

# PATHOLOGY ANNUAL:

series editors SHELDON C. SOMMERS  
PAUL PETER ROSEN

PART 1

# **PATHOLOGY ANNUAL**

**PART 1**

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# **PATHOLOGY ANNUAL**

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## **PATHOLOGIC STUDIES IN COLORECTAL CANCER**

### **A Guide to the Surgical Pathology Examination of Colorectal Specimens and Review of Features of Prognostic Significance**

**ALI H. QIZILBASH**

Cancer of the colon and rectum is becoming the most important malignancy in North America today. It is second in mortality to cancer of the lung in men and of the breast in women.<sup>1</sup> In 1981, approximately 120,000 new cases of colorectal cancer will be diagnosed in the United States.<sup>1</sup>

There are approximately 500,000 living persons in the United States who have cancer of the colorectum.<sup>2</sup> Mortality figures show that there has been little change since 1950<sup>1</sup> in the survival rate for such cancer; the 5-year survival rates for the period 1950 to 1959 were 42 percent for males and 46 percent for females. For the period 1965 to 1969 the rates were 43 and 46 percent, respectively.

Surgical specimens from patients with tumors of the colorectum continue to be among the tissue specimens most frequently examined by pathologists. The way in which this examination is done, and the final reporting of the results, play an important role in assessing the prognosis. The clinical staging of colorectal cancer is not accurate because of the difficulty encountered in clinically assessing the extent of the disease. However, the careful and systematic examination of surgical specimens gives the clinician valuable information regarding the configuration and grade of a lesion, the extent of spread, and the extent of vascular and lymphatic invasion if any—factors which have an important bearing on the patient's ultimate survival. Additionally, with increasing interest in more individualized methods of treatment for cancer of the large bowel, accurately compiled pathologic data assist in delineating patients suitable for local treatment or adjuvant chemotherapy.

Analysis of surgical pathology reports show that no uniform standard for reporting exists, and some workers have compiled essential information for pathology reports.<sup>3</sup> The American Joint Committee for Cancer Staging and End Result Reporting<sup>4</sup> has developed a system of clinical and pathologic staging—the

TNM system—for the purpose of standardizing the classification of cancer in various sites. The TNM system provides a basis for categorizing the extent of disease; essential site-specific information is recorded on standard data forms. The method of reporting used is not crucial as long as the factors important in making the prognosis are accurately recorded.

The surgical pathologist has an important role to play in the emerging multidisciplinary setting in the treatment of patients with cancer in various organs. The time-honored triad of pathologist, radiologist, and surgeon must now be expanded to include the radiotherapist and the oncologist or chemotherapist. It is not only enough to be able to make a diagnosis—prior knowledge of the patient and the results of previous investigations and biopsy are important in the subsequent handling of surgical specimens.

## GENERAL CONSIDERATIONS

The surgical pathologist is responsible for the pathology specimen once it is removed from the patient. It is his responsibility to make sure that the specimen is properly handled and promptly delivered to the processing laboratory. All large specimens should be sent in the fresh state to prevent distortion by fixatives. The bowel undergoes considerable shrinkage on fixation, with the result that the adequacy of the resected margins may be underestimated if measurements are taken following fixation. Bowel specimens should be examined right away and not left to be handled at the end of the day, after the other, smaller specimens have been examined.

An accurate and detailed gross examination of the specimen is important and cannot be overemphasized. This should be supplemented by photographs of the specimen in the fresh state where possible. In addition, we have found line drawings depicting the lesions and relationships to important landmarks and margins to be very useful. Fixation of the specimen is necessary before blocks are taken for sections, and care should be taken in handling specimens in preparation for fixation. If any washing is required—such as the flushing of feces out of the bowel—it should be done with a weak solution of formalin or isotonic saline, and not with tap water. The choice of fixative is a personal matter, but we have found a 10 percent dilution of 40 percent formaldehyde in normal saline, buffered to neutrality, to be a satisfactory fixative. Although formalin penetrates slowly, the tissues do not harden unduly even after prolonged fixation, and the results are good if prior specimen preparation is adequate. It takes from 24 to 48 hours before a specimen of bowel is fixed satisfactorily, enabling adequate blocks to be taken. In my experience, frozen sections are rarely employed unless the resection margin is very close to the tumor, or when they are necessitated by some unexpected finding at surgery.

