BEST PRACTICE

Management of colorectal cancer

A Leslie, R J C Steele

Postgrad Med J 2002;**78**:473–478

Colorectal cancer is the second most common cause of cancer death in the UK. Prompt investigation of suspicious symptoms is important, but there is increasing evidence that screening for the disease can produce significant reductions in mortality. High quality surgery is of paramount importance in achieving good outcomes, particularly in rectal cancer, but adjuvant radiotherapy and chemotherapy have important parts to play. The treatment of advanced disease is still essentially palliative, although surgery for limited hepatic metastases may be curative in a small proportion of patients.

In the UK there are approximately 30 000 new cases of colorectal cancer registered each year and the disease represents the second most common cause of cancer death after lung cancer with over 17 000 per annum.[1] The incidence is roughly equal in men and women but over the past 30 years there has been a gradual increase in the incidence among men, although not in women.[1] The aetiology of sporadic colorectal cancer is still poorly understood, although there is epidemiological evidence for a protective effect of vegetable intake,[2] and there is also evidence that a diet rich in red meat may represent a risk factor.[3] A family history of colorectal cancer is also significant and there are two well established inherited conditions: familial adenomatous polyposis and hereditary non-polyposis colorectal cancer. The majority of individuals with a family history, however, do not fall into either of these categories and subtle genetic polymorphisms are likely to be responsible in the majority of cases.

The treatment of colorectal cancer is now multidisciplinary, and guided by precise staging and histopathology. For this reason, all patients should be discussed and treated as appropriate by a team consisting of pathologists, radiologists, surgeons, oncologists, and colorectal nurse specialists. In this article the areas of diagnosis, screening, staging, surgery, follow up, adjuvant therapy, and the management of advanced disease will be covered in turn with particular emphasis on conclusions which can be based on firm evidence. For further detailed information the reader is encouraged to refer to recent guidelines for the management of colorectal cancer issued by the Association of Coloproctology of Great Britain and Ireland,[4] the United Kingdom Committee for Co-ordination of Cancer Research,[5] and the NHS Executive.[6]

The Best Practice series will provide a definitive guide to the care of patients with a wide range of conditions. Experts in the field have been asked to distill current evidence based practice into clear and authoritative reviews, and their purpose is to ensure that clinicians have quick and easy access to contemporary thinking. The series will only be a success if clinicians know that the contents are reliable and form a basis for good practice. In days when we all need to be committed to continuing professional education and development, the existence of such a series can help us maintain our own current awareness and help meet the requirements for revalidation.—John Mayberry, *Editor*

See end of article for authors' affiliations

Correspondence to: Professor R J C Steele, Department of Surgery and Molecular Oncology, University of Dundee, Ninewells Hospital and Medical School, Dundee DD1 9SY, UK; r.j.c.steele@dundee.ac.uk

Submitted 14 February 2002
Accepted 21 March 2002

DIAGNOSIS

The symptoms which suggest a diagnosis of colorectal cancer are well known and the most important consist of change of bowel habit, rectal bleeding of short duration, and blood in the stool.[7] Any of these symptoms should prompt a digital rectal examination, as up to 80% of rectal cancers are palpable,[8] followed by urgent investigation. It should also be remembered that iron deficiency anaemia is an important mode of presentation and this finding should always raise the suspicion of colorectal cancer particularly in an individual over the age of 50 years.[9] The gold standard investigation for suspected colorectal cancer is colonoscopy. This has been shown to be more sensitive and specific than barium enema,[10] but it must be acknowledged that small lesions can be missed on colonoscopy,[11] and even in expert hands a 100% caecal intubation rate is not achievable.[12] In addition, a colonoscopy service is highly dependent on sufficient expertise, and in the UK double contrast barium enema (DCBE) is still widely used. However, this investigation can miss cancers, particularly in a patient with severe diverticular disease of the sigmoid colon, and on the right side of the colon spasm can be misinterpreted as a malignant stricture.[13] Thus, unless the sigmoid colon is extremely well visualised, DCBE should be supplemented by flexible sigmoidoscopy and radiological evidence of lesions in the caecum should be treated with suspicion and confirmed by colonoscopy unless appearances are unequivocal.

SCREENING

Screening for colorectal cancer can be divided into two broad categories: screening of high risk groups and population screening.

Abbreviations: DCBE, double contrast barium enema; MRI, magnetic resonance imaging

Box 1: Diagnosis

- Colonoscopy is the gold standard investigation.
- Barium enema tends to underdiagnose cancer in the sigmoid colon and overdiagnose in the caecum.
- Double contrast barium enema should usually be supplemented by flexible sigmoidoscopy.

