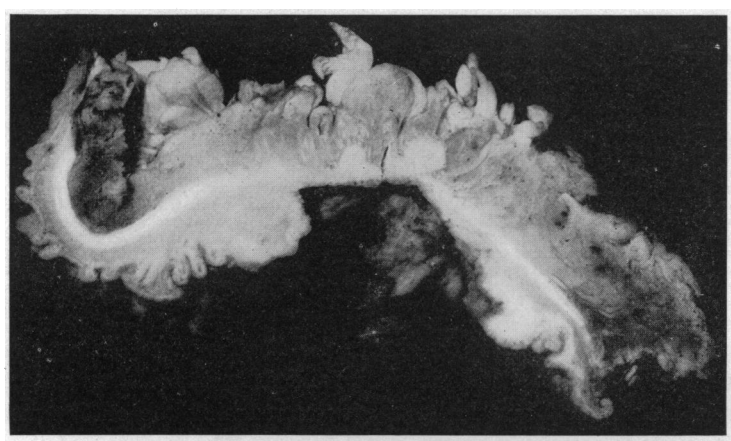

FIG. 5.—Longitudinal section of the growth shown in Figure 4.

to have demonstrated by mucicarmin staining of entire sections of the bowel. Cole, Monsarrat and Williams, and Cheatle were unable to confirm his findings.

Cancer of the rectum metastasizes slowly in most cases. Oehler had fifty-eight patients die from carcinoma of the rectum and thirty-four had no internal metastasis. Zinner found metastatic enlargement of retroperitoneal

lymph-nodes in only 3.5 per cent. of the 141 patients examined. Pennington collected data on 997 necropsies of patients dying from cancer of the rectum and in 324 the regional nodes were found to be involved. Metastasis, when it does occur, usually takes place in the liver. Oehler says that metastasis is most frequent in the liver and retroperitoneal lymph-nodes and that the lungs are seldom involved, and the remaining organs still more seldom. Rectal carcinoma may reach the liver through glandular metastasis or by the breaking off of emboli of carcinoma cells into the portal circulation, a method recognized and described by W. J. Mayo, McArthur, Smith, and others.

Materials and Methods.—One hundred specimens were studied which had been removed at operation at the Mayo Clinic. The size, location, form, extent, and character of the growth were studied as well as the normal mucosa, skin, surrounding fat, and fascia. Photographs were then made of the specimens, one showing the growth from the mucosal side, and one showing a cross-section cut through the centre of the growth in the longitudinal axis of the bowel. The character and extent of the invasion of the growth into the submucosa, muscular coats, glands, fat, and fascia were studied and sketches of the specimens were made, showing the relative location and size of the growth recorded in millimetres.

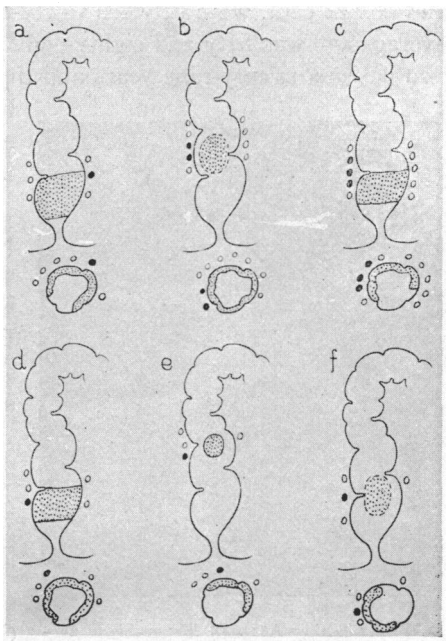

FIG. 6.—Diagram showing relative position of glands and growth in six cases of Group 2. Glands not involved are shown as clear circles; glands involved are shown in solid black. *a* (Case A174591). Growth on anterior wall measuring 95 by 60 mm.; 3 cm. from anus. *b* (Case A17 6669). Encircling growth measuring 50 by 60 mm.; 6 cm. from anus. *c* (Case A185201). Encircling growth measuring 45 by 40 mm.; 7 cm. from anus. *d* (Case A187873). Encircling growth measuring 80 by 55 mm.; 3 cm. from anus. *e* (Case A201505). Growth on posterior wall measuring 20 by 20 mm.; 12 cm. from anus. *f* (A250973). Growth on left wall measuring 50 by 50 mm.; 9 cm. from anus.

