Screening sigmoidoscopy for colorectal cancer: further pieces in the jigsaw

Consensus is yet to be reached on the optimal approach to screening

Australians have a 1 in 21 lifetime risk of developing colorectal cancer. The incidence of the disease and mortality resulting from it can be reduced by population-based screening programs, as has been demonstrated in several large randomised controlled trials of faecal occult blood testing (FOBT). The Bowel Cancer Screening Pilot Program currently under way in Queensland, South Australia and Victoria is assessing the practical application of FOBT.

While screening of asymptomatic, average-risk individuals for colorectal cancer is advocated by many authorities worldwide (including the National Health and Medical Research Council [NHMRC] in Australia1), uncertainty remains as to the screening test of choice. The numerous publications on the subject are indeed like jigsaw pieces waiting to be put together to reveal the complete picture. In addition to FOBT, the NHMRC-recommended screening options for asymptomatic, average-risk individuals include flexible sigmoidoscopy (FS), and it is timely to review its role here.

Colonoscopic studies on asymptomatic people show that 60% of adenomas and cancers occur in the distal colon and are potentially detectable by sigmoidoscopy. Case-control studies have shown that sigmoidoscopy can reduce the risk of subsequent fatal distal colorectal cancer by up to 60%, translating to an approximate 30% reduction in overall colon cancer mortality. Direct evidence of the magnitude of benefit from randomised controlled trials that are currently under way is awaited. A 5-yearly screening interval is recommended, based on data from these ongoing studies (which suggest that benefit from sigmoidoscopy extends up to 10 years) and on studies of repeat colonoscopy (which show that significant neoplasia is very uncommon 5 years after polypectomy or a normal examination).

What are the performance characteristics of FS? The procedure is typically done in an unsedated patient after administration of an enema and takes 5–10 minutes to perform. At our institution, generally eight procedures are done by one operator over 2 hours. The instrument is advanced as far as is tolerated with reasonable comfort (mean insertion depth, 60 cm; range, 30–110 cm) with biopsy or removal of polyps performed at the time. The finding of any adenomatous polyp or other suspicious lesion prompts further evaluation with colonoscopy. Fifteen percent of such screenings result in referral for colonoscopy. However, some have suggested that diminutive adenomas may not require follow-up — a policy that might reduce colonoscopy referrals to 5% of screenings. FS is a safe procedure, with a reported colonic perforation rate of about 1 in 50 000. Outpatient colonoscopy, which includes therapeutic procedures, has a perforation rate of about 1 in 1000.

Concerns are commonly raised about the potential miss rate of FS for lesions in the proximal colon beyond the reach of the instrument and of small lesions that are overlooked in the areas examined. Many heterogeneous studies have addressed the issues of missed proximal colonic lesions and of what distal colonic findings should trigger colonoscopic follow-up. The likelihood of a proximal advanced polyp (ie, one with pathological features that increase malignant potential, such as size or villous architecture) increases with a more advanced distal finding. In the absence of any distal adenoma, 2%–5% of asymptomatic people screened will have isolated proximal advanced lesions. Whether this is acceptable in the context of cancer screening may become clear from prospective studies. The fact that sigmoidoscopy may also miss lesions within the area of colon that is examined may have implications for the screening intervals used. It has been shown on repeat FS that polyps may be missed in up to 20% of cases, while with colonoscopy a 6% miss rate for adenomas larger than 1 cm has been reported. Schoen et al recently reported a 0.8% advanced adenoma or cancer rate (there were 6 cancers in 9317 repeat examinations) in patients having a repeat examination 3 years after an apparently normal examination; 80% of advanced lesions were in regions thought to have been adequately examined previously, indicating missed or newly evolved lesions. However, other studies have shown that after 5 years the rate of new findings is low enough to consider lengthening the screening interval.

The technical aspects of FS are sufficiently clear to enable us to define what FS can and cannot do. From the point of view of screening, FS clearly cannot completely exclude the presence of colon cancer in all asymptomatic people. A distinction must be made between screening the general population and testing the individual seeking screening. For the former, obtaining the greatest mortality benefit safely and at an acceptable cost to the nation is the crux of the matter. Recently published data indicate that FS is a cost-effective screening strategy, although colonoscopy and annual FOBT avert a greater number of cancer deaths.

