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# Contribution of the Pathologist to the Radiology and Management of Colorectal Polyps

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Most of the confusion and disagreement over the classification and malignant potential of polyps of the large bowel have resulted from controversy about nomenclature and wrong use of words. For these reasons it is important to define accurately the use of current terms and their synonyms.

It is essential in the first place to define the meaning of *polyp*. This is a clinical or gross description of any circumscribed tumor or elevation that projects above the surface of surrounding flat normal mucous membrane, and the term should not be used by itself as a histologic diagnosis. Polyps can be tumors on a long stalk, a short stalk, or no stalk at all. Commonly they are sessile, but clearly demarcated, elevations, but exceptionally they may be so flat as to be barely visible to the naked eye. Polyps with stalks are seldom larger than 3 cm in diameter, but sessile lesions can vary in size from 1 millimeter diameter to as much as 10 cm across. The elevation of sessile tumors above surrounding normal mucosa is also variable. Study of the shape and size of the various histologic types of polyps gives the radiologist valuable clues to diagnosis.

There are many histologic types of polyps which vary in their clinical significance and particularly in their malignant potential. In Table I a histologic classification is given of the common and most important benign polyps seen in clinical practice. There are 4 main classes, all of which can present as single or isolated multiple tumors or in the form of *polyposis*, a term usually reserved to describe the presence of hundreds or thousands of polyps covering the mucous membrane of the large bowel. Like "polyp," the word "polyposis" has significance only as a clinical or gross description.

There is no acceptable evidence that metaplastic or hyperplastic polyps have any malignant potential. When present in considerable numbers they may be confused with familial (adenomatous) polyposis. Juvenile polyposis has malignant potential for colorectal cancer, but present evidence suggests that the magnitude of risk is much lower than in adenomatosis. In the Peutz-Jeghers syndrome colorectal cancer is rare, and when malignancy complicates this disease the cancers are usually found in the stomach and small intestine. Inflammatory polyposis per se does not predispose to cancer. Polyps with significant malignant potential are those in the neoplastic (adenoma) group of tumors. *Neoplasia* is, of course, a term applicable to both adenoma and carcinoma, and

**Table 1.** Histological classification of colorectal polyps

| | Single | Multiple (polyposis) |
|---|---|---|
| Neoplastic | Adenoma – Tubular<br>– Tubulovillous<br>– Villous | Familial polyposis coli |
| Hamartomatous | Juvenile polyp<br>Peutz-Jeghers polyp | Juvenile polyposis<br>Peutz-Jeghers syndrome |
| Inflammatory | Benign lymphoid polyp | Inflammatory polyposis (e.g. in non-specific and specific forms of inflammatory bowel disease)<br>Benign lymphoid polyposis |
| Unclassified | Metaplastic (hyperplastic) | Metaplastic (hyperplastic) polyposis |

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**Table 2.** Neoplastic polyps

| | | |
|---|---|---|
| Adenoma | – Tubular | (syn. adenomatous polyp) |
| | – Tubulovillous | (syn. villo-glandular adenoma) |
| | – Villous | (syn. villous papilloma) |

the adenoma-carcinoma sequence is an expression that covers both the preinvasive and invasive stages of neoplasia.

## Histology of Adenomas

Colorectal adenomas are well-demarcated, circumscribed lumps of epithelial dysplasia (atypia) with or without a stalk, which can be categorized into 3 histologic types: tubular, tubulovillous, and villous [1] (Table 2). The histology of these 3 types of adenomas has been well documented, but it is important to remember that they are not sharply separable from one another, being only different manifestations of a spectrum of abnormal tissue architecture [2].

It is common to see differing grades of dysplasia within any one adenoma, and individual adenomas should be classified according to the part with the most advanced grade. Sometimes an area with one grade of dysplasia has a distinct boundary with the adjacent area showing a different grade, but more often there is a gradual transition. A focus of severe dysplasia in an adenoma often shows an expansive growth pattern and a sharp boundary with the adjacent mild to moderate dysplasia. There have been other studies on grading dysplasia [3–6], but it must be emphasized that grading is a subjective assessment encompassing both structural and cytologic changes.

Although there are differences, the cellular features of dysplasia in adenomas have much in common with those of the dysplasia seen as a consequence of longstanding ulcerative colitis [7] and the chronic colitis caused by *Schistosoma japonica* [8]. Similar changes of focal or diffuse epithelial dysplasia are seen in the stomach [9] and in the squamous mucous membrane of the esophagus [10]. Moreover, it has been pointed out [11] that the word "dysplasia" has general applicability in the description of histopathological precursor lesions for cancer in a variety of epithelial surfaces both within and outside of the gastrointestinal tract. Conceptually it now appears advantageous to think in terms of the dysplasia-carcinoma sequence rather than the polyp-cancer or adenoma-carcinoma sequence in the colorectum.

