In summarizing these findings it can be stated that carcinoma of the large bowel has a low incidence rate in Africa and in other populations living in rural tropical areas, and that the rate is high in most urbanized industrialized countries. The low incidence rates in Africa are paralleled by low incidence rates of adenomatous polyps which have a clear association with carcinoma in high incidence areas.

The rarity of ulcerative colitis and of diverticular disease in Africans is of importance because it indicates differences in bowel physiology and behaviour which may be relevant to an understanding of the etiology of carcinoma of the large bowel.

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Possible Relationships Between Bowel Cancer and Dietary Habits

I propose to try to construct a tentative hypothesis of the possible cause of bowel cancer which is consistent with the clinical, pathological and epidemiological information which has been presented by Dr Morson, Professor Hutt and Dr Templeton.

I would like first to reinforce the close relationship between bowel cancer and economic development which has been outlined by Professor Hutt and Dr Templeton, by considering the rise in incidence of this form of cancer which has accompanied or followed the adoption by American negroes of the food habits of the white population. It can be assumed that initially negro slaves got as little bowel cancer as do Africans today. Thirty years ago, when much more maize meal was eaten by American negroes, particularly in the south, than is the case today, their incidence of bowel cancer was little more than half that of Caucasians (Lawrence 1936), a difference which has subsequently almost completely disappeared (Doll 1969).

Other examples of growing evidence of bowel cancer with adoption of western ways of life, and diet in particular, are the steady rise in incidence of this tumour in Puerto Rico (1968) where American type diet is becoming increasingly popular, and the fact that Japanese emigrants to Hawaii and California quickly depart from the low incidence characteristic of Japan, and within a generation almost catch up with their white compatriots (Wynder & Shigematsu 1967, Stemmermann 1970).

Relationship between cancer and other noninfective diseases of the bowel: Other noninfective diseases of the large bowel, such as adenomatous polyps, diverticular disease, ulcerative colitis and, with a generation gap, appendicitis, have a geographical distribution similar to that of bowel cancer. Some of these conditions, polyps in particular, tend to occur concurrently in the same patient. This association suggests related causative factors (Burkitt 1969, 1970).

Dietary change as a probable causative factor: The following observations strongly suggest that bowel cancer is closely related to diet:

(1) Diet is the most important factor affecting the environment of bowel mucosa.
(2) Epidemiologically bowel cancer is closely associated with highly processed foods, being rare in all less developed communities.
(3) Bowel cancer is rare in all animals.
(4) The gastrointestinal canal and the bronchi are the only epithelial-lined ducts highly prone to cancer, and they are the only ones in which we can alter the contents.
(5) Bowel carcinogens given to experimental animals give rise to no tumours in a loop of bowel surgically isolated and consequently no longer conveying fæcal matter (Spjut & Spratt 1965).

Possible relationship between bowel cancer and cellulose deficiency in the diet: A close relationship has been demonstrated between the unabsorbable cellulose content of the diet and bowel behaviour and its contents. A diet rich in unabsorbable roughage passes more rapidly through the bowel and produces large, soft stools with little odour (Walker 1947, 1961, Walker & Walker 1969, Walker *et al.* 1970).

Diverticular disease of the colon, which is epidemiologically associated with bowel cancer, is now believed to be caused by increased intraluminal pressures resulting from the effects of a low-residue diet (Painter 1968, 1970).

Any potential carcinogen in a constipated colon will not only be concentrated in the reduced fæcal mass but will also be longer in contact with the bowel mucosa (Oettlé 1967, Higginson 1967). Both these factors could enhance the carcinogenicity of any noxious bowel contents.

Possible relationship between bowel cancer and bacterial flora: The following observed facts suggest that bacteria may play a part in the induction of bowel cancer.

(1) When carcinogens capable of producing intestinal cancer are given orally to experimental animals their maximum effect is normally in the proximal bowel, whereas the maximal incidence of bowel cancer in man is in the distal colon where bacterial proliferation is maximal.

(2) Tumours are rare in the small intestine which has rapidly passing and relatively abacterial contents.

(3) Carcinogens which produce intestinal tumours in normal rats are ineffective if the rats are kept in a sterile environment with resulting bacteria-free fæces (Stewart 1967).

(4) Epidemiologically bowel tumours are related to western-type diets which are known to alter the bacterial flora of the intestinal content (Aries *et al.* 1969).

(5) Bacteria can cause the degradation of normal bile salts to form known carcinogens (Hill *et al.* 1971).

(6) A greater proportion of bile salts can be recovered from the fæces of Bantu living on a high residue diet in South Africa than from the fæces of Europeans on a more refined diet (Antonus & Bersohn 1962). This suggests that part of the bile salts of the latter has somehow been disposed of, possibly by bacterial action.

(7) Differences between the bacteria in the fæces of Africans and Europeans have been demonstrated (Aries *et al.* 1969).

Facts which must be considered when formulating a hypothesis for the possible cause of bowel cancer:

(1) The association between bowel cancer and other types of noninfective disease of the bowel geographically and in individual patients.

(2) The relationship between these diseases and cellulose-depleted diets.

(3) The relationship between colon cancer and bacterial flora of the gut in experimental animals.

Tentative Hypothesis

Alterations in diet from traditional patterns to the more highly processed foods of economically developed communities, and particularly changes in the carbohydrate content, alter the bacterial flora in the gut (Hoffmann 1964). This could lead to degradation of bile salts and so to the formation of carcinogens (Hill *et al.* 1971).

With a cellulose-depleted diet and resultant colonic stasis, such carcinogens in the fæces would not only be concentrated in the smaller fæcal mass but would be in contact with the mucosa for a prolonged period. The potential activity of such carcinogens might be enhanced by a combination of these factors.

Benign adenomas and ulcerative colitis might be caused in a similar manner, whereas diverticulosis is believed to be solely due to the removal of fibre from the diet and the resultant stasis (Painter & Burkitt 1971).

Conclusion

There appears to be a direct relationship between the prevalence of noninfective disease of the large bowel and the cellulose content of the diet. It may therefore be possible to reduce the incidence of these diseases by retaining the cellulose in carbohydrate foods. Such action could be taken before the mechanisms of carcinogenesis are understood. The situation could be paralleled by that of smoking and bronchial carcinoma.

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