COLON CANCER-
NOW A PRESIDENTIAL DISEASE

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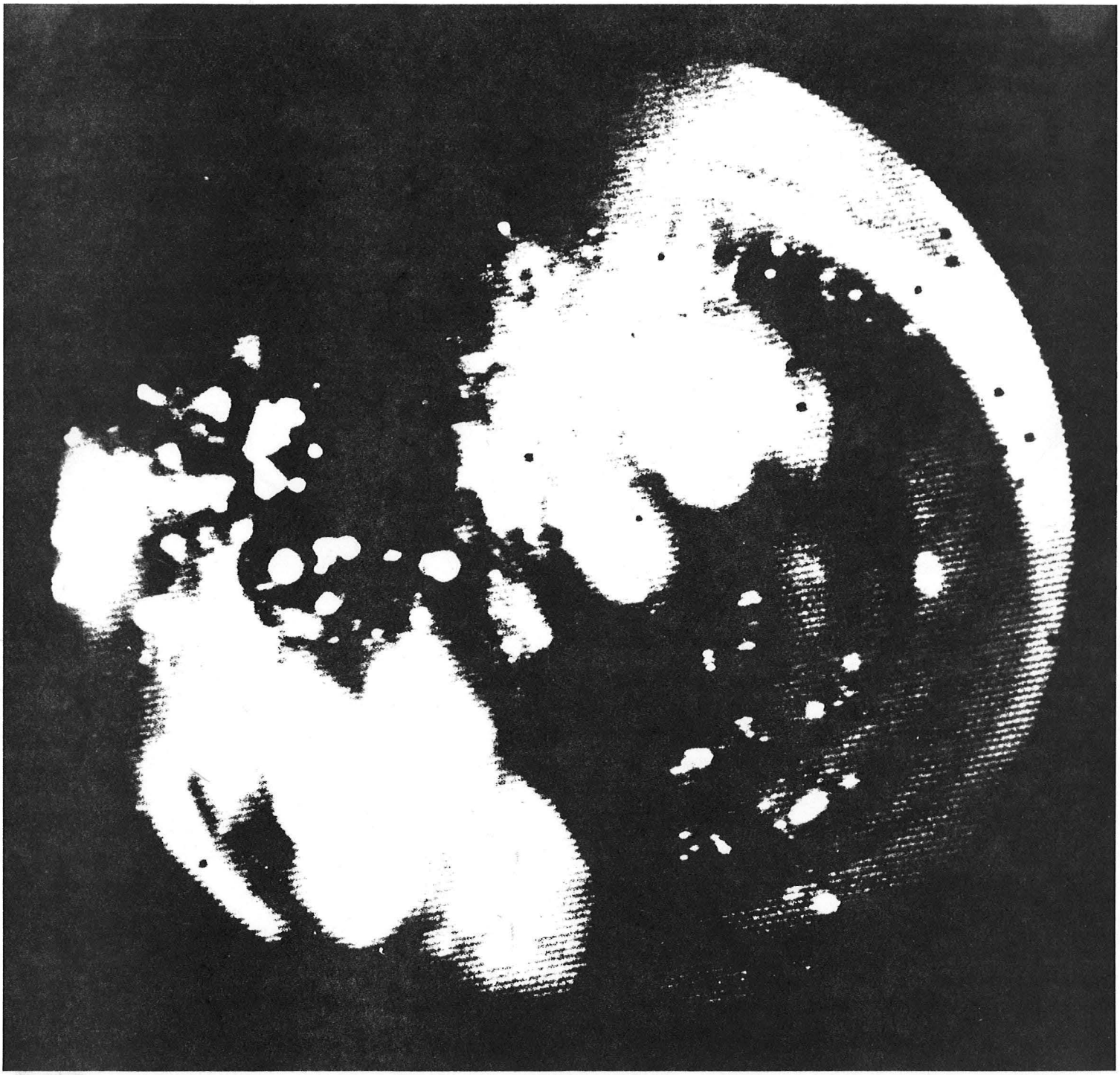

INTERNAL MEDICINE GRAND ROUNDS
SOUTHWESTERN MEDICAL SCHOOL
FEBRUARY 6, 1986

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This Grand Rounds presentation is dedicated to Mrs. Bertha L. Ahlschlager who for the last two years has coped with the disease described here.

Guenter J. Krejs, M.D.

Dallas, Texas Feb. 6, 1986

OUTLINE

INTRODUCTION

During the lifetime of today's Americans, one out of 25 will develop colon cancer. During 1986, it is expected that 140,000 new cases of colon cancer will be diagnosed in the United States. After lung cancer, colon cancer has become the second most frequent cancer (excluding common skin cancers) (Table 1) (1).

TABLE 1

ESTIMATED NEW CANCER CASES IN THE U.S. FOR 1986

ALL CANCERS	930,000		
RESPIRATORY		165,000	
LUNG			149,000
GASTROINTESTINAL		218,000	
COLON			140,000

Thus, the overall incidence of colon carcinoma is now approximately 55 per 100,000 population (lung cancer 60 per 100,000). The mortality rate of colorectal cancer is 24 per 100,000 (44%) . Applying these numbers to the city of Dallas (population 1 million), one can expect 550 new colon cancer cases in 1986 and in the Dallas-Fort Worth Metroplex (population 4 million) there will be 2200 new cases this year.

In addition to these impressive numbers, which illustrate the magnitude of the public health problems posed by colon cancer, the diagnosis and treatment of this cancer in the President of the United States, Ronald Reagan, has drawn enormous attention to this disease (2).

CASE REPORT

[redacted] is a [redacted] year old [redacted] lady who, apart from a previous history of jaundice and prolonged hepatitis, was in good health until [redacted] of 1983 when she tripped and fell backward in her home and sustained a lumbar compression fracture of L1 and L2. Admission laboratory at Presbyterian Hospital in Dallas revealed a low hemoglobin of 10 g/dl and Hct of 31%, and MCV was 61 μm^3. Because of the back injury, rectal examination was omitted on physical examination by the orthopedic surgeon. She was discharged after

three days, and her internist [redacted] initiated a workup for anemia. Serum Fe was 49 µg/dl and 2 fecal hemoccult tests were negative. Iron replacement therapy was commenced. Upper gastrointestinal x-ray studies in December of 1983 revealed a normal esophagus, stomach, duodenum and small bowel. In February 1984 a barium enema demonstrated a nodular filling defect on the lateral wall of the cecum measuring about 4x4 cm. No other lesions, particularly no polyps elsewhere in the colon, were seen. Colonoscopy was attempted for tissue diagnosis and to rule out synchronous lesions in the colon, but it was impossible to advance the colonoscope beyond the sigmoid colon. A partial colectomy was performed by Dr. C. T. Simonton on 3/2/84. A polypoid mass, 7 x 4.5 cm with 3 cm elevation was removed. Histological examination revealed poorly differentiated adenocarcinoma. Twenty-eight lymphnodes wer negative for tumor cells. The tumor was classified as a Duke's B colon carcinoma. The postoperative course was uneventful, and the patient has done extremely well during a two-year follow up. Barium enema examination one year after surgery was negative and colonoscopy two years after resection revealed a normal ileocolonic anastomosis and no polyps in the remainder of the colon. Her CBC has remained normal after surgery. Carcino-embryonic antigen (CEA) was normal preoperatively with 1.5 ng/ml (normal <3.0) and has remained at that low level during the two-year follow up.

WHO GETS COLON CANCER ?

In the United States the incidence of colon cancer is similar in men and women as well as in caucasians and blacks. The incidence of colon cancer varies widely throughout the world with up to forty-fold differences. For instance, the United States incidence of 55 per 100,000 population contrasts to the 1.5 per 100,000 incidence in Nigeria (3). High incidences are found in the highly developed countries of North America, northern and western Europe, and Australia and New Zealand. The lowest rates are seen in Asia, Africa, and most of the Latin American countries.

The incidence of colon cancer in the United States has been rising during the past few years (1980: 105 new cases, 1986: 140,000 new cases). Risk factors for colon cancer are listed in Table 2.

TABLE 2

RISK FACTORS FOR COLON CANCER

RISK FACTOR	INCREASED RISK
AGE	HIGH AGE
FAMILY HISTORY	OTHER FAMILY MEMBERS WITH COLON CANCER, FAMILIAL POLYPOSIS SYNDROMES
ETHNIC BACKGROUND	CZECH BACKGROUND IN RURAL NEBRASKA (4) (DIFFICULT TO SEPARATE GENETIC FROM ENVIRONMENTAL FACTORS: MIGRANT POPULATION TAKES ON CANCER RATE OF NEW COUNTRY)
DEGREE OF URBANIZATION	URBAN AND INDUSTRIALIZED AREAS
DIET	HIGH DIETARY INTAKE OF FATS (IN MEAT, MILK PRODUCTS, SALAD AND COOKING OIL AND MARGARINE)
HISTORY OF INFLAMMATORY BOWEL DISEASE	MORE THAN 10 YEARS OF ULCERATIVE COLITIS (SEE SEPARATE DISCUSSION BELOW)

The age distribution of colon cancer is shown in Figure 1. While colon cancer may occur at any age, the incidence rises after age 40 with 90% of cancers occurring above the age of 50.

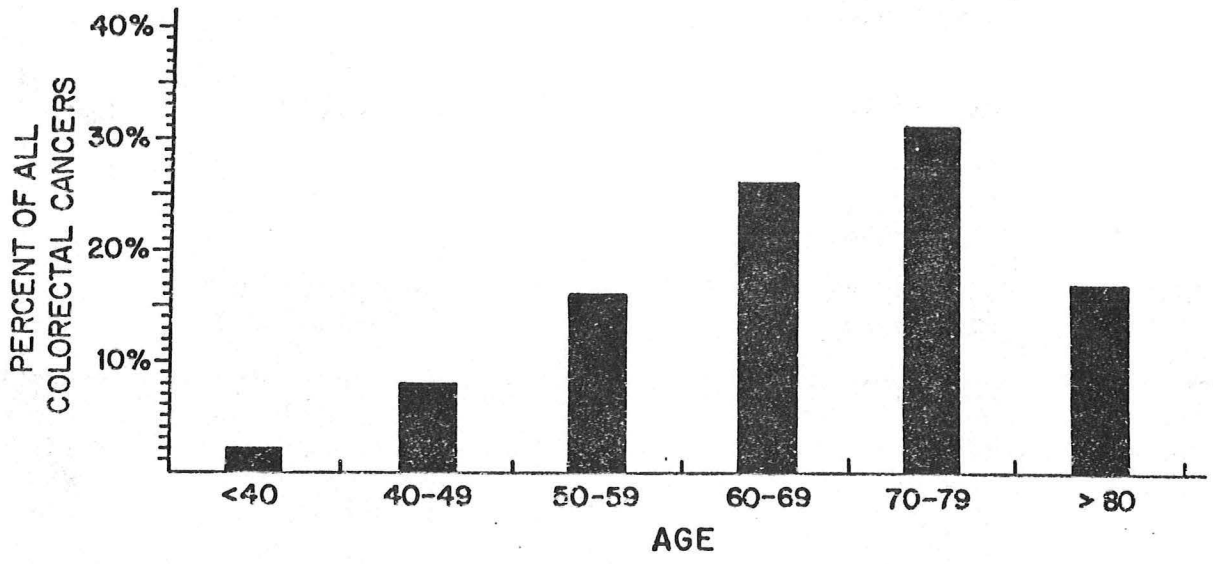


FIGURE 1: AGE DISTRIBUTION OF COLON CANCER

Table 3 indicates the changes in colon cancer incidence and death rate in the United States since 1950. In 1950 the yearly death rate amounted to 70% of the newly diagnosed cases of colon cancer, whereas in 1986 the death rate decreased to 44% of the newly diagnosed cases. Thus, despite the increased incidence there are now less deaths from the disease. This improved survival clearly is a consequence of earlier recognition and thus more effective treatment of colon cancer.