The anorectal lymph-nodes were then carefully dissected out, and as each gland was removed its location in the longitudinal and radial directions was recorded on the sketch. The glands were then placed in small phials correspondingly numbered and preserved in formalin. A section of the original growth was also made and similarly preserved. Frozen sections averaging about 10 microns in thickness were made of each gland and these were stained in hæmatoxylin and eosin and mounted in balsam.

The sections of the glands were studied for metastasis. On the sketches the results of the microscopic examinations were recorded for each gland with appropriate notes of any striking features.

The results were then recorded on printed diagrams. The diagrams were

made to represent the sigmoid, rectum, and anus as viewed posteriorly and also the rectum in cross-section. The growth was sketched in its relative position and the lymph-nodes were placed as near as possible in the relative position in which they were found. Glands which showed no carcinomatous involvement on microscopic examination were represented as clear circles, while those showing metastatic involvement were represented in solid black. The variation in the size of the glands is not indicated in the diagram.

Results.—Forty-seven per cent. of the patients were in the sixth decade and 96 per cent. were between thirty-one and seventy years (Table I). The average age was fifty and eighty-eight hundredths years. The youngest were two patients twenty-nine years and the oldest was seventy-nine. There were fifty-seven males and forty-three females. The average duration of symptoms was ten and four-tenths months.

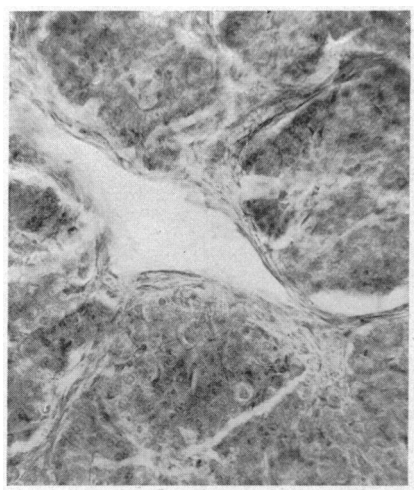

FIG. 7.—(Case A80564.) Metastasis in anorectal lymph-node. Cells show first degree of cytodifferentiation (X100).

Six hundred and twenty-three glands were obtained from the 100 specimens, or an average of six and twenty-three hundredths glands for each specimen. Fifty-three per cent. of the specimens did not show glandular involvement, 30 per cent. showed slight glandular involvement, and 17 per cent. showed marked glandular involvement. The cases may be readily classified into three groups: Group 1, cases of carcinoma of the rectum without metastatic involvement of the regional lymph-nodes. Group 2, cases of carcinoma of the rectum with metastatic involvement of less than one-half of the regional lymph-nodes, and Group 3, cases of carcinoma of the rectum with involvement of one-half or more of the regional lymph-nodes.

Group 1.—This group contained fifty-three patients (53 per cent.). Thirty were males and twenty-three were females. The average age was fifty-one and six-tenths years. The average number of glands for each specimen was six and nine-hundredths (Table II).

One of the most striking features is that the size of the growth (Figs. 1 and 2) apparently bears no relation to the extent of glandular involvement (Fig. 3). Most of the growths in this series were above the average in size and caused symptoms of equal or longer duration than the average for the series. Most were protuberant and appeared to be growing into the lumen of the bowel rather than into the bowel wall, as is seen in the cross-section of the growth. Little attempt at direct extension into the muscle and fatty layers is seen. The glands vary in size; many were much larger than those in the other groups, so that no attempt was made to demonstrate the relative size of the glands on the diagrams.