## METHOD OF EXAMINATION OF THE LARGE-BOWEL SPECIMEN

The unopened specimen received from the operating room should be carefully examined, with note taken of the external features. The segment of the bowel should be identified—as for example, whether it is from a right hemicolectomy, a sigmoid

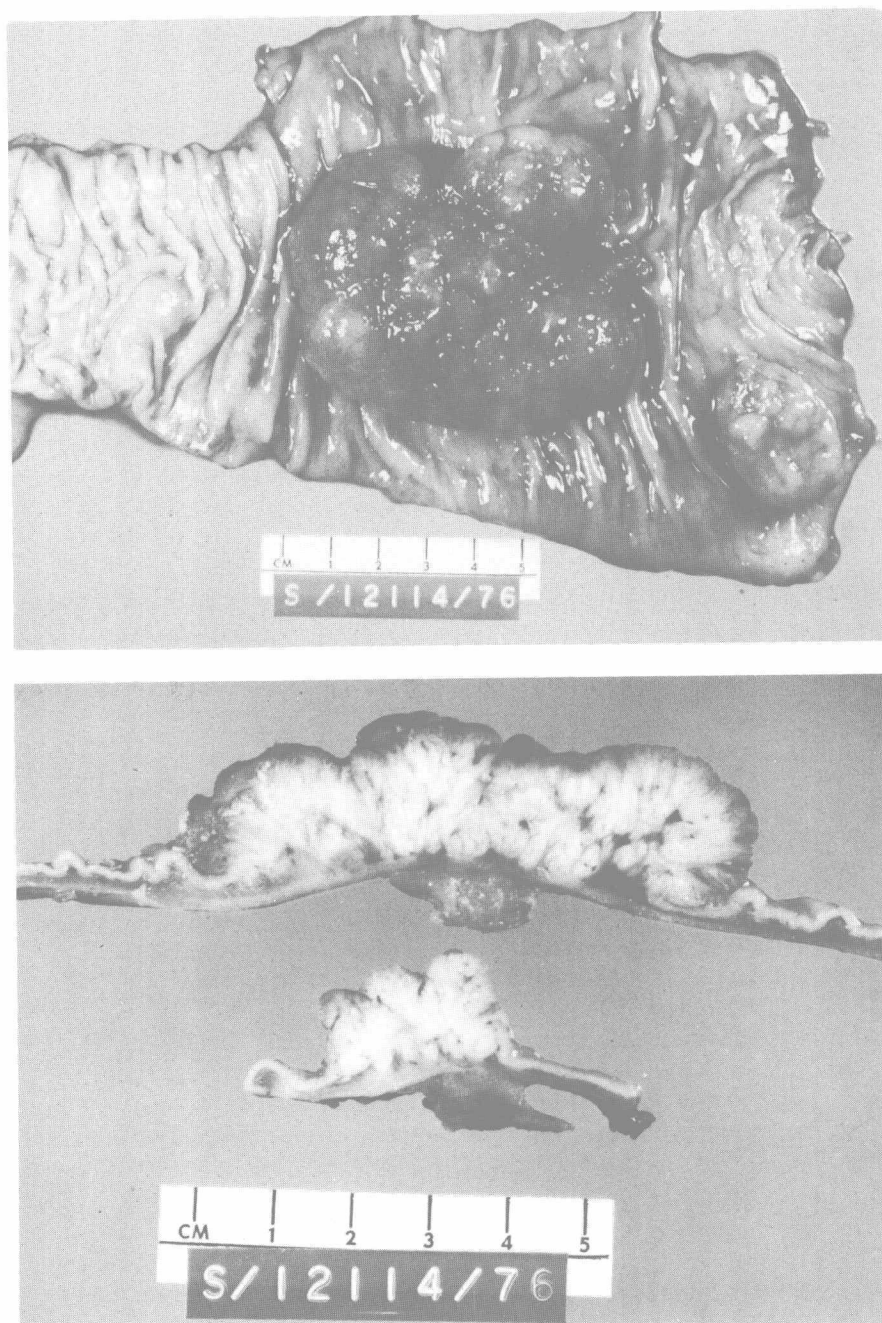
resection, or an abdominoperineal excision. The length of the bowel and its diameter both above and below the lesion are recorded. Note is made if the appendix or a segment of terminal ileum are present, and their measurements and characteristics are recorded. The amount and features of the mesentery are next recorded. Note is made of the appearance of the serosa of the bowel. Any other lesions noted grossly, such as diverticula, perforations, or tumor deposits, are recorded.

