Diet and Colon Cancer

An interview with
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Editor: In 1973, an estimated 37,000 people in the United States will die of colon cancer. I understand you and your colleagues at the American Health Foundation are currently investigating factors which relate to the etiology of colon cancer—studies which will hopefully lead to the prevention of this disease.

Dr. Wynder: That is correct. Initially, we studied pertinent incidence data and found marked differences in the incidence of large bowel cancer in various populations. For instance, in Japan the incidence of colon cancer is low and gastric cancer is high. In the United States, the reverse is true. Epidemiologic surveys also showed that when Japanese migrate to the United States, their incidence of gastric cancer decreases while their incidence of colon cancer increases. The same phenomenon is seen when eastern Europeans, who tend to have a low incidence of colon cancer, migrate to the United States and develop a higher incidence of this disease. Such epidemiologic studies suggest a factor in American life which relates to colon cancer and which is apparently not present to the same extent in these other countries.

Editor: Does the incidence of colon cancer also vary within a specific population?

Dr. Wynder: In the United States the incidence of colon cancer is relatively similar among different ethnic and socioeconomic groups. Recently, we conducted a large scale epidemiologic study of patients with colon cancer and normal controls in New York City and in Japan.
In the New York study there were no major differences between colon cancer patients and controls, except for a slightly higher rate of colon cancer in the Jewish population. In Japan, people in higher socioeconomic groups had a higher incidence of colon cancer than Japanese in lower socioeconomic groups.

**Editor:** *Do these findings suggest a common denominator?*

**Dr. Wynder:** We believe they do and that a diet high in animal protein and animal fat correlates with a high incidence of colon cancer. In the United States, according to the Department of Agriculture, almost everyone eats about the same total amount of fats, proteins and carbohydrates and consequently the incidence of colon cancer is relatively similar among different populations. In Japan, people in higher income groups tend to eat a more Western-type diet and have a higher incidence of colon cancer than those in lower economic groups who usually eat a typical Japanese diet.

**Editor:** *Are you also studying vegetarians in the United States who are not on a high protein, high fat diet?*

**Dr. Wynder:** Yes. We are now examining the incidence of colon cancer among Seventh Day Adventists who are largely vegetarians. In addition, we are studying a group of patients with Crohn’s disease who, according to several reports, have a low incidence of colon cancer and also patients with familial polyposis, who have a high incidence of colon cancer.

**Editor:** *Have etiologic factors other than diet been ruled out?*

**Dr. Wynder:** We believe that diet plays a major role in the etiology of colon cancer, but we cannot positively rule out other causes. The relationship of ulcerative colitis to cancer of the large bowel is well established. We do not believe alcohol and tobacco play a role and an association between a previous appendectomy and the development of colon cancer is probably artifactual. We have studied industrial chemicals as another possible cause, but also find it unlikely although some association has been reported between asbestosis and colon cancer.

**Editor:** *What about genetic characteristics as a contributory factor?*

**Dr. Wynder:** Although patients with multiple polyposis, a hereditary disease, have a high incidence of colon cancer, we believe genetics plays a relatively small role in the etiology of colon cancer. By and large, the human population is very heterogeneous and there is not a high correlation between genetic characteristics and colon cancer. There are many possible causes of colon cancer, but we feel that the evidence now points most strongly toward diet as an etiologic factor. The key question remains: How does a diet high in animal protein and animal fat relate to colon cancer?
Editor: Do you agree with Dr. Burkitt's thesis that transit time, the bulk and consistency of stools may cause changes in the bacterial flora of feces and relate to cancer of the large bowel?

Dr. Wynder: There is some evidence for, and some which contradicts, this concept. For instance, American women, who are significantly more constipated than men, do not have a correspondingly higher incidence of large bowel cancer. We have also interviewed patients with colon cancer and found no association with constipation. Dr. Jack Cole at Yale performed an experiment in which rats given magnesium sulfate as a laxative to speed up the transit time of stools showed the same incidence of chemically induced colon cancer as controls. Therefore, our emphasis is not on transit time as such, but rather on metabolic processes affected by diet and how these relate to colon cancer.

Editor: What specific metabolic processes are being investigated?

Dr. Wynder: We are presently studying the role of aerobes and anaerobes in the microbial flora of the gut and also the relationship between bile acids and cholesterol metabolism and the development of colon cancer.

Editor: Why do you suspect that these processes may be related to the development of colon cancer?

Dr. Wynder: Detailed studies have shown that people on a Western-type diet have many more anaerobes in the microbial flora of the gut than those on a Japanese-type or vegetarian diet. We also know that certain bile acids and cholesterol metabolites are significantly more common among populations with a high risk of colon cancer.

Editor: Do you attribute these metabolic changes more to high fat or to high protein consumption, or both?

Dr. Wynder: We are inclined to attribute these changes largely to the fat and cholesterol content in the diet. The animal protein content may modify the biochemical potential of tissues and gut microflora to metabolize fats and derived materials with the production of carcinogenic metabolites. Dr. Bandaru Reddy at our Institute is currently involved in studies dealing with this question.

Editor: Further clarification, I assume, involves studying the problem in the laboratory, as well.

Dr. Wynder: Yes. Dr. John Weisburger and his staff at this Institute are currently investigating the relationship between diet and colon cancer in animal models.

Editor: Wasn't this impossible as recently as five years ago?
Dr. Wynder: The discovery of synthetic chemicals which can induce colon cancer in animals, reliably and reproducibly, with a comparatively short latent period—six to 10 months—is quite new. In 1963, Dr. G. Laqueur and his associates at the Arthritis Institute of the National Institutes of Health found quite accidentally while examining another problem, that cycasin, a natural product obtained from the fruit of the cycad tree, caused cancer of the colon in rats. He also showed that the microbiological flora in the intestine was crucial to the action of cycasin since this agent was completely inert in germ-free rats. In 1967-1968, Dr. Druckrey tested a synthetic prototype, 1,2-dimethylhydrazine, for carcinogenic activity and found that this chemical could induce cancer of the large bowel in various rodent species such as mice, hamsters and rats, especially upon subcutaneous injection. Today, we have a battery of synthetic chemicals with which we can induce colon cancer and study in detail how diet modifies the response. Thus, we expect to gain definitive information on how all of these complex factors interrelate and operate. We hope that greater understanding will lead to rational, sound preventive measures.

Editor: Do you feel at this point in your research that Americans should eat less animal fat?

Dr. Wynder: This recommendation should be supported not only because of the apparent relationship between animal fat, cholesterol and cardiovascular diseases, but also because of the possible association with colon cancer.

Editor: Thank you, Dr. Wynder.

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