

# This Week's Citation Classic

Harris O D, Cooke W T, Thompson H & Waterhouse J A H. Malignancy in adult coeliac disease and idiopathic steatorrhea.

*Amer. J. Med.* 42:899-912, 1967.

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From a review of 202 patients with adult coeliac disease (ACD) or idiopathic steatorrhea (IS), evidence is given that both can be complicated by malignancy, either lymphoma or carcinoma (especially oesophageal). It is more significant for men, and a gluten-free diet appeared to decrease the risk of malignancy. [The SC<sup>®</sup> indicates that this paper has been cited in over 280 publications since 1967.]

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"This study was begun in early 1965 soon after my arrival from Australia. W.T. Cooke had a major interest in small and large bowel disease since 1941, and hence had a huge group of such patients attending his clinic. His nutritional and intestinal unit was a major referral centre from the Midlands of England.

"My research projects were to be centred around coeliac disease (CD). The major project was to review all of the coeliac patients and determine the occurrence of malignancy. Already, the literature contained anecdotal case reports of adenocarcinoma of the small bowel possibly complicating CD, and in 1962, Gough, Read, and Naish<sup>1</sup> had put forward the hypothesis that small bowel reticulosis may develop as a complication of idiopathic steatorrhea (IS). In 1960, Cooke and his colleagues<sup>2</sup> reported their experience with jejunal biopsy in adult CD (ACD); this produced similar results to the earlier English study by Shiner in 1957.<sup>3</sup> Thus, in my study, these two patient groups were studied—(1) the possibly heterogeneous group without jejunal biopsy (1941-1957) and identified as IS, and (2) the homo-

geneous group with jejunal biopsy criteria for CD.

"Early in the study a substantial group with lymphoma was found, along with an apparently significant excess of gastrointestinal carcinomas. It was then important to involve the Cancer Registry of the department of social medicine, Birmingham University. They could provide the expected incidence figures for all malignancies, and determine the observed incidence in our patients. Also, Henry Thompson (surgical pathologist) reviewed all jejunal biopsies and the lymphomas.

"The final paper thus represented a critical review of 202 patients with careful clinical and pathological documentation of 31 malignancies that developed in them over a mean follow-up period at this unit for 8.2 years. Of the malignancies, 14 were lymphoma in type, and 13 gastrointestinal. The mean follow-up period had been 7.8 years from the time of diagnosis of the CD (or IS) until the lymphoma was diagnosed. In 11 of these patients, there was asymptomatic follow-up of 8.4 years on a gluten-free diet before the lymphoma developed. This evidence permitted the only conclusion that ACD could be complicated by lymphoma. The remaining three patients were inconclusive in their relationship.

"This study documented that some gastrointestinal cancers (especially oesophageal) can also complicate CD. Lastly, there was some support (not statistically valid) for the beneficial effect of a gluten-free diet on reducing the incidence of malignant complications.

"This paper has become a *Citation Classic* because of the careful documentation of a big group of carefully diagnosed and followed coeliacs; and there were comparative data in the same district for malignancies. The lymphoma is now classified as a histiocytic lymphoma, and the most recent review is 'Coeliac disease and malignancy,' published in *Lancet*.<sup>4</sup>

1. Gough K R, Read A E & Naish J M. Intestinal reticulosis as a complication of idiopathic steatorrhea. *Gut* 3:232-9, 1962.
2. Fone D J, Meynell M J, Harris E L, Cooke W T, Brewer D B & Cox E V. Jejunal biopsy in adult coeliac disease and allied disorders. *Lancet* 1:933-8, 1960.
3. Shiner M. Small intestinal biopsies by the oral route—histopathologic changes in the malabsorption syndrome. *J. Mt. Sinai Hosp.* 24:273-85, 1957.
4. Swinson C M, Slavin G, Coles E C & Booth C C. Coeliac disease and malignancy. *Lancet* 1:111-15, 1983.