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# Gastrointestinal Polyps In The Bowel

Colonic polyps present an important clinical entity, as a precursor to malignant disease. Lives can be saved by finding and removing polyps. In the future, there may be a role for medication to prevent polyp recurrence.

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**G**astrointestinal polyps are often encountered in primary practice, and appropriate investigation and treatment is important, with cancer usually diagnosed following the detection of polyps. Colorectal cancer is common, the second leading cause of death in North America,<sup>1</sup> and screening for polyps in the pre-malignant phase is important.

In this article, we will review: the pathology of the various types of polyps; their clinical significance; familial syndromes associated with polyps and their relative malignant potentials; the role of the polyp-cancer sequence, appropriate screening regimens for familial syndromes and for the general public; treatment and follow-up of affected individuals; and the role of cyclo-oxygenase-2

(COX-2) inhibitors, ursodeoxycholic acid and nutrition as prophylaxis.

## Pathology

A polyp is a tumorous mass that protrudes into the lumen of the gut. Polyps may be pedunculated (having a stalk) or sessile (broad-based) (Figure 1). Histologically, polyps then are classified as non-neoplastic or neoplastic. The non-neoplastic polyps have no malignant potential, and include hyperplastic polyps, inflammatory polyps, hamartomas and lymphoid aggregates. The neoplastic polyps are adenomas, which are initially benign, but with malignant potential.

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## Non-neoplastic Polyps

**Hyperplastic polyps.** These are the most common polyps found in the colon, comprising approximately 90% of all polyps detected

(see Figure 1). They may be formed as the result of abnormal mucosal maturation, inflammation and architecture of the bowel. They are usually small—less than 5 mm—



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and found incidentally during endoscopy. They often present in multiples, and are found most commonly in the rectosigmoid and left colon. Grossly, they are smooth, small, nipple-like projections into the lumen. Histologically, they have a characteristic stellate appearance on cross section, with well-formed glands and crypts. They have virtually no malignant potential.<sup>2</sup> Hyperplastic polyps are not associated with more proximal lesions, and are not an indication for full colonoscopy, nor do they require follow-up.<sup>3</sup>

**Inflammatory polyps.** These are really pseudopolyps seen in inflammatory bowel disease. These are not actual polyps, but represent normal regenerating mucosa between areas of inflammation and destruction. At first glance, these projections appear as polyps, but closer inspection identifies abnormal surrounding tissue—all part of chronic inflammatory bowel disease. Imagine most of the colon's normal mucosa collapsing, leaving a few areas to remain standing; these areas represent the pseudopolyps. Inflammatory polyps vary in size and shape, occasionally being multi-lobed.

**Hamartomatous polyps.** These are rare, occurring in conjunction with familial syndromes. They are usually single, and are larger, being 1 cm to 3 cm. They have little to no malignant potential, but should still be removed, even if they are asymptomatic, to prevent complications, such as intussusception, obstruction and bleeding.<sup>4</sup> They are typically round and smooth, and may have stalks up to 2 cm long. On microscopy, they typically have a branching pattern of connective tissue and smooth muscle. The lamina propria makes up the majority of the polyp, and the surface may show dilated glands, or signs of erosion and inflammation.<sup>2</sup>

