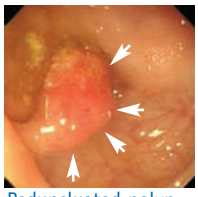
Improving outcomes in colorectal cancers: a NHS priority

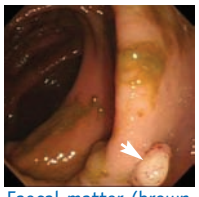
Pharmacy in Practice special supplement

Contents **Page**

This is a special supplement on colorectal cancer, which is one of the easiest cancers to prevent through early screening and detection. For colonoscopists to visualise abnormal cells the colon must be scrupulously clean (below, left) and not obscured by debris (right).



Pedunculated polyp (arrowed) extending into lumen



Faecal matter (brown stain) and sessile polyp (arrowed)

© *Images kindly provided by Mr Roger Leicester*

Box 1. Risk factors for colorectal cancer[1,3–9]

Anyone can develop colorectal cancer (CRC) but the following are associated with increased risk:

- Age.[3] 95% of all new CRC diagnoses occur in people older than 50 years.[1]
- Diet, exercise, alcohol and smoking. High caloric diets, high processed meat and alcohol intake, low fruit, fibre and vegetable intake, obesity and lack of physical exercise are linked with higher rates of CRC.[3,4]
- Presence of polyps on the inner colon and rectum wall,[3] which are common in people aged more than 50 years. Some types of polyps increase the risk of developing CRC.
- Personal medical history. Risk is increased in anyone who has experienced CRC.[3–5]
- Family medical history. First-degree relatives of a person who has had CRC are somewhat more at risk, particularly if the relative had the cancer at a young age. The risk increases with the number of family members who have had CRC.[3,6]
- Familial polyposis or hereditary non-polyposis CRC.[3,6] Rare, genetic syndromes. In both conditions, if untreated, there is a higher likelihood of developing CRC.[3]
- Ulcerative colitis increases the risk of CRC.[3,4,7,8]
- Crohn's disease.[4] Young onset of Crohn's (< 30 years) is associated with increased risk of CRC.[9]

Screening and diagnosis of colorectal cancer requires good bowel cleansing

Colorectal cancer (CRC) is the most common cancer after breast, prostate, and lung cancers,[1] with around 83% of CRC cases occurring in people aged more than 60 years in the UK.[1] In the EU in 2000, however, bowel cancer was the most commonly diagnosed cancer followed closely by breast and lung cancer.[2] In 2004 (the latest UK figures) around 30,000 new cases were registered and around half this number died from CRC.[3] Symptoms can include blood in the stool, change in bowel habit, abdominal pain and unexplained weight loss.[3]

Epidemiology

Anyone can develop CRC, but certain lifestyle and genetic factors can increase the risk (Box 1).[1,3–9] The 2004 data indicate that CRC incidence is rising[3] and there has been an age-specific increase, particularly in males aged 65–84 years.[1,3] The UK has poorer CRC survival rates (relative to age-matched groups without CRC) than found in Europe as a whole, which is thought to be a result of late diagnosis.[3] A major determinant of survival is disease stage at diagnosis,[3] and early detection of pre-malignant polyps allows their removal at colonoscopy, underlining the importance of screening.[3]

In 2004 NICE recognised the need to put systems in place in primary care and the community to improve detection of potential CRC symptoms and to ensure the rapid referral of people who might have CRC for endoscopy.[3] The NHS bowel cancer screening programme[10] began in England in June 2006[11] and in Scotland in June 2007[12] to address this.

NHS bowel cancer screening programme[10]

Five programme hubs have been set up in England[11] (one in Scotland[13]) to coordinate a national CRC screening programme.[10] This is being rolled out over three years and is based on a biennial guaiac faecal occult blood test (FOBT), which will be posted to people aged 60–69 years[10] (50–74 years in Scotland[13]). Because asymptomatic polyps or CRC can bleed a positive FOBT could highlight those people at risk of CRC.[3]

FOBT provides a first screen

Most CRCs result from a malignant change in polyps (adenomas) that develops over 10 years or more[3] and conservative estimates of the reduction in CRC mortality that could be achieved through offering biennial FOB testing are around 15%.[14] Previous studies indicate that of the returned FOBTs only 2% are expected to test positive and these people will be offered a colonoscopy in one of the local endoscopy centres.[10]

Colonoscopy can detect early changes

Colonoscopy technologies have advanced considerably in the last two decades and many pre-cancerous polyps can now be detected and removed before they progress (*see p*S2). However, good bowel preparation is essential to ensure optimal visualisation of the mucosa (*see p*S4). Important considerations in the choice of bowel cleansing agents are their cleansing efficacy, patient tolerability (*see p*S4) and cost-effectiveness (*see p*S7). A condition that must be satisfied by all accredited colonoscopy units is that they must visualise the *entire* colon, so any faecal debris that occludes full visualisation of the mucosa will inevitably lead to a repeat colonoscopy (*see p*S2). This could not only cause additional discomfort and inconvenience to the patient but might incur further cost to the NHS (*see p*S7). The importance of a scrupulous bowel preparation therefore cannot be over-emphasised (*see p*S4–7).

Tamara Lawrence, freelance writer, Reigate

This supplement of *Pharmacy in Practice* is sponsored by a non-restricted educational grant from Norgine Pharmaceuticals Limited. It has undergone independent peer-review and editorial control remains with *Pharmacy in Practice*. Job Code: MP/07/1285

Screening and diagnostic procedures for colorectal cancer

Population screening for colorectal cancers (CRCs) has begun in England for those at highest risk, aged 60–69 years, although faecal occult blood test (FOBT) kits can be requested by people aged 70 years or more.[10] In Scotland the age range is 50–74 years,[13] and when national coverage has been achieved in England for the 60–69 year age group consideration will be given to extend the age range here.[15]

The basis of the guaiac FOBT is detecting peroxidase-like activity in haem.[16] A strongly positive test indicates that blood is present in the stools.[10,14,16] This can arise because of malignancies,[17] or other causes such as haemorrhoids[10] or stomach ulcers.[18] A weak positive FOBT result will need to be confirmed by repeating the procedure.[10,18]

Box 2. FOBT screening outcomes[10]

- 94% of people will receive a normal result. They will continue with routine FOBT screening every two years.
- 4% may have an unclear FOBT, which may contain traces of blood caused by conditions such as haemorrhoids, and will be sent a further FOBT for confirmation. Most of the repeat tests will be negative.
- 2% will have an abnormal result and be offered a colonoscopy.