Box 2: Screening

- Patients with a family history, a history of adenomatous polyps, and a history of ulcerative colitis should be considered for colonoscopic surveillance.
- Faecal occult blood testing is the only population screening modality that has been shown to reduced colorectal cancer mortality.

Screening of high risk groups

Family history

In general, patients with a family history of colorectal cancer constitute a high risk group. Precise recommendations for follow up are difficult to prescribe but it is generally agreed that individuals at moderate risk of developing colorectal cancer on the basis of their family history should be advised to undergo a single colonoscopy at the age of 50 years. There are, however, two conditions, inherited as autosomal dominant traits, which put the patient at very high risk of developing the disease. The first of these, familial adenomatous polyposis, accounts for approximately 1% of all colorectal cancer cases and is due to a germline mutation in the APC gene.[14] The condition is characterised by the appearance of multiple polyps throughout the colon and the inevitable development of colorectal cancer at a mean age of about 40. The age at which polyps first appear is highly variable but it is usually in the late teens and early 20s. It is now possible to identify mutations of the APC gene of an affected individual and the offspring of such an individual can be offered genetic counselling and screening.[15] If an offspring does not carry a mutation then no further investigations are required. However, carriers of the mutation should be offered early sigmoidoscopy and colonoscopy every two to three years. When polyps begin to develop the patient should undergo either panproctocolectomy with or without pouch reconstruction or total colectomy and ileorectal anastomosis depending on the degree to which the rectum is affected.

The second inherited condition, hereditary non-polyposis colorectal cancer accounts for around 5% of colorectal cancer cases. The diagnosis of this condition is made using the following clinical criteria[16]:

(1) The affected individual should have at least three relatives with a confirmed colorectal cancer (one of whom should be a first degree relative of the other two).

(2) At least two consecutive generations should be affected.

(3) Colorectal cancers should be diagnosed at less than 50 years of age.

It is now known that the majority of individuals with this condition have a germline mutation in one of the DNA mismatch repair genes[17] and, in some specialist centres, it is possible to offer genetic screening to individuals who appear to be at risk on the basis of their family history. Once an individual is identified as carrying a mismatch repair gene mutation or fulfils high risk criteria, colonoscopy should be offered every two to three years starting at about the age of 20.

Sporadic adenomatous polyps

Patients who have had colonoscopic removal of adenomatous polyps are at higher risk than the general population of developing further polyps (approximately 40% risk at three years)[18] and presumably, therefore, of developing colorectal cancer. The strongest evidence for this contention is the recent finding that screening for colorectal cancer can reduce the incidence of the disease, most probably as a result of removal of adenomas at colonoscopy.[19] However, enthusiasm for colonoscopic follow up of patients with colorectal adenomas must be tempered with a realistic approach to the use of endoscopy services. There has been one randomised trial showing that three yearly colonoscopy is as effective as one yearly colonoscopy in detecting significant lesions after polypectomy,[20] and it is generally agreed that patients should be offered follow up colonoscopy at three to five years after polypectomy. It is reasonable to defer for five years if there are one or two tubular adenomas without severe dysplasia. If, however, there are multiple polyps or a polyp with a villous component or severe dysplasia, colonoscopy should be repeated at three years. If no adenomas are found at follow up colonoscopy then five yearly examination is indicated but if further adenomas are detected repeat colonoscopy at three years is advisable.

Inflammatory bowel disease

Patients with long standing ulcerative colitis or Crohn's colitis are known to be at higher risk of developing colorectal cancer than the general population.[21] In ulcerative colitis the cumulative risk of developing invasive cancer appears to be 2% at 10 years, 8% by 20 years, and 18% by 30 years.[22] Thus, it seems reasonable to offer patients with left sided colitis or pancolitis of 10 years' duration colonoscopy every three years with mucosal biopsies plus biopsy of any lesions which are suspicious of cancer. This regimen should be increased to yearly colonoscopy when the disease has been present for 20 years or when indeterminate dysplasia has been diagnosed. If, on the other hand, high grade dysplasia is found, colectomy should be advised as there is a 40% chance of such a patient harbouring an invasive colorectal cancer.

Population screening

As colorectal cancer is a common condition, particularly after the age of 50, and because there is a well defined premalignant lesion which is amenable to treatment, the disease would seem to be a prime candidate for population screening. The most widely used screening tests are faecal occult blood testing, flexible sigmoidoscopy, and colonoscopy. However, only faecal occult blood testing has been shown to be effective in reducing colorectal cancer mortality in population based randomised trials. Such trials are essential in order to eliminate biases such as lead bias, which can give a false impression of an improved prognosis in screen detected disease. The trials of faecal occult blood testing carried out in Minnesota, USA, Nottingham, UK, and Funen, Denmark[23] have all shown significant reductions in disease specific mortality, and in the UK a demonstration pilot of faecal occult blood test screening for colorectal cancer is in progress.[24] If this pilot demonstrates that introduction of this type of screening is feasible then it is hoped that a national programme will be forthcoming.

