ABC of colorectal cancer
Screening

John H Scholefield

Colorectal cancer is the third commonest malignancy in the United Kingdom, after lung and breast cancer, and kills about 20 000 people a year. It is equally prevalent in men and women, usually occurring in later life (at age 60-70 years). The incidence of the disease has generally increased over recent decades in both developed and developing countries. Despite this trend, mortality in both sexes has slowly declined. This decrease in mortality may reflect a trend towards earlier diagnosis—perhaps as a result of increased public awareness of the disease.

Surgery remains the mainstay of treatment for colorectal cancer, but early diagnosis makes it more likely that the tumour can be completely resected and thereby improves the chance of cure

Why screen?

Most colorectal cancers result from malignant change in polyps (adenomas) that have developed in the lining of the bowel 10-15 years earlier. The best available evidence suggests that only 10% of 1 cm adenomas become malignant after 10 years. The incidence of adenomatous polyps in the colon increases with age, and although adenomatous polyps can be identified in about 20% of the population, most of these are small and unlikely to undergo malignant change. The vast majority (90%) of adenomas can be removed at colonoscopy, obviating the need for surgery. Other types of polyps occurring in the colon—such as metaplastic (or hyperplastic) polyps—are usually small and are much less likely than adenomas to become malignant.

Colorectal cancer is therefore a common condition, with a known premalignant lesion (adenoma). As it takes a relatively long time for malignant transformation from adenoma to carcinoma, and outcomes are markedly improved by early detection of adenomas and early cancers, the potential exists to reduce disease mortality through screening asymptomatic individuals for adenomas and early cancers.

Colon cancer

Which screening test for population screening?

Education about bowel cancer is poor. A survey in 1991 showed that only 30% of the British population were aware that cancer of the bowel could occur. Such ignorance only adds to the difficulties of early detection for this form of cancer.

For a screening test to be applicable to large populations it has to be inexpensive, reliable, and acceptable. Many different screening tests for detecting early colorectal cancer have been tried. The simplest and least expensive is a questionnaire about symptoms, but this has proved predictably insensitive and becomes reliable only when the tumour is relatively advanced. Digital rectal examination and rigid sigmoidoscopy both suffer from the limitation that they detect only rectal or rectosigmoid cancers and are unpleasant and invasive.

Flexible sigmoidoscopy

Flexible sigmoidoscopy can detect 80% of colorectal cancers as it examines the whole of the left colon and rectum. A strategy of providing single flexible sigmoidoscopy for adults aged 55-65 years—with the aim of detecting adenomas—may be cost effective. A multicentre trial of this strategy for population screening is currently under evaluation.

Although flexible sigmoidoscopy is more expensive than rigid sigmoidoscopy, it is generally more acceptable to patients

Flexible sigmoidoscope: used for endoluminal visualisation and therapeutic removal of adenomas

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(it is less uncomfortable) and has much higher yield than the rigid instrument. Many nurses are now trained to perform flexible sigmoidoscopy, making potential screening programmes using this technique more cost effective. In a population screening programme, uptake of the offer of the screening test is crucial. Uptake is likely to be around 45%, and, of these, 6% will subsequently need full colonoscopy. The effect that this will have on the incidence of and mortality from colorectal cancer is uncertain until the completion of the multicentre trial in 2003.

Colonoscopy

Colonoscopy is the gold standard technique for examination of the colon and rectum, but its expense, the need for full bowel preparation and sedation, and the small risk of perforation of the colon make it unacceptable for population screening. Colonoscopy is, however, the investigation of choice for screening high risk patients (those at risk of hereditary non-polyposis colon cancer or with longstanding ulcerative colitis).

Barium enema

Barium enema, like colonoscopy, examines the whole colon and rectum, and, although it is cheaper and has a lower complication rate than colonoscopy, it is invasive and requires full bowel preparation. Whereas colonoscopy may be therapeutic (polypectomy), barium enema does not allow removal or biopsy of lesions seen. There are no population screening studies using barium enema.

