

Morson B C & Pang L S C. Rectal biopsy as an aid to cancer control in ulcerative colitis. *Gut* 8:423-34, 1967.
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The incidence and extent of epithelial changes suggestive of precancer or carcinoma were examined in 199 colectomy specimens from patients with a history of colitis alone or with cancer of the colon or rectum and in 148 rectal biopsies from patients with ulcerative colitis. Precancer was found in all colectomy specimens removed for colitis and cancer and in some patients with colitis alone. Rectal biopsy diagnosis of precancer accurately predicted precancer in subsequent colectomies. [The *SCC*® indicates that this paper has been cited in over 305 publications. It is among the six most highly cited articles in this journal.]

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I have a very clear recollection of how this investigation was born. A rectal biopsy was sent to me in 1964 by F. Avery-Jones (now Sir Francis Avery-Jones) from a patient with colitis. Very atypical epithelial changes amounting to carcinoma-in-situ were present in flat mucosa, and I reported these as "precancerous." Barium enema subsequently showed that the patient had a carcinoma of the sigmoid colon but that this was inoperable. In my report, I added that this was not the first time I had noticed premalignant appearances in rectal biopsies from patients with long-standing colitis and that subsequent examination of colectomy specimens confirmed the presence of diffuse epithelial changes of a precancerous nature in flat mucosa. It was clear that a comprehensive clinicopathological investigation was required to see whether the examination of rectal biopsies from patients with a long history of total colitis could be used as a "test" for the detection of a precancerous phase.¹

Throughout the article, no mention was made of the word "dysplasia." At the time, this nomenclature would have been unfamiliar to clinical gastroenterologists, whereas precancer was more emotive and

likely to arouse interest. It soon became clear, however, that precancer was an insufficiently precise word to cover the range of cellular changes seen. It had served its purpose and could now be replaced by a system of grading into mild, moderate, and severe epithelial dysplasia, which was a more appropriate and familiar system for use by pathologists. This grading system was adopted about the time of the 1967 publication, but the results of assessment of individual risk of cancer in colitis in which the term dysplasia and the use of rectal biopsy in follow-up were first mentioned were not published until 1974² and 1977.³

It is important that from the beginning I was concerned about the distinction between precancer and reactive hyperplasia, the consequence of active inflammation. This remains a problem for pathologists, and, currently, there is still overdiagnosis of epithelial dysplasia, as judged by my experience in referral practice. Recently, an international study group has recommended that dysplasia should be divided into low- and high-grade varieties because this appears to be more clinically appropriate.⁴ This study also addressed the difficulties of distinguishing dysplasia from reactive hyperplasia.

I think this paper has been so highly cited because for the first time it provided a method for identifying the *individual* patients with extensive colitis at increased risk of developing colorectal cancer, whereas formerly, it was a *population* of patients who were most at risk on the basis of extensive colitis and a history of symptoms longer than 10 years. When consideration is being given to prophylactic colectomy, the gastroenterologist has now become very dependent on the opinion of the pathologist because a confirmed report of high-grade dysplasia, even in a "well" patient, is an indication for proctocolectomy. Another factor was the original concept that precancerous epithelial changes were to be found in endoscopically flat mucosa rather than in polypoid lesions, but the latter have now been shown to have particular importance as well.⁵ Lastly, the whole concept of dysplasia complicating inflammatory bowel disease has been shown to provide opportunities for cancer prevention and cancer control⁶ as well as to contribute to the investigation of wider problems of intestinal carcinogenesis.

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