TABLE 3

CHANGES OF COLON CARCINOMA INCIDENCE
AND DEATH RATES BETWEEN 1950 AND 1986

Per 100,000 Population	1950	1986
New Cases	40	55
Deaths	28 (70%)	24 (44%)

DUKE'S STAGES

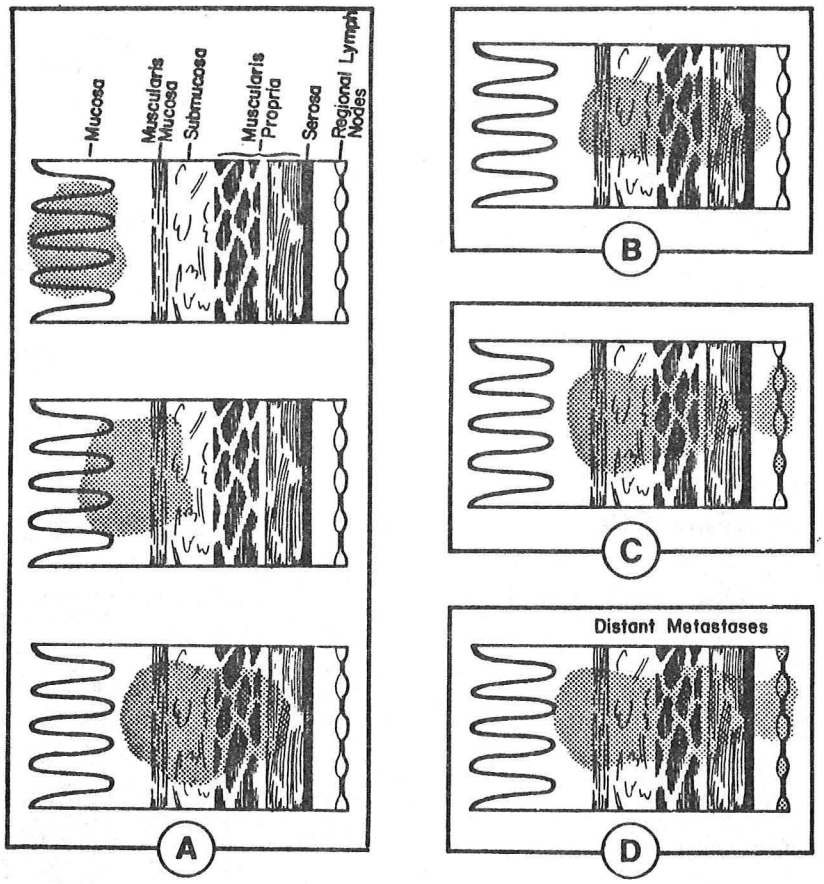


FIGURE 2: DUKE'S STAGING OF COLON CANCER

As expected, survival rates depend on the extent of cancer spread at the time of diagnosis. The commonly used staging according to Cuthbert Duke (a London pathologist in the 1930s) is illustrated in Figure 2.

Duke's A colon cancer involves varying levels within the bowel wall. Carcinoma in situ refers to a neoplasm in the mucosa that has not penetrated the muscularis mucosae. The latter is an important feature since - unlike the small bowel - the colonic mucosa does not contain lymph vessels above the muscularis mucosae. Duke's B extends through the wall of the large bowel but not to any lymph nodes, Duke's C involves regional lymph nodes; and Duke's D is defined by the presence of distant metastases, most commonly in the liver. The 5-year survival curves for each of these stages is shown in Figure 3.

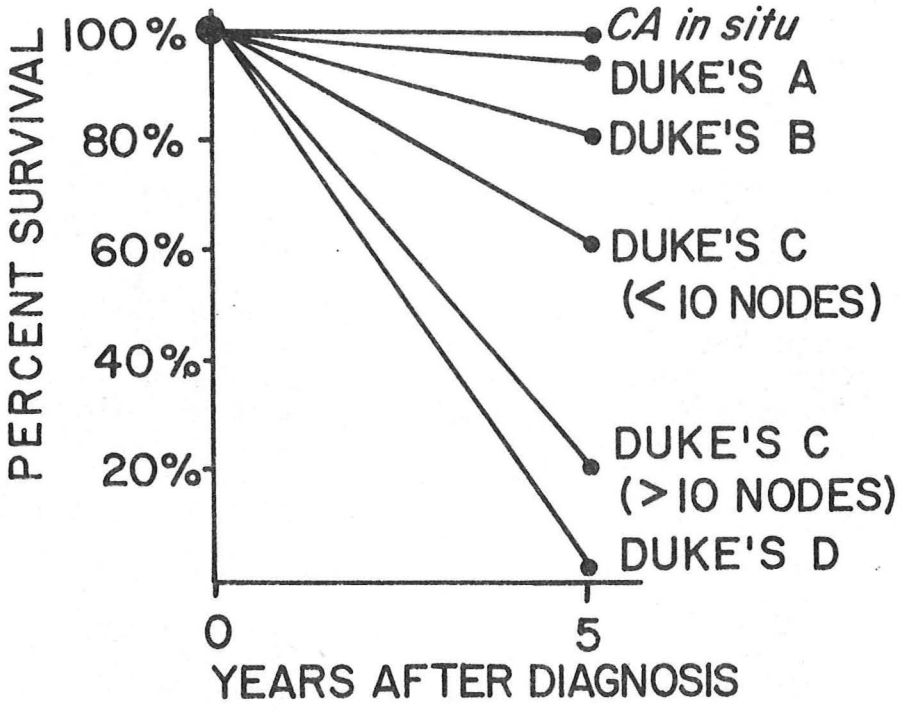
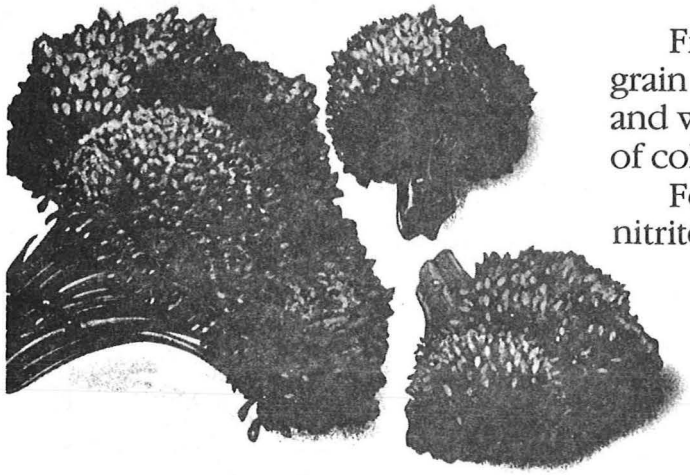


FIGURE 3: 5-YEAR SURVIVAL ACCORDING TO DUKE'S STAGE OF COLON CANCER

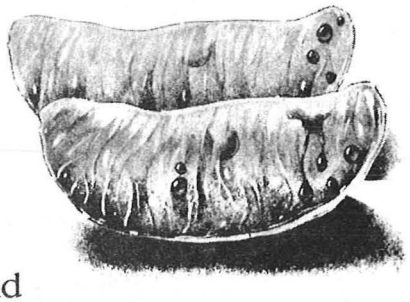
A colon cancer detected as carcinoma in situ (limited to mucosa) has a 99% 5-year survival. On the other hand, with Duke's D carcinoma (distant metastases) no one is alive after 5 years. Duke's B (as in patient [redacted] and President Reagan) has an 80% 5-year survival.

A defense against cancer can be cooked up in your kitchen.



Fruits, vegetables, and whole-grain cereals such as oatmeal, bran and wheat may help lower the risk of colorectal cancer.

Foods high in fats, salt- or nitrite-cured foods like ham, and



fish and types of sausages smoked by traditional methods should be eaten in moderation.

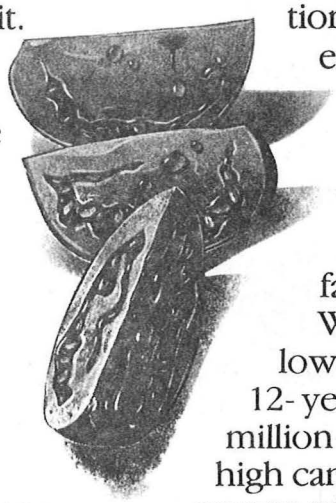
Be moderate in consumption of alcohol also.

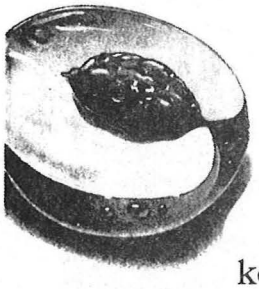
A good rule of thumb is cut down on fat and don't be fat.

Weight reduction may lower cancer risk. Our 12-year study of nearly a million Americans uncovered high cancer risks particularly among people 40% or more overweight.

There is evidence that diet and cancer are related. Some foods may promote cancer, while others may protect you from it.

Foods related to lowering the risk of cancer of the larynx and esophagus all have high amounts of carotene, a form of Vitamin A which is in cantaloupes, peaches, broccoli, spinach, all dark green leafy vegetables, sweet potatoes, carrots, pumpkin, winter squash and tomatoes, citrus fruits and brussels sprouts.





Foods that may help reduce the risk of gastrointestinal and respiratory tract cancer are cabbage, broccoli, brussels sprouts, kohlrabi, cauliflower.

Now, more than ever, we know you can cook up your own defense against cancer. So eat healthy and be healthy.

No one faces cancer alone.

