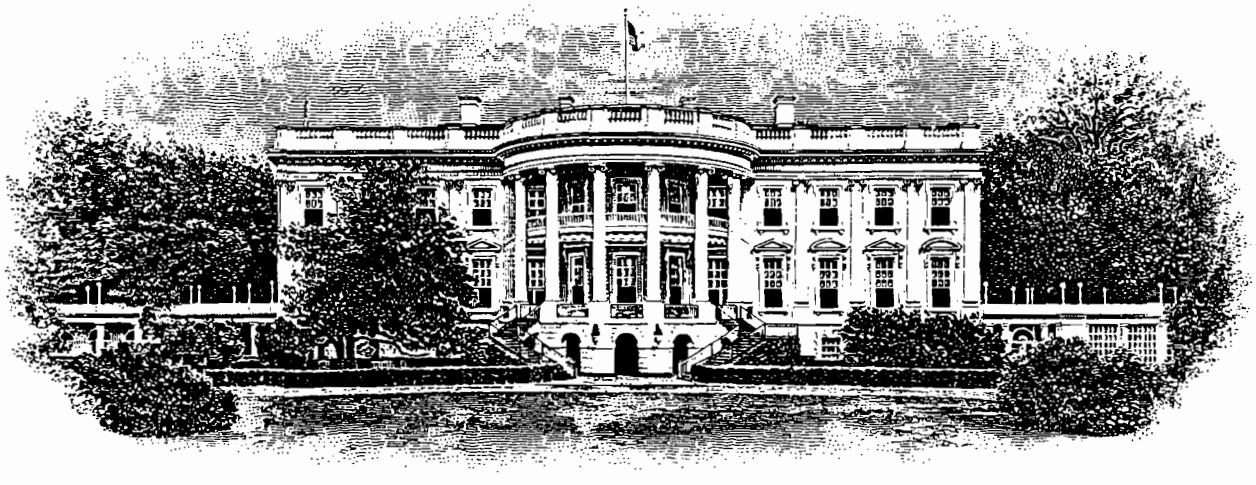
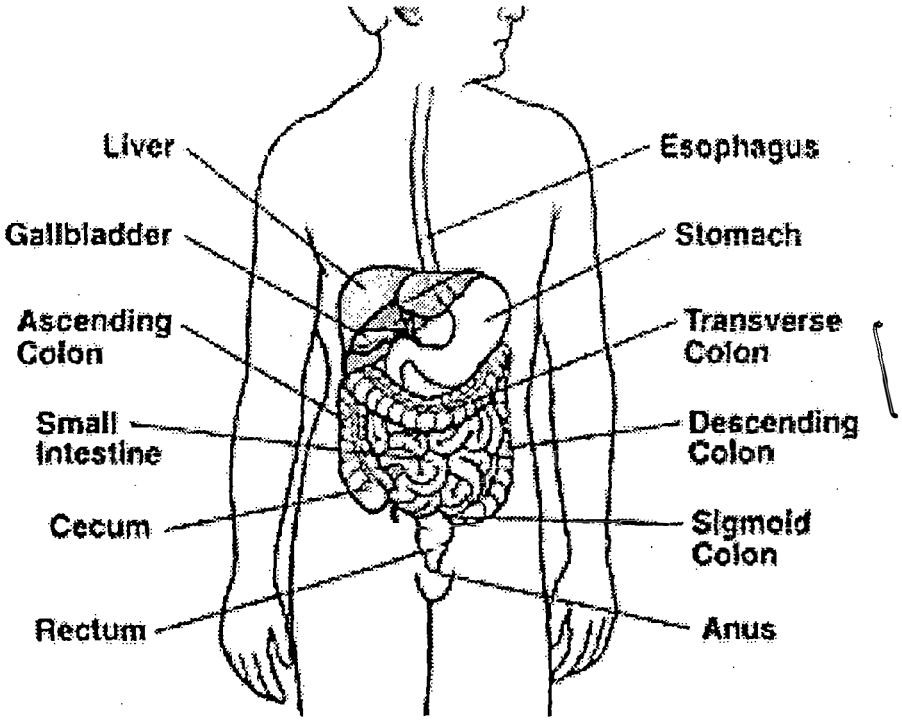
COLON CANCER

The White House




Liver
Gallbladder
Ascending Colon
Small Intestine
Cecum
Rectum
Esophagus
Stomach
Transverse Colon
Descending Colon
Sigmoid Colon
Anus

COLON CANCER SCREENING OPTIONS			
TEST		**MEDICARE COVERAGE AND COST SHARING REQUIREMENTS (Current Law)**	**PROPOSAL BEING ENDORSED TODAY / MEDICARE REFORM PROPOSAL**
Name	**Description**		
Fecal Occult Blood Test	Digital exam used to find hidden blood in feces.	Annual exams for beneficiaries over 50. No cost sharing requirement.	Annual exams for beneficiaries over 50. No cost sharing requirement.
Flexible Sigmoidoscopy	Flexible tube 60 cm long. Allows a view of roughly ½ the colon. Can be performed by primary care physician.	Exams every four years for beneficiaries over 50. ***Deductible and 25 percent copayment apply.***	Exams every four years for beneficiaries over 50. ***Cost sharing eliminated.***
Colonoscopy	Flexible tube allows a view of entire colon and removes possible cancers. Must be performed by a specialist.	***Beneficiaries who are not high risk may not receive this service.*** Exams every two years for beneficiaries with a family history of colon cancer or other high risk factors. ***Deductible and 25 percent copayment apply.***	***Provides colonoscopy once every 10 years to beneficiaries over 50.*** Exams every two years for those with a family history of colon cancer or other high risk factors. ***Cost sharing eliminated.***
Screening Barium Enema	Barium sulfate is used to inflate and fill the colon, allowing clear x-rays to be taken.	Exams every four years for individuals over the age of 50 or every two years for beneficiaries at high risk. ***Deductible and 20 percent copayment apply.***	Exams every four years for individuals over the age of 50 or every two years for beneficiaries at high risk. ***Cost sharing eliminated.***
NOTE: Endorsing this legislative proposal brings Medicare into line with the ACS recommendation on the use of colonoscopy as a primary screening device.			

Radio Address – Colon Cancer Announcement
Friday, October 6, 2000

List of Attendees

Agency Representatives

Dr. Barbara Rimer, Director of Cancer Control at NCI
Dr. Rick Klausner, Director of the National Cancer Institute
Dr. Bob Hyatt, Division of Cancer Control at NCI

Cancer Advocates

Fran Visco, President, National Breast Cancer Coalition
Ellen Stovall, President, National Coalition for Cancer Survivorship
Stacia Grosso, COO, National Coalition for Cancer Survivorship
Sonja Christopher, Walnut Creek, CA [breast cancer survivor from CBS television program, Survivor]
Jessica Turri, Bartlett, TN [12 year old acute lymphobiatic leukemia survivor. Featured in HBO Emmy-nominated documentary "Cancer: Evolution to Revolution.]
Jordan Turri, Bartlett, TN [sister to Jessica]
Dakota Max Ortiz, Royal Oak, MI [diagnosed with cancer as an infant, Dakota is featured on NCCS Rays of Hope posters posing on his tricycle with the bumper sticker, I am a cancer butt-kicker.]
Laura Ortiz, Royal Oak, MI [Mother of Dakota]
Susan Weiner, President, The Children's Cause
James Williams, Intercultural Cancer Council
Lois Williams, Intercultural Cancer Council
Kenneth Giddes, Alliance of/for Lung Cancer Advocacy, Support and Education
Ann Kolker, Executive Director, Ovarian Cancer National Alliance

Colon Cancer Advocates

Lilly Tartikoff, NCCRA, still pending
Lisa Paulsen, NCCRA, President, Entertainment Industry Foundation
Eric Davis, Major League Baseball
Angela Hunt, publicist for Eric Davis
Nick, Donna Constantinople
Alexandria Constantinople, NBC Vice President, still pending
Jeff Zucker, Executive Producer Today Show, still pending
Dan Smith, American Cancer Society
Wendy Selig, American Cancer Society
Bernard Levin, MD, Chair, National Colorectal Cancer Roundtable
Maurice Cerulli, MD, President, Digestive Disease National Coalition, Brooklyn, NY
Gavin Lindberg, Digestive Disease National Coalition
Priscilla Savary, Executive Director, Colorectal Cancer Network, Silver Spring, MD
Pamela McAllister, Science Liaison, Colon Cancer Alliance, Madison, WI
Dale P. Dirks, Digestive Disease National Coalition
Carolyn "Bo" Aldrige, Executive Director, Cancer Research Foundation of America

Final 10/6/00 1:30 p.m.
John Pollack

PRESIDENT WILLIAM JEFFERSON CLINTON
RADIO ADDRESS ON
RENEWING OUR FIGHT AGAINST CANCER
WASHINGTON, DC
October 6, 2000

Good morning. Every year, more than 56,000 Americans die from colorectal cancer, and another 130,000 are diagnosed with the disease. These are people we know and love: our families, our friends, our neighbors. Today I want to talk about our common fight against this quiet killer, and what we can do as a nation to save more lives.

