

Aries V, Crowther J S, Drasar B S, Hill M J & Williams R E O. Bacteria and the aetiology of cancer of the large bowel. *Gut* 10:334-5, 1969.

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The bacterial flora of faeces collected in England, an area with a high incidence of large-bowel cancer, was compared with that from Uganda where the incidence is low. In these populations, the frequency of large-bowel cancer was related to the bacterial flora. [The SCI® indicates that this paper has been cited in over 235 publications.]

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During the late 1960s and early 1970s, Michael Hill and I, working in the Bacteriology Department of the Wright-Fleming Institute with Sir Robert Williams, undertook a series of studies to explain the cause of large-bowel cancer. During our long collaboration, Hill's contribution has tended to be biochemical and mine bacteriological, but this demarcation has not been strict. For this investigation, we were joined by Vivienne Aries and John Crowther, who were doing research for their PhDs.

The story of these studies was told in part by Hill,¹ and I also must mention the support and help that we received from many other workers, particularly Albert Neuberger, Sir Francis Avery Jones, and Sir Richard Doll. Our choice of Uganda as the first study area was aided by the presence in Kampala of Robert Blowers, a collaborator of Williams. During 1967 I visited the US to present our results on bile acid metabolism at a symposium² and while in New York visited Russell Schaedler at the Rockefeller Institute. He introduced me to Ernest Wydner (then at the Sloan-Kettering Institute). We had valuable discussions on the

causes of cancer, particularly with respect to the role of diet.

The paper put forward the hypothesis that differences in the bacterial flora of the bowel, by leading to different degrees of degradation of bile acids, might be one cause of the variations in the geographical distribution of large-bowel cancer. The relationship of large-bowel cancer to diet was explained in terms of the influence of diet on the intestinal bacteria. Studies in London and Kampala supported this hypothesis. This was the first time that an explanation, supported by prospectively collected data, had been advanced for the geographical differences in the incidence of large-bowel cancer. The study brought together the insights of many investigators as to the role of diet and set them in the context of a testable hypothesis, thus holding out the prospect of cancer prevention.

The paper was caught up in and perhaps contributed to the upsurge of interest in the role of diet in the aetiology of disease in Western industrialised countries. It may be that the large number of citations in part reflects this. Consideration of the other aspects of Western diet including food additives might be part of the motivation of subsequent studies.³

Though the basic hypothesis has never been disputed, major changes have been made since first publication. These have come from several sources and reflect: (1) improvements in our knowledge of the composition and function of the intestinal flora, (2) changes in our perception of the cellular mechanisms of carcinogenesis, and (3) advances in the study of diet. It may be claimed with some justice that without our hypothesis many of these investigations would not have been carried out; however, the prospect of cancer prevention seems to me no closer than in 1969. The nature of the problem is made clear in recent publications.^{4,5} The ways in which we believe bacteria can cause cancer have multiplied, but our ability to control the flora has not advanced.

In 1976 I was awarded the British Gastroenterology Society's "Medal for Research" for my part in these studies.

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2. Drasar B S & Hill M J. Degradation of bile acids by human intestinal bacteria. (Schiif L, Cary J B & Dietschy J M, eds.) *Bile salt metabolism*. Springfield, IL: Thomas, 1968. p. 71-4.
3. Drasar B S, Renwick A G & Williams R T. The role of the gut flora in the metabolism of cyclamate. *Biochemical J.* 129:881-90, 1972.
4. Drasar B S, Montgomery F & Tomkins A M. Diet and faecal flora in three dietary groups in rural northern Nigeria. *J. Hygiene* 96:59-65, 1986.
5. Drasar B S & Cook P G S. *Intestinal bacteria and the initiation of cancer*. New York: Japan Scientific Societies Press, 1986. p. 221-9.