Polyps and colorectal cancer in South African Blacks

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SUMMARY This study reflects the fact that cancer of the large bowel is uncommon in South African Blacks, and that colorectal polyps do not appear to constitute a precursor to most colorectal cancers. Furthermore, it is shown that dietary factors associated with this cancer in Western populations are not evident in the Black population. In the South African White population, however, the disease behaves in a similar way to that observed in Western countries. Other definitive differences found were the absence of multiple synchronous cancers and diverticular disease in the Blacks with colorectal cancer. It is thus postulated that dietary factors are absent, or have not been present for a sufficient length of time to influence the development of polyps or polyp-cancer sequence in this population. It is also possible that the adenoma-carcinoma progression observed in Western countries may not be relevant to the development of all colorectal carcinomas in communities such as those reported here.

Colorectal cancer is the second most common cancer in many Western countries.¹ It is, however, uncommon in developing societies. The incidence in South African Blacks is one of the lowest in the world.² Thus the mortality rate for the period 1968-71 was 0.8 per 100 000 population. This is in striking contrast with the Johannesburg White population, with a mortality rate of 13 per 100 000 population (Unpublished data). (Table 1).

During a 12-year period (1957-68) 96 cases of large bowel cancer were diagnosed from an urban Black population of at least one million.³ During the same period, only six adenomatous polyps were observed as surgical specimens. Isaacson *et al.* (1978)² confirmed the low occurrence, and, in addition, showed that no significant alteration in incidence had occurred over the past 20 years.

The purpose of this study is (1) to examine some characteristics of colorectal cancer in Black and White patients treated at Baragwanath and the Johannesburg General Hospital, and (2) in particular to examine the relevance of the adenoma-carcinoma sequence in Black patients with carcinoma.

Background

Johannesburg, the largest city in South Africa, has a population of 1.5-1.75 million of whom over a million are Blacks.⁴ Most live in Soweto, on the outskirts of Johannesburg. The Soweto population comprises those urban born and bred, and rural immigrants of 30 to 50 years standing. Hospital services for Soweto are provided by Baragwanath Hospital, a 2714 bed hospital dealing with approximately 45 000 adult medical and surgical inpatients a year, and 140 000 outpatients. Two hundred more beds are provided at the central Johannesburg General Hospital, where 700 beds for White patients are available.

A single pathological service analyses all specimens from both institutions. The local White community consumes approximately the same diet as Whites in Western countries.⁵ The diet of the Black patients analysed in this study, is reported below.

Table 1 *Mortality rates for Johannesburg populations from colon cancer, 1968-71 (per 100 000 population)*

Age group (yr)	Whites	Blacks
All ages	13.1	0.8
45-64	24.5	2.2
65+	55.0	6.5

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Methods

PATIENTS

Two-hundred-and-five Black patients with colorectal cancer diagnosed between January 1969 and June 1978, and 123 White patients with colorectal cancer who were treated in the surgical wards from 1974 to 1976 inclusive, are described. The final diagnosis in all cases was based on histological evidence. The Black patients comprised two groups: (1) 179 patients seen from January 1969 to July 1977, when data were obtained from hospital files, and (2) 26 patients who were personally examined and interviewed by one of the authors between August 1977 and June 1978.

The variables assessed were age, sex, clinical presentation, site of tumour, and presence of associated adenomatous polyps and diverticular disease. In addition, the second group of 26 patients was questioned as to occupation, habitat, and diet. A semiquantitative assessment of their diet was undertaken.

All reports of the biopsies and resected large bowel specimens were retrieved from the routine surgical pathology files. The macroscopic description was studied in each report and the recorded absence of polyps was noted. Specimens of surgically resected colons were available for histopathological investigation in 79 Black and 75 White patients: these specimens were re-examined for polyps related to the actual malignancy, or separate from the tumour.

Results

SEX, AGE, AND SITE

The male:female ratios in the Black and White groups were 1.5:1 and 1.7:1 respectively.

The highest incidence in the Black and White patients was in the 6th and 8th decades respectively (Table 2). The former figure is the same as that found in Western communities. The latter figure may not reflect the true maximum age incidence in the Johannesburg White population, as selection is biased towards the older age groups at that particular hospital.

Table 2 Age distribution of patients with colorectal cancer

Age group (yr)	Black patients	White patients
15-19	1	2
20-29	8	1
30-39	21	3
40-49	44	7
50-59	52	12
60-69	44	37
70-79	19	46
80+	3	15
Unknown	13	—

There appeared to be little difference in the tumour site in the two racial groups. In Black patients 59% of tumours occurred in the rectum and rectosigmoid areas; 15.6% on the left side of the colon; 6.4% in the transverse colon; and 13.7% in the right side of the colon. The corresponding figures for the White group were 55.3%, 23.6%, 4.9%, and 15.4% respectively. These figures closely resemble those from Western countries. If the large bowel is divided into the left and right sides of the splenic flexure,⁶ the ratio of the right- to left-sided tumours is almost identical in Black (1:3.7) and White (1:3.9) population groups, a finding which applies to most reported series, whether from high or low incidence areas.