A false positive test result can arise by ingesting iron,[19] non-steroidal antiinflammatory agents, corticosteroids, phenylbutazone, reserpine or foods that have peroxidase activity such as red meat,[16] and false negative results can occur after ingesting large amounts of vitamin C.[16,19] However, individuals with a confirmed positive FOBT will be referred to colonoscopy (Box 2) at one of the local screening centres.[10,13,15] Many polyps can be removed at colonoscopy, but in cases where an intermediate-risk or high-risk polyp is found, the individual will transfer from biennial FOBT to colonoscopy surveillance within the NHS bowel screening programme (BSP). Where CRC is found, the individual will be referred for treatment as appropriate (Box 3).[10,15]

Screening centres must be accredited

Endoscopy units can be nominated by their Strategic Health Authorities (SHAs) to become local screening centres within the BSP.[15] Currently, in England there are 17 accredited centres.[11] In line with key recommendations from the British Gastroenterology Society (BGS),[20] nominated endoscopy units must satisfy several criteria for peer review accreditation by the Joint Advisory Group on Gastrointestinal Endoscopy (JAG)[21] at least three months before they can become operational.[15] They must achieve a high score on the Global Ratings Scale (GRS)[15,22] — a web-based tool designed to assess and audit clinical quality and safety, and the quality of the patient experience of the endoscopy service.

The BSG, together with NHS Cancer Screening Programmes, have developed quality assurance standards for the programme to facilitate continued monitoring of accredited centres.[23] This includes photographing the ileocaecal valve as evidence of examining the *entire* colon; being able to identify adenoma and CRC; excising polyps and subjecting these to pathology, and minimising harm to the patient.[23] Emphasis is placed upon timeliness across the whole Trust and units must aim to see people who have FOBT-positive results within six weeks for JAG accreditation.[24] Finally, the unit must have sufficient accredited colonoscopists to run the service without compromising waiting times for symptomatic patients.[15]

As is the case for breast and cervical screening, primary care trusts (PCTs) or clusters of PCTs will commission the services of the local screening centre for its own responsible population. Pilot studies have shown variability in uptake of FOBT and in following patients up, and PCTs will therefore benefit from undertaking a local needs assessment. PCTs will need to ensure the local infrastructure is in place, including professionals who can support informed choice about participation in the screening programme and ensure equity of access to the service.[15]

Box 3. Patients' route to colonoscopy[10,15,18,23]

60–69 year-old males and females* are sent the information leaflet *Bowel Cancer Screening: The Facts*[18] and invited by letter to participate in the programme

↓

One week later, a FOBT kit is sent out with instructions and return address for samples

↓

The hub laboratory processes the samples, returns the results within two weeks, sending a copy to the relevant GP. 2% will be positive

↓

The 2% of people offered colonoscopy will be seen by a specialist nurse who will assess their fitness for the procedure and answer any queries

↓

The people undergoing colonoscopy will be prescribed a cathartic to take (usually) the day before and/or morning of the procedure

↓

Colonoscopy is performed and the findings are discussed with the individual, who will either have a normal result or low-risk polyp and resume biennial FOBT, be at intermediate or high risk of CRC and enter into colonoscopic surveillance or have CRC and be referred to his or her local secondary care multidisciplinary team

**in England*

Colorectal examination techniques

A range of diagnostic strategies are available

to detect CRC, including colonoscopy,[3] sigmoidoscopy[3] and virtual colonography using computed tomography (CT).[3] Some of the advantages and disadvantages of these techniques, and some newer methodologies are described below.

Colonoscopy

Colonoscopy allows endoscopists to satisfy the BSG requirement of providing evidence of visualising the *entire* colon.[23] It usually takes less than 15 minutes to complete[25] and can allow the detection of flat lesions[26] and small polyps.[26–28] Importantly, this method allows polyps to be removed[26,28] or tattooed for future reassessment[29] during the diagnostic procedure. Disadvantages include the need for full bowel preparation,[26,28] the use of sedation[28] and the serious but small risk of complications such as perforation and bleeds.[30] Flexible sigmoidoscopy is a quicker procedure[31] and is conducted without sedation,[31] but has similar complications to colonoscopy[31] and is useful for examining the bowel only below the level of the descending colon,[31] which detects about two thirds of colonic disease,[30] but does not meet BSG criteria.[23]

Virtual colonoscopy

This technique involves taking serial CT scans through the abdomen and pelvis — in a matter of seconds[28] — and then reconstructing from these scans two- or three-dimensional images of the colon and rectum.[28] Sedation is not usually needed,[28] but colon distension with air or carbon dioxide insufflated via a small rectal tube may cause discomfort and antispasmodic agents may be needed.[27] Less invasive than colonoscopy,[28] CT colonography may be used as a diagnostic test both in symptomatic and asymptomatic patients with a high risk of developing CRC.[27,28]

Like colonoscopy, CT colonography is usually performed on an empty bowel,[27,28] but it is possible to use 'faecal tagging'[27] in which an iodinated contrast agent is ingested 48 hours before the scan.[27] Measurements from the tagged stools are digitally subtracted from image measurements.[28] This eliminates the need for bowel preparation,[27] and some centres use faecal tagging to increase sensitivity and specificity of polyp detection.[32] The malignant potential of an adenomatous polyp directly correlates with its size, histologic type, and degree of dysplasia.[32] Only a minority of advanced adenomas measure less than 10mm and these can be detected by CT colonography.[32] However, image analysis requires time[28] and although some centres offer a same day colonoscopy service for polypectomy for detected lesions measuring 10mm or more to *avoid* the need for repeat colonic cleansing[32] many patients will have to return for colonoscopy if polyps are identified.[28]

Capsule endoscopy

This technique is indicated mainly for obscure gastrointestinal bleeding.[33] It involves swallowing a small (11x27mm)[34] capsule containing a camera, light source and wireless circuit for the acquisition and transmission of signals.[33,34] Images, captured at two frames per second,[34] are sent to a radio-receiver worn on a belt[33,34] for later analysis. The capsule is usually swallowed after an overnight fast,[33] however, mucosal visualisation may be improved by a full bowel preparation.[35] The capsule is excreted[33] adding to costs, but it is a non-invasive technique and relatively free of complications.[33,34]

