Symposium

Inflammatory Disease of the Bowel:
The Risk of Cancer

JOHN ALEXANDER-WILLIAMS, M.D.*

Birmingham, England

First I want to remind you that there is a well recognized risk of development of colonic cancer in patients with ulcerative colitis. This risk is particularly great when the disease has been present for ten years or more; it is particularly great when the whole colon is involved and when the disease begins at an early age. Furthermore, there are certain characteristics of colonic malignancy in ulcerative colitis that differ from those of large-bowel carcinomas appearing in patients who do not have ulcerative colitis. In ulcerative colitis, the carcinoma has a tendency to be more undifferentiated; it frequently appears at multiple sites; it certainly occurs earlier in life and, what is extremely important, the carcinoma tends to occur in clinically silent areas, that is, apart from in the rectum or the sigmoid colon. Now the first question I want to put to you and to my fellow panelists is: as the risk of cancer in ulcerative colitis is high, and as it often occurs in silent areas, what should we do to detect or prevent it? Should we advise prophylactic colectomy to those patients at great risk? I have done this many times in the past, and I must say that I am now reluctant to do so. I am reluctant to take out the entire large bowel from a patient with quiescent disease just because the disease began when they were young and it involved the whole colon. What I prefer to do whenever possible is a total colectomy with a cecorectal or ileorectal anastomosis in patients at high risk who have quiescent rectal disease.

Should we advise regular total colonoscopy? I think the logistics of this exercise are, at the moment, rather daunting both for the patient and for the endoscopists. However, I believe that this will be a popular method of management in the future. How often should colonoscopy be performed? I think at least once a year.

Should we look for precancerous changes in the rectal biopsy? If you work with a pathologist who is as good as Dr. Basil Morson, you are fortunate, for he will be able to recognize precancerous changes in the colon in those people in whom colonic carcinoma is developing, or will shortly develop. However, as Evans and Pollock have shown recently, these precancerous changes can be patchy. You can be misled if you biopsy an area where there is no premalignant change, even from the colon of a patient who already has carcinoma complicating ulcerative colitis. However, with a
colonoscopic examination and multiple biopsies, the chances of detecting premalignant change should be increased.

Should we perform regular carcinoembryonic antigen estimations? This context promised to be one of the most important for carcinoembryonic antigen. However, recent reports have not been very enthusiastic.

Having established that there is a high risk of malignancy in chronic ulcerative colitis, we now turn to a question that is even more interesting: is there also a high risk of malignancy in Crohn's disease? In a recent report, Chevrel recorded the world literature and recorded 38 patients with long-standing Crohn's disease in whom cancer of the small bowel developed. It was of interest that 26 of the 38 cases involved the ileum and another 13, a bypassed segment.

This has been looked at in another way in the report by Frank and Shorey, who, also on the basis of a literature review, compared incidence of small-bowel carcinomas occurring apart from Crohn's disease with that of small-bowel carcinomas occurring in association with Crohn's disease. The average age at diagnosis was much younger in the patients who had carcinoma complicating Crohn's disease (38 years instead of 60). The duration of symptoms was, of course, much longer (12 years instead of 14 months). Now here there is difficulty, because the patients with Crohn's disease have had obstructive intestinal symptoms for many years and it may not be possible to detect symptomatically the development of carcinoma. The jejunum-to-ileum ratio is entirely different, with a much greater preponderance of carcinomas in the ileum in patients with Crohn's disease (one jejunum to two ileum) compared with the rest (3.5 jejunum to one ileum). The five-year postoperative survival rate for carcinomas of the small bowel complicating Crohn's disease was nil compared with 20 per cent for those without Crohn's disease.

In our series of 500 patients with Crohn's disease followed for a mean of 13 years, the ultimate fates of the patients are known in all but three cases. Malignant disease has developed in 19. Twelve malignancies occurred in the alimentary tract, two each in the esophagus, stomach, pancreas, and colon, one in the ileum, and three in the rectum.

With the help of our statistician colleagues and the use of life tables and certified causes of death, we have been able to show that the risk of developing these various malignancies is significantly greater in patients who have Crohn's disease than would be expected in a population of the same age and sex followed for the same length of time. These differences are highly significant, not only for the small and large bowel, but also for the esophagus and pancreas.

It appears that there is something about Crohn's disease that predisposes not only to the development of carcinoma within the commonly affected gut but possibly to carcinoma of the alimentary tract in general. Further work in our institution by MacLaurin et al. has shown that in some patients there is a failure of the lymphocyte immune response. The lymphocytes failed to "recognize" injected tumorcell antigen. It seems that there may be some basic immunologic deficiency in Crohn's disease that predisposes to malignancy.

Cancer of the large bowel has also occurred in series of Crohn's disease reported in the literature. Chevrel recorded 28 cases and noted that the site of the cancer in Crohn's disease is predominantly in the colon (25 cases) rather than in the rectum (three cases). This is, of course, a different ratio from what one would expect in patients who do not have Crohn's disease. Once again, the prognosis was extremely poor; only six of the 28 patients lived a year or more.

From this evidence it appears that the