Early diagnosis of colorectal cancer: a review[1]

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In the United Kingdom, 16430 persons died of colorectal cancer in 1978. This made large bowel cancer the second highest malignant cause of death after lung cancer. Over the last 20 years, however, there has been little improvement in the outlook, with 24% of patients registered in 1959 surviving 5 years compared with only 30% of those registered in 1975 (OPCS 1982).

It has been known for a considerable time that the most important single factor in determining prognosis in colorectal cancer is its spread at the time of resection. Dukes (1932) described a method of staging which, with modification, remains the most widely accepted. Cancer which remains confined to the bowel wall (Stage A) carries a 5-year survival of 80–90%. When the tumour has penetrated the bowel wall (Stage B) the 5-year survival is reduced to 45–58%, and the presence of lymph node spread (Stage C) reduces it still further to 12–27% (Stower & Hardcastle 1983, Gill & Morris 1978). When distant metastases are present, almost all patients are dead within one year. Regrettably the proportion of cancers in the good prognosis group (Stage A) presenting to a district general hospital is small (6–8%) (Stower & Hardcastle 1983, Gill & Morris 1978).

There is good evidence that the majority of colorectal cancers develop in benign adenomas (Morson 1974), and this premalignant lesion is often easily treated by endoscopic removal. If these adenomas can be identified and removed, the incidence of colorectal cancer may be decreased and subsequently the mortality from this disease reduced.

Early diagnosis in symptomatic patients

Symptoms which might be attributed to colorectal cancer may often be vague and are extremely common. In a randomly selected sample of the population aged over 45 years, 6.6% admitted to recent rectal bleeding, 12.3% to a change in bowel habit and 10.8% to abdominal pain (Farrands & Hardcastle 1983*a*). Screening on the basis of symptoms is not helpful. Of 1533 persons randomly selected from general practitioners' lists, 128 (8.3%) admitted to a symptom suggestive of bowel cancer: all were investigated but only two adenomas in one individual were detected (Farrands & Hardcastle 1983*a*).

The average delay between the onset of symptoms and surgical treatment is 8–9 months. Only a few weeks are attributable to hospital delay. Delay by the patient in consulting the doctor is due to many factors: the commonness of symptoms and the lack of insight into their significance, the wish not to 'bother' the doctor, fear of cancer, etc (Holliday & Hardcastle 1979). When the patient does see his family practitioner, he may be one of many with bowel symptoms or rectal bleeding and the doctor is faced with the problem of deciding whom to refer for investigation.

Early symptomatic diagnosis by faecal occult blood testing and flexible fibreoptic sigmoidoscopy in 129 symptomatic patients reduced time to diagnosis to 17.3 days in 4 carcinomas (3 Stage B, 1 Stage D) and 4 adenomas, compared to 141 days in 4 carcinomas in a control group (Hardcastle *et al.*, unpublished data). However, it is unlikely that this improvement will alter survival and, indeed, in the United States of America a reduction from 6 months to 2 months made no difference to survival (Welch & Donaldson 1978).

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Population screening for colorectal cancer

Detection of occult blood in faeces is at present the only practical method of population screening for colorectal cancer, and can be performed using a guaiac-impregnated slide test such as Haemoccult (Greegor 1971). Its use in studies will be discussed with particular reference to compliance, yield, workload generated and false-negative rate.

Compliance

The success of any screening programme depends on its acceptability to the group at whom it is aimed. The compliance rate of a population usually refers to the proportion of the whole group who participate in the programme. Many factors influence the acceptability of an occult blood slide test in the population to whom it is offered.

Firstly, the health consciousness of the individuals screened is an important factor. In the United States, individuals attending a 'check-up' clinic have an 80–90% compliance rate, as do members of the Armed Forces (Winawer *et al.* 1980, Glober & Peskoe 1974, Miller & Knight 1977). In the United Kingdom, a similar trend can be demonstrated as individuals who are health conscious have a higher compliance rate (Farrands, Chamberlain *et al.* 1983).

Secondly, the method of presentation directly affects compliance. If the tests are distributed through the post from a hospital department without prior warning, the compliance is low both in the United Kingdom and the United States (15–26%). If the tests come from the patients' own family doctors, the proportion completing the test increases (38–45%) (Farrands, Chamberlain *et al.* 1983). Prior education in the form of letters and interviews can also improve compliance – up to 51% in a group of patients from the Nottingham area (Farrands, Chamberlain *et al.* 1983).

Compliance is lower in the elderly, e.g. only 27% of those over 70 years accepted the invitation. Females are more likely to complete the tests, perhaps because they have greater opportunity to collect the specimens (Farrands, Chamberlain *et al.* 1983).

