Clinical Review

Colon Polyps

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Colonic polyps commonly occur in all age groups and are of varied significance depending on the type of polyp and the symptoms manifested. There is some debate in the medical literature regarding the appropriate clinical management of polyps and the follow-up of patients after polypectomy. This discussion addresses the significance of colon polyps, including their etiology, histology, complications, detection, and management.
Key words. Colonic polyps; colonic diseases; colonic neoplasms; adenoma. *J Fam Pract 1992; 35:194-200.*

Intestinal polyps, mucosal protuberances from the epithelial lining of the lumen of the colon and rectum, can vary in size and shape, occur anywhere in the colon or rectum, and vary in histopathology. They usually do not cause symptoms unless they are large enough to cause obstruction or are vascular and bleed. By gross appearance they are classified as *sessile*, *semisessile*, *flat*, or *pedunculated* (Plates 1–4), and can be either neoplastic or nonneoplastic. The result of histologic studies is the only final determinant of the nature of a polyp; the gross appearance or the size and shape of the polyp is of limited value in terms of management, treatment, and prognosis.

The greatest concern with polyps is their potential to become malignant. Studies have shown that early identification and removal of polyps can reduce the subsequent occurrence of invasive cancer. Studies have also shown that most colon cancers have developed within previously benign adenomas.[1–6] Therefore, currently accepted management is to remove all colonic adenomas.[7–14]

The epidemiology of colonic polyps indicates that prevalence is higher in North America and Europe than in other parts of the world. According to autopsy surveys in the United States, nearly one half of the population harbors at least one adenomatous colonic polyp.[7] Among persons over age 65 years, more than two thirds of the population have colonic adenomas.[7] The prevalence of adenomatous polyps increases with age. Polyps of larger size with a higher degree of dysplasia as well as multiple adenomas are a common occurrence in persons over 65 years of age.[7] Multiple polyps are found in 28% of patients who have at least one adenoma. One third of all surgical specimens containing colon cancer also contain an adenoma.[7]

Classification

Colon polyps are classified into two major histologic groups, *nonneoplastic* and *neoplastic* (Table 1). The nonneoplastic polyps include the mucosal polyps, hyperplastic polyps, juvenile polyps, Peutz-Jeghers polyps, and inflammatory polyps. The neoplastic polyps include the adenomatous polyp, which may be identified histologically as a *tubular adenoma*, *tubulovillous adenoma*, or *villous adenoma*.[1,7]

To understand the nature of the different types of polyps, it is helpful to review the normal histology of the mucosa of the colon (Figure 1). The normal colonic mucosa is made up of straight tubular glands, termed *crypts of Lieberkühn*, packed parallel to each other and perpendicular to the muscularis mucosa.[1,7] The normal proliferation of the cells lining the crypts occurs in the lower third of the crypts, which is lined with young immature dividing cells. These cells then migrate upward along the tubular crypt to the tip of the glands exposed to the lumen of the colon. They gradually differentiate into mature goblet cells or mature absorptive cells. The lower border of these cells that line the surface rests on a pericryptal sheath of collagen that is suspended in loose areolar connective tissue called the *lamina propria*. Fibroblasts proliferate in the lower areas of the crypts and migrate upward toward the epithelial lining of the lumen. They mature during this journey upward. The lamina propria is rich in mononuclear cells and small

