Early detection of colorectal cancer using faecal occult blood tests

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Summary
Five thousand and twelve asymptomatic patients over the age of 40 years who were on a normal diet were asked by their general practitioners to perform a Hemoccult (Röhn Pharma (Noristan)) faecal occult blood test over 3 days. Of the 3422 patients (68%) who completed the test, 99 (3%) had a positive result. The patients with a positive result then again performed the Hemoccult test, this time over 6 days on a restricted diet. Thirty-two of these patients had a positive result on the second test.

Only the 32 patients who had a positive result for the second test were fully investigated (including double-contrast barium enema and colonoscopy); 27 patients (84%) were found to have neoplastic disease. Twelve had invasive carcinoma (5 Dukes' A, 2 Dukes' B and 1 Dukes' C), 6 of these also having 10 adenomas, while the other 15 had 27 adenomas which were identified and removed at colonoscopy. Barium enema missed 3 carcinomas (all Dukes' A) and identified only 16 (43%) of the 37 adenomas. Those patients found to have a negative result for the second Hemoccult test are being followed up.

The case for the development of screening programmes for the detection of colorectal neoplasms has been forcefully made by various authors. Early detection of colorectal cancer improves the 5-year survival rate, and follow-up programmes directed at patients particularly at risk (viz. those with ulcerative colitis, polyposis coli and colorectal carcinoma in the family) may prevent malignant transformation.

Colorectal cancer is now the second most common malignant tumour in the Western world. In spite of the introduction of combination chemotherapy, radiotherapy, immunotherapy and improved surgical techniques, the overall survival rate has improved only very modestly during the past 30 years. Prognosis is directly related to the degree of centrifugal spread of the tumour. Patients with cancers limited to the bowel wall have a corrected 5-year survival rate of about 90%, whereas those with tumours with lymphatic spread have a 5-year survival rate of about 30%. Unfortunately, less than 50% of the colorectal cancers seen are localized at the time of diagnosis.

Colorectal adenocarcinomas probably pass through a benign adenomatous stage, and removal of adenomas should therefore reduce the risk of the development of invasive cancers. Patients who come to surgery for asymptomatic cancers rarely have metastases, and the 5-year survival rate approaches 90% in some series.

At present the only practical method of population screening for colorectal cancer is by the detection of occult blood in the faeces. Many screening programmes have been carried out and the majority show that approximately 65% of the tumours thus detected will be confined to the bowel wall. A successful screening programme must achieve both a high compliance rate and, in particular, a low false-positive rate. The present study was designed with these two points in mind.

General practice, where patients are seen on a continuing basis, is ideal for screening purposes. Seventy percent of patients are said to visit their doctor at least once a year, while 90% will have consulted their doctor once every 5 years. However, it is thought, that at least one member of the family will consult his general practitioner once a year, thus giving indirect contact to every family member.

Patients and methods
The screening programme was performed in five coastal towns in the Cape Province (Cape Town, Mossel Bay, George, Knysna and Plettenberg Bay). Ninety-five general practitioners affiliated to the research group of the South African Academy of Family Practice took part in the study. Doctors were asked to invite only asymptomatic patients between 40 and 75 years of age who were not receiving analgesic or anti-inflammatory agents to participate. Each participant was informed that there were no dietary restrictions. They were then asked to collect a stool sample, open the Hemoccult (Röhn Pharma (Noristan)) test card, smear faeces on the filter paper with a cardboard spatula and then reseal the address envelope. The cards were tested at the Gastro-intestinal Clinic of Groote Schuur Hospital by one of the authors or a trained research assistant. A blue discoloration occurring at 30 seconds was regarded as a positive result.

All patients with a positive result for the first test were immediately contacted and were asked not to eat red meat or to take vitamin C tablets before further collections of faecal samples. Each patient was then given another Hemoccult test card and was asked to repeat the sampling for a further 6 consecutive days.