A lot of people are uncomfortable talking about cancer, especially colorectal cancer. While all of us can certainly appreciate this reluctance, our silence protects nobody – least of all those we love the most. That's why tens of thousands of people, led by Katie Couric, have come to Washington this weekend to speak out and rally against colorectal cancer.

For almost eight years now, Vice President Gore and I have made the fight against cancer one of our top priorities. We've nearly doubled funding for cancer research and treatment. We've accelerated the approval of cancer drugs, while maintaining the highest standards of safety. We've strengthened Medicare to make prevention, screening and clinical trials more available and more affordable. And just a few days ago – during Breast Cancer Awareness Month – the Senate voted to fund our proposal to provide health coverage to uninsured women with breast and cervical cancer.

Our efforts are paying off. This year, for the first time, cancer deaths in the United States are no longer rising. We need to build on that progress by encouraging more early detection and treatment. Colorectal cancer is the second-leading cancer killer in America. The good news is that – caught soon enough – more than 90% of these cases can be cured. That's why, in 1998, my wife Hillary helped launch the first national campaign against colorectal cancer, much as we have been working for years to defeat breast cancer.

Hillary's leadership in promoting more cancer education and research has made a real difference in so many lives. Sadly, our family knows all too well the terrible toll that cancer can take, and we are doing everything we can to help others avoid that same loss.

Today, I am announcing several new actions in the war against cancer. First, the National Cancer Institute will invest $30 million over the next five years to help doctors expand and improve screening procedures for colorectal cancer. We need to address the chronic under-use of these life-saving tools, and this new investment will encourage physicians to make regular use of the most effective procedures.

Second, we are launching a new initiative to educate Medicare beneficiaries about the importance of regular checkups and cancer screenings. Beginning next year, every senior and

every American with a disability using Medicare will get a screening reminder – starting with one on colorectal cancer – every time they go to their doctor, or use Medicare's toll-free hotline.

Third, I am urging Congress to pass bipartisan legislation that expands Medicare to include more sophisticated colorectal cancer screening tests for people over the age of 50. Congress should not adjourn before sending me this legislation. They should also pass my proposal to eliminate all cost-sharing requirements for colorectal screening and other preventive procedures under Medicare. If we take these steps, we will remove major barriers to older Americans getting the preventive care they need.

And finally, once again, I am calling on Congress to pass a strong, enforceable Patients' Bill of Rights, one that assures that cancer patients – and all patients – have access to the specialty care they need. It's time to put progress before partisanship, and get people the medical care they deserve.

While the war against cancer is not yet won, we all have reason for new hope. Even as I speak, scientists are fast unlocking the secrets of the human genome, and revolutionary treatments are sure to follow. As they do, Americans should know that we will do everything necessary to safeguard their privacy, and to outlaw genetic discrimination in both employment and health insurance.

In the meantime, we must all stand watch against cancer, even if that means confronting – at times – our own worst fears. None of us will ever die of embarrassment, so go to the doctor and get that screening done. I did, and it was just fine. Remember, with early detection, quality care, love from our families and the grace of God, we can all lead longer, healthier and better lives.

Thank you.

RISK OF ADVANCED PROXIMAL NEOPLASMS IN ASYMPTOMATIC ADULTS ACCORDING TO THE DISTAL COLORECTAL FINDINGS

THOMAS F. IMPERIALE, M.D., DAVID R. WAGNER, M.S., CHING Y. LIN, B.S., GREGORY N. LARKIN, M.D., JAMES D. ROGGE, M.D., AND DAVID F. RANSOHOFF, M.D.

ABSTRACT

Background and Methods The clinical significance of a distal colorectal polyp is uncertain. We determined the risk of advanced proximal neoplasia, defined as a polyp with villous features, a polyp with high-grade dysplasia, or cancer, among persons with distal hyperplastic or neoplastic polyps as compared with the risk among persons with no distal polyps. We analyzed data from 1994 consecutive asymptomatic adults (age, 50 years or older) who underwent colonoscopic screening for the first time between September 1995 and December 1998 as part of a program sponsored by an employer. The location and histologic features of all polyps were recorded. Colonoscopy to the level of the cecum was completed in 97.0 percent of the patients.

Results Sixty-one patients (3.1 percent) had advanced lesions in the distal colon, including 5 with cancer, and 50 (2.5 percent) had advanced proximal lesions, including 7 with cancer. Twenty-three patients with advanced proximal neoplasms (46 percent) had no distal polyps. The prevalence of advanced proximal neoplasia among patients with no distal polyps was 1.5 percent (23 cases among 1564 persons; 95 percent confidence interval, 0.9 to 2.1 percent). Among patients with distal hyperplastic polyps, those with distal tubular adenomas, and those with advanced distal polyps, the prevalence of advanced proximal neoplasia was 4.0 percent (8 cases among 201 patients), 7.1 percent (12 cases among 168 patients), and 11.5 percent (7 cases among 61 patients), respectively. The relative risk of advanced proximal neoplasia, adjusted for age and sex, was 2.6 for patients with distal hyperplastic polyps, 4.0 for those with distal tubular adenomas, and 6.7 for those with advanced distal polyps, as compared with patients who had no distal polyps. Older age and male sex were associated with an increased risk of advanced proximal neoplasia (relative risk, 1.3 for every five years of age and 3.3 for male sex).

Conclusions Asymptomatic persons 50 years of age or older who have polyps in the distal colon are more likely to have advanced proximal neoplasia than are persons without distal polyps. However, if colonoscopic screening is performed only in persons with distal polyps, about half the cases of advanced proximal neoplasia will not be detected. (N Engl J Med 2000;343:169-74.)

THE clinical significance of distal colorectal polyps depends on two factors: whether the polyps are associated with advanced proximal neoplasms, and whether polyps with histologic features of advanced neoplasia (e.g., villous features) are clinically important. Although Stryker et al. reported that large polyps (>10 mm in diameter) left intact progress to colorectal cancer at a rate of about 1 percent per year,[1] it is unclear whether smaller polyps with histologic features of advanced neoplasia have a similar natural history. If early detection of such lesions is desirable, then the ability to estimate the risk of advanced proximal neoplasia with precision may be important both for deciding which patients should undergo examination of the proximal colon after sigmoidoscopic screening and for evaluating other screening strategies.

Previous studies of the association between polyps in the distal colon and advanced proximal neoplasia have lacked control groups of persons with no distal abnormalities,[2-5] making it difficult to identify risk factors for advanced proximal neoplasia. Furthermore, these studies have varied with respect to features that can affect the outcome, including the sample size and the criteria for classifying distal lesions (i.e., according to their size, number, location, or histologic features). Differences in reported risks have led to conflicting recommendations for the use of colonoscopy according to distal findings, particularly for patients with distal tubular adenomas, with important implications for the case of individual patients as well as for guidelines for colorectal-cancer screening.[2-5]

We analyzed data from a large cohort of persons at average risk who underwent colonoscopic screening for colorectal cancer. Our primary objective was to determine the relative risk of advanced proximal neoplasia in patients with distal polyps, either hyperplastic or neoplastic, as compared with persons with no distal polyps. A secondary objective was to determine the risk of large proximal neoplasms (≥10 mm in diameter) according to the distal findings.

From the Departments of Medicine, Indiana University Medical Center and Roudebush Veterans Affairs Medical Center (T.F.I., C.Y.L.); the Indianapolis Gastroenterology Research Foundation (D.R.W., J.D.R.); and Eli Lilly (G.N.L.) — all in Indianapolis; and the Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill (D.F.R.). Address reprint requests to Dr. Imperiale at Indiana University Medical Center, Division of Gastroenterology, 975 W. Walnut St., IB-424, Indianapolis, IN 46202-5121.

METHODS

Study Design

We performed a cross-sectional analysis of consecutive asymptomatic adults, 50 years of age or older, who underwent colonoscopic screening for the first time between September 1995 and December 1998. The study was approved by the institutional review board of Indiana University at Indianapolis.

Screening Program

In September 1995, Eli Lilly, which has its own health insurance plan for employees, retirees, and their dependents, began providing colonoscopic screening as a benefit. Persons 40 years of age or older receive a brochure about the screening program and are encouraged to call a toll-free number for more information or to make an appointment to be screened. A telephone interview is used to establish that persons who call to make an appointment for screening are asymptomatic (e.g., they report no visible rectal bleeding, no recent change in bowel habits, and no recent or current lower abdominal pain) and have no personal history of colorectal cancer, colorectal polyps, or inflammatory bowel disease. Thirty-six board-certified gastroenterologists and colorectal surgeons practicing in central Indiana participate in the screening program.

Study Procedures and Definitions

Polyethylene glycol lavage solution was used for bowel preparation. Fecal occult-blood testing was not performed before colonoscopic screening, and information on the presence or absence of a family history of colorectal cancer and the results of prior screening or diagnostic colorectal evaluations was not available, since such information is not routinely recorded.

During colonoscopy, the location and size of all polyps were determined before they were removed. Pathological specimens were evaluated by one of three board-certified pathologists, who classified polyps according to the criteria established by the World Health Organization.[6]

For the purpose of our analysis, the boundary between the proximal colon and the distal colon was defined as the junction of the splenic flexure and the descending colon, as assessed by the endoscopist. In the case of patients with more than one polyp in either the proximal or distal segment of the colon, the most advanced lesion in that segment was included in the analysis. The size of the polyp was estimated either with the use of open-biopsy forceps or on the basis of clinical judgment.