It is essential to obtain agreement on the use of the word *carcinoma* or *cancer* in the context of malignant change in adenomas. Severe dysplasia or atypia can be equated with carcinoma in situ. The meaning of this is readily understood among histopathologists but can give a wrong impression when used in histologic reports. It communicates a sense of anxiety to some surgeons, which can lead to unnecessarily radical operations. It cannot be emphasized too strongly that as long as tumor is confined above the line of the muscularis mucosae, there is no potential for metastasis even though the tissue changes satisfy all the cytologic criteria for adenocarcinoma. Because there are no lymphatics in colonic mucosa above the line of the muscularis mucosae [12], neoplastic epithelial cells can metastasize only after traversing this line. For this reason it is best to restrict the use of the word carcinoma to that stage of the adenoma-carcinoma sequence in which neoplastic cells have invaded the submucosal tissues. In these circumstances it is important to distinguish between pseudocarcinomatous and carcinomatous invasion [13].

*Focal cancer* is an expression that should also be avoided because it is used by some to mean a focus of carcinoma in situ or severe dysplasia (atypia), whereas for others it means a focus of early invasion (microinvasion) across the muscularis mucosae into the stalk or submucosal tissues of a tumor that otherwise has the structure of an adenoma.

**Table 3.** Persons at increased risk of colorectal cancer

1. Patients with a long history of extensive ulcerative colitis
2. Members of polyposis coli families
3. Members of colorectal cancer families
4. Patients who have had a colorectal cancer removed
5. Patients with isolated adenomas

## Patients at Increased Risk of Colorectal Cancer

There is an important distinction between a precancerous condition, which is a clinical state associated with a significantly increased risk of cancer, and a precancerous lesion, which is a recognizable histopathological abnormality in which cancer is more likely to occur than in its apparently normal counterpart [14]. The first 4 groups of patients listed in Table 3 all have precancerous conditions, whereas those with adenomas have a lesion that seldom gives rise to significant symptomatology and is usually discovered incidentally during investigation for a variety of abdominal and anorectal complaints. However, the adenoma is the histopathological precursor lesion for those clinical conditions recognized as polyposis coli, colorectal cancer occurring in families, and metachronous cancer. The histopathological marker for increased cancer risk in ulcerative colitis is epithelial dysplasia, which, although its gross appearance is different from that of the adenoma, is caused by essentially the same biological mechanism.

The magnitude of cancer risk in ulcerative colitis is very low; in contrast, the risk in adenomatous polyposis (polyposis coli) reaches 100% with time [6]. For colorectal cancer families the magnitude of risk is not clear but probably varies with the number of affected family members. The risk of a second primary or metachronous cancer in remaining bowel after partial removal of bowel for malignancy begins at about 2 years after the first operation and steadily increases with time [15, 27].

The pathologist has a special role in the study of histopathologic markers of increased cancer risk. In ulcerative colitis a severe grade of dysplasia has been shown to be a valuable marker in cancer surveillance programs, but the adenoma is a common lesion and a dilute marker of increased cancer risk. The task of the pathologist is to search for more selective markers of high risk within the adenoma group of tumors because only in this way will it be possible to identify, register, and follow-up populations of patients small enough to be manageable in terms of long-term surveillance, availability of technical expertise, and cost effectiveness.

## Colonoscopic Survey of Adenomas

The increasing role of colonoscopy and polypectomy in the diagnosis and management of colorectal adenomas during the past decade has provided the histopathologist with an abundance of valuable material for study. This material is especially useful because, in many patients subjected to colonoscopy, the entire colorectum has been visualized at one examination and all polyps removed for histologic diagnosis. Previous studies have relied on adenomas removed by proctosigmoidoscopy only, and surgical segments of bowel usually removed for carcinoma in which adenomas were a coincidental finding. Therefore, a colonoscopic survey should provide more detailed information about their distribution in the large bowel matched against other variables such as size, histologic type, and grade of dysplasia.

## Distribution and Size

Table 4 shows the site distribution of 1187 adenomas. The number of rectal adenomas should not be compared to the number in the colon because rectal adenomas are often treated separately from colonic adenomas. About half (47%) of adenomas removed were located in the sigmoid colon; the percentage decreased from the sigmoid proximally to the right colon (8.2%) in striking contrast to the distribution of adenomas in autopsy series [16–21]. Most reports of autopsy studies show a more or less even distribution with a slightly greater percentage in the right colon. It must be remembered, however, that adenomas found in autopsy studies were mostly smaller than those in this colonoscopic series.