AMERICAN CANCER SOCIETY®

NATIONAL GEOGRAPHIC January 1986

FIGURE 4

In 1978, Dr. Walter L. Peterson in his Grand Rounds "Current Concepts of Colon Cancer" (5) stated that if the cost, mortality, and suffering from colon cancer are to be reduced, three avenues are available:

1. DEFINE THE CAUSATIVE AND CONTRIBUTORY FACTORS
   -REMOVE THEM -

2. DEFINE ANY PREMALIGNANT LESIONS
   -REMOVE THEM -

3. DEVELOP EFFECTIVE SCREENING METHODS TO FIND EARLY OR PREMALIGNANT LESIONS
   -REMOVE THEM -

Dr. Peterson reviewed genetic and environmental factors, particularly epidermiological observations that suggest that a fiber-deficient diet and a high meat intake may be causally related to colon cancer. Dietary carcinogens were also reviewed and therefore will not be repeated here.

Recently Lipkin and Newmark from the Memorial Sloan-Kettering Cancer Center reported that a high calcium intake reduced cell proliferation in mucosal crypts of subjects at high risk for familial colon cancer (6). Whether this observation might have any practical implications for colon cancer in general is completely unknown at the present (7).

While it is reasonable for the American Cancer Society to recommend a diet rich in vegetable fiber and low in fat (Figure 4), present evidence is not sufficient to suggest a drastic change of the dietary pattern of this whole nation and expect a reduction in colon cancer incidence. Rather, it appears that progress in the treatment of colon cancer can only come from earlier detection at a stage when survival rates are high.

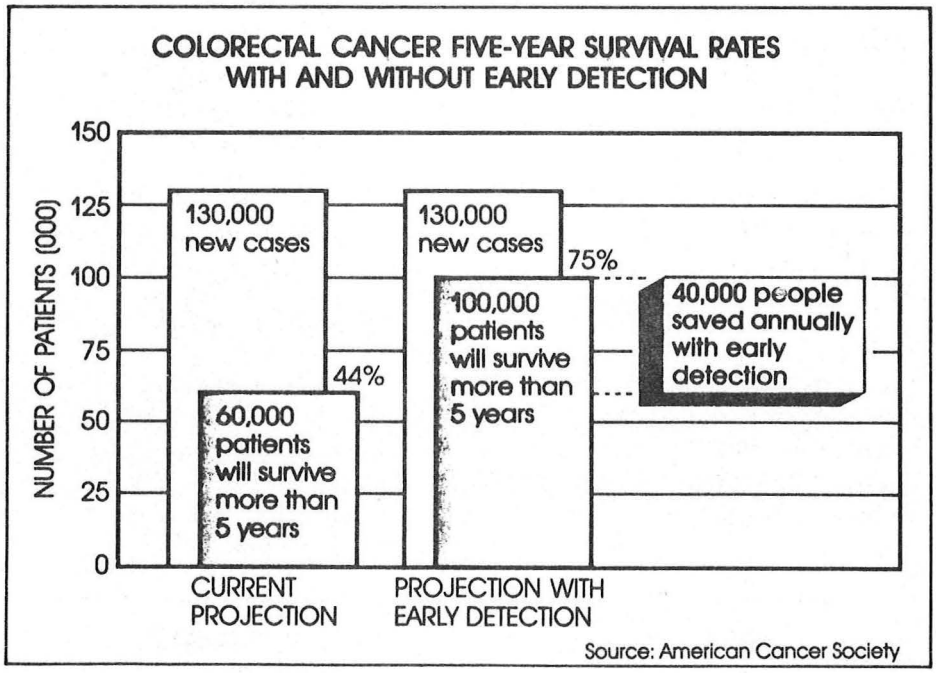


FIGURE 5

Figure 5 shows the impact of early detection on colon cancer as estimated today by the American Cancer Society. It is projected that the 5-year survival for all colon cancers could increase from 44% to 75% with early detection. This would save the life of 40,000 people annualy in the United States.

ADENOMA-CARCINOMA SEQUENCE

In the normal colonic mucosa, cell proliferation occurs in the crypts as demonstrated by tritiated thymidine incorporation which reflects DNA synthesis (8,9). Mature cells at the surface do not incorporate tritiated thymidine

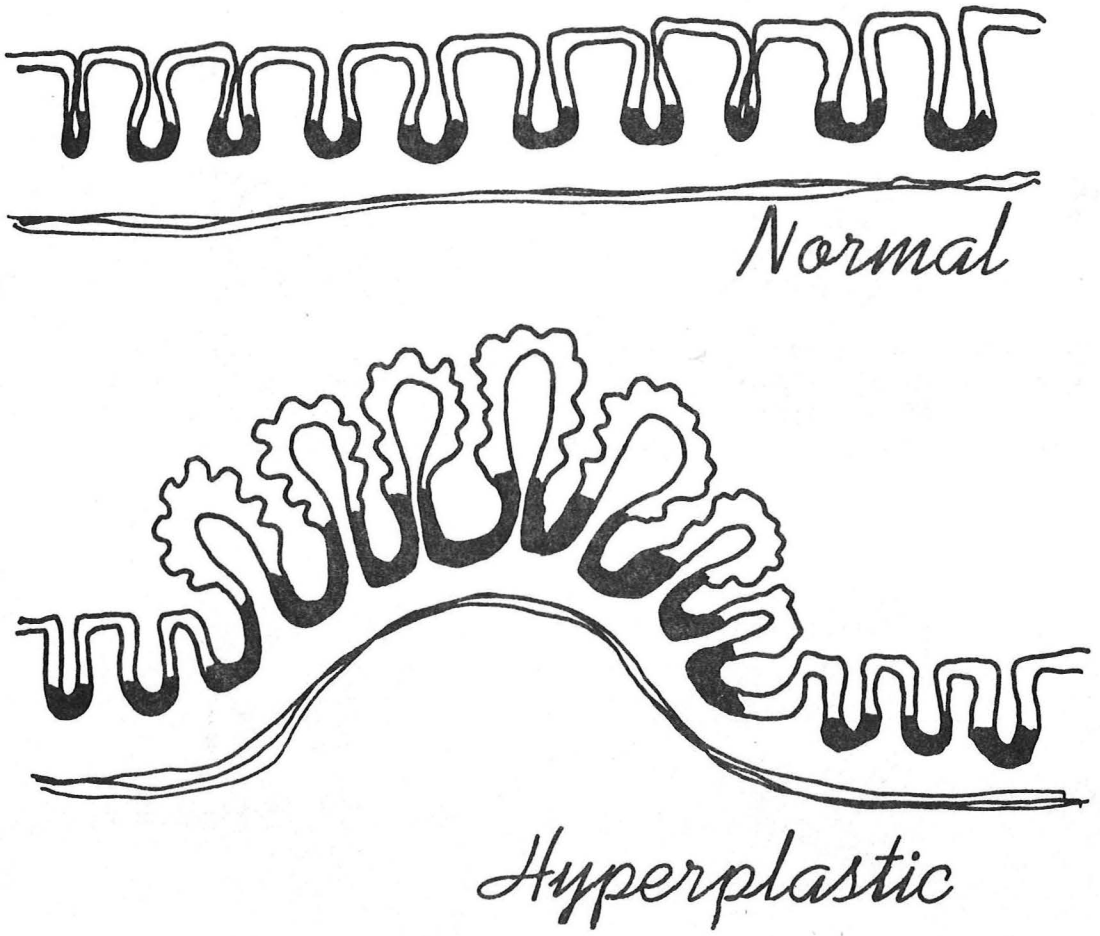


FIGURE 6: PROLIFERATIVE ZONE (HEAVY DARK LINE) IN NORMAL COLONIC MUCOSA AND IN HYPERPLASTIC POLYPS

indicating that no further cell division occurs once cells move from the crypts to the surface. This proliferative zone which is restricted to the deepest one-third of colonic crypts is schematically shown by the heavy dark line in Figure 6. When localized increased mucosal growth occurs polyps form in the colon. Thus, the term polyp denotes a growth protruding from the bowel mucosa. While the ratio of proliferative zone to zone of mature cells (1:2) is maintained in hyperplastic polyps (Figure 6), adenomatous polyps only consist of proliferating epithelial cells (Figure 7).

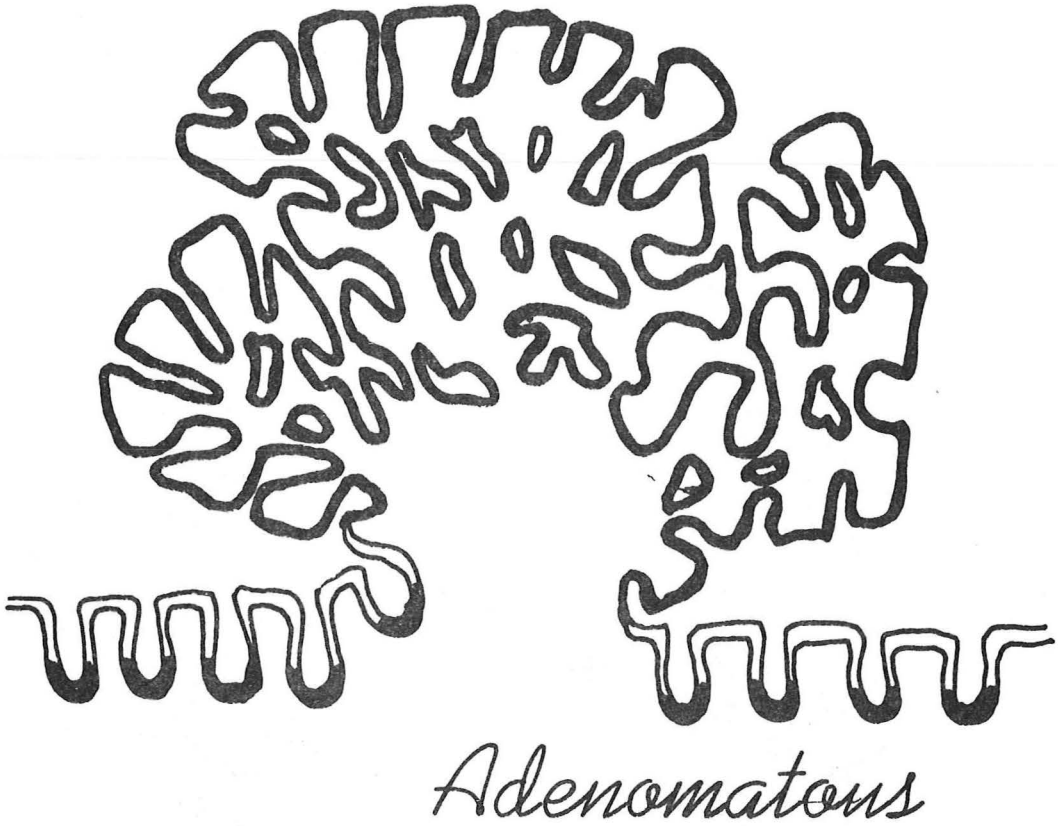


FIGURE 7: ADENOMATOUS POLYP. THE EPITHELIUM CONSISTS EXCLUSIVELY OF PROLIFERATING CELLS

With respect to colon cancer risk, polyps can be classified as "harmless" or "dangerous" dependent on the proliferative features of the epithelium (Table 4).