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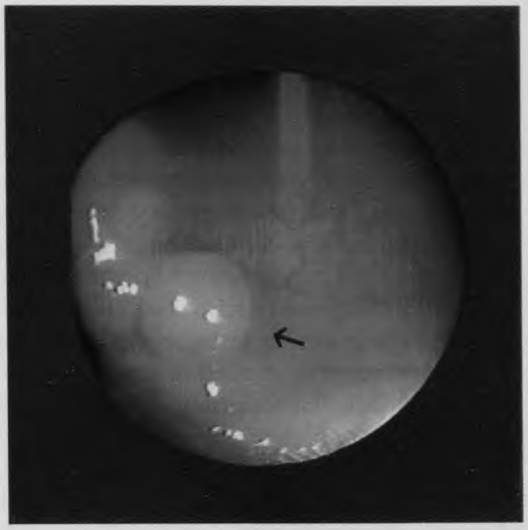
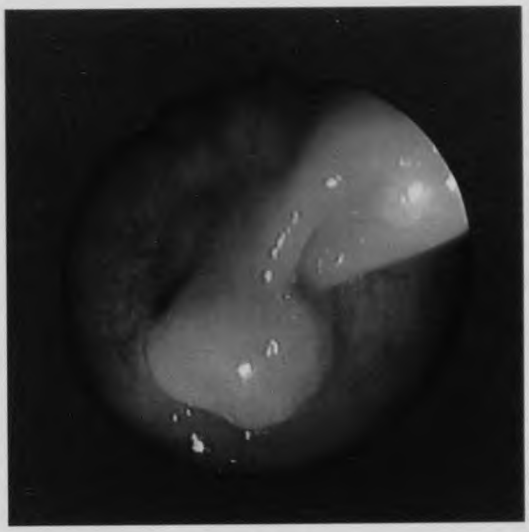


Plate 1



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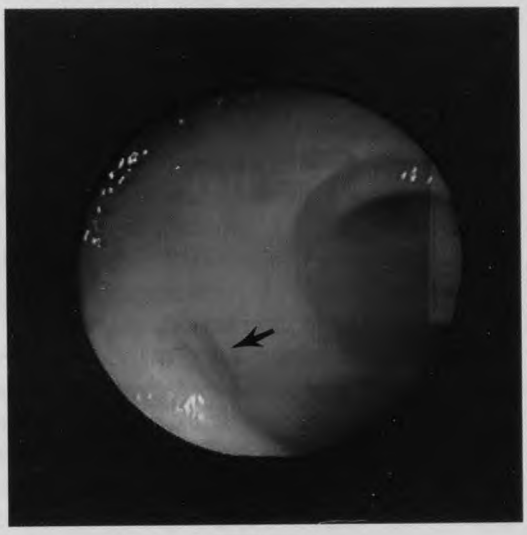

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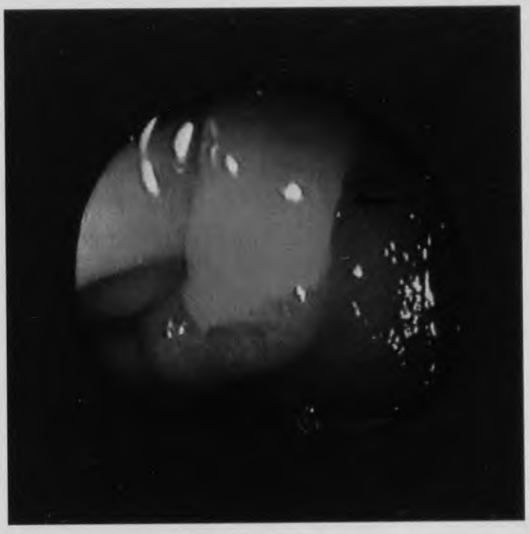

Plate 4

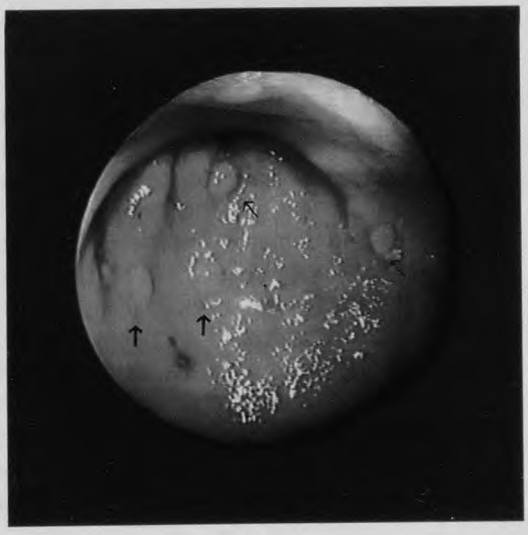

Plate 5

Plate 1. Sessile polyp. Note absence of a stalk. The base of the polyp is flush with the surface of the mucosa (tubular adenoma by histology). *Plate 2.* Semisessile polyp. Note the short stalk and broad base (tubular adenoma by histology). *Plate 3.* A flat polyp. Note the central vascularity suggestive of dysplasia (tubular adenoma with severe dysplasia by histology). *Plate 4.* Pedunculated polyp. The arrow indicates the polyp's long stalk (tubular adenoma by histology). *Plate 5.* Four small (2 to 3 mm) hyperplastic polyps, also called metaplastic polyps. Arrows indicate these small polyps.