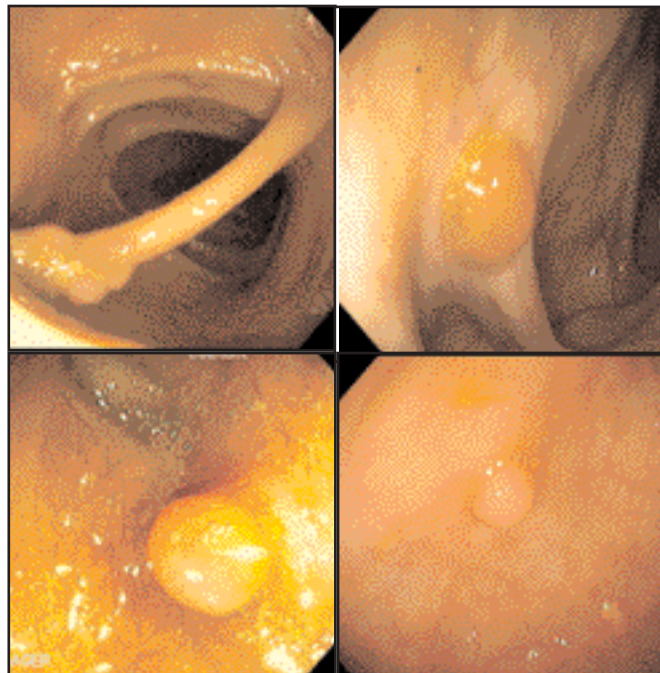


Figure 1. Top left is a pedunculated polyp. The remainder are sessile, hyperplastic polyps.

## Neoplastic Polyps

### Adenomas

*Adenomatous polyps* are a diverse group that may appear endoscopically to be round and lumpy, flat and shaggy, pedunculated or sessile (see Figure 2). They all are formed by a proliferation of cells in a well-circumscribed area of glandular epithelium, within the colonic mucosa. Depending on the volume of villous tissue, they are called tubular, tubulovillous or villous adenomas.<sup>5</sup> Tubular adenomas are formed of tubular glands, straight or branched; villous adenomas are formed of villous or finger-like projections of dysplastic epithelium; and tubulovillous adenomas are a combination of the two patterns.

*Tubular adenomas* are the most common



Populations that have a high prevalence of adenomas have a high prevalence of colorectal cancer, and vice versa.

adenomatous polyp, having an incidence of more than 80%. The majority are small and pedunculated, and more than 90% of them are found in the colon. They are solitary only 50% of the time, and they may vary in appearance, being smooth or rough, pedunculated or sessile. On histology, they have a tubular component of greater than 75%.

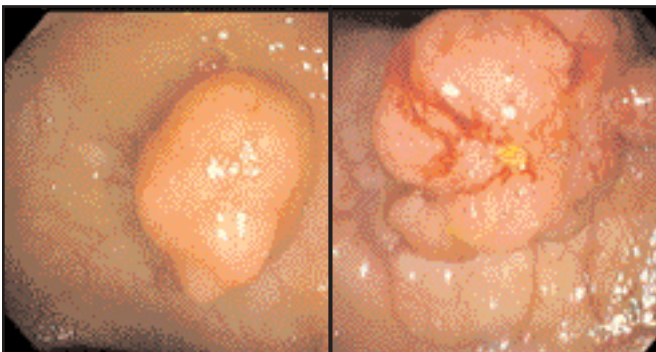


Figure 2. Adenomatous polyps.

They may have adenomatous epithelium extending down the stalk. They have a low malignant potential, particularly when they are small, but can include carcinoma *in situ* (severe dysplasia) to intramucosal carcinoma.<sup>2</sup> Invasion of the submucosal stalk denotes invasive adenocarcinoma.

*Villous adenomas* account for less than 5% of adenomatous polyps, and are more likely to progress to malignancy. They are generally sessile, and may grow up to 10 cm in diameter. Typically, they have a velvety appearance (see Figure 3). Villous histology is an independent risk factor for high-grade dysplasia within an adenoma.<sup>3</sup> On microscopy, frond-like extensions of the mucosa are seen, covered by dysplastic, disordered columnar epithelium.<sup>2</sup> These polyps must be at least 75% villous on histology to qualify as a villous adenoma.

*Tubulovillous adenomas* are intermediate between the other two, having between a 25% and 75% villous component.

### Significance

Once found, what is the significance of these gastrointestinal polyps? And in whom should we look for them? And what do we do if we find them?