TABLE 4

CLASSIFICATION OF POLYPS

"Harmless Polyps"

1. Juvenile ("retention polyps," hamartomas)
2. Hyperplastic (metaplastic)
3. Inflammatory (pseudopolyps)
4. Extrinsic polyps (lipomas, fibromas, leiomyomas)

"Dangerous Polyps" (malignant potential)

1. Adenomatous (tubular, tubulovillous, and villous adenoma)

Although in rare cases colon cancer may develop from a microadenoma in the colonic mucosa, it is now well established that most cancers develop on the basis of an adenomatous polyp. Evidence for the adenoma-carcinoma sequence is summarized in Table 5.

TABLE 5

EVIDENCE FOR ADENOMA-CARCINOMA SEQUENCE

Peak age for adenomatous polyps: 10 years before peak age for colon cancer

Cellular atypia increases with polyp size

Polypoid changes precede malignant changes (experimental cancer and serial clinical observations)

Potential for malignant transformation depends on polyp morphology (tubular 5%, tubulovillous 23%, villous 41%)

Number of colon adenomas:			
	One:	8%	Risk of cancer
	Two:	10%	elsewhere
	Three:	17%	in the colon
	Twenty-five:	100%	(10)

Familial polyposis syndromes (almost 100% cancer risk in some)

Removal of all rectal polyps detected reduced the subsequent incidence of carcinoma to 15% of expected rate in one community (11)

Because of the information presented in Table 5, it is my opinion that any colon polyp that is detected should be removed, provided that no contraindication for polypectomy exists. The method for colonoscopic polypectomy is shown in Figure 7. Polyps up to 6 cm in size can now be removed by colonoscopy, and surgical resection is not required.

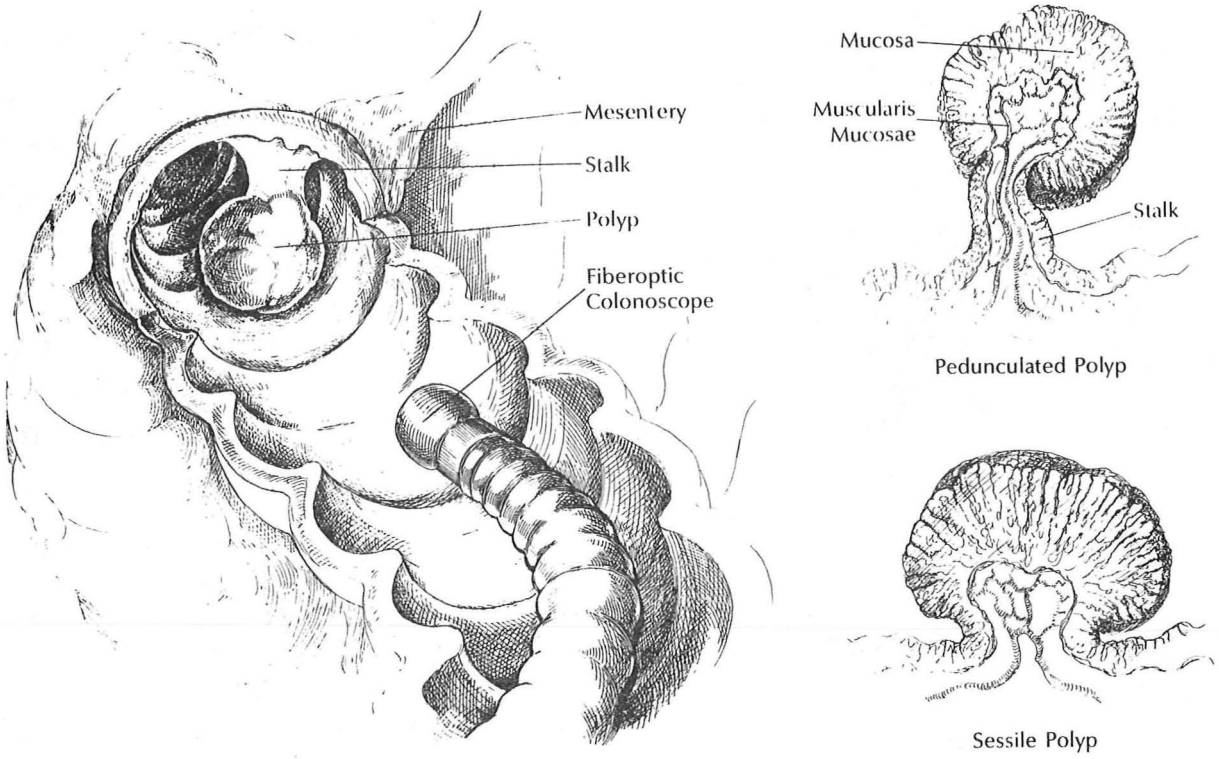
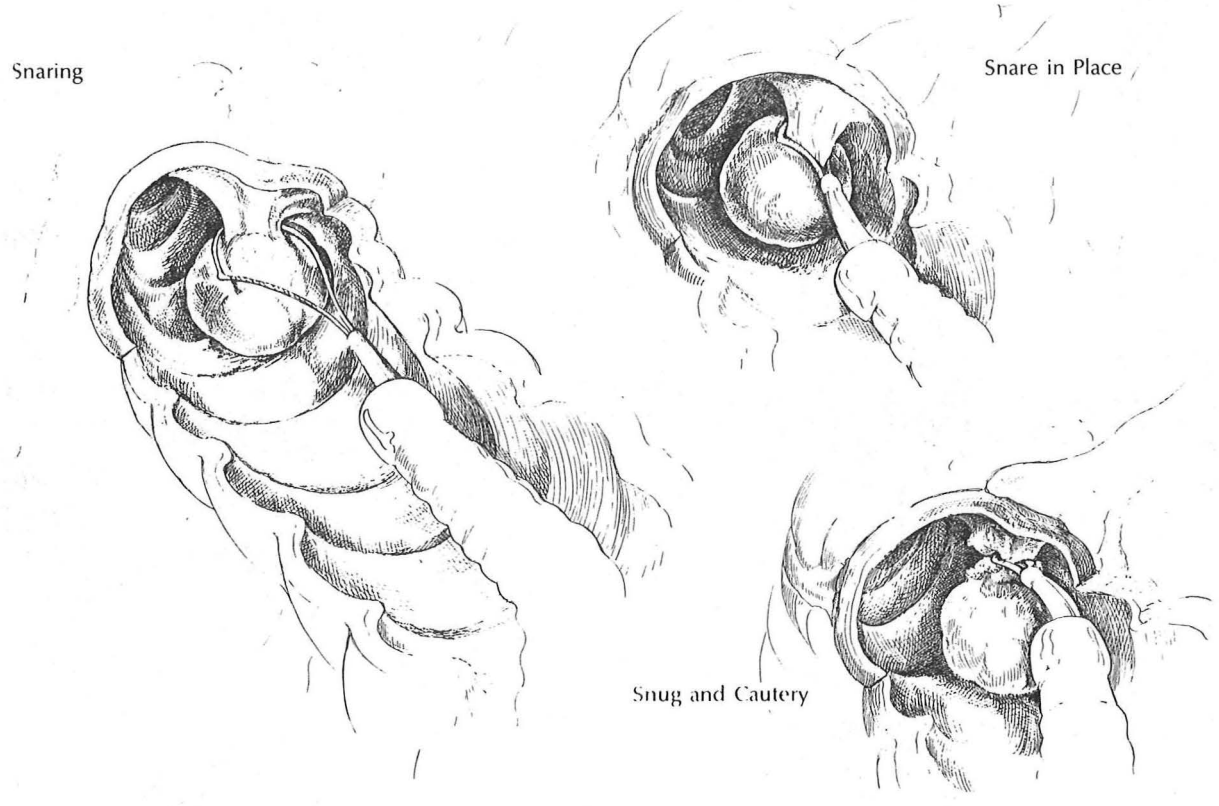


FIGURE 7: Polyp removal by means of a colonoscope. As the polyp is approached initially (above left), it is crucial to gauge accurately the nature of the growth. The thin-stalked pedunculated polyp (upper right) can usually be removed with only one application of the snare-cautery, while the sessile polyp (upper right) is almost invariably removed piecemeal. In excising the pedunculated polyp, the stalk is ensnared (lower left) by passing the wire completely over the head and positioned and tightened about the stalk, the polyp is tented toward the center of the bowel lumen, yet not so much that the head touches the opposite wall. As the cautery is applied (lower right), the polyp is oscillated gently as a precaution against perforation of the bowel (from 12).



If a histological evaluation reveals hyperplastic or inflammatory polyp, patients generally need no specific follow up, although the natural history of these patients awaits further study (President Reagan's first polyp removed on May 18, 1984, was an "inflammatory pseudopolyp," see below, Table 13).

Patients with adenomatous polyps develop new adenomas in 30% of cases if the initial polyp was a single ademona and 60% with multiple index adenomas (13).

For patients with a single adenoma, it is recommended that colonoscopy be repeated at one year, and if negative, every three years thereafter. Such a follow-up program has been implemented at Parkland Memorial Hospital in Dallas for the last three years. One year after "a clean colon" following removal of one to three adenomatous polyps we send the patient a letter explaining the tendency for new adenomatous polyps to form and the associated risk of cancer. If they don't respond by making an appointment for follow-up colonoscopy, we do not push further at this time for two reasons: 1) colonoscopy itself carries a certain risk, and 2) a National Polyp Study is now in progress to determine whether 1 or 3 year follow-up intervals are preferable.

The complications of colonoscopy with or without polypectomy are summarized in Tables 6 and 7. Table 6 gives the results of a large French survey concerning 55,124 polypectomies. The perforation rate was 1 in 500 and bleeding occurred in 1 out of 250. Such retrospective questionnaire-type surveys have to be considered with great caution since they are prone to underestimation of the true complication rate (14).

TABLE 6

COLONOSCOPY COMPLICATIONS - FRANCE, 1984

499 Centers - 711 Endoscopists

	293,215 Colonoscopists	55,124 Polypectomies
Perforation	0.4 / 1,000	2 / 1,000
Bleeding		4 / 1,000
Explosion		1 / 10,000
Death	1 / 10,000	1 / 10,000

At Parkland Memorial Hospital in Dallas, we have prospectively recorded all complications of gastrointestinal procedures and results for colonoscopy and polypectomy are given in Table 7.