**Table 4.** Distribution of adenomas (combined series)

| Right colon | Transverse colon | Descending colon | Sigmoid colon | Rectum | Total |
|---|---|---|---|---|---|
| 8.2% (97) | 13.6% (161) | 18.7% (222) | 47.0% (559) | 12.5% (148) | 100% (1,187) |

**Table 5.** Size and site of (1,187 adenomas)

| | Right colon | Transverse colon | Descending colon | Sigmoid colon | Rectum | Total |
|---|---|---|---|---|---|---|
| < 5 mm | 64.0% (62) | 69.2% (111) | 44.6% (99) | 22.2% (124) | 48.0% (71) | 39.3% (467) |
| 6–10 mm | 18.5% (18) | 17.4% (28) | 31.1% (69) | 38.8% (217) | 29.0% (43) | 31.6% (375) |
| > 10 mm | 17.5% (17) | 13.4% (22) | 24.3% (54) | 39.0% (218) | 23.0% (34) | 29.1% (345) |

**Table 6.** Size of rectal adenomas

| | < 5 mm | 6–10 mm | > 10 mm |
|---|---|---|---|
| Rectal adenomas in colonoscopic series | 52.6% (142) | 25.2% (68) | 22.2% (60) |
| All rectal adenomas 1976–1979 | 48.0% (71) | 29.0% (43) | 23.0% (34) |

Table 5 shows the size of 1187 adenomas by site. Colonic adenomas smaller than 5 mm show a comparatively even distribution, but in striking contrast those measuring 5–10 mm and greater than 10 mm are concentrated in the sigmoid colon; the difference is statistically highly significant ($X^2 = 162.17$; df = 8; $P \ll 0.001$).

A similar trend has been shown in other studies [18, 20]. The figures for the rectum in Table 5 are similar to those of a previous series of rectal adenomas (270) removed from 1976 to 1979 at St. Mark's Hospital (Table 6). The percentages of rectal adenomas measuring 6–10 mm and greater than 10 mm are less than those of sigmoid colon adenomas within the same size group. In Table 5 so far as the relationship between size and site is concerned, the rectum and the descending colon showed a similar tendency. However, broad-based adenomas often measuring 3.0 cm across or even larger are more common in the rectum than in the sigmoid or descending

**Table 7.** Percent grades of dysplasia by site (1,187 adenomas)

| | Right colon | Transverse colon | Descending colon | Sigmoid colon | Rectum | Total |
|---|---|---|---|---|---|---|
| Mild | 94.9% (92) | 90.7% (146) | 86.0% (191) | 74.8% (418) | 84.5% (125) | 81.9% (972) |
| Moderate | 4.1% (4) | 8.1% (13) | 8.1% (18) | 15.7% (88) | 10.1% (15) | 11.6% (138) |
| Severe | 1.0% (1) | 1.2% (2) | 5.9% (13) | 9.5% (53) | 5.4% (8) | 6.5% (77) |

**Table 8.** Grades of dysplasia in rectal adenomas

| | Mild | Moderate | Severe |
|---|---|---|---|
| Rectal adenomas in colonoscopic series | 84.5% (125) | 10.1% (15) | 5.4% (8) |
| All rectal adenomas 1976–1979 | 82.2% (222) | 12.6% (34) | 5.2% (14) |

**Table 9.** Histological type by site (1,187 adenomas)

| | Right colon | Transverse colon | Descending colon | Sigmoid colon | Rectum | Total |
|---|---|---|---|---|---|---|
| Tubular | 83.5% (81) | 89.4% (144) | 85.5% (190) | 78.8% (440) | 69.6% (103) | 80.7% (958) |
| Tubulovillous | 14.4% (14) | 9.9% (16) | 11.7% (26) | 18.2% (102) | 25.0% (37) | 16.4% (195) |
| Villous | 2.1% (2) | 0.6% (1) | 2.7% (6) | 3.0% (17) | 5.4% (8) | 2.9% (34) |

**Table 10.** Histologic type of rectal adenomas

| | Tubular | Tubulovillous | Villous |
|---|---|---|---|
| Rectal adenomas in colonoscopic series | 69.6% (103) | 25.0% (37) | 5.4% (8) |
| All rectal adenomas 1976–1979 | 70.7% (191) | 23.0% (62) | 6.3% (17) |

colon. In the right colon and in the transverse colon 67% of adenomas were less than 5 mm. Larger adenomas in the sigmoid colon and rectum may be detected more readily than large adenomas in other parts of the large bowel because of easier accessibility to endoscopic examination.