Technologies of the future

Chromoendoscopy is a technique in which a contrast dye, such as indigo carmine[26,36] or congo-red with methylene blue,[37] is sprayed through a catheter into the colon lumen,[26] which can be visualised at high magnification.[36,38] Recent reports suggest that chromoendoscopy may improve the detection of flat lesions[38] and could be a useful addition to the endoscopists' armamentarium for selected cases.[37,38] Emerging immunophotodiagnostic methods in which fluorescent dyes are linked with monoclonal antibodies that are directed against tumour-specific antigens,[39] may extend these chromoscopic techniques. Other methods manipulate light to selectively improve visualisation of bowel mucosa. With narrow-band imaging, for example, applied light of defined wavelengths allows visualisation of microvasculature in neoplastic tissue and differentiation between hyperplastic and adenomatous polyps.[40] Yet other new strategies explore the use of fluorescent probes specifically designed to target invasive CRC for endoscopic identification.[41] Many of these developing immunodiagnostic techniques are still under clinical evaluation.

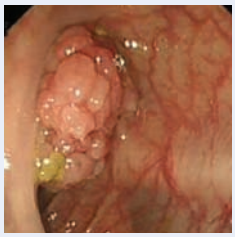
Conclusions

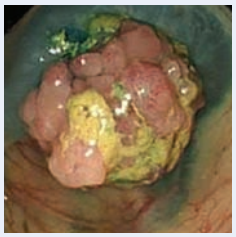
Colonoscopy is the only diagnostic technique in which during *full* examination of the bowel the surgeon can perform therapeutic intervention, take biopsies for histology[26,28] and tattoo lesions for surveillance colonoscopy.[29] Providing that good bowel preparation has been carried out colonoscopy is a sensitive, if invasive, technique.[26,28] If bowel preparation is not optimal, however, the procedure may need to be repeated.[26] Potentially, repeating a colonoscopy may cause additional discomfort and inconvenience to the patient and extra cost to the NHS; and will lead to a reduced GRS score[23] with a knock-on effect at JAG appraisal. Bowel preparation is discussed in the next article.

Geoff Saunders, Macmillan Network Oncology Pharmacist, Greater Manchester and Cheshire

Box 4. Colonoscopic imaging of the bowel

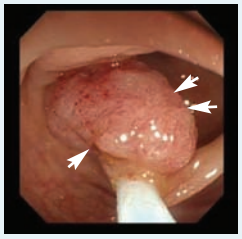
Colonoscopy is the standard bowel visualisation technique. The colonoscopist advances the colonoscope into the colon slowly, using small puffs of air to gently distend the colon. When the ileocaecal valve is reached the colonoscope is withdrawn very slowly — over a matter of around 6–8 minutes — and the colonoscopist can examine the mucsoal surface for signs of polyps or other lesions. The colonoscopic images opposite show a large, sessile polyp in the colon lumen. The image on the far right has been taken after injecting methylene blue solution under the mucosa to aid colonoscopic resection of the lesion, and reduce the risk of perforation. The colonoscopist can remove such polyps during the procedure and tattoo the colon to indicate the site of resection for future surveillance colonoscopy.





© Images kindly provided by Mr Roger Leicester

Bowel cleansing preparations



left: A colonoscopic image of a pedunculated tubulovillous adenoma (arrowed) extending into the lumen, just before removal using a snare.

© Image kindly provided by Mr Roger Leicester

The full potential of colonoscopy can only be realised if there is good visualisation of the bowel mucosa.[30,42] Failure to ensure the bowel is clean will inevitably lead to poor bowel visibility — and even low levels of residual stool could either simulate[32,43] or obscure[43,44] a clinically significant lesion. Clearly, inadequate visibility could potentially delay diagnosis,[45] lengthen colonoscopy duration[25] — perhaps increasing the amount of sedative needed — and require a repeat colonoscopy, thereby reducing the efficiency of the endoscopy service.[45] Optimising colonoscopy outcomes through appropriate choice of bowel cleansing preparation is therefore essential.

Agents in use

Currently available bowel cleansing preparations include the osmotic saline agents Citramag® and Fleet Phospho-soda®, the polyethylene glycol (PEG) based osmotic agents, Klean-Prep® and Moviprep®, and the stimulant, Picolax® (Box 5).[46–51]

Saline cathartics osmotically attract water from the circulation and maintain oral fluids in the intestinal lumen[52,53] until the salt solution becomes isotonic with the extracellular fluid.[52] The resulting bulk volume stimulates peristalsis and expulsion of the contents.[52,53] The high molecular weight PEG-based osmotic preparations are administered in an isotonic electrolyte solution, which is retained within the intestine[53] where it also acts as a bulk stimulant. Stimulant cathartics, such as sodium picosulphate (SPS) promote smooth muscle contractility[53] and increase bowel water content.[42,52,53]

Precautions and contraindications

When saline osmotic agents or low-volume stimulants transit through the intestine there is some absorption of magnesium, sodium and phosphate ions into the circulation, which are rapidly removed in people with good renal function.[52] However, in people with compromised renal function biochemical derangements can occur.[42,47,48,51] For example, sodium phosphate (NaP) ingestion has caused hyperphosphataemia[42,53] and hypokalaemia,[42,48,53] although this was clinically insignificant.[42] Similarly, SPS has induced clinically insignificant reductions in serum sodium and potassium,[54] and hypermagnesaemia.[55] However, clinically significant electrolyte shifts and dehydration are more likely with low volume preparations.[42,56] NaP, for instance, has caused tetany,[48] fatality in a patient with colonic ileus[42] and acute renal failure in two diabetic patients.[57] Hyponatraemia-mediated seizures have been reported in patients who took either NaP[58,59] or SPS with magnesium citrate.[58] NaP and SPS are therefore contraindicated in renal or cardiovascular impairment, congestive heart failure, ascites, gastrointestinal obstruction, ileus, megacolon, perforation and inflammatory bowel disease.[48,51] This also emphasises the importance of being alert to patients' comorbidities and regular medication that could induce inappropriate secretion of antidiuretic hormone and increase the risk of water retention and/or electrolyte imbalance,[48,51,58] such as tricyclic antidepressants, selective serotonin re-uptake inhibitors, antipsychotic drugs and carbamazepine.[51] Extreme caution should be exercised in the use of saline preparations in people taking medicines that could cause hypokalaemia, such as diuretics, corticosteroids, or cardiac glycosides.[51] Similarly, their use in patients taking medicines that can produce hypo-