Distal and proximal findings were categorized as indicating normal mucosa (no polyps), hyperplastic polyps, tubular adenomas, or advanced neoplasms. An advanced neoplasm was defined as a polyp or polypoid lesion with villous features, a polyp or polypoid lesion with high-grade dysplasia, or cancer. Findings such as lipomas, lymphoid aggregates, chronic nonspecific inflammation, and inflammatory or juvenile polyps were categorized as indicating normal mucosa. No specimens were considered to be nondiagnostic.

Statistical Analysis

The prevalence of both advanced proximal neoplasms and large proximal neoplasms was calculated on the basis of the distal colorectal findings. The unadjusted relative risk of each distal and proximal finding was calculated for men as compared with women.[7] Multivariate logistic-regression analysis was used to estimate the adjusted relative risk of advanced proximal neoplasia and large proximal neoplasms (≥10 mm in diameter), with the use of age, sex, and distal colorectal findings as independent variables.[8] For each distal finding, the "number needed to screen" was determined. Conceptually similar to the "number needed to treat,"[9] the number needed to screen is the number of persons with a particular distal finding who would have to undergo colonoscopy in order to detect one advanced proximal neoplasm. Analyses were performed with SPSS for Windows software (version 9.0, SPSS, Chicago).

RESULTS

From September 1995 through December 1998, a total of 2686 persons underwent colonoscopic screening. We excluded from the analysis 692 persons who were less than 50 years old. The study cohort thus consisted of 1994 persons. Their mean (±SD) age was 59.8±8.3 years, and 58.9 percent were men (mean age, 59.6±8.3 years). The mean age of the women was 60.1±8.4 years. Colonoscopy to the cecum was performed in 97.0 percent of patients.

A total of 12 cancers were detected: 8 in men and 4 in women; their mean age was 69.8±10.0 years. Seven patients had cancers in the proximal portion of the colon; in three of the seven, there were associated distal lesions (adenomas in two patients and a hyperplastic polyp in one). Five of the 12 patients had carcinoma in situ, 1 had a Dukes' stage A lesion, 4 had Dukes' stage B lesions, and 2 had Dukes' stage C lesions.[10] There were no deaths related to colonoscopy. One patient had a colonic perforation that was managed medically. Three patients who had bleeding after polypectomy went to an urgent care center or emergency room for evaluation; none required transfusion or surgery.

Distal and proximal findings are shown in Table 1. No polyps were present in the distal colon in 78.4 percent of the patients (mean age, 60.0±8.3 years). Hyperplastic polyps, tubular adenomas, and advanced neoplasms were present in the distal colon in 10.1 percent, 8.4 percent, and 3.1 percent of the patients, respectively. Men were more likely than women to have hyperplastic polyps (unadjusted relative risk, 1.49; 95 percent confidence interval, 1.12 to 1.97), tubular adenomas (unadjusted relative risk, 1.54; 95 percent confidence interval, 1.13 to 2.11), and advanced neoplasms (unadjusted relative risk, 2.39; 95 percent confidence interval, 1.32 to 4.31).

No polyps were present in the proximal colon in 84.6 percent of the cohort (mean age, 59.8±8.2 years) (Table 1). Hyperplastic polyps were present in 3.6 percent, tubular adenomas in 9.3 percent, and advanced neoplasms in 2.5 percent. Men were more likely than women to have tubular adenomas (unadjusted relative risk, 2.3; 95 percent confidence interval, 1.7 to 3.2) and advanced neoplasms (unadjusted relative risk, 3.7; 95 percent confidence interval, 1.8 to 8.0).

The prevalence of advanced proximal neoplasia according to the findings in the distal colon is shown in Table 2. Among the 1564 persons with no distal polyps, the prevalence of proximal neoplasia was 1.5 percent (95 percent confidence interval, 0.9 to 2.1 percent), and the prevalence increased linearly among persons with distal hyperplastic polyps (4.0 percent), tubular adenomas (7.1 percent), and advanced neoplasms (11.5 percent). The proportions were essentially the same when advanced proximal neoplasms and large proximal neoplasms were considered together. Twenty-three of the 50 patients with advanced proximal neoplasia (46.0 percent) had no polyps in the distal colon. Had these 23 patients undergone screening sigmoidoscopy, their proximal neoplasms would not have been detected, because of the absence of distal polyps.

TABLE 1. FINDINGS IN THE DISTAL AND PROXIMAL COLON IN THE COHORT OF 1994 PATIENTS.*

FINDING	DISTAL COLON		PROXIMAL COLON	
	PATIENTS	AGE	PATIENTS	AGE
	no. (%)	yr	no. (%)	yr
No polyp	1564 (78.4)	60.0±8.3	1686 (84.6)	59.8±8.2
Hyperplastic polyp	201 (10.1)	59.3±7.4	72 (3.6)	60.6±9.5
Tubular adenoma	168 (8.4)	62.0±9.4	186 (9.3)	62.1±8.8
Advanced neoplasm†	61 (3.1)	62.2±8.0	50 (2.5)	64.4±8.9

*Plus–minus values are means ±SD.

†An advanced neoplasm was defined as a polyp or polypoid lesion with villous features, a polyp or polypoid lesion with high-grade dysplasia, or cancer.

Table 2 also shows the relative risk of advanced proximal neoplasia, adjusted for age and sex, according to the distal findings, with patients who had no distal polyps serving as the reference group. The magnitude of the risk was related to the histologic features of the distal lesion.

The size of a distal adenoma alone was unrelated to the risk of advanced proximal neoplasia. Thirteen of 124 patients with distal adenomas that were 1 to 5 mm in diameter had advanced proximal neoplasia (10.5 percent; 95 percent confidence interval, 5.7 to 17.3 percent). Advanced proximal lesions were detected in 2 of 72 patients with adenomas that were 6 to 9 mm in diameter (2.8 percent; 95 percent confidence interval, 0.3 to 6.6 percent) and in 4 of 26 with distal adenomas that were 10 mm or more in diameter (15.4 percent; 95 percent confidence interval, 4.4 to 34.9 percent), respectively.

The prevalence of large proximal neoplasms according to the distal findings is shown in Table 3. Despite the small number of patients with large lesions, the risk of a large proximal neoplasm was significantly associated with the histologic stage of the distal lesion (two-tailed P value for trend, 0.02). The confidence intervals for the proportions indicate that the risk of large proximal neoplasms was greater for patients with distal tubular adenomas or advanced neoplasms than for those with distal hyperplastic polyps or no distal polyps. Table 3 also shows the adjusted relative risk of a large proximal neoplasm according to the distal findings, with persons who had no distal polyps serving as the reference group. The presence of distal neoplasia increased the age- and sex-adjusted relative risk of a large proximal neoplasm.

Multivariate analysis showed that after adjustment for sex and distal findings, age was significantly associated with the risk of advanced proximal neoplasia, with a relative risk of 1.3 (95 percent confidence interval, 1.3 to 1.4) for every successive five-year interval between the ages of 50 and 80 years. Likewise, male sex, adjusted for age and distal findings, increased the risk of advanced proximal neoplasia by 3.3 (95 percent confidence interval, 1.5 to 7.1).

DISCUSSION

If there were a reliable distal marker for clinically important proximal neoplasia (i.e., a sentinel lesion) or if normal findings in the distal colon were a reliable marker for the absence of clinically important proximal neoplasia, then sigmoidoscopic examination of the distal colon and rectum would help determine which persons should undergo examination of the proximal colon.

In our study, a polyp of any size or type in the distal colon was associated with an increased risk of histologically advanced proximal neoplasia. The magnitude of the risk was proportional to the histologic features of the distal lesion. The risk of a large proximal neoplasm was similarly related to the histologic features of polyps in the distal colon.

TABLE 2. PREVALENCE OF ADVANCED PROXIMAL NEOPLASMS ACCORDING TO THE DISTAL FINDINGS.*

DISTAL FINDING	TOTAL	ADVANCED PROXIMAL NEOPLASM		ADJUSTED RELATIVE RISK (95% CI)†
	no. of patients (%)	no. of patients	% (95% CI)	
No polyp	1564 (78.4)	23	1.5 (0.9–2.1)	1.0
Hyperplastic polyp	201 (10.1)	8	4.0 (1.3–6.7)	2.6 (1.1–5.9)
Tubular adenoma	168 (8.4)	12	7.1 (3.3–11.0)	4.0 (1.9–8.3)
Advanced neoplasm	61 (3.1)	7	11.5 (3.4–19.5)	6.7 (3.2–16.6)

*An advanced neoplasm was defined as a polyp or polypoid lesion with villous features, a polyp or polypoid lesion with high-grade dysplasia, or cancer. CI denotes confidence interval.

†The relative risk was adjusted for age and sex. The group of patients with no distal polyps was the reference group.