Once the initial gross examination described above is completed, the specimen should be prepared for fixation. Some workers<sup>5</sup> advocate inflating the specimens with formalin. Although this is a good method for preserving specimens for museum purposes, I personally favor, for routine purposes, the alternate method described below. Following gross examination, the specimen is opened lengthwise along the antimesenteric border. In case of the rectum and anus, it is cut open with scissors along the midline anteriorly. A slight deviation may be necessary to avoid cutting through the tumor. The mucosa is then gently rinsed to get rid of the feces. The size of the tumor (in three dimensions) and the site are next recorded. Multiple cancers should be described and labeled separately (Fig. 1). The relationship of the lesion to the pectinate line, ileocecal valve, or other landmarks is noted. The color, consistency, and configuration of the tumor should be recorded. It is important to accurately record if the tumor is polypoid and involving, for instance, only one-fourth of the circumference of the bowel, or whether it is a constrictive, napkin-ring type of lesion causing complete obstruction.

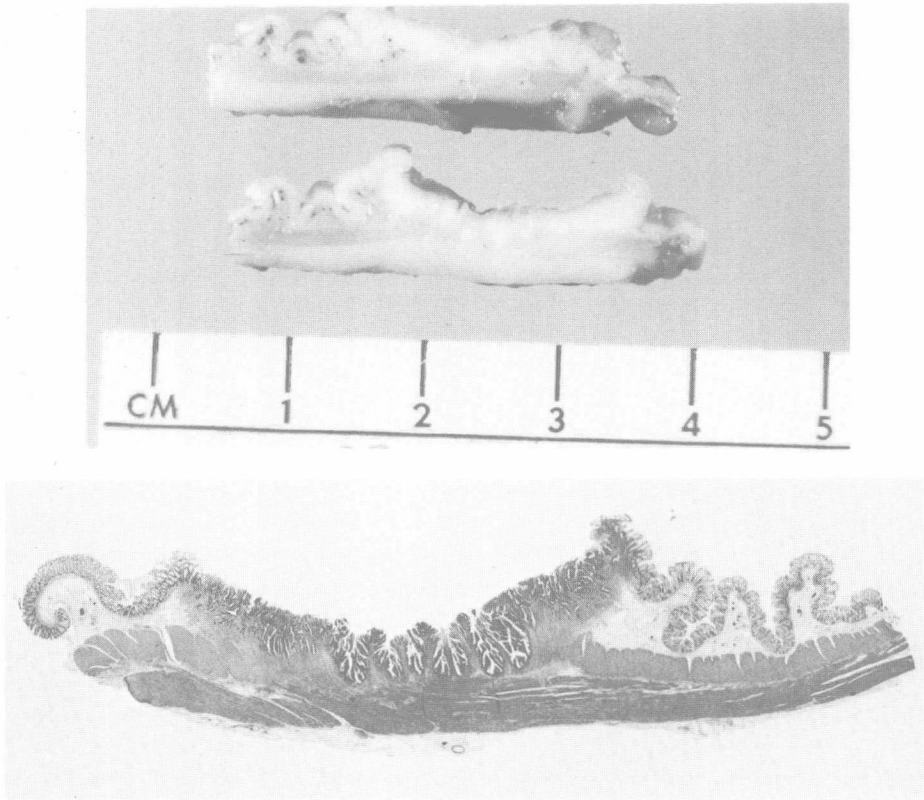
The tumor should next be sliced through the region of deepest penetration to note the extent of local spread (Fig. 2). In the majority of cases, gross examination will give a fairly good idea of the extent of local spread. However, this should always be confirmed histologically. The distance of the tumor from the resected margins should be recorded. Any other lesions—for example, polyps—and their size, number, location, etc., should be noted. The length of the stalks should be recorded. The presence of diverticula and changes of inflammatory bowel disease, such as ischemia or ulcerative colitis, should be documented.

The presence or absence of lymphatic spread is next studied. The best way to examine the lymph nodes is to turn the specimen over and cut a series of thin slices through the extrarectal and colonic tissues from the outside in, hinging these slices on the uncut wall of the bowel. The lymph nodes can easily be felt and seen, and can be removed for microscopic study. Another way of looking for lymph nodes is to remove the glands in groups, for example, fatty tissue containing lymph nodes is removed separately from the immediate vicinity of the cancer, as well as fatty tissue distal or proximal to the tumor. The topmost glands located at the point of ligation of the vascular pedicle should always be identified. Following separation of the fat containing the various groups of lymph nodes, the search for the lymph nodes is undertaken. The lymph nodes are separated from the fat and put in a fixative overnight. The nodes are identified as to location.