Box 5. Currently available bowel cleansing agents and adult doses[46–51]

Preparation	Total volume	Dosing notes
Osmotic agents:		
Citramag®[46,47] Heavy magnesium carbonate, 11.57g + anhydrous citric acid BP, 17.79g per sachet. Lemon and lime flavour.	1 sachet in 200ml hot water, cool when dissolved. Drink extra clear fluid. Repeat 6–8 hours later.	High fluid/low residue diet required on day before procedure and only clear fluids after dosing.
Fleet Phospho-soda®[46,48] Disodium phosphate dodecahydrate, 10.8g + sodium dihydrogen phosphate dihydrate, 24.4g per 45ml. Ginger-lemon flavour.	(a) Take at least 240ml clear liquid. (b) Take 45ml dose in 120ml cold water plus at least 240ml cold water. (c) Between doses take at least 960ml clear fluid. (d) Repeat b.	For am procedure — take at 7am and 7pm on day before procedure. For pm procedure — take at 7pm on day before and 7am on day of procedure. Clear liquids only during dosing period.
Klean-Prep®[46,49] Macrogol 3350, 59g + anhydrous sodium sulphate, 5.685g + sodium bicarbonate, 1.685g + sodium chloride, 1.465g + potassium chloride, 0.7425g per sachet. Vanilla flavour.	Dissolve each sachet in 1L water. Take 4L over 4–6 hours or, if preferred, 2L in evening before and 2L in morning of procedure.	Must be taken with sufficient fluid to produce clear fluid excrement. Aspartame is an excipient so avoid in phenylketonuria.[46] Allergic reactions have been reported.
Moviprep®[46,50] Sachet A: Macrogol 3350, 100g + sodium sulphate anhydrous, 7.5g + sodium chloride, 2.691g + potassium chloride, 1.015g. Sachet B: ascorbic acid, 4.7g + sodium ascorbate, 5.9g. Lemon flavour.	In 1L water mix 1 sachet A and 1 sachet B. Dose: 2L, taken either evening before or 1L evening before and 1L early morning of procedure. Take doses over 1–2 hours. Also drink 1L clear fluid during treatment.	Dosing must be completed at least 1 hour before colonoscopy. No solid food permitted during dosing. Aspartame is an excipient so avoid in phenylketonuria.[50] Ascorbate present so contraindicated in G6PD deficiency.[50]
Stimulant:		
Picolax®[46,51] Sodium picosulphate 10mg + magnesium oxide light, 3.5g + citric acid anhydrous, 12g Orange flavour.	Mix 1 sachet in 150ml cold water, let cool before drinking. Next dose 6–8 hours later. Take around 250ml fluid per hour during washout.	Low residue diet with copious intake of water/clear fluids recommended on day before procedure. Caution: heat generated when reconstituting powder.

volaemia, such as diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers or non-steroidal anti-inflammatory drugs, could increase their risk of acute renal failure and they should be advised to hydrate adequately during the cleansing period.[48,51] SPS and NaP can cause dizziness, which may arise from dehydration and electrolyte shifts,[42] and can occur in apparently healthy people.[53] These problems are largely obviated with PEG-based agents ingested in isotonic electrolyte solution, which minimise fluid and ion exchange across the colonic mucosal membrane.[42,53] Pharmacists should bear in mind the potential for purgatives to alter the absorption of regular medicines.[48–51]

Patient tolerability

Factors affecting patient tolerability fall into three categories — clinical sequelae resulting from biochemical derangements (described above); patients' response to the taste and volume of the preparation, and patients' response to dietary restrictions.

Volume and taste: The main disadvantage of most PEG-based preparations is that large volumes (around 4L) must be ingested.[42,56] This may be responsible for their association with nausea, vomiting and abdominal pain, making them somewhat less well tolerated compared with NaP or SPS and having a negative impact on patient adherence[42,45] — and, therefore, perhaps, upon thoroughness of bowel cleansing.[45]

When the doses of PEG-based agents are split they appear to be better tolerated.[53] A recent single blind, parallel group, equivalence study conducted to compare a 2L PEG plus ascorbic acid (PEG+ASC) combined preparation with NaP found comparable efficacy and a better tolerability profile for PEG+ASC.[56] This may be because patients in the PEG+ASC group had a liberalised diet and more of these rated it as being 'quite or very satisfactory' compared with NaP.[56]

Dietary restrictions: During most bowel cleansing regimens a clear liquid diet is required to help minimise the faecal material in the colon.[45,47–51] Because this may reduce patient adherence, allowing a low-residue breakfast on the day before colonoscopy has been studied and found not to impair colon cleansing.[45] This was confirmed in the PEG+ASC and NaP study in which subjects taking PEG+ASC were permitted a normal breakfast, lunch and light dinner on the day before colonoscopy.[56] This dietary regimen was found to be acceptable to most of this group, while those in the NaP group were less happy with their liquid diet regimen.[56]

Efficacy comparisons

Methodological differences between studies limit meaningful comparisons between preparations and make it difficult to draw clear conclusions.[42,53] The most commonly used preparation in the UK is SPS with magnesium citrate, but it has been studied less than PEG and NaP.[53] Some analyses found significantly more people completed NaP than the high volume PEG-based preparations[42,45] and — perhaps as a consequence — NaP was the more effective bowel cleanser.[42] Other studies found no overall difference between NaP and PEG in terms of efficacy.[53,56]

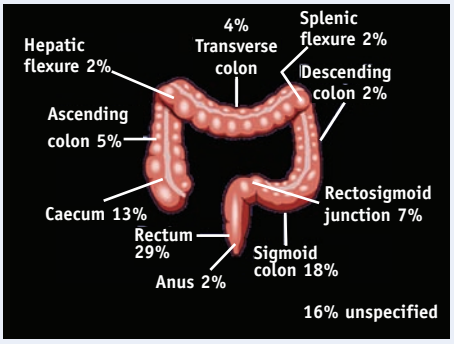
Interpretation of studies assessing bowel cleansing efficacy is hampered by the lack of a universally used grading scale, yet there is a clearly defined link between preparation quality and adenoma detection rate.[53] The comparisons between PEG+ASC and NaP described above were made using a newly devised rating system for objectively quantifying bowel cleanliness (Box 6),[56,60] which could allow meaningful comparisons to be made in future randomised controlled trials.