As a general rule, the larger and more vil-  
lous the polyp, the more likely the presence of carcinoma. All adenomatous polyps have a degree of dysplasia or cellular abnormality. Increasing grades of dysplasia, from low to high, signal increasing malignant potential. High-grade dysplasia may include changes referred to as carcinoma *in situ*.

All adenomatous polyps are dysplastic, and they all are pre-malignant. They are

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generally asymptomatic and relatively common, occurring in approximately one-half of all men and women over the age of 60. They are slow-growing lesions, growing at an average rate of 0.5 mm/year. The polyp-cancer sequence is well-established, and is based on a number of principles:

- Populations that have a high prevalence of adenomas have a high prevalence of colorectal cancer, and vice versa.
- The distribution of adenomas within the colorectum is more or less comparable to that of colorectal cancer.
- The peak incidence of adenomatous polyps antedates by some years the peak for colorectal cancer.
- When invasive carcinoma is identified at an early stage, surrounding adenomatous tissue is often present.
- The risk of cancer is directly related to the number of adenomas and, hence, the virtual certainty of cancer in patients with familial polyposis syndromes.
- Programs that assiduously follow patients for the development of adenomas reduce the incidence of colorectal cancer.<sup>2</sup>

As such, it makes sense to try and screen for (and treat) these lesions at an early asymptomatic stage. The aim is to reduce the incidence of colorectal cancer by treating cancers earlier, as well as to prevent some through the removal of known pre-malignant lesions.

## Screening for Polyps

There are many confusing and occasional-

ly conflicting guidelines surrounding the appropriate screening program, as highlighted in many recent articles in leading journals.<sup>1,6-12</sup> There are four standard tools available for screening: fecal occult blood testing (FOBT), double contrast barium enema, sigmoidoscopy and colonoscopy.

FOBT is easy, cheap, readily available and has no morbidity associated with it. It is generally considered an acceptable test by patients, however, it is neither sensitive nor specific. There have been many large population-based studies to evaluate the use of FOBT as a screening tool, which have demonstrated positive predictive values, ranging from 22% to 58% for adenomas and cancers together.<sup>8,13</sup> False-positive results may be caused by many different foods and medications, and could lead to further and costly work-up. False-negatives occur approximately 40% of the time due to the intermittent nature of tumor blood loss, leading to delays in diagnosis. Nonetheless, it has been shown to lead to a reduction in mortality, ranging from 12% to 57% when used as a screening tool in asymptomatic patients.<sup>8,14</sup> It is best used in conjunction with one of the other modalities.

Double contrast barium enema (DCBE) also is readily available. It is fairly sensitive for larger lesions, and will likely detect all clinically significant lesions. Reported sensitivity rates range from 70% to 90% for lesions greater than 1 cm,<sup>8</sup> however, for lesions smaller than 1 cm, it

Colonoscopy is the gold standard method for evaluating the colon. It is very sensitive, approaching 95%.

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is less sensitive, less than 50%.<sup>3,4,14</sup> DCBE also does not offer the possible therapeutic advantage that colonoscopy does with polypectomy. Its cost is usually intermediate, between that of sigmoidoscopy and colonoscopy.<sup>14</sup>

Sigmoidoscopy, either flexible or rigid, has the added advantage of being potentially therapeutic and has been advocated as a screening tool, in that case control studies have shown convincingly that it does lead to a significant reduction (60%) in mortality rates over one decade.<sup>8,12,14</sup> No patient sedation is required and complications are minimal. Opponents argue that, even with a flexible sigmoidoscope, one can only reach the splenic flexure, potentially missing 50% of the lesions. More formal training is required for flexible sigmoidoscopy, although some programs have begun to train paramedical personnel in this role with success.<sup>14</sup> Multicenter trials evaluating flexible sigmoidoscopy as a screening tool are ongoing.