Faecal occult blood tests

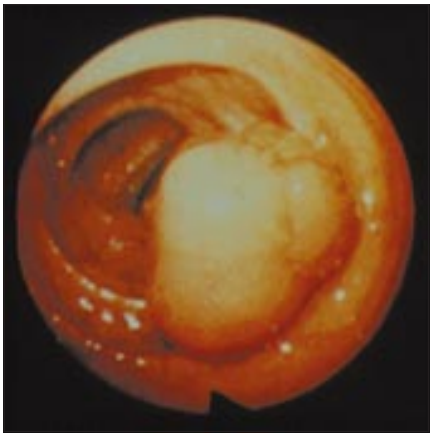
Faecal occult blood tests are the most extensively studied screening tests for colorectal cancer. These tests detect haematin from partially digested blood in the stool. Their overall sensitivity for colorectal neoplasia is only 50-60%, though their specificity is high. In screening studies of faecal occult blood tests, individuals are invited to take two samples from each of three consecutive stools. Compliance is around 50-60%, but with population education this might be improved. Individuals with more than four out of six positive tests (about 2% of participants) need colonoscopy.

Several large randomised studies have shown that screening with faecal occult blood testing is feasible, and two studies have shown that such screening reduces the mortality from colorectal cancer. In a study in Nottingham, for every 100 individuals with a positive test result, 12 had cancer and 23 had adenomatous polyps. The cancers detected at screening tended to be at an earlier stage than those presenting symptomatically (Dukes's A classification: 26% screen detected *v* 11% in controls). The disadvantage of screening with faecal occult bloods is its relatively low sensitivity—a third to a half of cancers will be missed on each round of screening. The Nottingham data suggest that screening every two years detects only 72% of cancers. This could be improved by testing annually and using more sensitive immunologically based faecal occult blood tests.

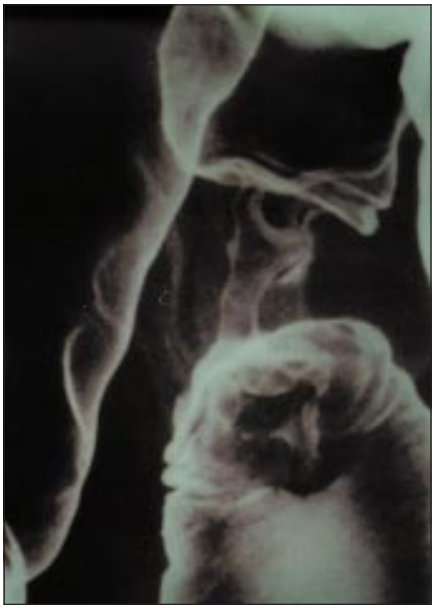
Who should be screened?

Although about 20% of the population will develop adenomatous polyps, only 5% of these will develop colorectal cancer. This equates to a 1 in 20 lifetime risk for colorectal cancer. The cancer occurs most often in the age group 65-75 years, but for adenomas the peak incidence is in a slightly earlier age group (55-65 years). Thus population screening for colorectal cancer should target both these age groups.

In addition, some people inherit a much higher susceptibility to colorectal cancer. Some inherit a well



Colonoscopic view of colonic adenoma (about 1.5 cm diameter)



Double contrast barium enema showing carcinoma of sigmoid colon

CT colography

- CT (computed tomographic) colography—virtual colonoscopy—is a new radiological technique that may have a role in population screening
- Although it requires full bowel preparation, highly expensive computed tomography scanners, and computing facilities, it is minimally invasive, and views of the whole colon can be obtained in five minutes
- Preliminary data suggest that this technique is as sensitive as colonoscopy or barium enema for detecting large polyps and cancers
- As yet, no trials of CT colography in population screening have been published
- CT colography has the potential to be cost effective and to reduce the need for colonoscopy in population screening

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recognised single gene disorder, such as familial adenomatous polyposis or hereditary non-polyposis colon cancer, whereas most inherit an undetermined genetic abnormality. These people tend to develop colorectal cancer before the age of 50, and therefore screening in this high risk population needs to be tailored to each individual's risk pattern. They may also be at risk for cancers at other sites, and screening for ovarian, breast, and endometrial cancers may be appropriate in some of these cases. The advice of clinical geneticists in these cases can be invaluable.

