Questions and Answers:
National Conference on Cancer of the Colon and Rectum

The presentations by participants in the National Conference on Cancer of the Colon and Rectum held in Los Angeles on January 7, 8 and 9, 1971, included a question and answer period. Because time did not allow all questions to be answered during the conference, the unanswered questions were forwarded to the participants. Their answers are published below.*

Question addressed to Martin Lipkin, M.D., Cornell University Medical Center, New York Hospital, New York, New York:

Would you discuss the fact that many intestinal tumors (even early ones) show considerable differentiating activity?

DR. LIPKIN: Despite morphological evidence that differentiation is present in neoplastic cells of the colon, normal development of the proliferative apparatus of the cell does not take place. The repression of DNA synthesis and mitosis that accompanies normal colonic epithelial cell maturation does not develop in colon carcinoma cells or in the cells of adenomatous polyps or villous adenomas. Errors appear to develop in the metabolic regulatory control of these activities within the cells and, as a result, the cells retain their ability to proliferate after they have wandered away from the basal crypt area of the mucosa, the area to which cell proliferation is normally restricted. Carcinoma cells develop additional abnormalities and are able to continue to proliferate and spread even further from their original location. However, characteristics of the carcinoma cell, the failure to repress DNA synthesis and mitosis, are present in the epithelial cells of benign neoplastic lesions of the colon of man despite morphologic evidence of cell differentiation. In some areas of histologically normal mucosa in the colon of man, where the cells are well differentiated, migrating epithelial cells also synthesize DNA during their entire life span.

Questions addressed to John H. Weisburger, Ph.D., National Cancer Institute, Bethesda, Maryland:

Are there sufficient controls over food additives that may be related to colon cancer?

DR. WEISBURGER: On the basis of model experiments, we have a fairly good idea of the four possible ways whereby colon cancer could be induced. It is visualized that naturally occurring environmental carcinogens are responsible rather than synthetic food additives. However, the latter possibility cannot be excluded. The Food and Drug Administration, however, sees to it that food additives are carefully tested before being admitted. Of course, the test procedures are continually refined and some of the older data must be reevaluated.

*The complete program of the National Conference on Cancer of the Colon and Rectum appeared in CA—A Cancer Journal for Clinicians 20: 280-285; September-October, 1970.
Do you believe that maintaining a relatively low bacterial count of the colon with antibiotics would reduce the incidence of cancer?

DR. WEISBURGER: Maintenance of a low bacterial count by chronic administration of antibiotics does not appear to be feasible. In fact, it could be harmful. Some types of intestinal bacteria are useful since they generate certain vitamins and other essential elements. Laboratory experiments have shown that certain bacterial variants are not susceptible to the antibiotic used. Furthermore, the enzymes required for resolution of carcinogen complexes are produced by certain yeasts or pathogenic organisms which are not affected by antibiotics and which would overgrow the intestinal tract, a hazardous condition.

We need to develop more knowledge on the relationship between specific diets and drugs under both acute and chronic conditions, on the composition of bacterial flora and its direct relevance to colon cancer induction, and on the problem of bacterial enzymes required to liberate the active carcinogen in the colon.

Is there a carcinogen available which could be used in an in vitro technique?

DR. WEISBURGER: Up to this point no long-term in vitro studies have been performed dealing with the general problem of colon carcinogenesis. My group is planning to do so. The first problem will be to insure continuing growth of appropriate cells or organ cultures. Once this is achieved, it would seem that many different types of carcinogens could be utilized, provided, however, that the tissue can perform the necessary biochemical activation which may be required. In vitro systems are different from in vivo techniques insofar as detoxification and circulatory schemes, which operate under in vivo conditions and selectively affect a given tissue, do not necessarily hold under in vitro conditions.

What influence would modifiers of intestinal flora like cultures of lactobacillus acidophilus, yoghurt, etc. have on cancer prevention?