Table 1. Classification of Colonic Polyps

Nonneoplastic	Neoplastic
Mucosal polyps	Tubular adenoma
Hyperplastic polyps	Villous adenoma
Juvenile polyps	Tubulovillous adenoma
Peutz-Jeghers polyps	
Inflammatory polyps	

blood vessels; however, there are no lymphatic channels in this layer. Below these crypts and the lamina propria is a thin layer of smooth muscle cells called *muscularis mucosae*, which forms the boundary between mucosa and submucosa and has a rich supply of lymphatic channels that form a *lymphatic plexus*. Deep in the muscularis mucosae are the layers of the submucosa, muscularis propria, and the serosa.

Nonneoplastic Polyps

Mucosal polyps are protuberances of the normal mucosa that resemble a polyp. They are often found in the colon but histologically consist of normal mucosa.[1,7]

Hyperplastic polyps, also termed *metaplastic polyps*, are commonly found in the rectum; however, they can occur anywhere in the large bowel (Plate 5, Table 1). These polyps develop from a focal abnormality in the cellular replication, resulting in the expansion of the proliferative zone of the crypts of Lieberkühn.[1,7,10] The individual cells differentiate and mature as usual. This is a true hyperplastic process leading to the formation of a protrusion into the lumen of the colon, a visible polyp. These polyps are typically small, varying from 1 to 5 mm in size, and they are usually sessile, sharply marginated

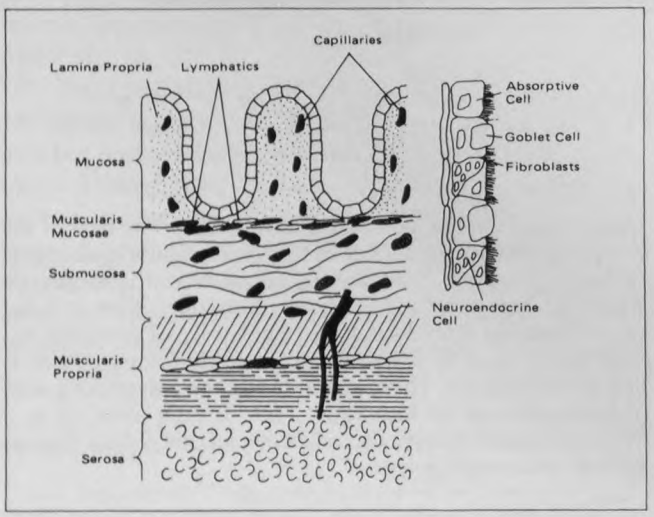

Figure 1. Normal histology of the colorectum. From CA 1985; 35:323. Reprinted with permission.

mucosal elevations. As a result of polyp formation, the cells in the lower zones of the crypt become crowded, hyperchromatic, and depleted of mucus, and contain numerous mitoses. The upper zones of the crypt lining consist of mature, differentiated, hyperdistended goblet cells. Despite polyp formation, cellular crowding, hyperchromatism, and mitotic activity do not occur in the upper zones of the crypts. The cells at the upper end of the crypts are hypermature. Further, the migration of cells from the bases of the crypts to the top is slow. The hyperplastic polyp seems to develop as a result of a failure of the mature cells to shed normally.[7] Hyperplastic polyps are usually flat-topped and found either in isolation or in association with adenomatous polyps. Adenomatous tissue has been found in up to 13% of hyperplastic polyps,[7,10–12] and foci of adenocarcinoma have also been found within such areas in hyperplastic polyps.[11,12] Autopsy studies have shown that up to 40% of persons under 40 years of age have hyperplastic colon polyps compared with 75% of persons over 40 years of age.[7] They are much more common in older patients and are sometimes found in clusters near and surrounding cancers in the colon. It has been suggested that hyperplastic polyps are markers of an increased risk of colorectal neoplasia, even though they are not neoplastic themselves.[13–15]