RELATIVE INCIDENCE IN MEN AND WOMEN

In Blacks, of the 121 (59%) tumours of the rectum, 59% were in men and 41% in women, while of 85 (42%) cancers of the colon, 56% were in men and 44% in women. The distribution was very similar in Whites. Of 68 (55%) rectal tumours, 53% were in men and 47% in women, and of 53 (44%) colon tumours, 57% were in men and 43% in women.

CLINICAL PRESENTATION

Details of clinical presentation were obtained in 131 Black and 123 White patients. The most common presentation in the former group was rectal bleeding (50.4%). Next in frequency were intestinal obstruction (18.3%), abdominal mass (9.3%), abdominal pain and weight loss (9.2%), rectal mass (4.6%), ascites (3.1%), and miscellaneous symptoms (3.8%). In a few cases, the mode of presentation was not clear. In the White group presenting symptoms were rectal bleeding (37%), change in bowel habits (26.6%), abdominal pain (16.1%), intestinal obstruction (10.6%), anaemia (6.5%), perforation (2.4%), and anal symptoms (1.6%). The greater frequency of obstruction, weight loss, ascites, and abdominal mass as presenting features in the Black patients suggests late presentation in this group.

Frequency of polyps

Two Black patients with multiple adenomatous polyposis had associated colon cancer (familial studies not performed). Four Blacks had polyps associated with the tumour and in two other cases polyps separate from the tumour were present. In 11 White patients there was histological evidence that the malignancy had arisen in association with a benign neoplastic polyp and two of these cases had polyps elsewhere in the colon. Another 14 cases showed microscopic evidence of benign neoplastic polyps not associated with the tumour. Thus, 25 cases had polyps in the resected specimens (33.3%) as against 8% in Blacks ($\chi^2=10.18$, $DF=1$, $P<0.05$).

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Multiple synchronous cancers

None of the Black patients had multiple cancers, whereas this occurred in seven White patients (6%).

Diverticular disease

None of the Black patients had diverticular disease, whereas this was present in 16 (13%) of the White patients.

Occupation and background

Regarding the occupation of 94 Black patients in whom this could be ascertained, 51 were either production workers or in the service industry, 16 were housewives, 10 were domestic servants, nine were pensioners, and only eight were in the higher socioeconomic categories. Of the 26 interviewed patients, five were referred to Baragwanath Hospital from rural areas, and 21 were either born in Johannesburg or had resided there for over 30 years.

Diet

The Black patients consumed a partially Westernised diet, with maize meal and bread the staple food. Additional foods included sugar, milk, tea, coffee, vegetables, soft drinks, and tinned fish. This is similar to the diet consumed by urban Blacks.⁵ Of the 26 patients questioned, meat was eaten once daily by 13, two to three times per week by seven and seldom eaten by six.

Discussion

In most Western populations the incidence of colorectal cancer ranks only second to lung cancer in men, and breast cancer in women. The epidemiology of colorectal cancer indicates that dietary agents play a vital role in the aetiology of the disease.¹ Genetic factors, however, are undoubtedly important in many instances.⁷ The exact nature of the dietary factors remains controversial. Burkitt *et al.*¹⁸ believe that a high crude fibre diet, leads, *inter alia*, to a more rapid transit of bowel contents, thereby reducing the opportunity for the bacterial production of carcinogens and also minimising the time of action of such carcinogens. Hill⁹ and Reddy and Wynder¹⁰ postulate that the most important fact is the amount of dietary fat; this determines the faecal concentration of bile acids and the nature of faecal bacterial flora, which promote the production of carcinogens or co-carcinogens from the bile acids. Another hypothesis links beef consumption with colonic cancer.¹¹ The evidence for hereditary factors is the increased incidence of colorectal cancer in relatives of probands with the disease.⁷ In addition, there is the definite

hereditary relationship in the development of large bowel cancer in familial polyposis and Gardner's syndrome. In this respect, it is noteworthy that familial polyposis is very rare in South African Blacks, only three cases having been reported.^{3,12} This indicates that the adenoma-carcinoma sequence can occur in this population in the presence of a strong predisposing factor.

The Johannesburg environment, with its two main divergent population groups, facilitates the study of the aetiology and pathogenesis of colorectal cancer. In the White population the incidence is similar to that in Western countries, and the findings in this study indicate that the sex ratio, site distribution, and incidence of coexisting adenomatous polyps and synchronous multiple cancers were all very similar to those found in Great Britain and North America. The similarity in diet, and the finding of an equal incidence of diverticular disease in the Johannesburg White population with colorectal cancer to that in Western countries, also suggests that some of the environmental factors which may effect colon physiology and pathology are similar.

The present study shows that among the Black population colorectal cancer is an uncommon disease. The differences in clinical presentation appear to indicate that Black patients present with late features such as obstruction, weight loss, and ascites, compared with earlier symptoms such as change in bowel habit and abdominal pain which occur more frequently in the White population.