Workload generated

The percentage of returned tests showing a positive result depends on the sensitivity of the particular test used. A sensitive test such as Fecatest has a high false-positive rate unless a restricted diet is observed, whereas a less sensitive test such as Haemoccult has only a 2–5% positive rate (Hardcastle *et al.* 1983, Farrands *et al.* 1981). Since those subjects with positive tests will require investigation, the workload generated will depend on the sensitivity rate.

Some of the 'false-positives' are due to dietary constituents such as red meat and vegetables containing peroxidases, such as horseradish. Conversely, foods containing much vitamin C may alter a test from positive to negative. Thus one means of increasing the specificity of a test is to ask the group to be screened to modify their diet for the period of the test. This may, however, reduce the compliance.

In the United Kingdom four major screening projects using Haemoccult have been conducted (Table 1). The overall positivity rate of those subjects who completed the test was

Table 1. Screening for colorectal cancer in the United Kingdom

Reference	Total offered screening	Total accepted (%)	Positive (%)	Yield (rate/1000 acceptors)	
				Carcinoma	Adenoma
Hardcastle *et al.* 1980	1638	713 (45)	27 (3.8)	2 (2.8)	4 (5.5)
Million *et al.* 1982	3481	1179 (34)	31 (2.7)	2 (1.7)	3 (2.5)
Farrands *et al.* 1981	8925	2439 (27)	124 (5.1)	4 (1.6)	8 (3.3)
Hardcastle *et al.* 1983	10253	3613 (37)	77 (2.1)	12 (3.3)	27 (7.5)
Total	22297	7944 (36)	259 (3.3)	20 (2.5)	42 (5.3)

3.3%. One hundred and eighty-two of these patients were investigated by rigid sigmoidoscopy and double contrast barium enema (Hardcastle *et al.* 1980, Million *et al.* 1982, Farrands *et al.* 1981); 8 (4.4%) cancers and 15 (8.2%) adenomas were detected. In the fourth study (Hardcastle *et al.* 1983) 77 persons were investigated by the same techniques but with the addition of flexible fibreoptic sigmoidoscopy. In this group, 12 (15.6%) cancers and 27 (35%) adenomas were detected. Whilst flexible fibreoptic sigmoidoscopy increases the work involved in screening, it also increases the yield substantially. This procedure is accurate in the diagnosis of lesions in the sigmoid colon, an area often difficult to examine radiologically (Farrands, Vellacott *et al.* 1983) particularly when diverticular disease is present.

False-negative rate

Diagnosis by occult blood tests depends upon tumours bleeding into the lumen of the bowel. Doran & Hardcastle (1982) have shown that cancers may bleed intermittently and it is not uncommon for no blood to be lost for several days. Clearly this will lead to a number of cancers being missed by an occult blood test.

Farrands & Hardcastle (1983*b*), testing 61 patients with known colorectal cancer using Haemoccult, showed a false-negative rate of 25% on 3-day testing, this being reduced to 9% by 6-day testing. Rehydration of the test slides increases the sensitivity of the test (Macrae & St Johns 1982) but at the price of increasing the false-positive rate and hence the workload.

Yield

A controlled study of colorectal screening has recently been completed using 20 000 persons identified from general practitioners' lists in Nottingham (Hardcastle *et al.* 1983). In 3613 persons accepting the test, 12 carcinomas were identified. Nine (75%) were Dukes' Stage A, 2 were Dukes' Stage B and one was a Stage C. Twenty-seven patients had a total of 40 adenomas, of which 12 were greater than 2 cm and severe dysplasia was present in 2, both of these factors being associated with a high risk of malignant change. These detected neoplastic lesions represent a rate of 3.3 for cancers and 7.5 for adenomas per 1000 individuals screened.

This study included a control population, with which direct comparisons may be made. In this group of 10 272, at one-year follow-up, 10 cancers (4 Stage B (2 palliative resections), 4 Stage C and 2 already with liver metastases) and 5 adenomas have presented. Thus the rate per 1000 in this group is 1.0 for cancers and 0.5 for adenomas.

By screening an asymptomatic population, therefore, it has been possible to increase the detection rate of cancers by 3 times and of adenomas by 15 times. Seventy-five percent of the cancers detected were Dukes' Stage A compared with the usual 6–8% presenting at this stage with symptoms. In addition, by removal of adenomas with a high risk of malignant change, the development of further cancers may be reduced. In West Germany a rise in the percentage of Dukes' Stage A colorectal cancers, from 4% to 35%, has been noted since the introduction of a free screening service for colorectal cancer (Cappel *et al.* 1984).

Conclusion

The ultimate aim of any early diagnosis/screening programme for colorectal cancer is to reduce the mortality from the disease. Screening has been shown to be effective in detecting colorectal cancer, and at a less advanced pathological stage than occurs in symptomatic patients. The question of whether survival is affected can only be answered by properly controlled studies carried out over a number of years. When this information is available it will be possible to determine whether population screening for colorectal cancer is a justifiable exercise to be employed in the Health Service.

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