DR. WEISBURGER: A preliminary check of this question with some of the experts at the Clinical Center, National Institutes of Health, has not given a clear-cut answer on the changes in intestinal flora by specific foodstuffs. Certainly much additional research is required before one can be in a position to modify intestinal flora in the desired way judiciously and deliberately. Dietary factors high in roughage seem characteristic of populations with low incidence of colon cancer. Sugar and fat should be low, a beneficial recommendation in any case since moderate body weight resulting from the reduction of high caloric value foods would by itself be a generally useful preventive health measure.

Question addressed to Phil Gold, M.D., Ph.D., McGill University Faculty of Medicine, Montreal, Quebec, Canada: Tumor-specific antigens are different
from each other in experimental carcinogen-induced tumors, whereas they are similar in virus-induced tumors. Do your findings have any bearing on the search for etiologic agents in colon cancer? i.e., do they suggest that colonic cancer is not carcinogen-induced?

Dr. GOLD: The fact that the carcinoma-embryonic antigen (CEA) is present in all entodermally-derived human digestive system cancers does not necessarily preclude the chemical induction of such lesions. It is true that the tumor-specific transplantation antigens (TSTA) of chemically-induced tumors in animals have been distinctive for each tumor, while the TSTA of tumors evoked by a particular virus, even in different strains of animals, have been the same. Nevertheless, it must be borne in mind that the vast majority of experimental studies in animals have examined only those neoantigens whose presence could be detected by the phenomenon of tumor graft rejection. Although such information has added enormously to our knowledge of malignant transformation and tumor growth, the term “tumor-specific transplantation antigen” is a semantic convenience based on a laboratory procedure, and almost certainly does not denote a functional priority. Moreover, a great deal of available information strongly suggests that a number of tumor antigens, other than those which stimulate a rejection process on the part of the host, develop in the course of malignant transformation. Until the origin and range of reactivity of these tumor cell constituents has been determined, it will be most difficult to draw conclusions concerning the etiology of human cancer from animal investigations.

Question addressed to Robert J. Bolt, M.D., University of California, School of Medicine, Davis, California:

Since asymptomatic cases are obviously found earlier in the natural history of the disease, is it appropriate to compare five-year survival from diagnosis of both asymptomatic and symptomatic patients?

Dr. BOLT: The ultimate value of any “routine” procedure must be based in terms of life years saved. We know that surgical intervention for symptomatic cancers of the rectosigmoid will result in an average five-year cure rate of plus-minus 50 percent. I have presented evidence from the literature to suggest that the cure rate for asymptomatic carcinomas will approach 80 percent. To detect these asymptomatic carcinomas requires routine sigmoidoscopic examination. Therefore, the basic issue is whether the mortality resulting from the procedure when done in large numbers of asymptomatic and cancer-free individuals nullifies this increase in five-year cures or life years gained. This review indicates that a real gain in life years does indeed result. To arrive at this conclusion it is obviously necessary to compare “cures” of the asymptomatic as contrasted to the symptomatic patients.

Questions addressed to B. F. Overholt, M.D., Knoxville Gastroenterology
Are fiberoptics applicable to colotomy at operation and colostomy proximal loop?

DR. OVERHOLT: At present, the flexible fiberoptic coloscopes have only minimal application at the time of colotomy. The rigid instruments are perhaps more satisfactory as they are easily sterilized and handled in the surgical situation. Colostomies, as well as ileostomies, can be endoscoped with a flexible instrument to great depths of penetration with satisfactory results.

Is fulguration advisable if there is evidence of uncontrolled bleeding due to biopsy obtained via coloscope?

DR. OVERHOLT: A small superficial biopsy measuring 1-2mm. in diameter is obtainable through the flexible coloscopes. Although bleeding is a potential hazard, it has not occurred. Because of the closed system involved, fulguration is not advisable because of the possibility of a spark and explosion. This would be highly unlikely but the possibility is not worth the risk.

How long does it take to do fiberoptic colosigmoidoscopy?

DR. OVERHOLT: The time required depends a great deal on the skill of the examiner and the type of patient examined. With teaching, use of photography and biopsy equipment, an experienced observer may take 30 to 45 minutes during the procedure. A satisfactory examination can be carried out in 20 to 30 minutes by a skilled examiner in a not too redundant sigmoid colon.