TABLE 3. PREVALENCE OF LARGE PROXIMAL NEOPLASMS ACCORDING TO THE DISTAL FINDINGS.*

DISTAL FINDING	TOTAL	LARGE PROXIMAL NEOPLASM		ADJUSTED RELATIVE RISK (95% CI)†
	no. of patients	no. of patients	% (95% CI)	
No polyp	1564	17	1.1 (0.6–1.6)	1.0
Hyperplastic polyp	201	4	2.0 (0.5–5.0)	1.8 (0.6–5.5)
Tubular adenoma	168	7	4.2 (1.7–8.4)	2.9 (1.1–7.2)
Advanced neoplasm	61	3	4.0 (1.0–13.7)	3.5 (1.0–13.0)

*A large neoplasm was defined as a lesion that was 10 mm or more in diameter. An advanced neoplasm was defined as a polyp or polypoid lesion with villous features, a polyp or polypoid lesion with high-grade dysplasia, or cancer. CI denotes confidence interval.

†The relative risk was adjusted for age and sex. The group of patients with no distal polyps was the reference group.

Because previous research has suggested that the histologic features of distal polyps may be a better marker for advanced proximal neoplasia than their size[11] and because the measurement of a polyp through the endoscope may be inaccurate,[12] we defined an advanced neoplasm on the basis of histologic findings instead of size. To make our findings comparable with those of other studies, however,[2,5] we also considered the relation between distal polyps and the combination of histologically advanced neoplasms and large tubular adenomas (≥10 mm in diameter) in the proximal colon. Because this relation was no different from that between distal polyps and histologically advanced proximal neoplasms alone, we have presented the results only for the definition of advanced neoplasm that we consider to be the more reliable of the two definitions.

In addition to distal polyps, we found that age was an important predictor of risk. For every five-year interval between the ages of 50 and 80 years, the risk of advanced proximal neoplasia increased by 32 percent. Few data are available to assess age as an independent risk factor for advanced proximal neoplasia. Levin and colleagues found that an age of more than 65 years was an independent risk factor for advanced proximal neoplasia.[5] In a study of colonoscopic screening among 621 asymptomatic persons who were 50 to 75 years old and who had negative fecal occult-blood tests, Rex and colleagues found that each five-year increase in age increased the odds of colonic neoplasia of any kind by 1.36.[13]

In our study, men were more likely than women to have both proximal and distal neoplasms and were more than three times as likely to have advanced proximal neoplasms, after adjustment for age and distal findings. Although men are known to be at increased risk for colorectal neoplasia, the effect of sex apart from age and distal findings has been uncertain.[11,14]

The prevalence of advanced proximal neoplasia in our patients with distal hyperplastic polyps was 4.0 percent (95 percent confidence interval, 1.3 to 6.7 percent). Although the 95 percent confidence interval for this estimate overlaps that for persons with no distal polyps, the relative risk of advanced proximal neoplasia, adjusted for age and sex, in patients with distal hyperplastic polyps as compared with the patients who had no distal polyps was 2.6 (95 percent confidence interval, 1.1 to 5.9). In part because of small samples, studies of the risk of proximal neoplasia in asymptomatic persons with distal hyperplastic polyps have had inconsistent findings. The risk of a proximal neoplasm of any size has ranged from 15 to 32 percent.[15-18] More important, the risk of advanced proximal neoplasia and the risk of large proximal neoplastic polyps have not been assessed. Otori and colleagues found K-*ras* mutations in 47 percent of hyperplastic polyps, suggesting that they could be precursors of neoplasia.[19] In the light of practice guidelines suggesting that hyperplastic polyps are not important[20,21] and the need to consider previous findings in the process of interpreting new data,[22] the importance of hyperplastic polyps remains uncertain and must be clarified by further research.

The efficiency of sigmoidoscopic screening in detecting proximal lesions can be assessed by calculating the number needed to screen — that is, the number of persons who would have to undergo sigmoidoscopic screening in order to detect one advanced proximal neoplasm. As the criterion for performing colonoscopy is relaxed (i.e., from the most stringent criterion of an advanced distal neoplasm to the criteria of a distal tubular adenoma or advanced neoplasm, any distal polyp, and finally, no polyp), the number needed to screen increases substantially (Table 4). However, the proportion of patients with advanced proximal neoplasia also increases. Further-

TABLE 4. NUMBER NEEDED TO SCREEN ACCORDING TO THE DISTAL FINDING USED AS A CRITERION FOR COLONOSCOPY.*

DISTAL FINDING AS CRITERION FOR COLONOSCOPY	ADVANCED PROXIMAL NEOPLASM DETECTED (N=50)	NO. NEEDED TO SCREEN (95% CI)	NO. SCREENED
	no. of patients (%)		
Advanced neoplasm	7 (14)	9 (5–25)	61
Tubular adenoma or advanced neoplasm	19 (38)	12 (8–21)	229
Hyperplastic polyp, tubular adenoma, or advanced neoplasm	27 (54)	15 (12–25)	430
No polyp, hyperplastic polyp, tubular adenoma, or advanced neoplasm	50 (100)	40 (31–55)	1994

*The number needed to screen is the number of patients who would have to undergo colonoscopic screening in order to identify one patient with advanced proximal neoplasia. CI denotes confidence interval.

more, even when colonoscopy is performed for any distal polyp, nearly half the cases of advanced proximal neoplasia are missed. These data indicate that a substantial proportion of advanced proximal neoplasms are not associated with any distal sentinel lesion. Physicians and policy makers could use this information to determine the appropriate threshold for performing a full colonoscopic examination. Although our data may be useful for deciding which screening techniques are best, other information is also important, such as the expense and complications of colonoscopy, the need for and frequency of repeated examinations, coexisting disease in patients undergoing screening, and the natural history of histologically advanced neoplasms.

The limitations of our study require comment. Despite the colonoscopic screening of 1994 persons, only 50 advanced proximal neoplasms were found. The small number of advanced and large proximal neoplasms precluded certain subgroup analyses. This limitation is not unique to our study. Some investigators have suggested that the size and number of distal tubular adenomas may affect the risk of proximal neoplasia.[2-4] In our study, only 12 of the 168 persons with distal tubular adenomas had advanced proximal neoplasms. The small size of this subgroup precluded the detection of any but the largest differences. Furthermore, we did not find a significant association between the risk of advanced proximal neoplasia and the size of a distal adenoma, in contrast to the results reported by Read and colleagues.[2] Yet because the two studies had small numbers of patients, with overlapping confidence intervals for each category of lesions, the results of the two analyses are not statistically different. Wide confidence intervals as a result of the small numbers of advanced proximal lesions account at least in part for the paradox of qualitatively different yet statistically similar findings among studies.

Both in our study and in previous studies, limited clinical information was available to supplement the endoscopic information provided by the screening examinations. Individual risk estimates for advanced proximal neoplasia might be derived from such information as race, body-mass index, the presence or absence of a family history of colorectal neoplasia, and the results of any previous colorectal screening and diagnostic tests. Although several groups have investigated the risk of proximal neoplasia on the basis of distal findings alone,[2-5,23-26] future studies should evaluate the risk by incorporating additional clinical information.

In summary, we found that increasing age, male sex, and the presence of polyps in the distal colon were independent risk factors for advanced proximal neoplasms in persons who were 50 years of age or older. Although our results are consistent with those of other studies with respect to the importance of advanced distal neoplasms as a marker of proximal neoplasia, our findings raise questions about the possible additional importance of hyperplastic polyps. Like other investigators,[27,28] we found that almost half the patients with advanced proximal neoplasms had no distal lesions. The current strategy of deciding who should undergo colonoscopy solely according to the findings in the distal colon should be reconsidered.

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USE OF COLONOSCOPY TO SCREEN ASYMPTOMATIC ADULTS FOR COLORECTAL CANCER

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ABSTRACT

Background and Methods The role of colonoscopy in screening for colorectal cancer is uncertain. At 13 Veterans Affairs medical centers, we performed colonoscopy to determine the prevalence and location of advanced colonic neoplasms and the risk of advanced proximal neoplasia in asymptomatic patients (age range, 50 to 75 years) with or without distal neoplasia. Advanced colonic neoplasia was defined as an adenoma that was 10 mm or more in diameter, a villous adenoma, an adenoma with high-grade dysplasia, or invasive cancer. In patients with more than one neoplastic lesion, classification was based on the most advanced lesion.

Results Of 17,732 patients screened for enrollment, 3196 were enrolled; 3121 of the enrolled patients (97.7 percent) underwent complete examination of the colon. The mean age of the patients was 62.9 years, and 96.8 percent were men. Colonoscopic examination showed one or more neoplastic lesions in 37.5 percent of the patients, an adenoma with a diameter of at least 10 mm or a villous adenoma in 7.9 percent, an adenoma with high-grade dysplasia in 1.6 percent, and invasive cancer in 1.0 percent. Of the 1765 patients with no polyps in the portion of the colon that was distal to the splenic flexure, 48 (2.7 percent) had advanced proximal neoplasms. Patients with large adenomas (≥10 mm) or small adenomas (<10 mm) in the distal colon were more likely to have advanced proximal neoplasia than were patients with no distal adenomas (odds ratios, 3.4 [95 percent confidence interval, 1.8 to 6.5] and 2.6 [95 percent confidence interval, 1.7 to 4.1], respectively). However, 52 percent of the 128 patients with advanced proximal neoplasia had no distal adenomas.