TABLE 7

COMPLICATIONS OF COLONOSCOPY AND POLYPECTOMY
AT PARKLAND MEMORIAL HOSPITAL IN DALLAS

Colonoscopy
(5000 Procedures)
1 Perforation (→ surgery, recovery)

Colonoscopy with Polypectomy
(521 Procedures)
1 Perforation (→ surgery, recovery)
2 Massive Bleeding (→ surgery, recovery)
3 Major Bleeding (requiring 2 to 6 transfusions each)
3 Minor Bleeding (no transfusions, observation only)
NO MORTALITY

Current recommendations concerning follow up after removal of adenomatous colon polyps may undergo changes pending the outcome of ongoing clinical trials including the National Polyp Study in the United States and studies in Sweden and Germany. In the United States the National Polyp Study (15,16) is examining whether one-year or three-year follow ups is better and most cost effective. Preliminary results are available in the group randomized to one-year follow up (Table 8). Seventy out of 117 patients had polyps on one-year follow up. Of 127 polyps removed, 101 (79%) were less than 5 mm in size, 59 (46%) were adenomatous and one had carcinoma in situ. While the number and type of polyps found at one year follow up are impressive, the randomized trial will show whether it would have been early enough to find these lesions at the three-year follow up. It is possible that at the present we are buying a small benefit for a big price. My personal prediction is, however, that in 3 to 5 years from now, the National Polyp Study will show a significant benefit of the one-year follow up.

TABLE 8

NATIONAL POLYP STUDY

546 Patients With Adenomatous Colon Polyps Randomized:

1 or 3 Year Follow up

117 1-Year Follow up Completed

70 / 117 (60%) Polyps
36 / 117 (31%) Adenomatous

127 Polyps Removed in 70 Patients:

79% <0.5 cm
46% Adenomatous
1% Ca in situ

DIMINUTIVE POLYPS

The National Polyp Study also allows a closer look at the very small polyps (17). Conventional wisdom has been that the majority of diminutive polyps (<5 mm in size) are hyperplastic and do not necessarily need to be removed when they are encountered on colonoscopy (18). This view is clearly wrong. Hyperplastic polyps don't convert to adenomatous polyps and adenomatous polyps naturally start very small early in their development. Table 9 shows that 51%

TABLE 9

NATIONAL POLYP STUDY

1124 DIMINUTIVE POLYPS (<0.5 cm)

% ADENOMAS	51
% TUBULAR	95
% MIXED OR VILLOUS	5
% MILD DYSPLASIA	97
% MODERATE DYSPLASIA	2
% SEVERE OR CA IN SITU	1
% INFILTRATING CA	0.2

out of 1124 diminutive polyps were indeed adenomatous, and severe dysplasia, carcinoma in situ, and infiltrating carcinoma were found. Thus, diminutive polyps should be considered part of the adenoma-dysplasia-adenocarcinoma sequence. A similar incidence of adenomas (49%) in diminutive polyps was found by Tedesco et al (19).

MALIGNANT POLYPS

The management of patients with carcinoma occurring in an adenomatous polyp has been controversial for a long time, but some clear concepts are now evolving based on a respectable number of studies and long enough follow up (21-25). The histological assessment is of utmost importance in the decision making whether segmental colonic resection should follow or whether colonoscopic polypectomy alone is sufficient. Levels of invasion need to be specified as outlined in Figure 8.

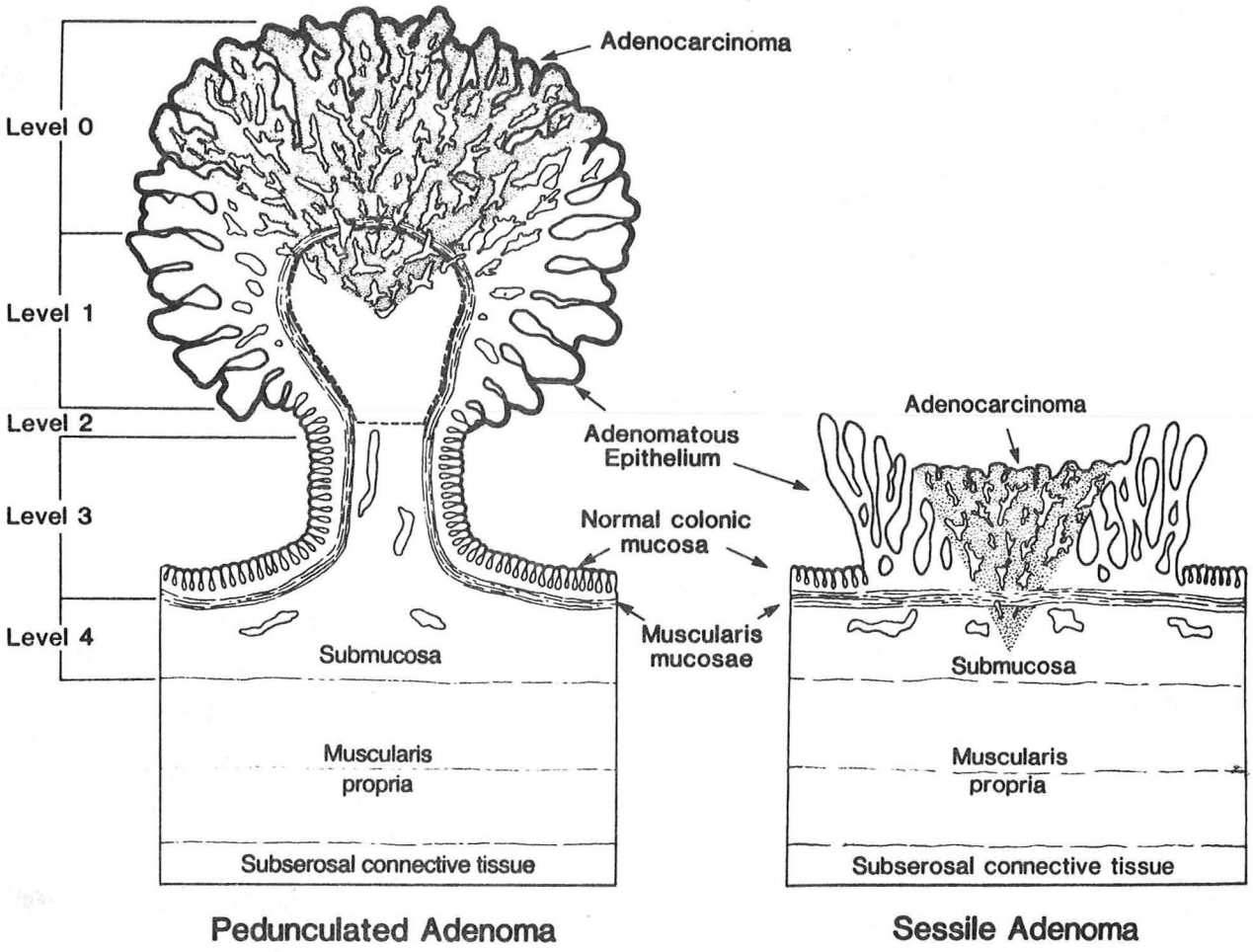


FIGURE 8: Levels of invasion in a pedunculated adenoma (left) and a sessile adenoma (right). The stippled areas represent zones of carcinoma. Note that any invasion below the muscularis mucosae in a sessile lesion represents level 4 invasion, i.e., invasion into the submucosa of the bowel wall. In contrast, invasive carcinoma in a pedunculated adenoma (left) must traverse a considerable distance before it reaches the submucosa of the underlying bowel wall. The dotted line in the head of the pedunculated adenoma represents the zone of level 1 invasion (from 21).

The importance of polyp size and histological type of adenoma with regard to the risk of carcinoma being present is illustrated in Tables 10 and 11.

TABLE 10

CORRELATION OF ADENOMA SIZE WITH THE RISK OF ITS CONTAINING INVASIVE MALIGNANCY (from 20)

ADENOMA SIZE	WITH CARCINOMA
<1 cm	1%
1-2 cm	10%
>2 cm	46%

TABLE 11

CORRELATION OF HISTOLOGIC CLASS WITH ADENOMA SIZE AND RISK OF ITS CONTAINING INVASIVE CARCINOMA (from 20)

HISTOLOGIC CLASS	WITH CARCINOMA (%)		
	<1 cm	1-2 cm	>2 cm
TUBULAR	1	10	35
TUBULOVILLOUS	4	7	46
VILLOUS	10	10	53

In the study by Haggitt et al (21) nodes were always negative with level 0, 1, and 2 invasion (Figure 8), and all patients in these 3 groups (n = 91) are alive and well with a mean follow up of 7 years.

The following recommendations concerning adenomatous polyps with malignancy can be made today (26):

1. Surgery cannot be justified in any adenoma containing carcinoma in situ, provided the lesion has been adequately excised.

2. The presence of well-differentiated to moderately differentiated invasive carcinoma in a pedunculated polyp should be treated conservatively with appropriate clinical follow up.

3. The risk of lymph node metastases exceeds the operative mortality (6-4.4%) when:

   a. Poorly differentiated invasive carcinoma is present.

   b. Endothelial-lined channels (lymphatic or blood vessels) are involved.

   c. Invasive carcinoma extends to the resected margin.

   d. Invasive carcinoma is present at the level of the submucosa of the wall of the adjacent large bowel.

DIAGNOSIS

The diagnostic approach to symptomatic patients includes digital rectal examination (which will allow recognition of about 10% of cancers), rigid sigmoidoscopy (30% of colorectal cancers can be detected), and flexible sigmoidoscopy (70% of colorectal cancers can be diagnosed). Barium enema and colonoscopy allow evaluation of the entire colon. Barium enema examination (even with air contrast technique) has a higher miss rate than colonoscopy for polyps and small carcinomas. Barium enema may miss 33% of the cancers and 66% of the polyps found during colonoscopy (27). The general availability and lower costs of barium enema still make it the first line test in the workup for suspected colon cancer in the United States. However, negative as well as positive findings often need confirmation by colonoscopy and many gastroenterologists now recommend colonoscopy as the primary test. Colonoscopy allows tissue diagnosis by forcep biopsies and in the patient with colon cancer synchronous neoplastic lesions such as adenomatous polyps or a second carcinoma elsewhere in the colon can be identified with high accuracy. About 2 to 5 percent of colon cancer patients have synchronous carcinomatous lesions. The colonoscopic appearance of colon cancer is shown on the cover and in Figure 9.

SCREENING

The high prevalence of colon cancer in the United States, the longer patient survival with earlier disease stage, and the potential to abort cancer by detection of premalignant polyps have raised great hopes in screening programs. The mainstay of these program is the detection of fecal occult blood. The hemoccult II test is commonly used. A positive test is caused by the penolic oxidation of the guaiac to a blue compound facilitated by the peroxidase-like enzymatic activity of hemoglobin (recommendations for use, see Table 12).