Questions addressed to David H. Greegor, M.D., Ohio State University, College of Medicine, Columbus, Ohio:

At what point do you refer the patient to a surgeon if the occult blood test is positive and the follow up with barium X-ray shows no lesions?

DR. GREEGOR: If the stool was guaiac positive and I had reason to suspect that the patient had definite pathology I would do an upper GI series, small bowel series and any other test that would help me find the cause. If, however, I had an obviously well patient with nothing but an occasional guaiac positive stool and negative barium enema I would probably not pursue the situation any further. There are too many innocent causes for an occasional positive guaiac.

Have there been many false positives in the occult blood test?

DR. GREEGOR: There have been very few false positives among the patients who had definite and repeated guaiac positive reactions. We usually find diverticulitis or a polyp or a carcinoma.

Questions addressed to William Martel, M.D., University of Michigan, Medical Center, Ann Arbor, Michigan:

Do you believe that proctosigmoidoscopy and the barium enema examination can be done on the same day with the same preparation?

DR. MARTEL: These two examinations can be done on the same day with the
same preparation but this is definitely not advisable and should be avoided. Invariably there is a great deal of residual gas in the colon following proctosigmoidoscopy and there is frequently a good deal of spasm of the rectosigmoid so that the barium enema examination which follows is usually suboptimal. Reversing the order of the examinations on the same day is also inadvisable inasmuch as barium coating of the mucosa interferes with the endoscopic examination.

Do you consider the lateral rectosigmoid view of value?

DR. MARTEL: The lateral rectosigmoid view is definitely of value, particularly for detecting flat lesions on the anterior and posterior rectal walls. I obtain lateral spot films or, in very large patients, lateral views with the overhead tube.

Question addressed to Warren H. Cole, M.D., University of Illinois, College of Medicine, Chicago, Illinois:

How low do you believe anastomosis should be done for rectal carcinoma, rather than abdominoperineal? When do you utilize proximal decompression or diversion? Do you drain? Do you leave in an intraluminal tube?

DR. COLE: There is no agreement as to the level in the rectosigmoid above which an anterior resection should be performed, and below which a Miles' procedure should be done. However, I personally will do an abdominoperineal operation unless the lower edge of the tumor is fully 2 cm. above the peritoneal reflection, as determined at the operating table. There are, of course, exceptions if the patient makes a strong request.

Ordinarily, I do not utilize proximal decompression following anterior resections, i.e., resection of the tumor with restoration of the lumen. Exceptions are the relatively few occasions when the resection was so low that a satisfactory suture line could not be achieved. On such occasions I prefer some type of drainage such as insertion of a Penrose rubber drain from the suture line through a stab wound in the perineum or to the exterior through a stab wound in the lowermost portion of the abdomen anteriorly. Under the latter circumstances the drain should be extraperitonealized as much as possible. Under no circumstances should the drain be wrapped around the bowel at the suture line, because in my opinion such a procedure will tend to encourage leaks and fistulae. When the suture line is insecure, and a drain has been inserted, the patient should be kept in bed for four or five days, and dietary intake of solid foods should be delayed a couple of days. With such precautions, serious peritonitis from a leak should not develop.

I have not used an intraluminal tube, and would discourage its use.

Question addressed to Lauren V. Ackerman, M.D., Washington University, School of Medicine, St. Louis, Missouri:
Questions

Do you advise segmental resection of a
1.5 cm. sessile polyp of sigmoid, or
polypectomy with frozen section of
stalk?

DR. ACKERMAN: No generalization
should be made as to an answer but
usually segmental resection would be
the treatment of choice.

Questions addressed to Robert C.
Horn, Jr., M.D., Henry Ford Hospi-
tal, Detroit, Michigan:

Would you comment on the discrep-
ancy between your frequency data for ade-
nomatous and hyperplastic polyps and
the data of Morson, Arthur and Lane
which show about a 9-1 preponderance
of hyperplastic polyps?