*Site and Grade of Dysplasia*

Table 7 shows the relationship between the grade of dysplasia and the site. The most striking difference is the high percentage (9.5%) of severe dysplasia in the sigmoid colon; 68% of adenomas with severe dysplasia are located in this part of the colorectum. Adenomas with moderate dysplasia, although more often seen, show a similar subsite distribution to adenomas with severe dysplasia. The difference is statistically highly significant ($X^2=44.19$; $df=8$; $P \ll 0.001$).

The percentage of each grade of dysplasia in the rectum is more or less similar to that obtained from the series of all rectal adenomas removed at St. Mark's Hospital from 1976 to 1979 (Table 8), and in this series is similar to that in the descending colon. The unexpectedly small percentage of severe dysplasia in the right colon and rectum could be due to biased selection of patients.

*Histologic Types*

The majority of adenomas (81%) are classified as tubular; 16% as tubulovillous (intermediate); and only 3% as villous (Table 9). Except for the percentage of villous adenomas, these figures are not significantly different when compared with a previous report from this hospital [6]. The percentage of villous adenomas in this study is smaller than that in the surgical series reported by Muto et al. [6] probably because in this colonoscopic series there was a smaller number of rectal adenomas.

It has been stated that villous adenomas are located almost exclusively in the rectum [22, 23]. In contrast, our study has shown that both tubulovillous and villous adenomas are more widely distributed with only a slightly higher incidence in the rectum and in the sigmoid colon. The percentage in the right colon, although not significantly different, is slightly higher than that in the transverse and descending colon. Again, the data for tubulovillous and villous adenomas of the rectum in this colonoscopy series (including adenomas removed by other methods) are similar to those for the previous surgical series of rectal adenomas removed at St. Mark's Hospital from 1976 to 1979 (Table 10)

*Grade of Dysplasia and Histologic Type*

The percentage of the different histologic types in relation to degree of dysplasia shows that as the histologic type becomes more villous, severe dysplasia becomes more common (Table 11). This trend is similar to that shown in other studies [4, 6].

**Table 11.** Percent grades of dysplasia by histologic type (1,187 adenomas)

| | Tubular | Tubulo-villous | Villous | Total |
|---|---|---|---|---|
| Mild | 88.2% (845) | 57.9% (113) | 41.2% (14) | 81.9% (972) |
| Moderate | 7.7% (74) | 26.2% (51) | 38.2% (13) | 11.6% (138) |
| Severe | 4.1% (39) | 15.9% (31) | 20.6% (7) | 6.5% (77) |

**Table 12.** Number of adenomas per patient (601 patients)

| | |
|---|---|
| 1 | 50% |
| 2 | 24% |
| 3 | 14% |
| >3 | 12% |

**Table 13.** Grade of dysplasia (%) and number of adenomas (601 patients)

| | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Mild | 73 | 63 | 59 | 51 |
| Moderate | 13 | 20 | 24 | 24 |
| Severe | 14 | 17 | 17 | 25 |

*Size and Grade of Dysplasia*

The influence of the size of adenomas on grade of dysplasia shows a trend similar to that previously reported from this hospital [6]. As the size of adenomas increases, so does the grade of dysplasia, in agreement with previous studies [4, 22, 24]. Size is the most simple and practical indicator and is closely related to grade of dysplasia.

*Multiplicity of Adenomas*

The number of adenomas per patient for this series is given in Table 12. Investigation of the relationship of size and number of adenomas per patient showed that with increasing number there is a trend toward a greater percentage of adenomas with severe dysplasia (Table 13). As the patient's age increases, there is also a trend for the percentage of patients with multiple adenomas to increase (Table 14).

There are reports relating increased numbers of adenomas to increased cancer risk [6, 25]. For example, Muto et al. [6] reported that as the number of adenomas per patient increased, so did the percentage of patients with invasive carcinoma.

Patients with multiple adenomas tend to have a greater risk of developing severe dysplasia, which suggests that these patients have a higher cancer risk than the patients with solitary adenomas. The evidence that the greater the number of adenomas per patient, the greater the cancer risk is supported by the example of familial polyposis coli, in which there are thousands of adenomas per patient, with an almost 100% risk of developing carcinoma.