Colonoscopy is the gold standard method for evaluating the colon. It is very

sensitive, approaching 95% sensitivity. It evaluates the entire colon, and allows both diagnostic and therapeutic intervention, with either biopsy or polypectomy. Recent studies have shown there is a significant risk of a solitary proximal lesion that would not be identified with sigmoidoscopy, and also of a synchronous proximal lesion in patients with a distal hyperplastic polyp, adenoma or malignancy.<sup>1,7</sup> These would be missed with sigmoidoscopy alone.

Skilled therapeutic endoscopists can safely resect the majority of polyps found during the colonoscopy. The techniques employed usually require electrocautery. When small polyps are numerous, and after representative biopsies have been taken, removal of these tiny polyps (< 1 mm) with biopsy forceps or ablation with cautery devices is an acceptable approach.

Most adenomatous polyps smaller than 1 cm remain static, rarely progressing to malignancy. Thus, a solitary adenomatous or hyperplastic polyp found on sigmoidoscopy is not deemed an indication for full colonoscopy. The indication for endoscopy in the first place, however, must be taken into account and each clinical situation evaluated on an individual basis.

Polypectomy and a resulting "clear" colon lowers the incidence of colon cancer by 76% to 90%.<sup>15</sup>

### Who Should Be Screened? Who Is At Extra Risk?

There are certain high-risk groups that physicians must be aware of, including

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patients with a history of inflammatory bowel disease, familial polyposis syndromes and patients with a personal or family history of colon cancer.

Patients with a history of inflammatory bowel disease are at a higher risk of developing colon cancer than the general population. Risk factors include pan-colitis for eight or more years, or left-sided colitis for

15 years. The risk of developing cancer in these patients is approximately 0.5% to 1% per year.<sup>9</sup> Current recommendations are for patients meeting the above criteria to have full colonoscopy performed every one to two years, although conclusive evidence for this is lacking.<sup>9-11</sup>

The tumors in Lynch syndrome are more often seen in the proximal colon and are frequently multiple.

## Familial Syndromes

There are numerous inherited familial polyposis syndromes that carry an increased risk of malignancy. Knowledge of their clinical features may help guide clinical management and investigation.

**Familial adenomatous polyposis (FAP)** is an autosomal-dominant inherited condition with innumerable adenomatous polyps, ranging from 100 to 2,500. Risk of progression to malignancy is nearly 100%. Once a firm diagnosis is established, prophylactic colectomy is warranted, and all first-degree relatives of the index case should be screened with colonoscopy. Genetic studies are now available. Patients with FAP also are at increased risk for malignancies of the

upper gastrointestinal tract, as well as desmoid tumors.<sup>10</sup>

**Gardner's syndrome** consists of intestinal polyps, such as those found in FAP, but is associated with multiple osteomas (particularly of the mandible, skull, and long bones), epidermal cysts and fibromatosis. There are rarer manifestations, including an increased frequency of medullary cancer of the thyroid, duodenal cancer and congenital hypertrophy of the retinal pigmentation.<sup>14</sup> Presentation with one of these rarer manifestations may warrant further investigation for signs of FAP. Turcot's syndrome is the same as Gardner's syndrome, with the addition of central nervous system tumors, particularly gliomas.<sup>14</sup>

**Hereditary non-polyposis colorectal cancer (Lynch syndrome)** is an autosomal-dominant inherited condition characterized by the development of cancer at an early age. The disease is defined as those individuals with three family members within two generations having developed colon cancer, and one of them before the age of 50. The tumors are more often seen in the proximal colon and are frequently multiple. They may arise spontaneously, rather than in pre-existing adenomas. When they do arise from adenomas, they are not associated with polyposis. The genetic defect is an inherited defect in one of four deoxyribonucleic acid (DNA) "repair" genes, and genetic testing is not available currently.<sup>2,10</sup>

Affected patients also are at an increased risk of developing extra-intestinal malignancies, particularly of the endometrium in women. Current recommendations suggest screening every two years, starting at age 25, or five years younger than the youngest relative to have developed a cancer.