Box 6. Classifying bowel cleanliness using the Norgine cleansing scale

Score	Description
0	Irremovable, heavy, hard stools
1	Semisolid, only partially removable stools
2	Brown liquid or semisolid stool
3	Clear, yellow or green transparent liquid
4	Empty and clean

Grade	Description
A	All 5 segments scored 3 or 4
B	1 or more segments scored 2
C	1 or more segments scored 1
D	1 or more segments scored 0

above: *Using the Norgine cleansing scale, all colon regions can be scored 0–4 according to cleanliness, with the cleanest segments scoring 4. A global cleanliness rating (A–D) can then be given to the whole bowel at colonoscopy.[56] Using this scoring system can allow bowel preparations to be compared.*



above: *Percentage of cancer cases by site in England 1997–2000.[60] The entire bowel must be examined to satisfy quality and safety indicators[23] and must, therefore, be clean.*

Summary

The key points to bear in mind about bowel preparations can be summarised as follows:

- *Efficacy.* No bowel cleansing agent has shown consistent superiority[42,45,53] over others. This suggests that when a regimen is followed correctly good bowel cleansing *could* be achieved, which is essential if repeat colonoscopies are to be avoided.
- *Tolerability.* Low volume preparations are preferred, such as NaP and SPS,[42,53] but they can cause dizziness[42,53] and electrolyte disturbances.[42,48,51] High volume PEG causes more nausea and bloating,[53] but low volume PEG+ASC has been found to have a better tolerability profile than NaP and to have comparable efficacy.[56]
- *Safety.* Clinically significant dehydration and electrolyte shifts may result from NaP[42,48,57–59] and SPS.[51,58] These are contra-indicated in renal or cardiovascular impairment and should be used with caution in people taking medicines that could cause hypokalaemia or hypovolaemia.[48,51] These problems are largely obviated with PEG-based agents, but they should also be used with caution in fragile patients in poor health or patients with severe renal insufficiency or cardiac impairment.[50]

Geoff Saunders, Macmillan Network Oncology Pharmacist, Greater Manchester and Cheshire Cancer Network, UK

Patients' experiences of the bowel screening programme

© Photograph kindly supplied by Vicki Hedley

Vicki Hedley is a specialist screening practitioner (SSP) for the NHS bowel cancer screening programme (BCSP) at St. Georges Hospital Endoscopy Unit in London. Like all SSPs, Vicki had to complete a course designed specifically for the BCSP. Vicki explains what happens at the pre-assessment appointment and some typical patients' concerns about the experience.

As a SSP in the endoscopy unit, part of my job is to assess people for their fitness to undertake colonoscopy. Understandably, most patients that attend the clinic are distressed and concerned about the outcome. Usually, it is the unknown that most concerns patients. During the consultation it is important to recognise and address their concerns and explain the purpose of the BCSP and what the faecal occult blood (FOB) test has shown.

The 45 minute consultation involves obtaining a past medical history and assessing a patient's appropriateness for colonoscopy. We also explain the BCSP; colonoscopy, including polypectomy and biopsies; bowel preparation and dietary restrictions; alternatives to colonoscopy and possible outcomes, such as surveillance. Consent for the colonoscopy and an appointment to have the procedure is also arranged. The importance of following the instructions for bowel preparation and adequate fluid intake is stressed and to date only 2% of screening cases have had inadequate bowel preparation. Indeed, our experience has been that patients referred through the BCSP have far better bowel preparations than those referred by GPs or as inpatients.

Typical patient experiences are illustrated by Mrs S, aged 61 years, who attended a pre-assessment clinic after a positive FOBT. Her past medical history included hyperlipidaemia, hypertension, type 2 diabetes, hysterectomy in 1980, and haemorrhoids. Medications included: Simvastatin 20mg nocte, aspirin 75mg daily, metformin 500mg twice daily, cod liver oil one tablet daily, and anusol cream applied prn. There was no family history of cancer. Mrs S arrived feeling very anxious, but said she found the appointment with the SSP nurse 'very helpful in putting my mind at rest and making the process less worrying, because I thought the poo sample I sent off had detected cancer'.

At colonoscopy, one polyp *was* detected and removed, but Mrs S had to come back for a repeat colonoscopy because her bowel preparation was not adequate. We have noticed that the 2% of patients with poor bowel preparation are diabetic (possibly a result of slow transit time) and we are now trialling dispensing an additional sachet of bowel cleansing medication to these patients. At Mrs S's repeat colonoscopy a further three polyps were detected and removed, underlining the importance of a good bowel preparation to avoid residual stool obscuring polyp visualisation.

Histology results are available 7 days after colonoscopy and an appointment is pre-arranged for patients to discuss these. Because of the size and extent of dysplasia detected within the polyps retrieved, Mrs S was invited onto the colonoscopy surveillance programme at the same screening centre by one of the approved screening colonoscopists.

Mr W, aged 72 years, who self-referred into the BCSP, also attended a pre-assessment clinic after a positive FOBT feeling rather distressed. He had experienced rectal bleeding and a change in bowel habit over the past 5 weeks, but because of the nature of the symptoms had not seen his GP. 'I have not even told my wife', he said 'I was hoping it would just go away'. His past medical history included: hypertension, transurethral resection of the prostate, appendicectomy as a child and hyperlipidaemia, but he had 'never really been ill'. His sister had breast cancer aged 65 and his father had lung cancer aged 50, and both were deceased.