No difficulty is usually encountered in finding large lymph nodes involved by cancer. However, finding normal-sized lymph nodes may pose a problem for the inexperienced. I have found that sampling lymph nodes is easier before fixation, when lymph nodes appear light pink to gray in color in contrast to the yellow color of the surrounding fatty tissue. After fixation in formalin, the nodes appear pale



**FIG. 1. Top.** Gross appearance of two polypoid cancers of the rectum. The smaller one is very close to the distal resected margin. **Bottom.** Slices through the center of the tumors reveal that both are confined to the bowel wall.



**FIG. 2. Top.** Slices of an ulcerated adenocarcinoma from the area of deepest penetration show that the lesion is confined to the bowel wall. **Bottom.** The large section confirms the gross impression. H&E.  $\times 3$ .

gray, and separation from the surrounding fatty tissue becomes more difficult. Clearing techniques have been used to identify lymph nodes; the mesentery is immersed in graded alcohols followed by xylene to remove fat. This, however, is time-consuming, expensive, and not recommended for routine work. Following the search for lymph nodes, the veins should be carefully examined for the presence of tumor.

With the gross examination completed, the specimen is then pinned on a corkboard and fixed for 24 hours in formalin. After overnight fixation, I usually remove the specimen from the corkboard and let it lie flat in formalin until the late afternoon, when blocks are taken. The numbers of blocks one takes depend on the size of the cancer. Small lesions may require taking only two blocks, whereas larger ones may necessitate examining 6 to 12 sections, especially if the tumor is necrotic. On the average, I find four sections of the tumor quite adequate. The blocks taken should include the junction of the tumor and the adjacent bowel mucosa, and at least one block should be routinely taken from the region of deepest penetration, consisting of about equal parts of tumor and apparently normal tissue. Sections



should be taken of the proximal and distal margins. If the tumor is situated in close proximity to the resected margin, I usually take a longitudinal section, to include the tumor and the margin. Otherwise, transverse sections, which would comprise most of the circumference, are taken. The use of India ink to determine surgical margins is to be recommended; however, fixed tissues do not take the ink as successfully as fresh tissue, so that margins should be inked prior to fixation.

If more than one tumor is present, the blocks from each tumor must be separately labeled. Polyps and other mucosal lesions should be sectioned. With rare exceptions, sections should be taken from all polyps. Small polyps can easily be embedded whole; however, large ones may require trimming. The polyps should be blocked in such a way so as to include the head and the stalk. In patients with familial polyposis it may be necessary to examine dozens of polyps. Large villous adenomas are notorious for harboring small foci of carcinoma; therefore, multiple sections of these should be taken. Random sections of the colon away from the tumor should be routinely taken. All lymph nodes identified and removed previously should be blocked and appropriately labeled. The highest lymph nodes at the point of vessel ligation should be separately blocked. Sections from the extracolonic tissues should be included, for the study of mesenteric vessels. Sections from right hemicolectomy specimens should include the appendix and the terminal ileum. In abdominoperineal resections, blocks from the anus should be taken for histologic study.

The size of the tissue blocks taken for histologic study varies in different laboratories, and thus one cannot arbitrarily recommend the optimum number of blocks. I personally take a minimum of four blocks, including one through the center, to include the area of deepest penetration of the tumor, and multiple sections from the periphery of the tumor and the adjacent nonneoplastic tissues. In addition, I usually take, in selected cases for a large section, a longitudinal block of tissue of the entire tumor and surrounding fatty tissue.

## STUDY OF COLORECTAL CANCER BY LARGE SECTIONS

For the past 10 years I have been using large sections cut on a Leitz sledge microtome for the study of tumors of the gastrointestinal tract. After 24 hours fixation in formalin, longitudinal or cross-sections of bowel, including the entire tumor and surrounding tissues, are cut. A thin slice of tissue from the center of the lesion, of approximately 0.75 cm thickness, is selected. Care should be taken not to make the blocks very thin since a fair amount of rough cutting is necessary before a satisfactory slide is obtained. The size of the blocks varies, depending on the lesion; however, blocks of up to approximately 9.0 cm by 7.0 cm can be cut. These are mounted on large glass slides 10.0 cm by 8.0 cm in size, and are studied both grossly and microscopically.

The total time involved from the time that a slice of tissue is selected to the time that the stained slide is made is approximately a week; however, this largely depends on the size of the block. I routinely fix a large slice of tissue for an additional 12 hours before beginning processing. The volume of the fixative should be