*Peutz-Jeghers syndrome* is an autosomal-dominant condition with multiple hamartomatous tumors throughout the gastrointestinal tract. It is associated with melanotic mucosal and cutaneous pigmentation around the lips, oral mucosa, face, genitalia and palms. Although these polyps are not pre-malignant, the patients are at an increased risk of cancer of the pancreas, breast, lung, ovary and uterus. As stated previously, if polyps are discovered endoscopically, they should still be removed because of the risk of complications.

## General Population Screening

Currently, there is not a generally accepted recommendation for screening asymptomatic individuals with no other risk factors for colorectal cancer. Although one of the general principles of a screening program is to apply it to a population that is at added risk for the disease, there is increasing evidence in the literature that a one-time colonoscopy may be of benefit for the general population. A recent paper in the *American Journal of Gastroenterology* found that a one-time colonoscopic screening between ages 50 and 54 was cost-effective compared to no screening. It appears further investigation is needed in this area to see if such a model would be effective in the Canadian health-care system. Obviously, such a screening program would face significant logistical difficulties, as waiting lists for indicated elective colonoscopy in Canada are already lengthy.

*Follow-up after polypectomy and a "clear" colon.* The American College of

Gastroenterology recommends repeat colonoscopy at three years for high-risk situations, including those with multiple adenomas (more than two), large adenomas (> 1 cm), or a first-degree relative with colorectal cancer.

Patients with a low risk of adenoma recurrence include those with one or two small adenomas less than 1 cm and no family history of colorectal cancer. For these patients, the first follow-up may be delayed for five years.

*Surveillance of families of patients with adenomas.* Surveillance should start in families at age 40, or five years younger than the age of initial diagnosis if a parent or sibling has colon cancer or an adenoma. This advice is prompted by the National Polyp Study, showing first-degree relatives have an increased risk of colon cancer and would benefit from surveillance.<sup>15</sup>

*Can adenomatous polyps be prevented?* Maybe. Epidemiologic studies suggest diets high in animal fats and low in fruits, vegetables and fiber are linked to colon cancer. Thus, the National Cancer Institute encourages a diet with less fat, more fruit, vegetables and fiber. Studies to support this recommendation, however, are lacking. New polyp growth was not affected by wheat bran or a low-fat diet,<sup>16</sup> nor in studies with antioxidants.<sup>17,18</sup> In a more recent randomized trial of a high-fiber diet, there was no protective effect shown against recurrent colorectal adenomas.<sup>19</sup>

Currently, no recommendations are made for the widespread use of NSAIDs to prevent colorectal cancer.

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Bile acids and fatty acids are potentially toxic to colorectal epithelium. Binding bile acids with calcium carbonate (3 g/day) promoted a significant reduction in the risk of recurrent adenomas.<sup>20</sup> Ursodeoxycholic acid is undergoing a clinical trial to assess its potential for polyp prevention by altering bile's constituents.

COX enzymes regulate the conversion of arachadonic acid to prostaglandins. Two forms of COX exist. COX-1 is present in normal gastrointestinal mucosa, while COX-2 is not found in normal mucosa, but is induced by cytokines, oncogenes and tumor promoters. COX-2 overexpression is found in adenomas and colonic neoplasia.<sup>21</sup> COX-2 inhibitors decrease tumor-cell growth and angiogenesis in the lab, as well as in animal models. Sulindac, an NSAID, has been shown to prevent colonic polyp growth in FAP.<sup>22</sup> COX-2 inhibitors are now being assessed for possible prevention of polyp growth in patients with sporadic adenomas. Time will tell, but for now, no recommendations are made for the widespread use of NSAIDs to prevent colorectal cancer.

## Summary

Colonic polyps present an important clinical entity, as a precursor to malignant disease. Lives can be saved by finding and removing polyps. In the future, there may be a role for medication to prevent polyp recurrence. **Dx**

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