During the consultation Mr W spoke freely about his symptoms saying he had 'felt a weight lifted off my shoulders after talking about it and that something was going to be done to see what the problem is.' He was especially worried because of his family history of cancer and, as a keen golfer, the symptoms were interfering with his hobby. At colonoscopy a sigmoid tumour was detected and biopsied. After the procedure the possible diagnosis was discussed with Mr and Mrs W by a Colorectal Nurse Specialist who took over his care until after surgery and beyond, arranging scans and surgical appointments as needed. The Dukes A tumour had not spread and he had a left hemicolectomy within three weeks of diagnosis. Mr W will need regular scans and yearly colonoscopies for a 5-year period but has recovered well and is now playing golf regularly.

Vicki Hedley, SSP, St. Georges Hospital, London

Cost-effectiveness of screening for colorectal cancer

In 1997 a PRISM study revealed that early deaths from cancers of the colon, rectum, rectosigmoid junction and anus placed a significant cost burden on the UK economy through loss of person years and through NHS costs.[61] Similar conclusions were reached in 2006 using the latest 2004 data.[62] The increasing incidence of colorectal cancer (CRC)[3] and poor 5-year survival rates in the UK — thought to be mainly due to late diagnosis[3] — provided further justification for population screening. To help inform decision-making about the optimal screening modality, the Government funded a faecal occult blood test (FOBT) pilot study during 2000–2002 to screen people aged 50–69 years in England and in Scotland with normal population risk of CRC.[63] The usefulness of flexible sigmoidoscopy for screening was evaluated through randomised, controlled trials.[63]

What screening option is best?

The Department of Health (DH) commissioned the School of Health and Related Research (ScHARR) in Sheffield to appraise the screening options in 2004. Options they considered included biennial FOBT for those aged 50–69, 60–67, 60–69, 60–71 or 60–73 years; and once-only flexible sigmoidoscopy at 55 or 60 years, or at 60 years followed by biennial FOBT at 61–70 years.[64] The authors stated that each of the options they considered was likely to have a cost-effectiveness compared to no screening, but the uncertainty of the prevalence of pre-clinical cancer within the general population made it difficult to ascertain which was most cost-effective.[64] Because each option had differing impacts on resource needs and all appeared to be economically attractive compared with no screening, the key issue concerned the viability of each option within NHS resource capacity. The authors concluded that if total endoscopy services are constrained then the favoured option was likely to be biennial FOB testing between the ages of 60 and 69 years.[64]

The UK Colorectal Cancer Screening Pilot Group study investigators found FOBT uptake to be around 57% of those invited.[65] Around 2% of the FOBTs were positive (5050 cases) and these people were offered colonoscopy. Around 89% (4116) took up this offer, and of these 552 had invasive cancer, 1388 had adenoma and the remainder showed no neoplasia.[65] The authors estimated the cost of FOBT screening to be about £5,900 per life year saved, concluding that this is well below the threshold most European countries are willing to pay and therefore represents a cost-effective intervention.[65] These costs also balance favourably against the estimated cost of each life year gained through intensive follow-up after CRC surgery of £3,402 (at 2002 prices).[66]

Colonoscopy

NICE recognise the difficulty in drawing definitive conclusions about the costs of the bowel screening programme and anticipate that full costs are unlikely to be known for several years.[3] Currently, £6.9billion has been included in the strategic health authority (SHA) bundle of central budgets for 2007–8 for bowel screening.[15] Clearly, these funds are allocated towards a *single* screen per person, so if screening could not be completed and a repeat procedure was needed the repeat costs would, presumably, have to be borne by the responsible SHA. The costs of repeat colonoscopies *could* be significant — of the 478,250 pilot study population offered FOBT there were 416 'incomplete' colonoscopies.[65] Using the 2004 national average unit cost of conducting an inpatient colonoscopy of £633[67] as an example, repeating 416 colonoscopies in inpatients might have incurred additional costs of around £263,328. Although outpatient colonoscopy costs are likely to be less, this does emphasise the importance of optimising colonoscopy preparation.

Box 7. Bowel cleansing agent costs

Preparation	Cost per screen[46]
Citramag®	£2.98
Fleet Phospho-soda®	£4.79
Klean-Prep®	£8.56
Moviprep®	£10.27
Picolax®	£3.53

Clean bowels could reduce failure rates

One of the modifiable factors that can impact upon failure rates for colonoscopy is bowel cleansing (*see p*S4–5). The costs of preparing single patients for colonoscopy using the various bowel cleansing agents are given in Box 7.[46] It will be important to ensure that the most cost-effective agent is used that has the greatest cleansing ability and the least risk of causing harm. NaP[48] and SPS[51] are contra-indicated in renal or cardiovascular impairment and should be used with caution when medicines that could cause hypokalaemia or hypovolaemia are taken.[48,51] There are fewer clinically serious electrolyte shifts reported for the more expensive PEG-based agents, but the costs of good bowel preparations are far outweighed by those of repeat colonoscopies — both in financial terms and in terms of patient discomfort and inconvenience.

Conclusions

The NHS bowel screening programme will build, with complete coverage of the target English population planned by 2009–10.[15] Screening is likely to result in a reduction in cancer-specific mortality[64] and, therefore, to be a cost-effective intervention.[65] An important consideration in maximising the cost-effectiveness of colonoscopies is ensuring patients are properly prepared through good bowel cleansing (*see p*S4).