DR. HORN: I am not familiar with
frequency data that show a 9-1 pre-
ponderance of hyperplastic over ade-
nomatous polyps. Morson, in the two
papers referred to, (J.A.M.A. 179:
316-321, 1962; Dis. Colon Rectum 5:
337-344, 1962) does not list comparative
figures. Lane (Cancer 16: 751-764, 1963)
does state that “among minute colonic
polyps the hyperplastic type is by far
the more common” but adds “With
increasing size, the proportion changes,
and just the reverse is true among
larger colonic polyps.” Arthur (J. Clin.
Path. 21: 735-743, 1968) reports a
predominance of metaplastic (my hyper-
plastic) over adenomatous polyps of
3 or 4 to 1. However, he limited his
study to nodules less than 5 mm. in
diameter discovered by careful scrutiny
of the entire mucosal surface of the
rectum (removed at surgery or autopsy)
by reflected and transmitted light.

This is in contrast to my study of
nodules removed at proctosigmoidos-
copy (or surgery) and studied routinely
in the surgical pathology laboratory.
In the light of these differences in
material and study methods, there
may well be no significant discrep-
ancy.

What attributes do you give the term
“adenomatous polyps with villous
changes”? Could this be an explana-
tion of your lower incidence of cancer
in “villous adenomas”?

DR. HORN: There seems to be general
agreement that the adenomatous polyp
and papillary adenoma are but different
anatomic patterns of essentially the
same neoplastic process. A degree of
papillary change is frequently seen in
the superficial portions of otherwise
typical adenomatous polyps. It may
be that the term “adenomatous polyp
with villous changes” refers to this,
although I believe it is generally re-
served for a more nearly equal mixture
of the two growth patterns. The fact
that I have not used this term (or one
like it) and have classified lesions by
predominant growth pattern may ac-
count at least in part for the relatively
low incidence of cancer in my series of
villous adenomas; however, I think the
low incidence more likely results from
the inclusion of many lesions smaller
than those in many series. It is in-
teresting in this connection that Morson
(Dis. Colon Rectum 5: 337-344, 1962)
uses the term “papillary adenoma” to
designate those lesions having features
of both the adenomatous polyp and
villous adenoma.
Question addressed to John S. Spratt, Jr., M.D., Ellis Fischel State Cancer Hospital, Columbia, Missouri:

*Can you speculate on why the incidence of colon cancer drops in a population undergoing regular sigmoidoscopy with removal of polyps (i.e. Wangensteen's studies)?*

**Dr. Spratt:** Colon cancer data has to be viewed several ways. First, the cancers themselves grow slowly and evolve over a number of years. Consequently, the first time a population is examined, the prevalence rate tends to be severalfold greater than the annual incidence rate. Further, some small cancers are undoubtedly mistaken for polyps and are fulgurated. The slowness of evolution after clearance can result in a several year reduction in the incidence since more than several years may be required to grow a detectable batch of colon cancers.

Proctosigmoidoscopy is a sound and beneficial examination when done by adequately equipped and trained hands. Many small cancers of the nonmetastasizing variant can probably be cured very simply by transproctoscopic examination and local ablation. Occasionally, the ablation of a benign polyp may prevent a cancer.

However, for proctosigmoidostomy to be used as an integral part of a truly effective cancer control program, planning, distribution, motivation, manpower and equipment must be looked at realistically. Most strategies, including public health strategies, fail for logistical reasons. An occasional study showing a slight drop in incidence for a small carefully examined population cannot be extrapolated to the entire public without facing these logistical and strategic realities.

Questions addressed to Maus W. Stearns, Jr., M.D., Memorial Hospital for Cancer and Allied Diseases, New York, New York:

*What is the smallest infiltrating adenocarcinoma you have ever seen or know of?*

**Dr. Stearns:** The smallest infiltrating adenocarcinoma we have seen at Memorial Hospital is approximately 1 cm. in size. We have seen infiltrating carcinoma in polyps which are approximately 8 mm. in size. We have heard of patients who have smaller lesions but when those specimens were measured they all approximated a centimeter. Undoubtedly smaller lesions do exist, but I have not seen them nor have my colleagues.

