

Hill M J, Drasar B S, Arles V, Crowther J S, Hawksworth G & Williams R E O.  
Bacteria and aetiology of cancer of large bowel. *Lancet* 1:95-100, 1971.  
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London, England]

In a study of populations from the UK, US, Uganda, India, and Japan, the incidence of large-bowel cancer correlated well with the faecal bile-acid concentration (particularly of deoxycholic acid) and with the faecal bacterial flora, supporting the hypothesis that colorectal cancer is caused by a bacterial metabolite of the bile acids. [The SCJ® indicates that this paper has been cited in over 455 publications since 1971.]

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In 1966, Bohumil Drasar and I were working in the Bacteriology Department at St. Mary's Hospital on bacterial degradation of bile acids in relation to blind-loop syndrome. Two of the patients being studied developed adenocarcinoma of the small bowel. We were already wondering about the role of bile acids in those lesions when Robert Williams, the head of the laboratory, introduced the question of colorectal carcinogenesis and its relation to diet. After much further discussion among the three of us, a hypothesis was formulated involving bacteria, bile acids, and colorectal carcinogenesis. The comparison of populations in various countries to test this hypothesis was

funded by the Cancer Research Campaign.

In the early years of the work, discussion of the ideas in public usually generated disbelief and disdain, thereby providing us with a considerable driving force to get through vast amounts of work in a relatively short time. During this time, Williams (now Sir Robert Williams) was the major source of strength in the group, but we also received considerable help and moral support from Avery Jones (now Sir Francis Avery Jones) and Albert Neuberger.

The results were a great relief to us. The paper has received considerable attention because it offered hope of finding the cause of the second commonest cancer in Western countries at a time when optimism was high following the confirmation of the link between smoking and lung cancer. The work has been repeated many times, and it is now accepted that there is a clear correlation between the mean faecal bile-acid concentration in populations and the risk of colorectal cancer. However, although in population studies colorectal cancer can be considered as a single-stage disease determined by bile acids and bacteria (and therefore by diet), when case-control studies are attempted, other factors are important and the results consequently are much less clear-cut. Our recent investigations, based on histopathological and epidemiological studies, suggest a mechanism for colorectal carcinogenesis involving at least three stages,<sup>1</sup> and more recent investigations suggest that bile acids and bacteria are not involved in the first stage<sup>2</sup> but are probably involved in some of the subsequent stages.

1. Hill M J, Morson B C & Bussey H J R. Etiology of adenoma-carcinoma sequence in large bowel. *Lancet* 1:245-7, 1978. (Cited 55 times.)
2. Hill M J. Metabolic epidemiology of large bowel cancer. (De Cosse J & Sherlock P, eds.) *Gastrointestinal cancer*. The Hague: Martinus Nijhoff, 1981. p. 187-226. (Cited 2 times.)