Tamara Lawrence, freelance writer, Reigate

References

1. Office of National Statistics. *Cancer statistics registrations. Registrations of cancer diagnosed in 2004, England*. Series MB1 no. 35, London, HMSO, 2006. http://www.statistics.gov.uk/statbase/Product.asp?vlnk=8843.*
2. Cancer Research UK. *Incidence and mortality in the European Union*. http://info.cancerresearchuk.org/cancerstats/geographic/cancerineu/incidenceandmortality/.*
3. National Institute for Health and Clinical Excellence. *Guidance on cancer services. Improving outcomes in colorectal cancers*. May 2004. http://www.nice.org.uk/pdf/CSGCCfullguidance.pdf.*
4. Cancer Research UK. *Bowel cancer risk factors*. http://info.cancerresearchuk.org/cancerstats/types/bowel/riskfactors/.*
5. Lewis C. Colorectal cancer screening. *BMJ Clinical Evidence*. http://www.clinicalevidence.com/ceweb/conditions/dsd/0414/0414_background.jsp.*
6. Hobbs FDR. ABC of colorectal cancer. The role of primary care. *BMJ* 2000; **321:** 1068–70.
7. Eaden JA, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. *Gut* 2001; **48:** 526–35.
8. Collins PD, Mpofu C, Watson AJ, Rhodes JM. *Strategies for detecting colon cancer and/or dysplasia in patients with inflammatory bowel disease.* Cochrane Database of Systematic Reviews 2006, Issue 2. Art No: CD000279. DOI: 10.1002/14651858.CD000279.pub3.
9. Gillen CD, Andrews HA, Prior P, Allan RN. Crohn's disease and colorectal cancer. *Gut* 1994; **35:** 651–5.
10. Department of Health England. NHS bowel cancer screening programme. Details of the programme, patient information leaflets; pilot study reports and the ScHAAR report are available at http://www.cancerscreening.nhs.uk/bowel/index.html.*
11. Department of Health England. NHS bowel cancer screening programme. For details of the hubs and screening centres see http://www.cancerscreening.nhs.uk/bowel/roll-out.html.*
12. National Health Service Scotland. The Scottish bowel cancer screening programme. Timetable of screening start dates in the NHS Boards. http://www.bowelscreening.scot.nhs.uk/wp-content/uploads/2007/06/timetable.pdf.*
13. The Scottish Bowel Cancer Screening Programme. Information about the programme and how it will be run. http://www.bowelscreening.scot.nhs.uk/?p=6.*
14. Hewitson P, Glasziou P, Irwig L *et al. Screening for colorectal cancer using the faecal occult blood test, Hemoccult*. Cochrane Database of Systematic Reviews, 2007, Issue 1. Art. No.: CD001216. DOI:10.1002/14651858.CD001216.pub2.*
15. National Cancer Screening Programmes. National Endoscopy Programme. *NHS Bowel cancer screening programme Wave 2: 2007–08. Advice to the NHS*. January 2007. http://www.grs.nhs.uk/documents/NHSBCSP-ADVICE-TO-NHS-JANUARY-07.pdf.*
16. Beckman Coulter Laboratories. *Hemoccult®. Physicians' #1 choice in fecal occult blood testing. Product instructions*. Available at http://www.beckmancoulter.com/literature/ClinDiag/462478-E_HO.pdf.*
17. du Toit J, Hamilton W, Barraclough K. Risk in primary care of colorectal cancer from new onset rectal bleeding: 10 year prospective study. *BMJ* 2006; **333:** 69–70.
18. Department of Health England. NHS bowel screening programme. *Bowel cancer screening: the facts* with details on FOB testing, preparing for and experiencing colonoscopy are available at http://www.cancerscreening.nhs.uk/bowel/publications/index.html.*
19. Bjpharmacol.org. *Stool occult blood test*. http://www.bjpharmacol.org/encyclopedia/fecal-occult-blood-test-fobt.html.*
20. British Society of Gastroenterology strategy group. *Care of Patients with Gastrointestinal Disorders in the United Kingdom A Strategy for the Future*. British Society of Gastroenterology, March 2006. http://www.bsg.org.uk/pdf_word_docs/strategy06_final.pdf.*
21. Joint Advisory Group on Gastrointestinal Endoscopy. Information available at http://www.thejag.org.uk.*
22. National Endoscopy Programme. Global Rating Scale. Information available at http://www.grs.nhs.uk.*
23. National Endoscopy Programme. Global rating scale quality and safety indicators. Available at http://www.grs.nhs.uk/instantkb13/attachments/BSG%20quality%20and%20safety%20indicators%202007%20final-GUID4lem2g55vknrbh555xzjkozs.pdf.*
24. National Endoscopy Programme. Global Rating Scale. *Endoscopy. Meeting the challenges. Working towards a sustainable future,* March 2007. http://www.grs.nhs.uk/instantKB13/attachments/1.%20Meeting%20the%20Challenges%202007-GUIDz5elhaa2fyfini5553d1md45.pdf.*
25. Kim WH, Cho YJ, Park JY *et al*. Factors affecting insertion time and patient discomfort during colonoscopy. *Gastrointest Endosc* 2000; **52(5):** 600–5.
26. Parra-Blanco A, Nicolás-Pérez D, Gimeno-García A *et al*. The timing of bowel preparation before colonoscopy determines the quality of cleansing, and is a significant factor contributing to the detection of flat lesions: A randomized study. *World J Gastroenterol* 2006; **12(38):** 6161–6.
27. National Institute for Health and Clinical Excellence. *Computed tomographic colonography (virtual colonoscopy). Interventional Procedure Guidance 129, June 2005*. http://www.nice.org.uk.*
28. Yee J, Akerkar GA, Hung RK *et al*. Performance characteristics of CT colonography for detection in 300 patients. *Radiology* 2001; **219:** 685–92.
29. Aboosy N, Mulder CJJ, Berends FJ *et al*. Endoscopic tattoo of the colon might be standardized to locate tumors intraoperatively. *Roman J Gastroenterol* 2005; **14(3):** 245–8.
30. Bowles CJA, Leicester R, Romaya C *et al*. A prospective study of colonoscopy practice in the UK today: are we adequately prepared for national colorectal cancer screening tomorrow? *Gut* 2004; **53:** 277–83.
31. McLoughlin RM, O'Morain CA. Colorectal cancer screening. *World J Gastroenterol* 2006; **12(42):** 6747–50.
32. Pickhardt PJ. Differential diagnosis of polypoid lesions seen at CT colonography (virtual colonoscopy). *RadioGraphics* 2004; **24:** 1535–59.
33. National Institute for Health and Clinical Excellence. *Wireless capsule endoscopy for investigation of the small bowel. Interventional procedure guidance 101, December 2004*. http:// www.nice.org.uk.*