Those patients with a positive test result for both tests had a full history taken and underwent clinical examination (including digital rectal examination, proctoscopy and rigid sigmoidoscopy). All of these patients subsequently had a double-contrast barium enema and colonoscopy. Those patients who had a positive result only for the first test were not fully investigated and underwent a further Hemoccult test 6 months later. Each Hemoccult slide kit contained slides for three stool specimens, three spatulas and an envelope with clear instructions.

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Results

Of the 5,012 patients on a normal diet who were invited to participate, 3,422 (68%) completed and returned their Hemoccult tests. Ninety-nine of these patients (3%) had a positive result. All patients who had a positive result underwent a second test over 6 days on a restricted diet (compliance rate 100%). Thirty-two of these patients had a positive result, and examination revealed neoplastic disease in 27 (84%) of these. Twelve patients had adenocarcinoma of the large bowel (9 Dukes' A, 2 Dukes' B and 1 Dukes' C) and, in addition, 6 of these 12 patients were found to have 10 further adenomas. The remaining 15 patients had 27 adenomas (1 patient having 10 adenomas).

On close questioning 4 of the 12 patients with adenocarcinoma were found to have symptoms, while 4 of the patients with adenomas were also asymptomatic.

Investigations

None of the carcinomas was identified by digital examination. Rigid sigmoidoscopy demonstrated 2 of the 12 adenocarcinomas (17%) and 3 of the 37 adenomas (8%). Double-contrast barium enema examination identified 9 of the 12 carcinomas (75%) and only 16 of the 37 adenomas (43%). Twenty-four of the 32 barium enemas were performed at Groote Schuur Hospital.

Of the 32 patients investigated, 28 (88%) underwent colonoscopy through to the caecum. The other 4 patients had already been diagnosed as having carcinoma by means of the barium enema, and preferred not to undergo an additional investigation before surgery. Colonoscopy identified the 3 carcinomas that were missed by double-contrast barium enema. These were all polypoid Dukes' A lesions and were situated in the caecum, transverse colon and sigmoid colon. Twenty-one of the 37 adenomas (57%) were identified at colonoscopy only.

Neoplasms

Nine of the 12 carcinomas (75%) were Dukes' A lesions, of which 4 showed no invasion beyond the submucosa. Two patients had a Dukes' B lesion and 1 patient a Dukes' C lesion. Eleven of the patients were treated by bowel resection and 1 by colonicoscopy polypectomy. Eight of the carcinomas were situated in the sigmoid colon, 3 were in the caecum and 1 was in the transverse colon.

Thirty-seven adenomas (≥ 5 mm) were found in 21 patients. Thirty-three of the 37 adenomas (89%) were situated distal to the splenic flexure. Thirty-five of the adenomas were removed by colonicoscopy polypectomy and 2 by colonoscopic resection. Ten of the adenomas were over 2 cm in size. Severe atypia was present in 3 adenomas (2 tubulovillous and 1 tubular adenoma).

All patients found to have a negative result for the second Hemoccult test are being followed up. Follow-up at present varies at between 3 and 11 months. All patients are asymptomatic. Thirty of the 67 patients underwent a third Hemoccult test while on a restricted diet 6 months after the initial test. All had negative results.

Discussion

The justification for population screening for a particular disease depends on the severity and incidence of that disease, and the cost and benefit of early detection. We believe that the high incidence of colorectal cancer among Whites and patients of mixed race in this country justifies the consideration of a screening approach.

The testing of stool samples for the presence of occult blood as an indication of gastrointestinal cancer is an old concept. Many authors have shown that approximately two-thirds of asymptomatic cancers diagnosed by faecal occult blood testing will be limited to the bowel wall; however, no study is available to determine whether the overall mortality rates in the long-term will be altered.

Any programme designed to make asymptomatic patients 'healthier' through screening must be able to demonstrate clearly that its benefits outweigh any costs or harm. We believe that the design of our study has produced an exceedingly low false-positive rate, with 84% of the patients investigated having neoplastic disease.