The site distribution is very similar in the two groups, especially when considering this in terms of the ratio of left- to right-sided large bowel cancers. It has previously been pointed out that this ratio does not differ between other low or high incidence areas or populations.¹³

The most definitive differences found between the two population groups in this study relate to the absence of macroscopic polyps and synchronous cancers, and the absence of diverticular disease in the Black population with colorectal cancer. Although colonoscopy was not carried out on patients with cancer, and it is possible that adenomas were present undetected in other parts of the colon, the extreme rarity of adenomas has been confirmed by other workers. Thus, Bremner and Ackerman (1970)³ reported the absence of adenomatous polyps in 14000 necropsies. If it is accepted that diverticular disease develops as a result of dietary factors, in particular a lack of fibre, the absence of this disease indicates that these dietary factors have been absent, or at least have not been present for a sufficient length of time to allow for the development of diverticular disease in this cancer population.

The diet of Black patients with colorectal cancer

who were interviewed showed that meat and fat intake was low in most cases, the staple foods being maize meal and bread. This is in keeping with the diet of Soweto Blacks, who, despite increasing Westernisation, still consume a diet containing more fibre and less animal fat and protein than the diet consumed by White populations.⁵ Also, the socioeconomic status of most of the patients makes it highly improbable that an expensive item such as meat was consumed in appreciable amounts.

This, plus the supposed long time interval between the appearance of a dietary aetiological factor and the subsequent development of colorectal cancer, makes it unlikely that suspected aetiological factors such as animal fat, meat, a high calorie and low fibre diet played a major part in the development of cancer in this particular group of patients.

Another important difference between the population groups is the usual appearance of colorectal cancer without accompanying adenomatous polyps in the Black patients. This is in clear contradistinction to the White patients where the incidence of this association is similar to that found in Western countries. This difference is unlikely to be due to observer error, as all tissues are examined by the same group of pathologists. Furthermore, all the resected specimens of both Black and White patients

were originally examined by the same group of pathologists and re-examined by one pathologist who confirmed the presence of an intramucosal adenoma in one Black. Other non-Western communities, including several regions in Africa and Iran, have also reported the rarity of colorectal cancer and particularly the rarity of polypoid adenomas.^{14 15}

A causal association between polypoid adenomas and colonic carcinomas has been demonstrated on a pathological basis. Thus it has been shown that most, if not all, colorectal carcinomas arise in preformed adenomas.^{16 17} There consequently seems little doubt that this pattern of cancer development does occur in Western populations. This, however, may not necessarily be the only route of cancer development in the Black population studied here.

If the adenoma-carcinoma sequence were a common event, and as in this situation polyps tend to precede the appearance of cancer by a number of years, it might be expected that polyps would be more common in Black patients with cancer and in the general population, and that any change in diet, which might be responsible for the development of cancer in this manner, would lead initially to the appearance of adenomatous polyps. This does not appear to occur. The reason for the low incidence of neoplastic polyps in the Black patients is that the

Figure Photomicrograph showing a large area of dysplasia involving flat colonic mucosa. $\times 72$ (original magnification).

cancer could theoretically have arisen *de novo*—that is, without a precursor lesion. This is, however, unlikely in view of current concepts of cancer development.¹⁸ Another possible mechanism is that the cancer originated in a single neoplastic polyp which was destroyed by the malignancy as it progressed. Another, and more likely, alternative is the presence of a precursor lesion in flat mucosa, examples of which have been described by Bussey.¹⁹ Preliminary results of a prospective study on the examination of apparently 'normal mucosa' in Black patients with large bowel cancer shows the presence of flat mucosal lesions in which dysplasia of epithelium is present (Figure). It is possible that these flat mucosal lesions progress to cancer without initially developing into polyps. The fact that the adenoma-carcinoma sequence does not occur in most of the Black patients and does indeed occur in a significant number of the White group is consistent with the hypothesis of Hill *et al.* (1978),¹⁷ that an environmental agent (dietary fat, meat) would cause adenomas to form and grow in adenoma-prone persons. And, on the basis of this substrate, a carcinogen would cause malignancy in a high proportion of large adenomas.

This would apply to the White group. The infrequent occurrence of adenomas in the Blacks could be similarly explained by the low intake of dietary fat and meat and perhaps a high fibre intake. If we pursue Hill's hypothesis, a carcinogen can occasionally induce malignancy in normal tissue, and the risk of carcinoma developing in persons who are not adenoma-prone is very small. This could explain the formation and low incidence in the Black population. This study indicates that the classical adenoma-carcinoma sequence observed in Western countries may not be relevant to the development of all colorectal cancers in communities such as reported here. Furthermore, it is suggested that dietary factors are protective against the formation of polyps and carcinoma in the Black population.

We wish to thank the Superintendents of the Baragwanath Hospital and Johannesburg General Hospital for permission to publish. In addition we wish to thank Dr A R P Walker for assistance in the preparation of this article.

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