**Table 14.** Multiplicity and age (601 patients)

| | <50 | 51–70 | >70 | Total |
|---|---|---|---|---|
| Single | 56.4% (66) | 49.0% (190) | 43.8% (42) | 49.6% (298) |
| Multiple | 43.6% (51) | 51.0% (198) | 56.2% (54) | 50.4% (303) |

**Table 15.** Number of adenomas in colorectal cancer families

| Group | Total no. of families | Total no. of adenomas | Average no. per patient |
|---|---|---|---|
| Patients from: | | | |
| 1 case families | 148 | 172 | 1.2[a] |
| 2 case families | 66 | 145 | 2.2 |
| 3 or more case families | 22 | 95 | 4.3[a] |
| Total | 236 | 412 | 1.7 |

[a] Mann-Whitney $U$ test, $P<0.01$

## Adenomas in Colorectal Cancer Families

Lovett [26] has illustrated the importance of taking a careful family history from all patients with colorectal cancer. By careful questioning of patients and relatives, she elicited a family history of colorectal cancer in 26% of 209 patients. The majority had only 1 affected relative (1 case families), but 28% were 2 case families and about 10% had 3 or more affected relatives. The average number of adenomas per patient (who also had cancer) increased with the number of affected family members (Table 15). Moreover, it can be shown that the incidence of severe dysplasia in adenomas from cancer family cases is significantly greater than that in a control group (Table 16).

## Adenomas in Metachronous Cancer Cases

The risk of developing a second primary cancer years after a partial large bowel resection for a first primary carcinoma is greatest in patients who had associated adenomas in the first operation specimen [27]. If the grades of dysplasia of the adenomas in the metachronous cancer cases are compared with those of

**Table 16.** Grades of dysplasia of associated adenomas in cancer family cases and noncancer family cases

| | Cancer family cases | Noncancer family cases (control) |
|---|---|---|
| Mild | 15 (65.2%) | 47 (92.1%) |
| Moderate | 5 (21.7%) | 3 (5.9%) |
| Severe | 3 (13.0%) | 1 (2.0%) |
| Total | 23 | 51 |

$X^2 = 8.65$; df = 2; $0.01 < P < 0.02$

**Table 17.** Grades of dysplasia of associated adenomas in metachronous and single cancer cases

| | Metachronous cancer cases | Single cancer cases (control) |
|---|---|---|
| Mild | 14 (66.7%) | 32 (84.2%) |
| Moderate | 2 (9.5%) | 2 (5.3%) |
| Severe | 5 (23.8%) | 4 (10.5%) |
| Total | 21 | 38 |

$X^2 = 5.57$; df = 2; $0.05 < P < 0.1$

a control group of adenomas from single cancer cases (i.e., those who did not develop a second primary cancer), it can be shown that there is a significant excess of severe dysplasia in the adenomas from the metachronous cancer cases (Table 17).

## Discussion

Colorectal adenomas are common and most never become malignant. In other words, the adenoma is a dilute marker of increased colorectal cancer risk. The objective must be to search for more selective markers of especially high cancer risk by studying the histopathological features of adenomas. It is already well established that those greater than 1.0 cm diameter, tumors with a pronounced villous component, and adenomas with severe dysplasia have the greatest malignant potential [6], but other evidence is presented here which suggests that severe dysplasia per se may be the most selective histopathologic marker of increased cancer risk and that this is closely linked with the site distribution of colorectal cancers, number of adenomas per patient, and increasing age. Moreover, severe dysplasia in adenomas appears to be a selective marker for increased cancer risk in members of colorectal cancer families as well as for the risk of developing a metachronous or second primary colorectal carcinoma. Severe dysplasia and multiple adenomas could be valuable markers for selecting out from the total population of patients with adenomas those most deserving of close surveillance in follow-up cancer prevention programs, but this could be satisfactorily demonstrated only by prospective studies.

Barium enema radiography (especially the air contrast technique) has an important role to play in the detection and follow-up surveillance of colorectal adenomas. The advantage of colonoscopy, of course, is that it can be accompanied by polypectomy, thus allowing the pathologist to make an accurate tissue diagnosis, not only of the variety of polyp but also of the detailed features of adenomas, such as histologic type and grade of dysplasia. However, total colonoscopy is difficult in some patients and also carries a recognized morbidity. Endoscopic studies so far have shown that large adenomas with the greatest malignant potential as well as most early cancers (malignant polyps) are usually detected in the left colon and comparatively few in the cecum and ascending colon [28]. Yet the right colon is an area with a significant risk for cancer, especially in women, and should provide a corresponding number of adenomas and early cancers by endoscopic examination or barium studies. Bias due to the way in which patients are selected for examination is inherent whether they come from a surgical, radiologic, or endoscopic series, but it does appear from current information that the most satisfactory procedures for screening purposes are various combinations of air contrast barium enema radiography with fiberoptic endoscopy (including the short instrument) to suit differing situations and types of patient.

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