In spite of the two-stage design of our study, the overall yield of large-bowel neoplasms is very similar to that of other groups. Obviously the risk of increasing the incidence of false-negative reports will only become known through careful follow-up of these patients. Dietary restriction was deliberately not included in the first stage of our trial protocol in the hope that participation would be made less onerous. Compliance varied markedly in various practices, the range being 9 - 100%. The possible reasons for this will be discussed in another article.

Nevertheless, in relation to other studies our overall compliance rate of 67% compares favourably and would support the hypothesis that this test can be routinely introduced into the day-to-day activity of the general practitioner. The 3% positivity rate is similar to that of other studies of patients receiving a normal diet.

Bleeding from colorectal neoplasms is thought to be an intermittent event. A number of specimens are therefore preferable, in order to avoid missing any blood loss. For the same reason a single positive occult blood test cannot be ignored. In our study 3 of the patients who had adenocarcinomas had only 1 positive test out of 6 samples (Table 1).

There is still occasional controversy as to the relative value of the single-contrast and double-contrast barium enema, but considerable evidence now strongly favours the double-contrast examination as being superior for the diagnosis of colorectal cancer and adenomas. Double-contrast barium enema has been

| TABLE I. MEAN NUMBER OF POSITIVE HEMOCCULT SLIDES IN PATIENTS RECEIVING NORMAL OR RESTRICTED DIETS |
|---------|-----------------|-----------------|
| No. of | 1st test (normal diet; 6 slides) | Mean No. of slides positive (range) |
| patients | | |
| Adenomas | | |
| < 1 cm | 6 | 2/6 (1-3/6) |
| 1 - 2 cm | 8 | 4/6 (3-6/6) |
| > 2 cm | 7 | 5/6 (4-6/6) |
| Adenocarcinomas | | |
| Dukes' A | 9 | 3/6 (1-6/6) |
| Dukes' B | 2 | 4/6 (3-5/6) |
| Dukes' C | 1 | 2/6 |
| | | 3/12 (2-7/12) |
| | | 9/12 (1-12/12) |
| | | 9/12 |
| | | 9/12 |
| | | 9/12 |

![Image](https://via.placeholder.com/150)
shown to be unreliable in the detection of neoplasms in the caecum and sigmoid colon, particularly in the presence of diverticular disease\textsuperscript{20} or inadequate bowel preparation.\textsuperscript{21,22}

In our study 3 of the 12 adenocarcinomas and 21 of the 37 adenomas were missed by this examination. These rather depressing figures are almost identical to those from a recent screening programme in Nottingham, UK.\textsuperscript{41} It is therefore essential that all patients who have a positive result for Hemoccult testing while on a meat-free diet undergo colonoscopy even if results of a previous double-contrast barium enema examination are normal.\textsuperscript{23}

Thirty-seven adenomas were identified and removed. This is of great importance, for much evidence is available that many of these lesions are premalignant.\textsuperscript{9} If one assumes that the majority of flexible sigmoidoscopic examinations only reach the junction of the sigmoid and the descending colon, the potential for the detection of colorectal neoplasia has been enhanced tremendously by the addition of colonoscopy to traditional radiographic examination. The false-negative result of colonoscopy for adenomas measuring more than 1 cm has been reported to be of the order of 5 - 8%.\textsuperscript{24}

Barium enema, radiography and colonoscopy complement each other well. Colonoscopy enhances the sensitivity of the barium enema throughout the colon (especially in the upper sigmoid and distal descending colon), while the barium enema is especially useful in complementing colonoscopy at the hepatic and splenic flexures.

In conclusion, there is a fair possibility that continued screening using the Hemoccult test may result in a definite decrease in the mortality rate from cancer of the colon and rectum. Until prevention of this cancer becomes feasible, early detection will remain the best weapon in reducing the mortality.

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