Inflammatory polyps usually occur during the regenerative phases following inflammation of the large bowel mucosa as seen in ulcerative colitis, Crohn's colitis, amebic colitis, and bacterial dysentery. Inflammatory polyps form, however, as a result of ulceration with no discernible cause, so their presence does not necessarily indicate chronic inflammatory bowel disease. The lesions can be small or large, and the large lesions may mimic a neoplasm. In the postinflammation period, the polyp may contain a tremendous amount of granulation tissue, but later the tissue is distorted normal mucosa. These lesions are often found in the colons of people who are at increased risk of developing colon cancer, and therefore the polyps should be evaluated.[7,16,17]

Juvenile polyps are hamartomatous epithelial retention polyps and are nonneoplastic. Generally, they are stalked but occasionally are sessile and are composed of cystically dilated glands that are filled with mucus and inspissated inflammatory material. The dilated cystic glands have an abundance of mature mucus-secreting cells, and some neuroendocrine and Paneth cells. The surfaces are often eroded and replaced by granulation tissue. In areas adjacent to the erosions, the regenerating epithelium may be cytologically atypical. The disorderly arrangement of glands is separated by abundant lamina propria infiltrated with neutrophil cells, eosinophils, and lymphocytes, and has an abundant blood supply, which

explains the tendency to bleed profusely. The stalks are lined with normal mucosa and have a core of submucosal areolar connective tissue. These polyps are usually solitary and found in the rectum and sigmoid colon. They range in size from 2 to 20 mm. Juvenile polyps occurring in the rectum have a tendency to prolapse during defecation, particularly if the polyps have stalks. They are rare before 1 year of age and are usually found between 1 and 7 years of age, but can occur in adults. Once they are removed they seldom recur. When multiple lesions occur, the condition is known as *juvenile polyposis syndrome*.[1,7,17]

Peutz-Jeghers polyps are pedunculated nonneoplastic lesions that range in size from 1 mm to 3 cm and are typically multiple. They are composed of mature intestinal epithelial cells that are organized into arborizing glands that are surrounded by a delicate stroma of smooth muscle bundles. The epithelial cells include goblet cells, neuroendocrine cells, absorptive cells, and Paneth cells. Regenerative activity is present on the surface. The stalks of the polyps are lined by normal mucosa and have a central submucosal core. At times the pseudoinvasive glandular structures extend from the polyp into the submucosa, the muscularis propria, and the serosa. The lesions are considered hamartomas and have very low if any malignant potential.[1,7,17]

Neoplastic Polyps

Neoplastic polyps are also termed *adenomas*. They are tumors made up of benign neoplastic epithelium. Adenomas result from the unrestricted proliferation of the cells in the crypts of Lieberkühn, and mitotic activity is present throughout the length of the epithelium of the crypt. The cells do not differentiate into mature goblet cells or mature absorptive cells, but remain as immature cells. These immature cells continue to proliferate beyond the replacement needs of the crypt, resulting in a larger, more dysplastic lesion.

Tubular adenomas are composed of a mass of tubular glands, producing a polyp with a rounded surface. Villous adenomas are composed of fingerlike epithelial projections extending outward from the surface. Mixed tubular and villous adenomas are composed of both types of tissue.

An unrestricted cellular division and an absence or failure to differentiate into mature cells is the essential characteristic of the adenoma. Adenomas are believed to originate from a failure in the normal steps of cellular proliferation, maturation, and differentiation. Nuclear hyperchromatism and crowding are features of all adenomas. Greater degrees of nuclear irregularity and mitosis develop in some of these adenomas, giving rise to numerous cell abnormalities termed *dysplasia* or *atypia*, which in turn can be of mild, moderate, or severe degrees. Mild and moderate degrees of dysplasia are not uncommon in adenomas. Severe dysplasia, however, suggests intraepithelial malignancy. On gross appearance, adenomas can be pedunculated, sessile, or semisessile.[1,6,7,12,17–20]