Cost effectiveness of screening

If screening for colorectal cancer is to be acceptable to healthcare providers it must be shown to be cost effective. Estimates of the cost of screening for colorectal cancer range from £1000 to £3000 per life year saved, depending on the screening technique used. The cost of using faecal occult blood testing would be the lowest—similar to estimates for breast cancer screening.

Cost estimates are associated with several unknown factors. The factors that cause greatest concern to those considering funding screening programmes are the cost of cancers missed and the potential damage caused to asymptomatic individuals by invasive procedures such as colonoscopy.

Potential harm from screening

Although it has been suggested that considerable anxiety and psychological morbidity may be caused by inviting populations to participate in screening for colorectal cancer, little evidence exists to substantiate this. Indeed in the Nottingham trial no longstanding psychological morbidity from the screening programme was found. Similarly, no evidence exists that screening for colorectal cancer leads to false reassurance from negative tests.

Complications from colonoscopy (perforation and haemorrhage), however, can occur. The incidence of these complications is around 1 in 2000 procedures, and complications usually occur in therapeutic colonoscopy (endoscopic polypectomy) rather than in diagnostic procedures. Mortality from such events is rare.

Conclusions

- Screening for colorectal cancer using faecal occult blood tests is feasible; increasingly compelling evidence shows that such programmes can save lives at a cost similar to that of the existing breast cancer screening programme
- Once-only flexible sigmoidoscopy presents a promising alternative to faecal occult blood screening, but conclusive data will not be available for about five years
- For a screening programme to operate in the United Kingdom, considerable investment in colonoscopy facilities and expertise would be needed
- Several countries, including the United States, have screening programmes that use faecal occult blood tests or once-only flexible sigmoidoscopy, or both of these procedures. The United Kingdom has undertaken a pilot study in three areas to determine the feasibility of delivering a practicable, population based screening programme

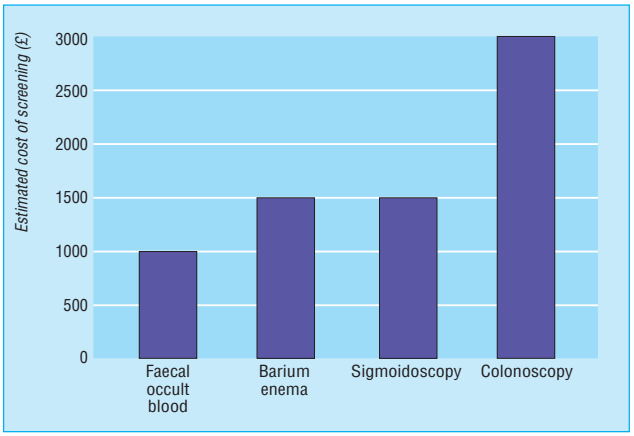
The picture of the flexible sigmoidoscope is published with permission from Endoscopy Support Services.

Inherited risk of colorectal cancer

High risk
- Familial adenomatous polyposis
- Hereditary non-polyposis colon cancer

Medium risk
- One first degree relative with colorectal cancer presenting at <45 years
- Two or more first degree relatives with colorectal cancer

Low risk
- Only one first degree relative with colorectal cancer presenting at >55 years
- No family history of colorectal cancer



Estimates of costs for different methods of screening for colorectal cancer. Costs are based on biennial testing (faecal occult blood), testing at intervals of 5 years (barium enema and colonoscopy), or once-only testing (sigmoidoscopy)

Further reading

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The ABC of colorectal cancer is edited by D J Kerr, professor at the Institute for Cancer Studies, University of Birmingham; Annie Young, research fellow at the School of Health Sciences, University of Birmingham; and F D Richard Hobbs, professor in the department of primary care and general practice, University of Birmingham. The series will be published as a book by the end of 2000.

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