34. Swain P. Wireless capsule endoscopy. *Gut* 2003; **52(Suppl IV):** iv48–iv50.
35. Dai N, Gubler C, Hengstler P *et al*. Improved capsule endoscopy after bowel preparation. *Gastrointest Endosc* 2005; **61:** 28–31.
36. Kato S, Fu KI, Sano Y *et al*. Magnifying colonoscopy as a non-biopsy technique for differential diagnosis of non-neoplastic and neoplastic lesions. *Gastroenterol* 2006; **12(9):** 1416–20.
37. Shaw D, Blair V, Framp A *et al*. Chromoendoscopic surveillance in hereditary diffuse gastric cancer: an alternative to prophylactic gastrectomy? *Gut* 2005; **54:** 461–8.
38. Kiesslich R, Neurath MF. Surveillance colonoscopy in ulcerative colitis: magnifying chromoendoscopy in the spotlight. *Gut* 2004; **53:** 165–7.
39. Dekker E, van Gulik T. Colorectal cancer: what the clinician wants to know. *Cancer Imaging* 2005; **5(Spec No A):** S127–S132.
40. Gheorghe C. Narrow-band imaging endoscopy for diagnosis of malignant and premalignant gastrointestinal lesions. *J Gastrointest Liver Dis* 2006; **15(1):** 77–82.
41. Kelly K, Alencar H, Funovics M *et al*. Detection of invasive colon cancer using a novel, targeted, library-derived fluorescent peptide. *Cancer Res* 2004; **64:** 6247–51.
42. Tan JJ, Tjandra JJ. Which is the optimal bowel preparation for colonoscopy — a meta-analysis. *Colorectal Disease* 2006; **8:** 247–58.
43. Silva AC, Vens EA, Hara AK *et al*. Evaluation of benign and malignant rectal lesions with CT colonography and endoscopic correlation. *RadioGraphics* 2006; **26:** 1085–99.
44. Yee J. CT Screening for colorectal cancer. *RadioGraphics* 2002; **22:** 1525–31.
45. Hookey LC, Vanner S. A review of current issues underlying colon cleansing before colonoscopy. *Can J Gastroenterol* 2007; **21(2):** 105–11.
46. *British National Formulary 53*, March 2007. BMJ Publishing Group Ltd and RPS Publishing 2007.
47. Sanochemia UK Ltd. *Summary of Product Characteristics, Citramag®*, January 2002. http://www.sanochemia.de/objectfile/1338/citramag.pdf.*
48. EC De Witt and Company Limited. *Summary of Product Characteristics, Fleet Phosphosoda®*, June 2006. http://emc.medicines.org.uk/emc/assets/c/html/displaydoc.asp?documentid=541.*
49. Norgine Limited. *Summary of Product Characteristics, Klean Prep®*, October 2003. http://emc.medicines.org.uk/emc/assets/c/html/DisplayDoc.asp?DocumentID=1243.
50. Norgine Limited. Summary of Product *Characteristics, Moviprep®*, March 2007. http://emc.medicines.org.uk/emc/assets/c/html/displaydoc.asp?documentid=19285.*
51. Ferring Pharmaceuticals Ltd. *Summary of Product Characteristics, Picolax®*, December 2003. http://emc.medicines.org.uk/emc/assets/c/html/displaydoc.asp?documentid=670.*
52. Gelfand DW, Chen MYM, Ott DJ. Preparing the colon for the barium enema examination. *Radiology* 1991; **178:** 609–13.
53. Belsey J, Epstein O, Heresbach D. Systematic review: oral bowel preparation for colonoscopy. *Aliment Pharmacol Ther* 2007; **25:** 373–84.
54. Ryan F, Anobile T, Scutt D *et al*. Effects of oral sodium picosulphate Picolax® on urea and electrolytes. *Nurs Stand* 2005; **19(45):** 41–5.
55. Hamilton D, Mulcahy D, Walsh D *et al*. Sodium picosulphate compared with polyethylene glycol solution for large bowel lavage: a prospective randomised trial. *Br J Clin Pract* 1996; **50(2):** 73–5.
56. Bitoun A, Ponchon T, Barthet M *et al*. Results of a prospective randomised multicentre controlled trial comparing a new 2-L ascorbic acid plus polyethylene glycol and electrolyte solution vs. sodium phosphate solution in patients undergoing elective colonoscopy. *Aliment Pharmacol Ther* 2006; **24:** 1631–42.
57. Ma RCW, Chow CC, Yeung VTF *et al*. Acute renal failure following oral sodium phosphate bowel preparation in diabetes. *Diabetes Care* 2007; **30:** 182–3.
58. Frizelle RA, Colls BM. Hyponatraemia and seizures after bowel preparation: report of three cases. *Dis Colon Rectum* 2005; **48:** 393–6.
59. Lui SYW, Cheung FKY, Siu WT, Ng EKW. Hyponatremic convulsion after oral sodium phosphate for bowel preparation in a patient with previous gastrectomy. *Endoscopy* 2006; **38:** 854–5.
60. Cancer Research UK. *UK Bowel Cancer incidence statistics*. http://info.cancerresearchuk.org/cancerstats/types/bowel/incidence/?a=5441.*
61. Lewison G. *Gastroenterology in the UK: The burden of disease*. PRISM project 9608, Second report, The Welcome Trust, 26 June 1997.
62. Williams J (Editor). *Gastroenterology services in the UK. The burden of disease, and the organisation and delivery of services for gastrointestinal and liver disorders: a review of the evidence*. Centre of Health Improvement Research, Swansea. March, 2006. http://www.medicine.swan.ac.uk/giservicesreview.*
63. Beating Bowel Cancer. *Screening — background information for health professionals*. http://www.bowelcancer.org/medical/pdf/Background%20to%20Screening%20Summary%20April%202005.doc.*
64. Tappenden P, Eggington S, Nixon R *et al*. *Colorectal cancer screening options appraisal. Cost-effectiveness, cost-utility and resource impact of alternative screening options for colorectal cancer*. Report to the English Bowel Cancer Screening Working Group, September 2004. Sheffield: School of Health and Related Research, 2004. http://www.cancerscreening.nhs.uk/bowel/scharr.pdf.*
65. UK Colorectal Cancer Screening Pilot Group. Results of the first round of a demonstration pilot of screening for colorectal cancer in the United Kingdom. *BMJ* 2004; **329:** 133–7.
66. Renehan AG, O'Dwyer ST, Whynes DK. Cost effectiveness analysis of intensive versus conventional follow-up after curative resection for colorectal cancer. *BMJ* 2004; **328:** 81–4.
67. Department of Health. *NHS reference costs 2003 and national tariff 2004 (Payment by results core tools 2004)*. 2004 Crown Copyright. The main document and reference costs for 2004 are available at http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4070195.*

**= website was last accessed on 29 July 2007.*

A slide set is available to accompany this supplement from Norgine Pharmaceuticals Limited. Please call 0800 269865 for a copy.