Mixed adenomatous-hyperplastic polyps comprise less than 1% of adenomas. They are made up of both hyperplastic and adenomatous tissue. They are often pedunculated and usually larger than typical hyperplastic polyps. This type of adenoma has as much potential of becoming cancerous as other adenomas of similar size, and hence requires close attention.[1,17]

Adenoma to carcinoma sequence. As discussed above, the neoplastic adenoma, whether tubular, villous, or tubulovillous, contains varying degrees of atypia or dysplasia. Over the past decade, researchers have come to the conclusion that most colon cancers arise from adenomas, although a few may arise de novo from flat epithelium.[20–24] Most foci of carcinomas are found within adenomas. Persons in whom adenomas are found tend to develop colon cancer within 10 to 15 years. Morson[25] was among the first to propose the polyp-to-cancer sequence. In 1975, Muto, Morson, and Bussey[5] published a paper documenting the adenoma-to-carcinoma sequence in the large bowel.

Relation of Polyps to Cancer

There is no evidence to suggest that hyperplastic polyps are precursors of colon cancer. The purely hyperplastic polyp is not a premalignant lesion. However, debate over the relationship continues.[26–36] It is also difficult to distinguish between diminutive polyps (<6 mm) that are hyperplastic and those that are small adenomas. In a retrospective review of 329 diminutive polyps (smaller than 5 mm), Tedesco et al[12] found that, although their small size suggests hyperplasia as the etiology, a number of these small polyps are neoplastic and represent a risk of progressing to cancer. Not all small adenomas grow large, but all large adenomas developed from small ones.

Inflammatory polyps are nonneoplastic; however, they are often associated with diseases of the colon that sometimes precede the development of cancer, eg, ulcerative colitis and rectal schistosomiasis. Their presence therefore warrants a complete evaluation of the colon and careful study of mucosal biopsies.[16,33]

Juvenile polyps. Although juvenile polyps are nonneoplastic, juvenile and adenomatous polyps sometimes occur concomitantly. Relatives of patients with juvenile polyps are at increased risk of developing cancer of the gastrointestinal tract. Since these polyps occur in child-

hood, and they present either with rectal bleeding or prolapsed stalked polyps or both, the entire colon needs to be evaluated early in order to rule out the polyposis syndrome.[1,7] Some researchers believe that juvenile polyps pose only a small cancer risk.[37]

Peutz-Jeghers polyps. No strong association between Peutz-Jeghers polyps and cancer has been proven; however, their neoplastic potential has been a matter of debate for decades. Approximately 3% of patients with Peutz-Jeghers polyps develop cancer. The direct origin of cancer from these hamartomatous lesions has been suggested,[1] but the concept has not received total acceptance. Nevertheless, areas of adenomatosis and cancer have been reported within a Peutz-Jeghers polyp.[1]

Adenomas. The adenoma is a benign glandular neoplasm; however, it can contain a focus of malignant cells confined within the basement membrane of the crypts of Lieberkühn. These areas are designated as *intraepithelial* cancers. An extension beyond the basement membrane into the lamina propria of the mucosa is called *intramucosal carcinoma.* Neither the intraepithelial or the intramucosal carcinomas have any significant potential of metastasis since there are no lymphatic channels in the lamina propria or in the crypt basement membrane. If the malignant cells spread beyond the basement membrane, the cancer is termed *microscopically invasive* but can still be intramucosal. When the malignant cells spread beyond the lamina propria into the muscularis mucosa and submucosa where there are an abundance of lymphatic channels, there is the potential for metastatic spread. In the process of the adenoma enlarging in size, the muscularis mucosa becomes distorted, and entrapment of malignant cells is facilitated.