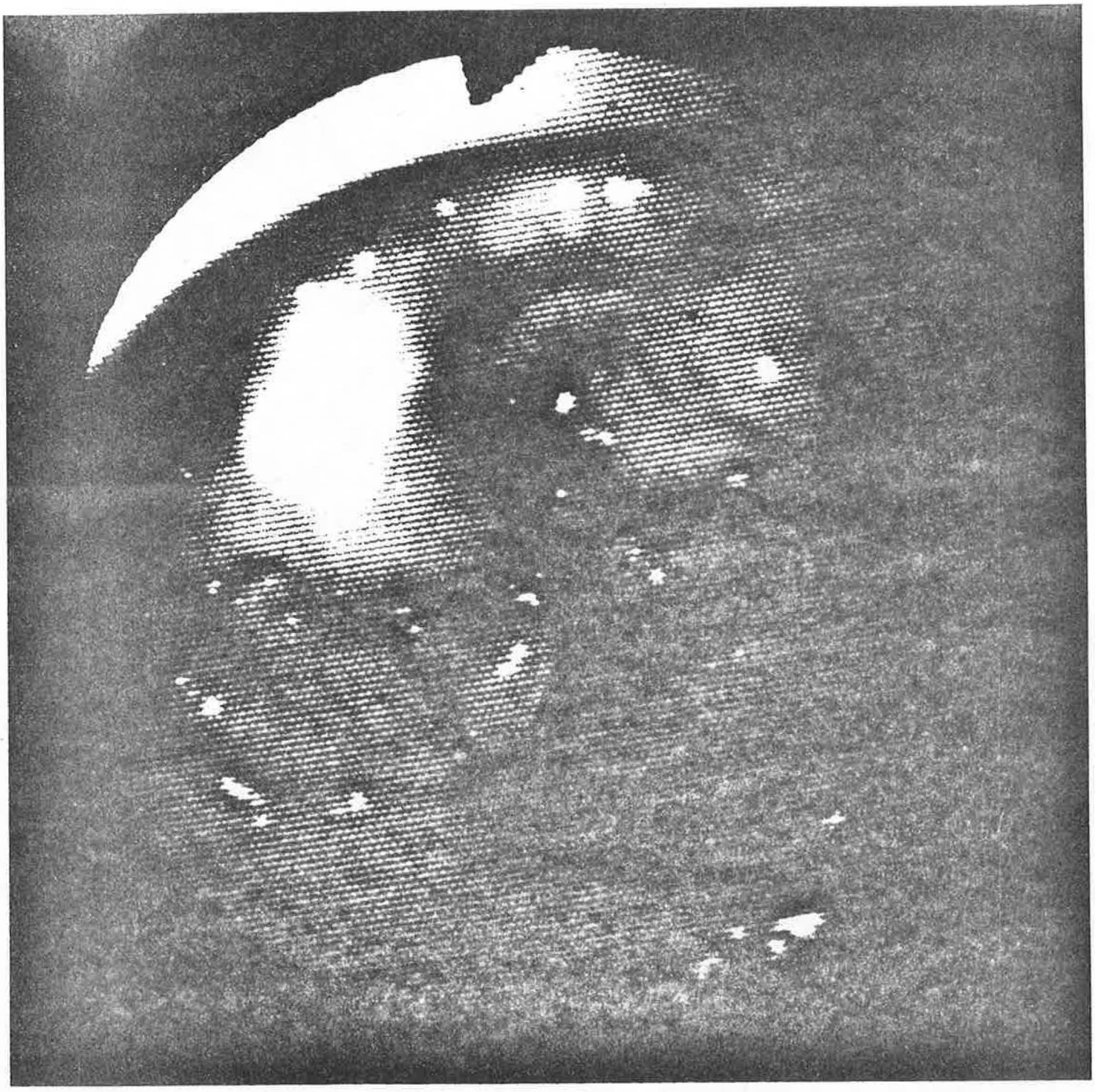


FIGURE 9 : COLONOSCOPIC VIEW OF AN ADENOCARCINOMA. NORMAL COLON MUCOSA IS SEEN IN THE LOWER HALF OF THE IMAGE. IN THE UPPER HALF THE LUMEN IS NARROWED BY A NODULAR MASS.

TABLE 12

RECOMMENDED USE OF HEMOCCULT II® (SMITH KLINE DIAGNOSTICS).

THE PATIENT SHOULD AVOID RARE RED MEAT AND HIGH PEROXIDASE FOODS FOR THREE DAYS BEFORE AND DURING TESTING.

VITAMIN C, IRON TABLETS, AND NONSTEROIDAL ANTI-INFLAMMATORY DRUGS SHOULD BE AVOIDED.

TWO SAMPLES OF EACH OF THREE CONSECUTIVE STOOLS SHOULD BE TESTED, FOLLOWING THE COLLECTION PROCEDURE AS RECOMMENDED BY THE MANUFACTURER.

THE DELAY BETWEEN PREPARATION AND LABORATORY TESTING SHOULD NOT EXCEED SIX DAYS.

SLIDES SHOULD NOT BE REHYDRATED.

A SINGLE POSITIVE SMEAR SHOULD BE CONSIDERED AS A POSITIVE TEST AND LEAD TO APPROPRIATE INVESTIGATION, EVEN IN THE ABSENCE OF DIETARY RESTRICTION. A POSITIVE RESULT NEED NOT BE REPEATED BEFORE DIAGNOSTIC WORKUP.

Two major controlled studies are currently in progress, and comprehensive results will be available in 3-4 years from the Minnesota program (27,28) and the Sloan-Kettering program (29,30).

Such extensive screening programs have not been universally accepted, and the following criticisms have been voiced (31):

1. Positive hemoccult reactions are only found in 50-66% of patients with proven malignancy, left sided cancers are particularly likely to be missed.

2. Homoccult is positive in only 25-41% of patients with endoscopically proven adenomatous polyps (31,32).

3. In screening surveys 33-50% of cancers will be missed and only about 5% of positive tests will turn out to be due to colon cancer.

4. Compliance is highly variable.

5. Follow up diagnostic studies are highly variable.

Despite these problems, for the time being, the American Cancer Association maintains the recommendation of yearly hemoccult testing in people of 40 years and older. This may, however, change when the Minnesota and

Sloan-Kettering trial results become available. At the present, evaluations of more sensitive and specific tests for detecting occult blood are in progress (33,34).

In Dallas, Baylor University Medical Center has performed three major screening campaigns for colon cancer using hemoccult tests (Dr. Loyd Kitchens, Projector Director). Preliminary results are listed in Table 13 (data kindly provided by Ms. L. Polter, Project Manager, Colorectal Cancer Screening Program).

TABLE 13

PRELIMINARY RESULTS OF COLON CANCER SCREENING PROGRAMS CONDUCTED BY BAYLOR UNIVERSITY MEDICAL CENTER IN DALLAS

	1982	1984	1985
TOTAL NUMBER OF CARDS DISTRIBUTED	74,210	94,227	36,317
CARDS PROCESSED	16,555	16,200	19,389
PATIENTS WITH POSITIVE CARDS	457	564	365
% OF CARDS PROCESSED	2.8	3.5	1.9
CANCERS FOUND	14	15	18
% OF POSITIVE CARDS	3.1	2.7	4.9
POLYPS FOUND	37	38	33
% OF CARDS PROCESSED	8.1	6.7	9.0
NEGATIVE EVALUATION	101	95	Follow up not yet complete
INCOMPLETE	59	255	

The latest (1985) numbers show a 2% incidence of positive cards. Of the positive cards, approximately 5% of patients have cancer, and in 9% polyps are found. These positive findings have to be weighed against the high costs for negative evaluations. Long-term follow up will allow better evaluation of the benefit of this type of screening.

SIGMOIDOSCOPY

Sigmoidoscopy in healthy subjects above the age of 40 is recommended every 3 years for screening for colon cancer. Rigid sigmoidoscopy will detect 2 cancers and about 60 polyps per 1,000 exams in asymptomatic patients (35,36). This yield can be markedly increased by using the 65 cm flexible sigmoidoscope: 20 cancers and 90-150 polyps can be detected per 1,000 patients examined (37,38).

In this context of screening, it might be of interest to look at the medical management of President Reagan's cancer since some criticism had been voiced by "doctors not connected to the case" (Table 13).

TABLE 13

DIAGNOSIS AND MANAGEMENT OF RONALD REAGAN'S COLON CANCER
(Source: Los Angeles Times, Friday, July 19, 1985, Page 14)

THE EVENTS	MY COMMENTS
May 18, 1984	
Reagan undergoes his first complete physical examination in 2½ years. A small "inflammatory pseudopolyp" is partly removed by sigmoidoscopy. Several hemoccult tests were negative. Reagan's personal physician (Dr. Daniel Ruge) on July 14, 1984, says that doctors have decided not to conduct a further examination of the colon.	Appropriate screening for person above 40 years of age. Inflammatory polyps are considered harmless with regard to malignant potential and no special follow up was needed in the presence of negative hemoccult tests.
March 8, 1985	
Sigmoidoscopy reveals a new polyp and removal is suggested. Fecal hemoccult tests positive. Hostage crisis (June 1985) delays planned removal of polyp by colonoscopy.	Colonoscopy and polypectomy indicated at that time. Procedure suggested by Dr. Edward Cattau, the Bethesda hospital gastroenterologist.
July 12, 1985	
Colonoscopy reveals a small polyp in the descending colon (adenoma sneared) and a large villous adenoma in the cecum which when resected the next day turned out to contain Duke's B carcinoma.	Delay of colonoscopy for 4 months undesirable but understandable due to urgent business affairs.
January 17, 1986	
Follow-up colonoscopy. Three adenomatous polyps are removed.	Appropriate 6 months follow up with polypectomy. Tendency of rapid polyp formation suggests repeat colonoscopy in another 6 months.

DUKE'S D

There has been a remarkable resurgence of interest recently in the treatment of liver metastases. However, as new modalities for treatment have been introduced, controlled clinical trials have in the main not been performed. Moreover, it is most unlikely that they will ever be performed with no-treatment arms as a control. The reason for this is the natural and understandable reluctance of clinicians to seek informed consent from patients with an inevitably fatal disease where one arm is no-treatment and the other a therapy which may be beneficial even if associated with side-effects (39).

The survival of patients with liver metastases is given in Table 14 (39,40).

TABLE 14

MEDIAN SURVIVAL IN PATIENTS WITH LIVER METASTASES FROM COLON CANCER

EXTENT OF LIVER INVOLVEMENT	SURVIVAL (MONTHS)
FEW METASTASES	18
SEVERAL METASTASES	9
MULTIPLE METASTASES	5

However, it is noteworthy that in a series of 101 patients with liver metastases, 14 had solitary metastases and 2 of these were still alive at 5 years.

From reviewing all treatment options for the patient with liver metastases (including surgery, systemic chemotherapy, radiotherapy, hepatic arterial ligation and devascularization, hepatic arterial embolization and hepatic arterial infusion techniques) the following conclusions can be reached (39-43):

1. Truly solitary liver metastases in the absence of tumor elsewhere should be considered for resection.

2. For patients with multiple liver metastases, the outlook is bleak, and treatment should be directed primarily at palliation. In the presence of severe pain percutaneous hepatic arterial embolization has a role but probably does not affect survival. There are theoretical advantages to hepatic arterial ligation and portal vein cytotoxic perfusion, but this approach requires laparotomy, and

survival may not be improved. There is insufficient evidence at present to recommend continuous hepatic artery infusion, and the side-effects (as well as expense) probably do not justify its routine use outside a clinical trial. This view may be modified when the results of on-going trials are available.