Group 2.—There were thirty patients (30 per cent.) in this group. Seventeen were males and thirteen were females. The average age was forty-eight and six-tenths years and the average duration of symptoms was eleven and

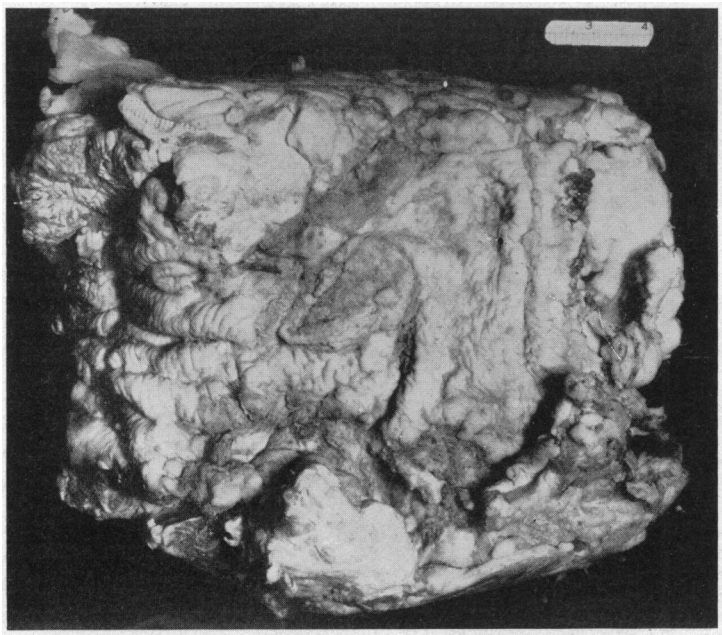

FIG. 8.—(Case A121346.) Typical specimen of Group 3.

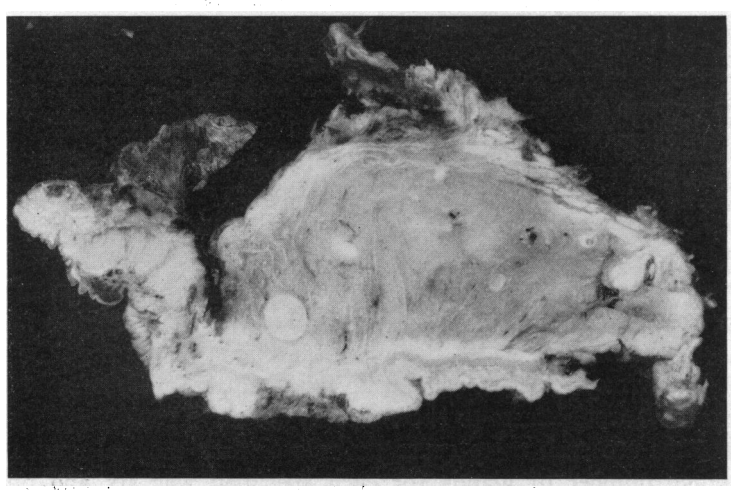

FIG. 9.—Longitudinal section of growth shown in Figure 8.

one-tenth months. The average number of glands for each specimen was six and five-tenths. The sex, age, duration of symptoms, number of glands found, and number of glands involved in each specimen are shown in Table III.

The photographs of this group (Figs. 4 and 5) also show that the size of the growth bears no direct relation to the amount of glandular involvement (Fig. 6). The protuberant type of growth occurred less often; most of the growths showed excavated ulcers. The growths showed a tendency to grow into the muscular tissue and the fatty tissue around the bowel wall, and thus to disseminate by direct extension. The gland or glands usually involved are those nearest the point of greatest direct extension. In other words, the metastasis is slow and the microscopic pictures show that the majority of the cells in most of the affected nodes, as seen in Figure 7, reach the state of secondary cyto-differentiation.[11] In many of the involved glands the cells are arranged in acinar form and in some this differentiation is advanced to the point of mucous production. This can only happen if the migration of the cells is slow and the tendency to return to the original type is strong.