Conclusions Colonoscopic screening can detect advanced colonic neoplasms in asymptomatic adults. Many of these neoplasms would not be detected with sigmoidoscopy. (N Engl J Med 2000;343:162-8.)

COLORECTAL cancer is the second leading cause of death in North America. There is evidence that the rate of mortality from colorectal cancer can be reduced by screening asymptomatic persons at average risk, beginning at the age of 50 years.[1-5] The Preventive Services Task Force has endorsed screening with the use of a fecal occult-blood test or sigmoidoscopy.[6] Colonoscopy is generally reserved for patients with positive results of screening tests or those with a higher-than-average risk of colorectal cancer. A multidisciplinary panel of experts has recommended that screening with colonoscopy be considered for persons at average risk.[7] Experience with colonoscopy as a primary screening procedure has been limited to a few case series.[8-10] There have been no direct comparisons between examinations limited to the distal colon and full colonoscopy to determine the potential additional benefit of a full examination in asymptomatic persons.

We conducted a study to determine risk factors for neoplastic lesions with a diameter of 10 mm or more in asymptomatic persons between the ages of 50 and 75 years. Patients enrolled in the study underwent colonoscopic examination, during which all

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*Participants in the study group are listed in the Appendix.

polypoid lesions were removed and evaluated histologically. The purpose of the study was to determine the prevalence and location of colonic neoplasia in asymptomatic patients, the risk of proximal advanced neoplasia in patients with and in those without neoplasia in the distal colon, and the likelihood that advanced proximal neoplasia would be detected on the basis of the presence of an adenoma in the distal colon.

METHODS

Patients

The study protocol was approved by a central human-rights committee and by the corresponding committee at each participating center. Patients were enrolled in the study between February 1994 and January 1997. They were recruited from 13 Veterans Affairs medical centers, representing each major region of the United States. Patients were recruited in one of three ways: by random selection from the center's clinic list on the basis of age, by the selection of asymptomatic patients referred for screening sigmoidoscopy, and by advertisement for patients with a family history of colorectal cancer. Oversampling for patients who had one or more first-degree relatives with colorectal cancer was performed in order to have an adequate number of patients with a family history in the sample.

A study nurse asked each patient to complete a brief questionnaire designed to determine eligibility for the study. Patients were excluded if they reported symptoms of lower gastrointestinal tract disease, including rectal bleeding, on more than one occasion in the previous six months, a marked change in bowel habits, or lower abdominal pain that would normally require medical evaluation. Other exclusion criteria were current participation in other studies, a history of disease of the colon (colitis, polyps, or cancer) or colonic surgery, a colonic examination within the previous 10 years (sigmoidoscopy, colonoscopy, or barium enema), a medical condition that could increase the risk associated with colonoscopy (active cardiac or pulmonary disease or other serious disease) or that would preclude a benefit from colonoscopic screening (cancer or any terminal illness), a prosthetic heart valve, anticoagulant therapy, nonmedical problems (psychiatric disorders, lack of transportation, homelessness or lack of support at home, or excessive use of alcohol), and a need for special precautions in performing colonoscopy (i.e., antibiotic prophylaxis). In addition, women of childbearing potential were excluded.

Study Protocol

Eligible persons who provided informed consent completed detailed questionnaires that covered diet, physical activity, drug use, and family history of cancer. A physical examination was performed, and laboratory studies were ordered to evaluate coagulation. The patients received a polyethylene glycol–based electrolyte solution for bowel preparation, along with instructions for use. A complete colonoscopic examination was performed while the patients were under conscious sedation with an intravenous agent. All examinations were performed at the participating centers by the study investigators, who were selected because of their extensive experience with colonoscopy. During the examination, the location and size of all polypoid lesions were noted by study nurses. The size of each polyp was estimated with the use of an open-biopsy forceps, which is 7 mm in diameter. Investigators were required to provide photographic documentation of cecal landmarks and of all polyps and other important lesions.

If the colonoscopic examination was incomplete because of problems with bowel preparation or failure to reach the cecum, the patient was asked to return for a second attempt. If a complete examination was performed within six months after the first attempt, a complete examination was reported, and the combined results of the two examinations were included in the analysis. If the second examination was also incomplete, the results were excluded from the analysis. If the patient underwent surgery within six months after the initial examination and if the resected specimen could be evaluated, then a complete examination was reported, and the results were included in the analysis.

Histologic Evaluation

All retrieved polypoid lesions were sent to local pathology laboratories for histologic evaluation. Slides were sent to a designated expert in pathology at the Veterans Affairs Medical Center in Hines, Illinois, for an independent, blinded review. When there was agreement between the local pathologist and the pathologist at the coordinating center, a final pathological classification was made. When there was disagreement, the slides were sent to a pathologist at the Veterans Affairs medical center in Minneapolis or in Portland, Oregon. The results of the third review were used to classify the lesion.

Patients were classified on the basis of their most advanced lesion in order to determine the prevalence of pathological features. For example, a patient who had a villous adenoma and a tubular adenoma was classified as having a villous adenoma. The most advanced lesions in the entire colon, distal colon, and proximal colon were determined. Patients were classified separately according to the number of adenomas in the distal colon and the number in the entire colon. The distal colon was defined as the rectum, sigmoid, and descending colon up to but not including the splenic flexure. The proximal colon was defined as the splenic flexure and other, more proximal portions of the colon. The risk of proximal neoplasia associated with distal colonic lesions was determined.

Advanced colonic neoplasia was defined as an adenoma with a diameter of 10 mm or more, a villous adenoma (i.e., at least 25 percent villous), an adenoma with high-grade dysplasia, or invasive cancer. Patients with intramucosal carcinoma or carcinoma in situ were classified as having high-grade dysplasia. Cancer was defined as the invasion of malignant cells beyond the muscularis mucosa.

Statistical Analysis

Data-base management and all statistical analyses were performed with SAS software (SAS Institute, Cary, N.C.). Rates and proportions were calculated for categorical data, and means and standard errors for continuous data. In addition, standard logistic-regression methods were used to calculate odds ratios for advanced neoplasia, with 95 percent confidence intervals.[11] Odds ratios were adjusted for age and family history of cancer in analyses of the risk of advanced neoplasia in the distal and proximal colon.

RESULTS

A total of 17,732 patients were screened for enrollment in the study, and 3196 eligible patients were enrolled. Selected demographic characteristics of the study population are shown in Table 1. The proportion of patients who were recruited by random selection from clinic lists was 48.8 percent; 45.0 percent of the patients had been referred for sigmoidoscopy, and 6.2 percent had responded to the advertisement for patients with a family history of colorectal cancer. The prevalence of a family history of colorectal cancer (one or more affected first-degree relatives) was 13.9 percent in the final study population but 8.2 percent in the overall group of patients who were randomly selected from clinic patients, with the difference due to oversampling. The most frequently reported reasons for exclusion are shown in Table 2. A total of 1463 patients met the criteria for enrollment but declined to participate.

Colonoscopy was completed to the cecum in 3121 of the 3196 patients (97.7 percent). In 14 patients,

TABLE 1. CHARACTERISTICS OF THE 3121 PATIENTS.

VARIABLE	VALUE
Age — yr	
Mean ±SE	62.9±0.13
50–59 yr — no. (%)	1044 (33.5)
60–69 yr — no. (%)	1481 (47.5)
>69 yr — no. (%)	596 (19.1)
Male sex — no. (%)	3021 (96.8)
Race — no. (%)	
White	2609 (83.6)
Other	512 (16.4)
Family history of colorectal cancer — no./total no. (%)*	
Final study population	434/3121 (13.9)
All patients randomly selected from clinic lists	462/5617 (8.2)
Recruitment method — no. (%)	
Random selection from clinic lists	1524 (48.8)
Sigmoidoscopy referral	1404 (45.0)
Advertisement for patients with family history*	193 (6.2)

*A family history of colorectal cancer was defined as one or more affected first-degree relatives.

TABLE 2. REASONS FOR EXCLUSION FROM THE STUDY.

REASON FOR EXCLUSION*	NO. OF PATIENTS
Colonic examination in previous 10 yr	6486
History of colon disease	2221
Serious medical disorder†	1052
Anticoagulation therapy	712
Nonmedical problem‡	433
Age (<50 yr or ≥75 yr)	397
Participation in other studies	296
Need for antibiotic prophylaxis	167
Prosthetic heart valve	48
Childbearing age	8
Declined clinic survey	2346
Patients who met inclusion criteria but declined participation	1463

*Some patients were excluded for more than one reason.

†Serious medical disorders included disorders that could increase the risk associated with colonoscopy (e.g., active cardiac or pulmonary disease or other serious disease) or that would preclude a benefit from colonoscopic screening (cancer or any terminal illness).

‡Nonmedical problems included psychiatric disorders, lack of transportation, homelessness or lack of support at home, and excessive use of alcohol.

more than one procedure was required to complete the examination. Patients were classified on the basis of the most advanced lesion found in the colon (Table 3). A total of 1441 patients (46.2 percent) had no polypoid lesions. In the other 1680 patients (53.8 percent), a total of 5218 polyps were removed. In

TABLE 3. COLONOSCOPIC FINDINGS ACCORDING TO THE MOST ADVANCED LESION.