3. Hepatic artery ligation, hepatic dearterialization, liver irradiation and systemic chemotherapy have not been shown to produce worthwhile benefits either in terms of palliation or survival.

A number of other therapeutic modalities are being assessed experimentally and clinically in selected patients with liver metastases. These include isolated regional liver perfusion, the administration of drug-containing microspheres which are trapped in the liver, intraperitoneal chemotherapy, hyperthermia, and liver transplantation. Further information is needed before these approaches can be evaluated.

FOLLOW-UP AFTER CURATIVE RESECTION

Overall recurrence rates after curative resection for colorectal cancer average 30% (44). The value of intensive follow-up protocols has to be viewed with great skepticism. For instance, a protocol as intensive as the one suggested by Langevin and Wong may be an overkill (Table 14).

TABLE 14

FOLLOW-UP PROTOCOL FOR PATIENTS WITH COLORECTAL CARCINOMA AS PROPOSED BY LANGEVIN AND WONG (44)

Procedure	Frequency
History-taking, physical examination and Hemoccult test	Every 3 mo for 2 yr, then every 6 mo for 2 yr, then yearly
Colonoscopy	At 3 mo if not done preop. Yearly for 4 yr then every 3 yr
Sigmoidoscopy	For rectal carcinoma as for history-taking
Barium enema examination	As for colonoscopy if former not available
Liver function testing	As for history-taking
Chest roentgenography	Every 3 mo for 2 yr, then every 6 mo for 10 yr
Determination of carcinoembryonic antigen (CEA) level	Every 2 mo for 2 yr, every 4 mo for 2 yr, then every 6 mo to 10 yr
Second-look operation	Based on CEA level, with or without confirmatory testing

It appears that recurrent colon cancer can be detected at an early stage by such a program and that repeat surgery with a second attempt for curative resection may be possible. However, to date no improvement of survival has been documented by such an aggressive approach. Until more data are available the rationale for intensive follow up appears acceptable.

CEA

Carcinoembryonic antigen (CEA) is one of a class of oncofetal antigens that are normally present during fetal life, occur at low concentrations in adults, and circulate in high concentrations in patients with certain malignancies, particularly epithelial tumors. Since the first description of CEA in 1965 (45), it was recognized that the concentration of the antigen in body fluids, particularly blood, might serve as a useful guide in the care of patients with cancer. Twenty years after introducing the antigen in the management of colon cancer, the usefulness can be summarized as listed in Table 15 (46).

TABLE 15

USEFULNESS OF CEA IN THE MANAGEMENT OF COLON CANCER (from 46)

POTENTIAL USE	USEFULNESS	RATIONALE
Screening	Not useful	Sensitivity and specificity are not high enough and are lowest in early stages of disease.
Diagnosis	Limited value	Serum levels alone cannot establish the diagnosis. They may be useful, in conjunction with findings of other noninvasive tests, in deciding how actively to pursue a diagnostic workup colorectal cancer.
Prognosis	Limited value	Serum levels predict recurrence of colorectal cancer independently of stage, but this information cannot be used to improve prognosis.
Monitoring	Limited value	Serum levels can detect recurrence of colorectal cancer after surgery earlier than other methods, but this information does not increase the opportunity for effective therapeutic interventions in most patients.

Thus, CEA-directed second look operations appear to be the main indication for determining the antigen level during follow up. Additional observations are necessary to establish the value of CEA monitoring.

FAMILIAL POLYPOSIS SYNDROMES

The importance of the above discussed adenoma-carcinoma sequence is illustrated by a group of genetic diseases leading to polyp formation and cancer in early adulthood. The three syndromes, familial polyposis coli, Gardner's and Turcot's syndromes are characterized by multiple adenomatous polyps in the colon.

Familial polyposis coli is the most common of the polyposis syndromes (one in 8300 births). Transmission is autosomal dominant. The polyps are usually not present at birth but appear after the age of 10 years and then rapidly increase in size and number in the second and third decade. Colon cancer is invariably present by age 40 but may occur as early as the teenage years. Treatment consists of total colectomy when rapid polyp growth is present prior to progression to carcinoma (47,48).

Gardner's syndrome. Polyposis of the large intestine associated with soft tissue tumors and osseous abnormalities characterize Gardner's syndrome (49). The incidence is 11 in 14025 births (47) and transmission is autosomal dominant. The high incidence of colon cancer requires the same aggressive diagnostic and therapeutic approach as in familial polyposis coli.

Turcot's syndrome. The exceedingly rare association between malignant central nervous system tumors and polyposis coli is known as Turcot's syndrome (50,51). Most patients succumb to their central nervous system tumors.

HIGH RISK GROUPS

Table 16 gives other groups that have an increased risk for colon carcinoma compared to the control population.

TABLE 16

RISK GROUPS FOR COLON CANCER

HIGH RISK

- FAMILIAL POLYPOSIS SYNDROMES (INHERITED ADENOMATOSIS, GARDNER'S SYNDROME, TURCOT'S SYNDROME)
- PEUTZ-JEGHERS SYNDROME
- JUVENILE POLYPOSIS IN PAST
- FAMILIAL COLON CANCER
- MULTIPLE COLORECTAL CANCERS
- SINGLE AND MULTIPLE SPORADIC COLON ADENOMAS
- A PRIOR HISTORY OF COLORECTAL CANCER
- ULCERATIVE COLITIS
- CROHN'S COLITIS
- IMMUNODEFICIENCY SYNDROMES

STANDARD RISK

- AGE > 40 YEARS

U.C.

There is no doubt that patients with ulcerative colitis carry a higher risk of developing colon cancer than the normal population, although the magnitude of this higher risk is disputed (52-54). Duration of illness and extent of disease are the two major factors that have been related to cancer risk. Management options for patients with long-standing colitis include: a) ignoring the risk, b) prophylactic proctocolectomy, or c) surveillance to recognize a precancerous state or early cancer. In recent years, emphasis has been placed on the last of these options because the survival rate of patients with colitis-associated cancer discovered in the ordinary way is low (12% at 5 years) (55) and epithelial dysplasia has been suggested as a useful marker for patients at risk to develop malignancy (54).

Waye recently reviewed 479 cases of patients reported in the world literature that have had colonoscopic surveillance. Of these, 55 patients (12%) have been found to have dysplasia. Nine cancers (2% of all patients, 16% of patients with dysplasia) were found because of the previous endoscopic finding of dysplasia (59). Whether these nine patients were cured of their cancers and whether the 46 patients who underwent colectomy but did not have cancer benefited from this intervention is unknown.

The utility of surveillance is unknown at present. The direct costs for a total colonoscopy with biopsy are in the neighborhood of $1,000 and for protocolectomy about $12,000. Thus, in the above example, over 1.1 million dollars were spent to find nine cancers ($125,000 per cancer). In addition, colonoscopy carries a risk of perforation of 1/1000, and its mortality rate is 1/10,000 (14). Disagreement between pathologists in assessing and classifying dysplasia may be considerable, making use of surveillance even more questionable.

In a recent debate presented at the Postgraduate Course of the American Gastroenterological Association in San Antonio (September, 1985), Dr. John Fordtran debated Dr. F. Warren Nugent regarding the usefulness of surveillance in ulcerative colitis. I agree with Dr. Fordtran's summary that:

1. The risk of colon cancer in ulcerative colitis has been exaggerated by results from specialized referral centers.

2. At the moment no absolutely convincing evidence of benefit of surveillance exists.

3. The bias in all uncontrolled studies on this subject is enormous.

Unfortunately, no controlled studies are in progress or are planned at this time to settle this issue.

LASER

Dr. R. Lambert from Lyon (60) recently presented a study involving 93 elderly patients in whom surgery for adenocarcinoma of the rectum was contraindicated. Rapid relief of symptoms was achieved by Nd:YAG LASER treatment in all patients with noncircular tumors (65% of group). In some patients biopsies were negative for tumor at 6 months follow up.

At Parkland Memorial Hospital we have successfully treated one patient with rectal cancer for 2 years by Nd:YAG LASER. Although the tumor was not eradicated, lumenal growth and bleeding was prevented by repeated treatment every 3-4 months. Two large rectal villous adenomas have also been treated at Parkland. One patient is asymptomatic and LASER therapy is given every 4 months. In the other patient, a rectal perforation occurred and surgical repair was required.

Table 17 lists common misconceptions about colon cancer held by the public.

TABLE 17

PUBLIC MISCONCEPTIONS ABOUT COLON CANCER

1. UNAWARE OF HIGH INCIDENCE
2. UNAWARE OF RISK FACTORS
3. UNAWARE OF SCREENING TESTS
4. UNAWARE OF DIAGNOSTIC TESTS
5. FEAR OF COLOSTOMY
6. UNIFORMLY FATAL DISEASE

SUMMARY

In 1986, colon cancer ranks as the second most frequent cancer in the United States; 140,000 new cases will be diagnosed during this year. While certain risk factors such as high fat and meat diet can be identified, removal of such risk factors does not appear feasible in the near future.

Adenomatous colon polyps have been identified as premalignant lesions, and removal of polyps is expected to decrease the incidence of colon cancer. Earlier detection of cancers is expected to increase the 5-year survival rate from 44 to 75% over the next few years.

Screening for colon cancer by fecal occult blood tests may allow early recognition of polyps and the diagnosis of carcinoma can be made at an early stage when survival rates are high. However, the cost/benefit ratio of mass screening needs further evaluation.

The results of chemotherapy for metastatic disease have been disappointing and chemotherapy can only be recommended in the setting of controlled clinical trails. The greatest hope for recurrent cancer lies in attempted second "curative resection" or partial hepatectomy in the face of solitary metastases.

REFERENCES

1. Cancer Statistics 1986. Ca-A Cancer Journal for Clinicians, published by the American Cancer Society, 36:9-25, 1986.

2. Reagan's Toughest Fight. TIME Magazine, July 19, 1985, p 16-19.

3. Waterhouse J, Muri C, Correa P, et al (eds): Cancer Incidence in Five Continents, Vol. 3, IARC Scientific Publication No. 15. Lyon, France: International Agency for Research on Cancer, 1976.

4. Pickle LW, Greene MH, Ziegler RG, et al. Colorectal cancer in rural Nebraska. Cancer Res 44:363-369, 1984.

5. Peterson WL. Current Concepts of Colon Cancer. Internal Medicine Grand Rounds, University of Texas Southwestern Medical School Library, Dallas, Texas 7 August 1978, p 1-59.

6. Lipkin M, Newmark H. Effect of added dietary calcium on colonic epithelial-cell proliferation in subjects at high risk for familial colonic cancer. N Engl J Med 313:1381-1384, 1985.