*What are your feelings regarding the malignant potential of “the benign sessile and pedunculated adenoma”?

**Dr. Stearns:** I have come to the conclusion that most of our attitudes about the malignant potential of the benign sessile and pedunculated adenomas are feelings rather than facts. I believe that the majority of apparently benign sessile and pedunculated adenomas are treated before their malignant potential is ever known. There are undoubtedly many which never be-
come malignant. However, we have seen a number of patients who had been advised to disregard colonic polyps which had all the clinical characteristics of benignity. These people were eventually seen with carcinoma in the same location with no benign polyp present. After years of failing to find the small "de novo" cancer that presents as a 2-3 mm. excrescence which proves to be a malignant tumor and yet continuing to find small 2-3 mm. cancers in polyps, either sessile or pedunculated, it is our impression that the majority of cancer of the bowel does arise in pre-existing adenomas much more frequently than it arises "de novo" from the bowel mucosa.

Questions addressed to Lloyd G. Bartholomew, M.D., Mayo Graduate School of Medicine, Rochester, Minnesota:

Are certain systemic syndromes in patients who are otherwise asymptomatic, occultly related to cancer or are they overlooked symptoms of the specific cancer?

DR. BARTHOLOMEW: Many of these systemic syndromes are the first indication of the presence of an abnormal condition. Even in retrospect, it is very difficult in many instances to find any indication of symptomatology that might turn one's attention to the presence of an underlying malignancy. For example, in acanthosis nigricans, complete examinations short of diagnostic abdominal laparotomies have failed to reveal any underlying malignancy for periods of time as long as one year before symptoms of the malignancy were apparent.

Is colon cancer associated with the myasthenic syndrome?

DR. BARTHOLOMEW: Carcinoma of the colon has not been reported in association with the myasthenic syndrome. The most frequently associated tumor is that of a small cell carcinoma of the lung.

Question addressed to Justin J. Stein, M.D., University of California, School of Medicine, Los Angeles, California:

What is your opinion of the latest work in which routine preoperative radiation, in Dukes C group of patients with cancer of the rectum and rectosigmoid, is not used?

DR. STEIN: There is a sound radiobiologic basis for the combined use of preoperative radiation and surgery in the treatment of operable carcinoma of the rectum and rectosigmoid.

Moss and Axtell analyzed data collected from the End Results Group and noted that there has been practically no improvement in prognosis for cancer of the colorectum even among patients with localized lesions who are treated by surgery alone.¹ The latest published data by Allen, by Tepper and Associates and by Roswit and Higgins indicate that preoperative radiation to the rectum and rectosigmoid can be beneficial.²-⁴

¹ Moss, N. H., and Axtell, L. M.: Cancer of the gastrointestinal tract. Trends in method treatment
Question addressed to Harry E. Bacon, M.D., Temple University, School of Medicine, Philadelphia, Pennsylvania: How are patients selected for the “pull-thru” and anterior resection procedures?

DR. BACON: Since 1940 it has been my policy to employ the “pull-thru” operation, otherwise termed abdominoperineal proctosigmoidectomy without colostomy and with preservation of the sphincter muscles, for all patients with operable cancerous lesions between the rectosigmoid (12 cm. and the 7 cm. level) above the anal margin. The only contraindication is the presence of acute intestinal obstruction. The size and shape of the pelvis, as they are on occasion with low anterior resections, is not a deterring factor.

Question addressed to Harvey R. Butcher, Jr., M.D., Washington University, School of Medicine, St. Louis, Missouri:

What is the place of pelvic exenteration in the treatment of cancer of the rectum involving the urinary tract?

DR. BUTCHER: Pelvic exenteration is indicated as therapy for colorectal cancers invading the lower urinary tract when the neoplasm is otherwise confined to the pelvis. In this situation approximately 40 percent of patients live five years without recurrence. Also, pelvic exenteration is occasionally indicated as a palliative procedure when the urinary bladder is involved and distant or extrapelvic spread has occurred. Such is the case when the life expectancy of the patient is significant and the urinary tract involvement has caused or is likely to cause fistula formation.