FINDING	NO. OF PATIENTS (%)
No polyps	1441 (46.2)
Nonadenomatous lesion	118 (3.8)
Hyperplastic polyp	391 (12.5)
Tubular adenoma	
<10 mm	842 (27.0)
1 or 2	687
3 or 4	112
≥5	43
≥10 mm	155 (5.0)
Villous adenoma*	
<10 mm	24 (0.8)
≥10 mm	69 (2.2)
High-grade dysplasia	
<10 mm	11 (0.4)
≥10 mm	40 (1.3)
Invasive cancer	30 (1.0)

*A villous adenoma was defined as a lesion that was at least 25 percent villous.

391 patients (12.5 percent), the most advanced lesions were hyperplastic polyps. In 118 patients (3.8 percent), biopsy of what appeared to be a polyp revealed either normal mucosa or nonpolypoid, miscellaneous findings. In all, 62.5 percent of the patients had no evidence of neoplasia.

A total of 1171 patients had one or more adenomas of any type or invasive cancer (37.5 percent). In 842 patients, the most important finding was a tubular adenoma that was less than 10 mm in diameter. Of these patients, 687 had one or two adenomas, 112 had three or four, and 43 had five or more.

Advanced disease (defined as an adenoma with a diameter of at least 10 mm, or villous features, high-grade dysplasia, or invasive cancer) was present in 329 patients (10.5 percent). In 155 patients (5.0 percent), the most advanced lesions were large tubular adenomas (≥10 mm). Ninety-three patients (3.0 percent) had adenomas with villous features, 51 (1.6 percent) had adenomas with high-grade dysplasia, and 30 (1.0 percent) had invasive cancer. Among the patients with cancer, the stage was T1N0 in nine patients, T2N0 in six, and T3N0 in seven; six patients had nodal involvement (N1 or N2), and two had metastatic disease.

The most advanced lesions in the distal colon and in the proximal colon were identified separately for each patient (Table 4). In the primary analysis, the distal colon was defined as the rectum and the sigmoid and descending colon. According to this definition, 228 patients (7.3 percent) had advanced disease in the distal colon (i.e., distal to the splenic flexure) and 128 (4.1 percent) had advanced disease in the proximal colon. We also determined the prevalence of advanced disease in the distal colon defined as only the rectum

TABLE 4. PREVALENCE AND LOCATION OF ADVANCED NEOPLASIA.

DEFINITION OF DISTAL COLON	ADVANCED NEOPLASIA		ADVANCED NEOPLASIA WITH DISTAL ADENOMA	
	DISTAL	PROXIMAL	TOTAL*	PROXIMAL†
	no. of patients/total no. (%)			
Rectum and sigmoid colon	188/3121 (6.0)	169/3121 (5.4)	224/329 (68.1)	64/169 (37.9)
Rectum and sigmoid and descending colon	228/3121 (7.3)	128/3121 (4.1)	263/329 (79.9)	62/128 (48.4)

*Total refers to all patients with advanced neoplasia who had adenomas in the distal colon.

†Proximal refers to all patients with advanced proximal neoplasia who had adenomas in the distal colon.

and sigmoid colon. With the more restricted definition, 188 (6.0 percent) had advanced disease in the distal colon, and 169 (5.4 percent) had advanced disease in the proximal colon.

The likelihood that advanced proximal neoplasia would be detected on examination of the distal colon was determined by noting the presence or absence of an adenoma in the portion of the colon that was distal to the splenic flexure (Table 4). Among the patients with advanced proximal neoplasia, 48.4 percent (62 of 128) had at least one adenoma in the distal colon, and 14.1 percent (18 of 128) had large adenomas (≥10 mm in diameter) in the distal colon. With the distal colon defined as the rectum plus the sigmoid colon, only 37.9 percent of the patients with advanced proximal neoplasia (64 of 169) had a distal adenoma.

Among the patients with no adenomas distal to the splenic flexure, 2.7 percent had advanced proximal neoplasia. These patients served as the reference group in an analysis of the risk of advanced proximal neoplasia according to the distal findings. The odds ratios (with 95 percent confidence intervals), adjusted for age and the presence or absence of a family history of colorectal cancer, are shown in Table 5, according to the two definitions of the distal colon. The patients with distal hyperplastic polyps did not have a higher risk of advanced proximal neoplasia than the patients without distal polyps. However, the patients with small or large adenomas in the distal colon had a significantly increased risk of advanced proximal neoplasia: odds ratio for patients with small adenomas, 2.6 (95 percent confidence interval, 1.7 to 4.1); odds ratio for patients with large adenomas, 3.4 (95 percent confidence interval, 1.8 to 6.5). Among patients with small tubular adenomas (<10 mm in diameter) in the distal colon, the presence of one or two adenomas was significantly associated with an elevated risk of proximal advanced neoplasia, but the presence of a larger number of adenomas did not further increase the risk. When the distal colon was defined as the rectum and sigmoid colon, the presence of distal adenomas, whether small or large, was still associated with an increased risk of advanced proximal neoplasia. The odds ratio for proximal advanced neoplasia was higher for the patients with distal villous adenomas (4.7; 95 percent confidence interval, 2.1 to 10.4) than for the patients with distal tubular adenomas (2.6; 95 percent confidence interval, 1.7 to 4.0), but the difference was not statistically significant.

The effect of age on the prevalence of advanced neoplasia was assessed as an independent variable. The prevalence of advanced neoplasia increased from 5.7 percent in the youngest patients (50 to 59 years old) to 13 percent in the oldest patients (70 to 75 years old). There was a trend toward an increased prevalence of advanced proximal neoplasia with age ($P<0.001$): the prevalence was 2 percent for patients who were 50 to 59 years old, 4.9 percent for those 60 to 69 years old, and 5.9 percent for those 70 to 75 years old.

There were no differences in the rates of advanced neoplasia according to the method used to recruit patients ($P=0.32$). Patients with a family history of colorectal cancer who were recruited by any of the three methods had a higher age-adjusted risk of advanced neoplasia than patients with no family history (14.3 percent vs. 9.9 percent; odds ratio, 1.5; 95 percent confidence interval, 1.1 to 2.0).

Ten patients (0.3 percent) had serious complications during or immediately after colonoscopy: six patients had gastrointestinal bleeding that required hospitalization, and one each had a myocardial infarction, a cerebrovascular accident, Fornier's gangrene that required hospitalization, and thrombophlebitis. Three patients died within 30 days after colonoscopy; none of the deaths were directly related to the procedure. There were no perforations.

DISCUSSION

We evaluated the use of colonoscopy as a primary screening procedure in a large number of asymptomatic adults. The combined prevalence of invasive

TABLE 5. RISK OF ADVANCED PROXIMAL NEOPLASIA ACCORDING TO THE DISTAL FINDINGS.

DISTAL FINDING	TOTAL NO.	NO. (%) WITH ADVANCED PROXIMAL NEOPLASIA*	ODDS RATIO (95% CI)†
Distal colon defined as rectum and sigmoid and descending colon			
No polyps	1765	48 (2.7)	1.0
Hyperplastic lesion	464	13 (2.8)	1.1 (0.6–2.1)
Adenoma			
<10 mm	561	38 (6.8)	2.6 (1.7–4.1)
≥10 mm	151	14 (9.3)	3.4 (1.8–6.5)
High-grade dysplasia	35	4 (11.4)	4.5 (1.5–13.4)
Invasive cancer	24	6 (25.0)	9.8 (3.6–26.4)
Histologic features			
Tubular adenoma			
Any size	648	44 (6.8)	2.6 (1.7–4.0)
<10 mm	543	35 (6.4)	2.5 (1.6–3.9)
≥10 mm	105	9 (8.6)	3.2 (1.5–6.8)
Villous adenoma	64	8 (12.5)	4.7 (2.1–10.4)
No. of small tubular adenomas (<10 mm)			
1 or 2	499	31 (6.2)	2.6 (1.6–4.2)
3 or 4	37	4 (10.8)	4.4 (1.5–13.1)
≥5	7	0	—
Distal colon defined as rectum and sigmoid colon			
No polyps	1912	71 (3.7)	1.0
Hyperplastic lesion	489	25 (5.1)	1.5 (0.9–2.4)
Adenoma			
<10 mm	426	37 (8.7)	2.4 (1.6–3.7)
≥10 mm	128	17 (13.3)	3.6 (2.0–6.3)
High-grade dysplasia	30	4 (13.3)	3.8 (1.3–11.3)
Invasive cancer	18	6 (33.3)	11.4 (4.1–31.7)
Histologic features			
Tubular adenoma			
Any size	501	47 (9.4)	2.6 (1.8–3.9)
<10 mm	414	36 (8.7)	2.5 (1.6–3.7)
≥10 mm	87	11 (12.6)	3.4 (1.7–6.7)
Villous adenoma	53	7 (13.2)	3.5 (1.5–8.1)
No. of small tubular adenomas (<10 mm)			
1 or 2	394	34 (8.6)	2.4 (1.6–3.7)
3 or 4	16	2 (12.5)	3.7 (0.8–16.7)
≥5	4	0	—

*Patients with nonadenomatous lesions were excluded.

