

## A New Era in Colorectal Cancer Screening and Surveillance

***The following is a distillation of my beliefs, primarily about endoscopic screening and surveillance of average-risk subjects, as formulated from my clinical experience, research, and knowledge of the literature. One of several general viewpoints, but one I hold quite strongly, it contains statements and recommendations that can be considered controversial, although to a lessening extent, it appears, as further studies are reported. The list of references also is highly selective, limited to the landmark and review papers that, for the most part, form the basis for my views.***

In the United States during the 1940s through the 1970s, cancer clinics in urban areas offered rigid sigmoidoscopy to persons who wanted screening for rectal cancer. These were probably very effective in reducing rectal cancer deaths as demonstrated by Gilbertsen and Nelms.<sup>1</sup> In the 1970s, the St. Mark's Hospital group showed that virtually all colorectal cancers develop from adenomas, usually large and villous, and that the process occurs very slowly, over 5 to 35 years;<sup>2</sup> advances in fiber-optics and engineering led to development of the colonoscope; and its implementation was accelerated by the introduction and widespread use of standardized fecal occult blood testing. In the 1980s, the flexible sigmoidoscope replaced the rigid proctoscope and afforded the ability to find the majority of colorectal cancers and advanced adenomas.<sup>3</sup>

The subsequent profusion of published studies, few of which were prospective or controlled, led the American Cancer Society and the gastroenterologic societies to publish guidelines,<sup>4</sup> which included, starting at age 50 years, lifelong annual stool Hemoccult testing, sigmoidoscopy every 3 years, colonoscopic follow-up of any adenoma found, then lifelong surveillance colonoscopies. These guidelines were based largely on the fear

that 1) all adenomas must be considered premalignant; 2) the presence of a single adenoma of any size or type puts the patient at high risk for malignancy; and 3) new polyps arise quickly and must be removed, lest they progress to fatal malignancies.

### The Flaw in the Guidelines

Understanding what was wrong with those concepts comes from reexamination and comprehension of the true role of the small tubular adenoma (TA), defined as a TA < 1 cm in diameter. (Another definition: advanced adenoma = TA > 1 cm in diameter or containing villous elements or severe dysplasia.)

It has been known for almost two decades that small TAs only occasionally develop villous elements and rarely contain severe dysplasia or carcinoma<sup>1</sup> and that they grow very slowly, if at all.<sup>5</sup> Several studies have demonstrated that a small TA in the distal bowel does not serve as a marker for proximal precancerous or malignant neoplasms.<sup>6,9</sup> In a 1989 Kaiser Permanente study, Grossman et al showed that only 3% of subjects who had only a single small tubular adenoma removed at proctoscopy were found to have a proximal advanced adenoma on total colonoscopy: the same findings that would be expected in the general population.<sup>6</sup> A similar study in 1994 verified those results.<sup>7</sup> At St. Mark's Hospital, Atkin

et al showed that after removal of their small rectal TAs and no further procedures, patients were at less-than-expected risk for eventual development of colorectal cancer.<sup>8</sup> On the other hand, all of these studies showed clearly that when the index lesions are advanced adenomas, patients are at increased risk of having advanced neoplasms proximally and should therefore have colonoscopy. The large, ongoing Kaiser Permanente sigmoidoscopic screening program<sup>9</sup> has not yet reported its data, which show that even subjects found on screening to have large TAs in the left colon do not have increased prevalence of advanced neoplasms in the right colon when compared with control subjects. Nor is the presence of several small TAs at screening sigmoidoscopy an indication for colonoscopy.

Periodic follow-up colonoscopy after initial clearing of the colon has been reported in large surveillance studies to show "unimportant pathology." Of the adenomas found at such surveillance colonoscopies, 84% to 90% are small (<1 cm) and mainly tubular; they are evenly distributed and rarely have high-grade dysplasia.<sup>10,11</sup> Careful analysis of costs and benefits of frequent colonoscopic surveillance after clearing a patient's colon shows it is usually not appropriate<sup>12</sup>—the most important exception being the universally accepted need for aggressive surveillance after removal of a sessile villous polyp.

In recent years, there has been partial acceptance of these concepts of less aggressive colonoscopy with the allowance that perhaps the finding of a 5 mm tubular adenoma at screening sigmoidoscopy does not mandate a colonoscopy and that routine sigmoidoscopy can be done as infrequently as every 5 years.

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SEYMOUR GROSSMAN, MD, retired in 1995 after 30 years with The Permanente Medical Group, Oakland, where he was Chief of Gastroenterology for the last 25 years. He continues as Clinical Director of the Colorectal Cancer Prevention (CoCaP) Program for TPMG, and as Clinical Professor of Medicine at the University of California San Francisco School of Medicine.

### Sigmoidoscopic Screening

The 1978 Gilbertsen report was uncontrolled and had poor documentation of data but suggested that screening proctoscopy could protect against rectal cancer. In a 1992 case control study from Kaiser Permanente, Selby et al showed convincingly that subjects who had rigid proctoscopic clearing of colorectal mucosa were 70% less likely to die from cancer of the rectum or distal sigmoid colon, and that they were protected for at least 10 years.<sup>13</sup>

Flexible sigmoidoscopy reaches 50% to 75% of advanced neoplasms (advanced adenomas plus adenocarcinomas).<sup>3</sup> Additional advanced neoplasms will be found in the right colon when sigmoidoscopic discovery of advanced neoplasms leads to colonoscopy. For a sigmoidoscopic screening program to be logistically feasible, total colonoscopy as a follow-up for sigmoidoscopic findings must be limited to patients who have had more than a small TA in their left colon. Subsequent surveillance must also be limited as described.