7. A Daily Quart. Milk may cut risk of colon cancer. TIME Magazine, December 9, 1985, p 73.

8. Lipkin M. Proliferation and differentiation of normal and neoplastic cells in the colon of man. Cancer 28:38-40, 1971.

9. Lipkin M, Blattner WE, Fraumeni JF Jr, Lynch HT, Deschner E, Winnawer S. Triated thymidine ($\emptyset_p$, $\emptyset_h$) labeling distribution in the identification of hereditary predisposition to colon cancer. Cancer Res 43:1899-1904, 1983.

10. Shinya H, Wolf WI. Morphology, anatomic distribution and cancer potential of colonic polyps. Ann Surg 190:679-683, 1979.

11. Hardison WGM. Polyps of the colon: When and how should they be removed? Medical Times 106:44-51, 1978.

12. Shinya A, Wolff WI. Colonoscopic polypectomy: Technique and safety. Hospital Practice 10:71-78, 1975.

13. Dworkin BM, Winawer SJ. Neoplastic colonic polyps: A review. Current Concepts in Gastroenterology 10:3-9, 1985.

14. Krainik F, Gavillon C, Christoforov B, Pouletty J, Pequignot H. Les accidents de la coloscopie et de la polypectomie endoscopique. Commentaires a propos d'une enquete francaise rassemblant 293.215 coloscopies et 55.124 polypectomies. Livro de Resumos XII Congresso Internacional de

Gastroenterologia and V Congresso Internacional de Endoscopia Digestiva, Lisboa, Portugal, 1984, p1075.

15. Winawer SJ, Stewart E, Gottlieb L, Andrews M. National polyp study: Organization and statement of purpose. Gastroenterology 80:1316, 1981.

16. Winawer SJ, Gottlieb LS, Stewart ET, Zauber A, Diaz B. National polyp study progress report. Gastrointestinal Endoscopy 30:147, 1984

17. Gottlieb LS, Winawer SJ, Sternberg S, Magrath C, Diaz B, Zauber A, O'Brien M. National polyp study (NPS): The diminutive colonic polyp. Gastrointestinal Endoscopy 30:143, 1984.

18. Fenoglio-Preiser CM, Hutter RVP. Colorectal polyps: Pathologic diagnosis and clinical significance. Ca-A Cancer Journal for Clinicians 35:322-344, 1985.

19. Tedesco FJ, Hendrix JC, Pickens CA, Brady PG, Mills LR. Diminutive polyps: histopathology, spatial distribution, and clinical significance. Gastrointestinal Endoscopy 28:1, 1982.

20. Boland CR, Kim YS. Colonic polyps and the gastrointestinal polyposis syndromes. In: Gastrointestinal Disease, 3rd edition, Sleisinger MH, Fordtran JS, eds. Saunders: Philadelphia, London, Toronto, 1983, p 1196-1219.

21. Haggitt RC, Glotzbach RE, Soffer EE, Wruble LD. Prognostic factors in colorectal carcinomas arising in adenomas: Implications for lesions removed by endoscopic polypectomy. Gastroenterology 89:328-336, 1985.

22. Listrom MB, Fenoglio-Preiser CM. The malignant polyp. An analysis of the procedures for handling polyps. Endoscopy Review, September/October, 1985, p 21-37.

23. Fucini C, Wolff, BG, Spencer RJ. An appraisal of endoscopic removal of malignant colonic polyps. Mayo Clin Proc 61:123-126, 1986.

24. Macrae FA, Whiteway J, Jones E, Morson BC, Williams CB. Malignant polyps: Five year follow up confirms colonoscopic polypectomy as adequate treatment for selected patients. Gastrointestinal Endoscopy 29:1983.

25. Blundell CR, Earnest DL. Cancer in a colonic polyp, or malignant colonic adenomas - is polypectomy sufficient? Gastroenterology 81:625-630, 1981.

26. Riddell RH. Hands off "cancerous" large bowel polyps. Gastroenterology 89:432-441, 1985.

27. Gilbertsen VA, McHugh RB, Schuman L, et al. The earlier detection of colorectal cancers. A preliminary report of the results of the occult blood study. Cancer 45:2899-2901, 1980.

28. Gilbertsen VA, Church TR, Crewe FJ. The design of a study to assess occult-blood screening for colon cancer. J Chron Dis 33:107-114, 1980.

29. Winawer SJ, Andrews M, Flehinger B, et al. Progress report on controlled trial of fecal occult blood testing for the detection of colorectal neoplasia. Cancer 45:2959-2964, 1980.

30. Winawer SJ, Sherlock P. Surveillance for colorectal cancer in average-risk patients, familial high-risk groups, and patients with adenomas. Cancer 50:2609-2614, 1982.

31. Simon JB. Occult blood screening for colorectal carcinoma: A critical review. Gastroenterology 88:820-837, 1985.

32. Gabrielsson N, Granqvist S, Nilsson B. Guaiac tests for detection of occult faecal blood loss in patients with endoscopically verified colonic polyps. Scand J Gastroenterol 20:978-982, 1985.

33. Ahlquist DA, McGill DB, Schwartz S, Taylor WF, Owen RA. Fecal blood levels in health and disease. A study using HemoQuant. N Engl J Med 312:1422-1428, 1985.

34. Yoshida Y, Saito H, Tsuchida S, Kakizaki R, Aisawa T, Munakata A. A simple sensitive immunologic fecal occult blood test suitable for mass screening for colorectal cancer. Gastroenterology 90, May 1986, in press.

35. Hertz RE, Deddish MR, Day E. Value of periodic examination in detecting cancer of the rectum and colon. Postgrad Med 27:290-294, 1960.

36. Gilbertsen VA. Proctosigmoidoscopy and polypectomy in reducing the incidence of rectal cancer. Cancer 34:936-939, 1974.

37. Hocutt Jr JE, Jaffe R, Owens GM, Walters DT. Flexible fiberoptic sigmoidoscopy in family medicine. AFP 29:131-138, 1984.

38. Dubow RA, Katon RM, Benner KG, van Dijk CM, Koval G, Smith FW. Short (35-cm) versus long (60-cm) flexible sigmoidoscopy: a comparison of findings and tolerance in asymptomatic patients screened for colorectal neoplasia. Gastrointestinal Endoscopy 31:305-308, 1985.

39. Taylor I. Colorectal liver metastases - to treat or not to treat? Br J Surg 72:511-516, 1985.

40. Nielson, J, Balsley I, Jensen HE. Carcinoma of the colon with liver metastases. Acta Chir Scand 137:463-465, 1971.

40a. O'Connell MJ, Adson MA, Schutt AJ, Rubin J, Moertel CG, Ilstrup DM. Clinical trial of adjuvant chemotherapy after surgical resection of colorectal cancer metastatic to the liver. Mayo Clin Proc 60:517-520, 1985.

40b. Oliver GC, Shorb, Jr. PE. The totally implantable infusion pump in

treatment of metastatic colorectal cancer. Dis Colon Rectum 28:18-23, 1985.

41. Johnson LP, Rivkin SE. The implanted pump in metastatic colorectal cancer of the liver. Risk versus benefit. Am J Surg 149:595-598, 1985.

42. Cohen AM, Kaufman SD, Wood WC. Treatment of colorectal cancer hepatic metastases by hepatic artery chemotherapy. Dis Colon Rectum 28:389-393, 1985.

43. Bengmark S, Hafstrom L. Jeppsson B, et al. Metastatic disease in the liver from colorectal cancer: an appraisal of liver surgery. Wld J Surg 6:61-65, 1982.

44. Langevin JM, Wong WD. What is appropriate follow-up for the patient with colorectal cancer? Can J Surg 28:424-427,1985.

45. Gold P, Freedman SO. Demonstration of tumor-specific antigens in human colonic carcinomata by immunological tolerance and absorption techniques. J Exp Med 121:439-462, 1965.

46. Fletcher RH. Carcinoembryonic antigen. Ann Int Med 104:66-73, 1986.

47. Wennstrom J, Pierce ER, McKusick VA. Hereditary benign and malignant lesions of the large bowel. Cancer 34(Suppl):850-857, 1974.

48. Bussey HJR. Familial polyposis coli. Johns Hopkins Univ Press, Baltimore, 1975.

49. Gardner EJ, Richards RC. Multiple cutaneous and subcutaneous lesions occurring simultaneously with hereditary polyposis and osteomatosis. Am J Hum Genet 5:139-147, 1953.

50. Turcot J, Despres JP, St. Pierre F. Malignant tumors of the central nervous system associated with familial polyposis of the colon. Dis Col Rect 2:465-468, 1959.

51. Schroder S, Otto HF. Das Turcot-Syndrom. Dtsch med. Wschr 109:187-190, 1984.

52. Gilat T, Rozen P. Risk of colon cancer in ulcerative colitis in low incidence areas; a review. In: Colorectal Cancer: Prevention, Epidemiology and Screening. Winawer S, Schottenfeld D, Sherlock P, eds. Raven Press, New York, 1980. p 335.

53. Katzka I, Brody RS, Morris E, Katz S. Assessment of colorectal cancer risk in patients with ulcerative colitis: experience from a private practice. Gastroenterology 85:22-29, 1983.

54. Yardley JH, Ransohoff DF, Riddell RH, Goldman H. Cancer in inflammatory bowel disease: how serious is the problem and what should be done about it? (editorial). Gastroenterology 85:197-200, 1983.

55. Hulten L, Kewenter J, Ahren C, Ojerskog B. Clinical and morphological characteristics of colitis carcinoma and colorectal carcinoma in young people. Scand J Gastroent 14:674-678, 1979.

56. Morson BC. Rectal and colonic biopsy in inflammatory bowel disease. Am J Gastroent 67:417-426, 1977.

57. Nugent FW, Haggit RC, Colcher H, Kutteruf GC. Malignant potential of chronic ulcerative colitis. Gastroenterology 76:1-5, 1979.

58. Riddell RH, Goldman HM, Ransohoff DF, et al. Dysplasia in inflammatory bowel disease: standardized classification with provisional clinical implications. Human Pathology 14:931, 1983.

59. Waye JD. Endoscopic assessment of inflammatory bowel disease. Endoscopic Fundamental and Fine Points; The New York Course - 1984. New York Society for Gastrointestinal Endoscopy, New York, November 12-13, 1984.

60. Lambert R, Sabben G, Guyot P, Chavaillon A, Descos F. Nd:YAG LASER therapy for adenocarcinoma of the rectum. Gastroentestinal Endoscopy 30:144, 1984.

The President's Polyp

President Reagan's bout with colon cancer [NATION, July 29] has left everyone wondering how he or she might be affected by a similar condition and what preventive action to take. History may

TIME, AUGUST 19, 1985

Letters

record that one of the greatest benefits of the Reagan presidency was the decline in colon cancer.

Jack Blankley
Los Angeles