†CI denotes confidence interval.

cancer and adenoma with high-grade dysplasia was 2.6 percent. Most of the patients with cancer (73.3 percent) were identified before there was nodal involvement or distal spread and were therefore candidates for curative treatment. These data suggest that screening with colonoscopy in asymptomatic men can detect early and potentially curable advanced neoplasia. In the National Polyp Study,[12] patients who underwent colonoscopy, with the removal of all polyps, had a lower incidence of colorectal cancer during six years of follow-up than did the reference populations. Although our study was not designed to determine whether colonoscopic screening would reduce the rate of mortality from colorectal cancer, the results indicate that many cases of advanced neoplasia would be detected as part of a colonoscopic screening program.

Our findings can be used to determine the yield of a screening examination limited to the distal colon. There has been controversy about the importance of detecting small adenomas (<10 mm in diameter) in the distal colon.[13-19] In our study, all patients were asymptomatic and underwent full colonoscopy, irrespective of the findings in the distal colon. Patients with no polyps of any kind in the rectum or sigmoid or descending colon had a risk of advanced proximal neoplasia of 2.7 percent. Among patients with no polyps in the rectum or sigmoid colon, the prevalence of advanced proximal neoplasia was 3.7 percent. The risk of proximal advanced neoplasia increased significantly with age. Patients with distal hyperplastic polyps had a risk of advanced proximal neoplasia that was similar to the risk among patients with no polyps. However, patients with distal adenomas of any size had a higher risk of advanced proximal neoplasia than patients with no distal adenomas.

We determined the prevalence of advanced proxi-

mal neoplasia in asymptomatic patients and the likelihood that such patients would have any adenomas in the distal colon (Table 4). When the distal colon was defined as the rectum and the sigmoid and descending colon, 48.4 percent of the patients with advanced proximal neoplasia had adenomas in the distal colon. When the distal colon was defined as the rectum and sigmoid colon, only 37.9 percent of the patients with proximal advanced neoplasia had distal advanced neoplasia. Therefore, the majority of advanced proximal neoplasms would not have been detected if the distal colon had been examined either to the junction of the sigmoid colon and the descending colon or to the splenic flexure.

These data can be interpreted in two ways. Examination of the distal colon to the splenic flexure, followed by full colonoscopy if an adenoma of any size had been found, would have identified the 79.9 percent of patients with advanced neoplasia. However, if the distal colon had been examined only to the junction of the descending colon and the sigmoid colon, then the advanced neoplasia in 31.9 percent of the patients would not have been detected. Failure to detect advanced neoplasia may be more likely in older patients than in younger patients, since the prevalence of advanced proximal disease increases with age.

Our study population included a disproportionately large number of patients who had one or more first-degree relatives with colorectal cancer. These patients had an increased age-adjusted risk of advanced neoplasia, a finding that is consistent with the results of other studies.[20-22] These data support the recommendation of an expert panel that colonoscopy be offered to such patients.[7]

Our study has several important limitations. First, the results are applicable only to men. There is considerable evidence that men have higher age-adjusted rates of cancer than women.[23] In addition, a definition of the distal colon that includes the left colon to the splenic flexure may not reflect the actual depth of insertion of a sigmoidoscope. Therefore, we determined the yield of an examination that reached the junction of the sigmoid colon and the descending colon. Our data demonstrate that a more extensive examination of the colon leads to a higher rate of detection of advanced neoplasia. Finally, the effectiveness of colonoscopy depends on the expertise of the endoscopist.[24] In our study, all the endoscopists had substantial experience with colonoscopy, as reflected by the high rate of successful cecal intubation. The results of examinations performed by less experienced endoscopists may be different.

We believe that the use of colonoscopy to screen asymptomatic men for colorectal cancer is feasible and that such screening can identify patients with advanced neoplasia who may benefit from the detection and removal of the lesions. The majority of advanced lesions are distal to the splenic flexure. However, our data show that more than half the cases of advanced proximal neoplasia would not be detected with sigmoidoscopy to the splenic flexure. Patients with distal adenomas of any size have a higher risk of advanced proximal neoplasia than patients with no distal adenomas. In the group of patients in our study who had no distal adenomas, 2.7 percent had advanced proximal lesions, which would not have been detected with sigmoidoscopy alone. It remains to be determined whether a full colonic examination will lead to a greater reduction in the rate of mortality from colorectal cancer than other methods of screening.

Supported by a grant from the Veterans Affairs Cooperative Studies Program.

APPENDIX

The following persons participated in Veterans Affairs Study Group 380: *Data Monitoring Board* — B. Levin (chairman), C.R. Boland, M. Brown, R. Burt, R.B. D'Agostino, and D.K. Rex; *Executive Committee* — S. Prindiville (special consultant, Denver), A. Schatzkin (Bethesda, Md.), W. Willett (Boston), and J.F. Collins (Perry Point, Md.); *Planning Committee* — J. Selby and C. Quesenberry; *Veterans Affairs Cooperative Program Office* — J.R. Feussner, D. Deykin, and P. Huang.

Study personnel — Dallas: M. Prebis; Denver: S. Frederick and B. Ciminelli; Durham, N.C.: C. Rose, M.J. Timmins, and R. Smith; Hines, Ill.: S. O'Connell; Kansas City, Mo.: R. Corbett; Long Beach, Calif.: S. Van Schoick, C. Nordin, E. Dumitrescu, B. Bagnol, and M. Du; Minneapolis: S. Schwartz; Palo Alto, Calif.: D. Tizer; Phoenix, Ariz.: R. Sanowski and S. Medlin; Portland, Oreg.: M. Garrard; San Francisco: S. Woodford; Tucson, Ariz.: P. Martinez; White River Junction, Vt.: L. Miraldi; *study chairman's office* — M. Sutton; *Veterans Affairs Cooperative Studies Program Coordinating Center* — B. Calvert, J. Collins, C. Crigler, M. Lee, R. Ortiz, and E. Spence; *central laboratory* (Tucson, Ariz.): L. Ramsey.

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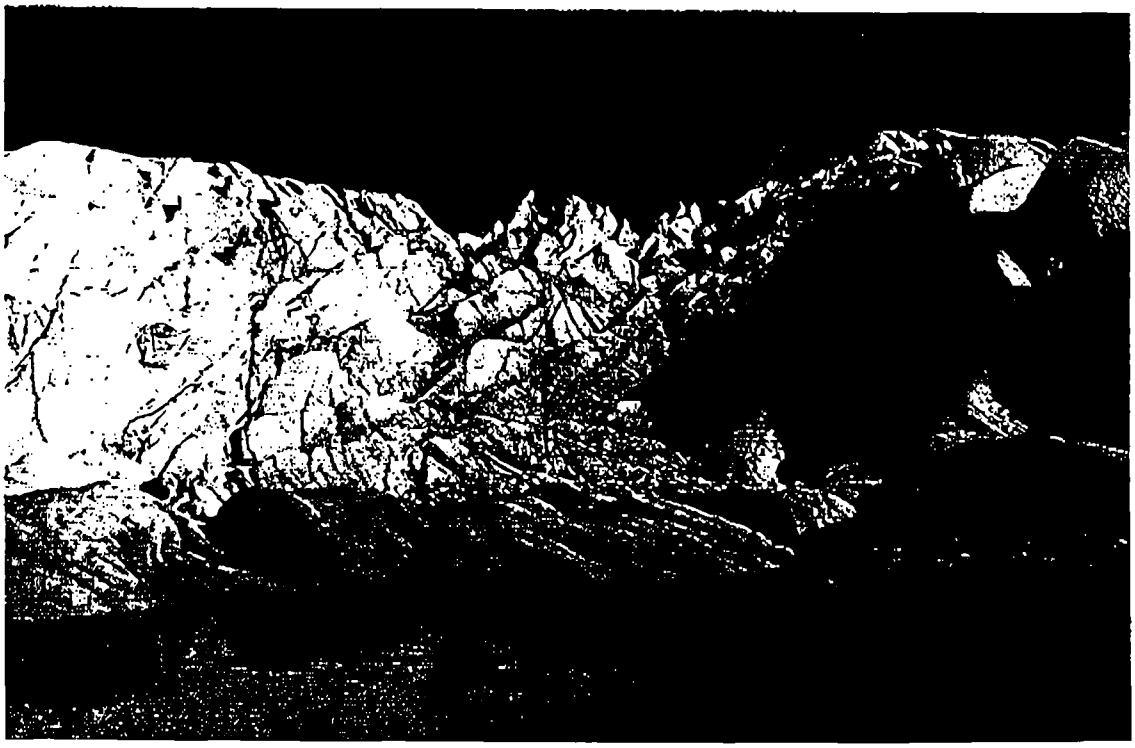

MALABIKA DE, M.D.