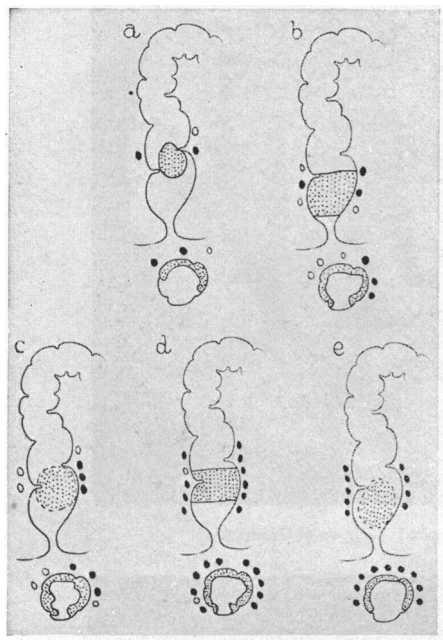

FIG. 10.—Diagram showing relative position of glands and growth in five cases of Group 3. Glands not involved are shown as clear circles: glands involved are shown in solid black. *a* (Case A110220). Encircling growth measuring 40 by 30 mm.; 9 cm. from anus. *b* (Case A121346). Encircling growth measuring 70 by 50 mm.; 5 cm. from anus. *c* (Case A139873). Growth on anterior wall measuring 80 by 60 mm.; 7 cm. from anus. *d* (Case A168690). Encircling growth measuring 55 by 60 mm.; 7 cm. from anus. *e* (Case A217336). Growth on anterior wall measuring 35 by 40 mm.; 3 cm. from anus.

Group 3.—There were seventeen patients (17 per cent.) in this group. Ten were males and seven were females. This is about the average for the entire series, so that sex apparently does not play a part in determining malignancy. The average age was fifty-one and two-tenths years and this also seems to show that the age does not determine malignancy to any great extent. It is true in carcinoma of the rectum as in all carcinomas in the body, that the most malignant types of growth occur in very young persons. The average duration of symptoms was seven and four-tenths months, which is almost four months less than the average for the other groups. While this group is too small for definite conclusions to be drawn, it would seem to show that in the more rapidly growing types the symptoms are such as to cause patients to seek medical advice earlier. The average number of glands for each specimen was six and one-tenth. Table IV gives the sex, age, duration of symptoms, total number of glands found and total number of glands involved for each specimen in the group.

The characteristic type of growth in Group 3 is seen to be the ulcerative (Figs. 8 and 9) and most of the growths were much smaller than the average of Group 1. The specimens (Fig. 9) resembled the growths in Group 2 in breaking through the muscular coats of the bowel, but their dissemination

into the fatty tissue surrounding the bowel was much less. Metastasis occurs early to the nodes (Figs. 10 and 11) before direct extension far into the surrounding tissues has taken place.

Early glandular involvement affects so small a part of the gland that it can only be ascertained by microscopic examination. The lymph sinuses at the edge of the gland are first affected (Fig. 12).

Smith says, "There is need for further investigation on this subject (speaking of glandular involvement in carcinoma of the rectum), but I think sections of all glands from a series of rectal growths would prove that

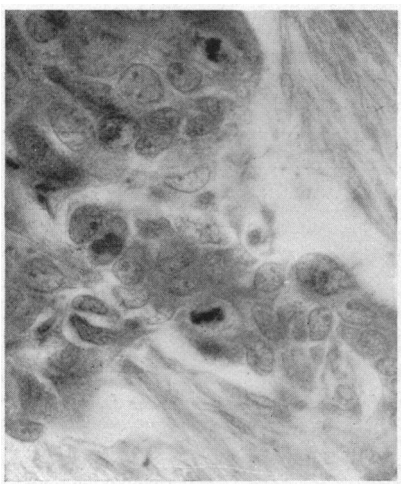

FIG. 11.—(Case A85834.) Metastasis in lymph-node. First degree of cytodifferentiation. Cells have large, clear nuclei with prominent nucleoli; two mitotic figures may be seen (X500).