The results of randomised controlled trials of screening FS and colonoscopy, currently being conducted, will allow us to make a more accurate comparison with the established data regarding FOBT.

Participation rates in sigmoidoscopy screening (23% in initial screening and 54% in follow-up screening at our institution) are encouraging given the invasive nature of FS screening. The ability of Australian gastroenterologists to accommodate increased demand for colonoscopy, whether as a follow-up to FOBT or FS, remains to be seen.

Pieces of the jigsaw continue to fall into place, although it is likely to be some years before a clearly superior screening modality is determined. The emergence of new technologies
such as virtual colonoscopy\textsuperscript{14} and faecal genetic testing will continue to add to the available armamentarium.

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IN SEPTEMBER 2003, the National Health and Medical Research Council (NHMRC) approved the new Australian Standard Vaccination Schedule recommended by the Australian Technical Advisory Group on Immunisation (ATAGI) (Box). The schedule includes inactivated poliomyelitis vaccine (IPV), varicella vaccine and seven-valent pneumococcal conjugate vaccine (7vPCV) for infants and young children. Earlier, in late 2002, routine meningococcal C conjugate vaccine was approved and funded for children aged 12 months, together with a cross-sectional catch-up program for young people to the age of 19 years (media release, Senator Kay Patterson, 24 November 2002). For the first time since 1994 — when all vaccines recommended on the schedule were funded for children vaccinated by both private and public providers under the National Immunisation Strategy\textsuperscript{1} — the childhood schedule recommended by NHMRC contains vaccines (IPV, varicella and 7vPCV) not available free of charge to parents.

As well as adding these four vaccines to the childhood program, the NHMRC also approved changes to the pertussis vaccination schedule. Since the diphtheria–tetanus vaccine was replaced by a combined diphtheria–tetanus–acellular pertussis (DTPa) vaccine at 4–5 years in 1995,\textsuperscript{2} the peak age of pertussis has progressively risen to 13–18 years.\textsuperscript{3} Based on recent evidence that three doses of DTPa in the first year of life provide good protection until the age of 6 years,\textsuperscript{3} it was decided to adjust the schedule so that the fifth dose is now given to adolescents at 15–17 years, using an adult-formulated vaccine (dTpa). This was done by removing the 18-month dose, thus making the 4-year dose the fourth dose. This is not expected to lower preschoolers’ protection from pertussis,\textsuperscript{4} but should help reduce the number of large local reactions seen when the dose was given at 18 months.\textsuperscript{5}

Inactivated poliomyelitis vaccine was recommended because it does not cause the extremely rare (1 in 2.4 million doses) live-vaccine-associated paralytic polio. The United States has already changed to inactivated vaccine,\textsuperscript{6} and other countries are considering doing so. The change to this vaccine in Australia may take time, as it is many times more costly than the oral vaccine and has had limited availability. Although various combinations of IPV with diphtheria, tetanus, acellular pertussis, \textit{Haemophilus influenzae} type b and hepatitis B vaccines are licensed in Australia,\textsuperscript{7} they are not yet available, as the companies producing them are uncertain of the potential market. In the interim, the Australian Government’s National Immunisation Program will continue to provide free oral live-attenuated poliomyelitis vaccine.

In making recommendations about the inclusion of each new vaccine in the childhood vaccination schedule, ATAGI took into account a wide range of factors. These included:

- vaccine safety and efficacy;
- the preventable burden of the disease targeted by the vaccine;
- the ease with which the vaccine could be integrated into the existing schedule;
- any likely effects on herd immunity, reduction in antibiotic resistance or impact on disease epidemiology; and
- cost-effectiveness and equity issues.

Some of the information used by ATAGI as the basis for its recommendations is contained in the \textit{The Australian immunisation handbook} (8th edition), while the levels of evidence for the new recommendations are available on the