PRESIDENT CLINTON LAUNCHES NEW EFFORT TO FIGHT COLORECTAL CANCER
October 6, 2000

Today, in his weekly radio address, President Clinton will join with cancer advocates from across the country to launch a new effort to fight colorectal cancer, encourage all Americans over the age of 50 to receive their annual colorectal cancer screening, and celebrate Breast Cancer Awareness Month. Today, the President will announce that the National Cancer Institute will invest $30 million over the next five years to help doctors expand and improve screening procedures for colorectal cancer and address the chronic under-use of these life-saving tools. He will also launch new efforts to educate all Medicare beneficiaries about the importance of preventive care. Finally, the President will encourage the Congress to remove major barriers facing older Americans and people with disabilities seeking preventive care under Medicare, challenging them to pass legislation expanding Medicare to include more sophisticated colorectal cancer screening tests for people over 50 and the Administration's budget proposal to eliminate all cost-sharing requirements for colorectal screening and other preventive procedures under Medicare.

COLORECTAL CANCER KILLS THOUSANDS OF AMERICANS EACH YEAR. Although death rates from colorectal cancer are at their lowest point in decades and the risk of developing this disease continues to decline, research demonstrates that more needs to be done.

- **Colorectal cancer is the second leading cancer killer in the United States.** An estimated 130,000 new cases and 56,000 deaths from colorectal cancer are expected in 2000. Americans spend $5 billion a year on treatments for colorectal cancer, which is the second most expensive cancer to treat after prostate cancer.

- **Timely screening for colorectal cancer saves lives.** Early colorectal cancer is a curable disease. Because colorectal cancers grow slowly, early detection significantly increases survival. When detected early, the five year survival rate is 90 percent; however, less than 40 percent of colorectal cancers are discovered at that stage. After the cancer has spread, the five year survival rate drops to 65 percent.

- **Recent evidence indicates that aggressive screening of individuals at risk for colon cancer increases the likelihood of early detection by over 50 percent.** There is excellent evidence that regular screening for colorectal cancer saves lives. People over the age of 50 should have a simple stool blood test once a year. They should also have a sigmoidoscopy or a colonoscopy every 5 to 10 years. Recent research, although not conclusive, indicates that using colonoscopies to screen individuals over the age of 50 for colon cancer rather than flexible sigmoidoscopy may identify polyps that would otherwise go undetected over half of asymptomatic patients. However, Medicare does not currently reimburse physicians for colonoscopies unless the patient has a family history of colon cancer or is otherwise at risk.

- **Screening rates for colorectal cancer are dangerously low, and rates decrease as individuals age.** Studies indicate that less than 40 percent of adults over the age of 50 have ever had a sigmoidoscopy. In addition, a recent GAO report indicates that even though Medicare covers colorectal screenings, the use of these tests remains dangerously low. For example, fecal occult blood tests, the least invasive of the screening tests, are supposed to be provided once a year to Americans over the age of 50 – but less than 10 percent of Medicare beneficiaries received this test in 1999.

- **Barriers to proper screening include a lack of patient and provider awareness.** A 1997 study indicated that many primary care physicians do not appropriately screen patients for colorectal cancer because of concerns about the effectiveness of screening and misconceptions about patients' willingness to be screened. In addition, many patients are concerned that the screening exam might be unpleasant and are embarrassed to discuss the tests with their physicians.

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- **Announce new efforts to educate Medicare beneficiaries about the importance of preventive care.** Beginning next March, Medicare beneficiaries will receive reminders about the importance of colorectal cancer screenings and other preventive services, in addition to the information on mammography and influenza they already receive, on the Statement of Benefits sent to them every time they use a Medicare service. In addition, Medicare's toll-free hotline will automatically remind seniors about the importance of preventive care when they call for information on their benefits. 1800 MEDICARE gets over 200,000 calls each month.

- **Challenge the Congress to eliminate barriers to Medicare beneficiaries seeking preventive services.** Today, the President will endorse bipartisan legislation to provide Medicare reimbursement for colonoscopies provided once every 10 years to beneficiaries over 50. This legislation, estimated to cost $200 million over 10 years by CBO, ensures that Medicare coverage policies are in-line with the latest medical research. Although this proposal does not mandate a particular screening schedule, it ensures that physicians have the option to provide these enhanced screening services. The President will also challenge the Congress to take the next step and eliminate all Medicare cost-sharing for colorectal screening and other preventive procedures.

CHALLENGE THE CONGRESS TO PASS A STRONG, ENFORCEABLE PATIENTS' BILL OF RIGHTS AND TAKE A STAND AGAINST GENETIC DISCRIMINATION. Today, the President will urge the Congress not adjourn before passing a strong, enforceable Patients' Bill of Rights that assures that cancer patients – and all patients – have access to the specialty care they need. He will also challenge them to finish the job begun by the bipartisan Health Insurance Portability and Accountability Act and pass legislation ensuring that genetic information used to help predict, prevent, and treat disease will not be used to discriminate against Americans seeking employment or health insurance. Studies demonstrate that the fear of discrimination is so pervasive that almost one-third of individuals offered the opportunity to participate in a clinical trial to identify the gene linked with breast cancer declined, citing concerns about discrimination and loss of privacy.

STATE HIS INTENTION TO SIGN INTO A LAW NEW TREATMENT OPTIONS FOR UNINSURED WOMEN WITH BREAST AND CERVICAL CANCER. Today, the President will praise the Senate's recent unanimous passage of the Breast and Cervical Treatment Act of 1999, legislation providing States with an important new Medicaid coverage option for low-income, uninsured women with breast and cervical cancer. This action virtually assures that the Congress will present the President with legislation that he was pleased to include in this year's budget and that he will be proud to sign into law, and he will urge the Congress to pass the final bill without further delay.

BUILDS ON THE CLINTON-GORE ADMINISTRATION'S LONGSTANDING COMMITMENT TO FIGHTING BREAST AND CERVICAL CANCER. The Clinton-Gore Administration has responded to the significant threat posed by cancer with increased efforts in research, prevention and treatment. During the Clinton-Gore Administration, funding for breast and cervical cancer research, prevention and treatment increased from approximately $283 million in FY 1993 to $623 million in FY 2000. President Clinton enacted the Mammography Quality Standards Act to ensure the quality of mammograms. This year, the President announced that Medicare would begin to cover the routine care costs associated with participation in clinical trials, removing a major barrier to study participation. Fighting the spread of this disease has also been a high priority for both Vice President Gore and First Lady Hillary Clinton. Al Gore successfully fought for historic increases in funding for cancer research, prevention and treatment at the National Cancer Institutes during the Clinton-Gore Administration. Hillary Clinton launched the Medicare Mammography Campaign to urge older women to get mammograms and to promote the use of Medicare coverage for mammography and helped develop and implement the National Action Plan on Breast Cancer, a public-private partnership coordinated at the Department of Health and Human Services.

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CHALLENGE THE CONGRESS TO PASS A STRONG, ENFORCEABLE PATIENTS' BILL OF RIGHTS AND TAKE A STAND AGAINST GENETIC DISCRIMINATION. Today, the President will urge the Congress not adjourn before passing a strong, enforceable Patients' Bill of Rights that assures that cancer patients – and all patients – have access to the specialty care they need. He will also challenge them to finish the job begun by the bipartisan Health Insurance Portability and Accountability Act and pass legislation ensuring that genetic information used to help predict, prevent, and treat disease will not be used to discriminate against Americans seeking employment or health insurance. Studies demonstrate that the fear of discrimination is so pervasive that almost one-third of individuals offered the opportunity to participate in a clinical trial to identify the gene linked with breast cancer declined, citing concerns about discrimination and loss of privacy.

STATE HIS INTENTION TO SIGN INTO A LAW NEW TREATMENT OPTIONS FOR UNINSURED WOMEN WITH BREAST AND CERVICAL CANCER. Today, the President will praise the Senate's recent unanimous passage of the Breast and Cervical Treatment Act of 1999, legislation providing States with an important new Medicaid coverage option for low-income, uninsured women with breast and cervical cancer. This action virtually assures that the Congress will present the President with legislation that he was pleased to include in this year's budget and that he will be proud to sign into law, and he will urge the Congress to pass the final bill without further delay.

BUILDS ON THE CLINTON-GORE ADMINISTRATION'S LONGSTANDING COMMITMENT TO FIGHTING BREAST AND CERVICAL CANCER. The Clinton-Gore Administration has responded to the significant threat posed by cancer with increased efforts in research, prevention and treatment. During the Clinton-Gore Administration, funding for breast and cervical cancer research, prevention and treatment increased from approximately $283 million in FY 1993 to $623 million in FY 2000. President Clinton enacted the Mammography Quality Standards Act to ensure the quality of mammograms. This year, the President announced that Medicare would begin to cover the routine care costs associated with participation in clinical trials, removing a major barrier to study participation. Fighting the spread of this disease has also been a high priority for both Vice President Gore and First Lady Hillary Clinton. Al Gore successfully fought for historic increases in funding for cancer research, prevention and treatment at the National Cancer Institutes during the Clinton-Gore Administration. Hillary Clinton launched the Medicare Mammography Campaign to urge older women to get mammograms and to promote the use of Medicare coverage for mammography and helped develop and implement the National Action Plan on Breast Cancer, a public-private partnership coordinated at the Department of Health and Human Services.