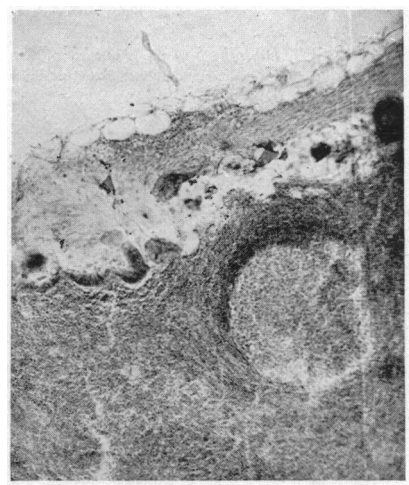

FIG. 12.—(Case A110220). Beginning involvement in peripheral lymph sinus, which could be determined by microscopic examination only (X50).

glandular invasion is not widespread in the stages early enough to be operable." This statement, based on clinical experience, is partially borne out by this study. Fifty-three per cent. of the patients did not have involvement of the glands, 30 per cent. had partial involvement, and 17 per cent. had marked involvement. Oehler reports that 38 per cent. of the fifty-four patients who died from carcinoma of the rectum and on whom necropsies were performed had glandular involvement in the retroperitoneal lymph-nodes. In Pennington's collected cases, 32 per cent. showed some involvement of the regional lymph-nodes. In neither instance was it stated that all the nodes were systematically examined. MacCarty and Blackford found 52 per cent. of 200 patients with carcinoma of the stomach to have glandular involvement. The close agreement of their percentages for the stomach and of those presented in this paper for the rectum is striking. It may mean that about one-half of the growths of the gastro-intestinal tract give rise to metastatic glandular involvement.

A systematic examination of the glands affords a more accurate idea of the prognosis in a given case. In studying the glands in Case A80564 (Fig. 7), the following note was made: Sections show but little evidence of differen-

tiation; the tumor should be rapidly growing. One should expect a short history and a poor result. When the history of the patient was consulted later, it was found that the symptoms had been present only six weeks. Operation was performed by the Mayo-Kraske method and the growth entirely removed. The patient returned to the Clinic six months later, and it was found that the disease had metastasized to the liver. He died shortly afterwards. The question of operability is often clinical, but the question of prognosis, aside from operative prognosis, is one which can only be accurately and safely answered by the aid of the microscope.

TABLE I

Distribution in Decades of the 100 Cases of Carcinoma of the Rectum

Age	Patients
21 to 30 years (29, 29, 30)	3
31 to 40 years	12
41 to 50 years	22
51 to 60 years	47
61 to 70 years	15
71 to 80 years (79)	1
Total	100

TABLE II

Group 1. Cases of Carcinoma of the Rectum Without Metastatic Involvement of the Lymph-nodes

Case	Sex	Age	Duration of symptoms, months	Glands dissected out	Case	Sex	Age	Duration of symptoms, months	Glands dissected out
669-½J	F	50	(?)	6	A120405	F	47	12	10
A2252	F	53	5	2	A121876	M	54	15	6
A3663	F	34	11	2	A123863	F	61	12	10
A7676	F	46	6	10	A124529	M	55	24	11
A7769	M	42	4	8	A132394	M	55	18	4
A8928	F	41	3	6	A136043	M	69	24	7
A715	F	58	12	5	A138027	F	51	4	3
A1484	F	53	36	5	A142982	F	47	36	1
A6354	F	54	8	3	A147264	F	67	3	2
A25364	F	61	12	2	A148799	M	69	5	11
A26283	F	70	(?)	6	A154180	M	34	12	4
A43441	F	57	12	9	A157347	M	54	12	7
A47322	F	53	18	10	A163565	M	43	24	10
A57201	F	51	10	9	A170796	M	57	8	4
A68756	M	51	12	1	A179420	M	48	36	9
A70580	F	56	3	7	A189827	M	55	11	7
A70730	M	53	12	5	A198743	F	53	3	4
A81871	M	52	7	4	A200441	F	38	5	6
A97023	M	60	18	3	A204879	M	57	13	9
A100372	M	50	12	12	A208438	M	44	3	5
A102258	M	45	6	5	A212669	F	40	24	5
A103155	M	64	12	6	A216300	M	39	9	4
A104886	M	46	8	11	A216842	M	43	7	7
A107782	M	44	4	4	A215439	M	51	12	4
A111786	M	50	12	10	A251281	M	54	3	5
A113133	F	51	12	9	A250263	M	54	7	2
A113219	M	53	12	6					