The role of family history in making decisions about screening and surveillance remains ill-defined. If a subject has a first-degree relative who had colorectal cancer at age 55 years or younger, or two first-degree relatives who had the disease at any age, we perform early screening colonoscopy, in conformity with the recommendations of the American Cancer Society.

### Hemoccult Screening

Hemoccult II, the most studied fecal occult blood test (FOBT), is usually positive in 1% to 4% of subjects and has sensitivity for cancer as low as 25% to 50%.<sup>14-15</sup> Cancer is found in about 10% of patients testing positive. In the highly publicized Minnesota study, slides were rehydrated, increasing sensitivity at great cost (in both dollars and complications). Ten percent of subjects had positive tests, and cancer was found in only 2% of the resulting colonoscopies.<sup>16</sup> Subsequent analysis of this study suggested that much of the reduction in cancer deaths was due to chance colonoscopy, not to FOBT.<sup>17</sup> In 1996, Allison et al showed that by using a combination of two fecal occult blood tests, one highly sensitive and the second highly specific, as much as 65% of cancers could be found.<sup>18</sup> Thus, one could add such fecal occult blood testing to a sigmoidoscopic screening program and succeed in diagnosing 85% of colon cancers and nearly that percentage of villous adenomas.

### Surveillance After Colon Cancer Resection

In the 1989 AGA/ASGE position paper,<sup>4</sup> all patients having curative surgery for colorectal cancer were man-

dated to undergo an intensive, multifaceted follow-up protocol. The protocol includes frequent interviews and examinations, blood tests, chest films, and colonoscopies for the rest of the patient's life. This aggressive surveillance regimen was based on several questionable premises: first, that every patient with colorectal cancer is at high risk for development of another colorectal cancer; and second, that discovery and treatment of recurrences can save enough lives to make worthwhile both the immense cost and the life-long ordeal of following that protocol.

Everyone agrees that perioperative (preferably preoperative) colonoscopy should be performed in all colorectal cancer patients to establish the presence or absence of synchronous neoplasms, and to remove any lesions found. However, the rest of the mandate has little evidence to support it. The risk for subsequent development of a second colorectal cancer is quoted variably from 2% to 6%, which is less than the risk of developing a first colorectal cancer in the general population. This risk holds for someone whose cancer is an isolated neoplasm. However, the cancer patient who is young (in 40s or younger) or has, in addition to the cancer, synchronous advanced neoplasms, is at high risk for development of a second cancer and should be in a surveillance protocol. As for curing patients with recurrences, studies using aggressive systematic follow-up protocols have usually proved futile. Suture line recurrences generally occur in patients who already have disseminated disease, so that survival rates are improved by < 0.5% by the occasional successful resection of these recurrences. Analysis of CEA monitoring shows it is expensive, inefficient, and potentially harmful because of the many unsuccessful operations, particularly in elderly, poor-risk candidates.<sup>19</sup>

### Main Concepts

1. Screening sigmoidoscopy performed on most people every 10 years starting in their sixth decade of life would result in a significant reduction in colorectal cancer mortality.

2. The small (<1 cm) colorectal TA is a common age-related finding. It rarely grows to become a malignancy—nor is it a marker for synchronous advanced neoplasms. Larger TAs now appear to share this non-marker quality. Conversely, adenomas containing villous or highly dysplastic architecture are the main participants in the adenoma-carcinoma sequence and are markers for synchronous and metachronous advanced neoplasms.

3. As fecal occult blood tests evolve and improve, stool testing will become a more effective part of screening programs.

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4. The development of cancer from a colonic adenoma is a very slow process, taking from 5 years to 25 years.

5. After a colon cancer is resected, searching for and treating recurrent cancer is usually futile. If the primary cancer was not accompanied by other advanced neoplasms, the likelihood of a second colon cancer developing is similar to the chance an average-risk person has of developing a first colon cancer (about 5%).

### Recommendations

1. Start colorectal cancer screening at about age 55 years with a flexible sigmoidoscopy. If results are negative (90%), tell the patient to return in 10 years for another sigmoidoscopy.

2. Remove small polyps at sigmoidoscopy, or measure and biopsy each small polyp. If the polyp is a TA and fully removed, repeat sigmoidoscopy in 5 years.

3. When sigmoidoscopy reveals a large polyp or biopsy shows a polyp to contain villous elements or high-grade dysplasia, total colonoscopy is indicated.

4. If colonoscopy shows no other lesions, or only a few tiny TAs in addition to the completely removed index lesion, do sigmoidoscopic follow-up in 5 years.

5. If a patient undergoing cancer resection is shown to have no other advanced neoplasms by perioperative colonoscopy, surveillance sigmoidoscopy or colonoscopy in 5 years is appropriate follow-up. If a cancer patient is unusually young or has other advanced lesions removed at perioperative colonoscopy, the first surveillance colonoscopy should be done in 3 years. ♦

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### Living Life

“We make a living by what we get, but we make a life by what we give.”

*Norman MacEwan*