The likelihood of invasive cancer occurring in an adenoma is dependent on size. Large sessile adenomas are more likely to be villous in nature and pose a greater propensity for malignant transformation. Foci of invasive cancers occur in about 3% of adenomas smaller than 2 cm. Factors that influence the malignant potential of an adenoma include whether it is sessile or pedunculated, the depth of penetration by the malignant cells, the ratio of malignant cells to normal cells, and the degree of differentiation of the cells. The rate of spread is higher in poorly differentiated or undifferentiated tumors.[1,7,12,38–45]

For the past decade research was focused on the molecular biologic events underlying carcinogenesis. Vogelstein et al[46] examined a number of small and large adenomas, adenomas bearing carcinomas, and carcinomas of the colon and rectum. Their findings suggested a multistage process of gene alteration in chromosome 5, subsequent ras-gene mutation, and allelic loss in chromosomes 18 and 17, as the normal mucosa progressed to fully developed carcinoma. The ras-gene mutation fits the model of a dominant acting oncogene, but the loss of genetic material in the three chromosomes suggests loss of a tumor suppressor function. Loss of tumor suppressor activity is the focus of much promising new research.[46]

Discussion

Polyps present a major epidemiological dilemma. On gross appearance, the adenoma may appear large or small, sessile, semisessile, or pedunculated. It can bleed, ulcerate, or fungate. There is no definite way to determine the histology on the basis of gross appearance. At most, based on size, vascularity, presence of ulceration or fungation, and fixation to the bowel wall, one can speculate as to whether the lesion is malignant. In the absence of these features, however, there is absolutely no way of correctly predicting the histology of an adenoma. This is especially true of smaller lesions.

Smaller adenomas cause the most confusion in reference to their malignant potential, management, and follow-up. The majority of colonic polyps are smaller than 1 cm, with most between 1 and 5 mm.[6,18,19–45]

The significance of colonic polyps became a matter of great interest and concern when, in the early 1970s, reports indicated that the adenoma was possibly a precursor of colon cancer.[3,5,21,30,32,40] In 1975, Muto, Morson, and Bussey[5] proposed the polyp-to-cancer sequence. In 1979, Shinya and Wolff[2] published their report on the analyses of 7000 polyps, 5786 of which were adenomas, which stated that all categories of neoplastic polyps demonstrated malignant changes. In the 1980s, several reports emerged to support the polyp-to-cancer sequence and the importance of minute adenomas. Almost 50% of small polyps are adenomas, and most of the remaining polyps are hyperplastic. In 1982, among other reports on the importance of diminutive polyps, Tedesco and his colleagues[12] suggested that a larger proportion of diminutive polyps were adenomas and hence they had the potential to progress to carcinoma. As a result of these and other reports it was recommended that all adenomas be removed and all diminutive polyps be biopsied and thereby removed.[12,15,17,40–45]

In relation to the nonneoplastic hyperplastic polyps, there have been concerns that these were associated with concomitant adenomas elsewhere in the colon.[4,13,14] This association was asserted by Church and his group.[4] In 1989, Ryan and colleagues[42] recommended that all small polyps be biopsied, since it is visually difficult to determine whether they are hyperplastic or neoplastic. The reported range of adenomatous change in these diminu-

tive colon polyps was 30% to 50%. Controversy still exists over the significance of hyperplastic polyps and small adenomas. Provenzale and his co-workers[45] assert that distal hyperplastic polyps are not indicators of proximal adenomas.

The question then arises, how does one distinguish between a 4-mm hyperplastic polyp and a 4-mm adenoma in the rectosigmoid found during sigmoidoscopy? Ansher et al[13] have suggested that left-sided hyperplastic polyps are indicators of proximal adenomas. Blue et al[14] recently stated that patients with left-sided hyperplastic polyps were at the same risk for proximal adenomas as patients with left-sided adenomas. The reported prevalence of hyperplastic polyps is 30% to 40%. Achkar and Carey[43] have reported that when a hyperplastic polyp was present in the sigmoid, there was a 29% prevalence of proximal neoplastic polyps, and when the sigmoid polyp was an adenoma, the prevalence of proximal adenomas was 33%.

The authors recommend that all diminutive polyps detected during flexible sigmoidoscopy should be biopsied or removed. When tubular adenomas are found on the left side of the colon, a full colonoscopy should be performed. Patients who have had a polypectomy should have a follow-up colonoscopy annually until the colon is clear, and then a colonoscopy every 3 to 5 years.[10–15]

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