TABLE III

Group 2. Cases of Carcinoma of the Rectum With Metastatic Involvement of Less Than One-half of the Lymph-nodes

Case	Sex	Age	Duration of symptoms, months	Glands dissected out	Glands involved
A19499	M	36	3	3	1
A26781	F	52	7	3	1
A43021	F	30	12	7	2
A44196	M	66	2	9	1
A47912	M	39	12	7	1
A64157	M	29	36	5	1
A66903	F	53	10	7	1
A69046	M	59	9	8	2
A73143	F	68	3	9	2
A79532	M	48	24	7	1
A80562	M	56	1.5	8	1
A99562	F	45	6	5	2
A101064	F	53	9	5	2
A109751	F	59	10	7	1
A159369	F	38	24	8	1
A164471	F	58	18	8	3
A166175	M	50	2	7	2
A168277	F	52	5 (?)	5	2
A169130	M	58	12	11	3
A169140	F	56	24	6	1
A174098	M	42	18	7	1
A174591	M	60	12	6	1
A176669	M	51	12	9	2
A185201	F	40	12	10	3
A187873	M	59	9	5	1
A201505	F	51	12	4	1
A250973	M	79	3	4	1
A2360	M	63	8	5	1
A5092	M	56	6	6	1
A69290	M	66	12	6	1

TABLE IV

Group 3. Cases of Carcinoma of the Rectum With Metastatic Involvement of One-half or More Than One-half of the Lymph-nodes

Case	Sex	Age	Duration of symptoms, months	Glands dissected out	Glands involved
928M	F	69	3	2	2
4831-½J	M	50	6	5	4
A7039	F	65	24	7	7
A7624	F	64	8	5	3
A7631	F	60	12	5	3
A21961	M	33	4	5	5
A23639	M	54	5	6	3
A52248	M	54	3	6	3
A74532	F	43	36	12	6
A78911	M	39	3	8	7
A85834	M	56	4	4	2
A108406	M	55	7	5	3
A110220	M	64	1.5	3	2
A121346	F	29	6	6	3
A139873	M	60	2.5	6	3
A168690	M	40	1.5	11	10
A217336	F	36	1.?	9	9

SUMMARY

Rectal carcinomas are the most common form of intestinal neoplasms and make up 4 per cent. of all the cancers of the body. The majority of patients are in the sixth decade. The males predominate slightly. The location of the growth on the rectal wall varies. About as many occupy the anterior wall as the posterior. The greater number of the growths are from the ampulla to the rectosigmoidal juncture. Adenocarcinoma is the most common type. Metastasis to the glands usually takes place slowly and the liver is the organ most affected by secondary growths. The other organs of the body are only rarely affected.

The size of the growth in the rectum cannot be relied on as an accurate index of the probable lymphatic involvement. The growths without lymphatic involvement tend to grow into the lumen of the bowel. The growths with slight lymphatic involvement tend to spread by direct extension and are slow growing. Carcinomas of the rectum with extensive lymph-glandular involvement tend to metastasize through the lymph-stream early. Occasionally metastasis may take place by emboli breaking off into the portal veins.

Metastatic lymph-glandular involvement can only be definitely determined by systematic microscopic study of all the regional lymph-nodes. The size of the lymph-node is not an efficient means of determining whether or not there is metastatic involvement. This is especially true if the amount of involvement is small, or if the process is an early one.

Systematic microscopic examination of all the regional lymph-nodes in carcinoma of the rectum offers, as it does in cancer of the stomach, the best method of establishing an accurate prognosis for the case.

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