STAGING

Once the diagnosis of colorectal cancer has been made it is important to establish the extent of the disease both locally and in terms of distant spread. All patients should have preoperative chest and liver imaging, and there is good evidence that computed tomography is the most sensitive modality for both liver and lung metastases.[25] As rectal cancer is not infrequently inoperable due to its confinement within the pelvis, many surgeons also use preoperative computed

Box 3: Staging

- All patients should have a contrast enhanced computed tomography of the liver and chest to look for metastatic disease.
- MRI is the most accurate means of preoperative staging for rectal cancer.
- Endoluminal ultrasound is particularly useful in distinguishing benign rectal tumours from early cancer.

tomography or magnetic resonance imaging (MRI) of the rectum. However, evidence that this approach is superior to digital rectal examination by an experienced surgeon in terms of determining operability is so far lacking.

There is now a great deal of interest in imaging rectal tumours with a view to planning preoperative radiotherapy, and there is no doubt that MRI is the most accurate modality for predicting histological spread of the tumour through the rectal wall and surrounding mesorectum.[26] However, its precise utility in this respect has yet to be fully established. Endoluminal ultrasound is also widely used but this is more valuable in distinguishing between benign rectal adenomas and invasive carcinoma.[27] Endoluminal MRI has a similar role but is less widely available. As synchronous tumours occur in about 5% of patients with colorectal cancer[28] it is also very important to ensure the entire colon has been imaged before surgery if at all possible. Although this can be achieved by DCBE, colonoscopy is preferable as this will also allow removal of any benign adenomatous polyps remote from the malignant tumour. If preoperative colonoscopy is not feasible because of an obstructing tumour, visualisation of the remaining large bowel should be performed within six months of surgery.

SURGERY

There is no doubt that surgery remains the definitive treatment for localised colorectal cancer and it is important that the patient undergoes appropriate preoperative preparation. Mechanical bowel preparation is widely employed but evidence from randomised trials fails to show that it has a significant effect.[29 30] However, for aesthetic reasons if for no other, the vast majority of surgeons employ bowel preparation certainly for left sided lesions, though less commonly for right sided tumours. Prophylaxis against deep vein thrombosis is important and the most commonly used method is low dose subcutaneous heparin.[31] Likewise, prophylactic antibiotics to reduce the incidence of wound infection are well established and current best practice is to give a single dose of intravenous antibiotics providing both aerobic and anaerobic cover within 30 minutes of induction of anaesthesia.[32] The surgery itself can be subdivided into surgery for colonic cancer and for rectal cancer.

Colonic cancer

In the elective situation, right sided cancers are treated by right hemicolectomy and left sided cancers by left hemicolectomy or sigmoid colectomy as appropriate. For tumours in the region of the splenic flexure there is debate as to whether segmental resection or extended right hemicolectomy is appropriate, although there is some evidence that extended right hemicolectomy is more likely to result in loose bowel action.[33] In the emergency situation with an obstructing colonic cancer a right hemicolectomy with primary anastomosis is appropriate for right sided lesions. For left sided lesions, particularly in the sigmoid colon, it is still standard practice to carry out a Hartmann's procedure with an end colostomy and closure of the rectal stump. In favourable situations and when an experienced surgeon is present, left sided cancers can be treated either by segmental resection with on-table colonic irrigation

Box 4: Surgery

- Surgery is the only potentially curative treatment for colorectal cancer.
- Anastomotic dehiscence rates should be less that 5% in colonic surgery.
- The outcome of rectal cancer surgery is highly dependent on the quality of the surgery, which is based on mesorectal excision.
- Anastomotic dehiscence rates after total mesorectal excision tend to be high, and consideration should be given to a defunctioning stoma.

or with subtotal colectomy and primary anastomosis. However, one randomised trial has shown that the latter procedure is associated with poorer functional outcome.[33] Clinical anastomotic dehiscence rates after colonic resection should be less than 5% but there is no consensus as to the best method of anastomosis. Randomised trials of stapling versus hand sutured anastomosis show no difference,[34] but the technique associated with the lowest anastomotic dehiscence rates in the literature is the interrupted serosubmucosal technique as described by Matheson.[35 36]

Rectal cancer

In recent years it has emerged that the most important concept in rectal cancer surgery is mesorectal excision.[37] This involves careful dissection in the plane immediately outside the mesorectum (fatty tissue surrounding the rectum in the pelvis) so that the rectum and tumour can be removed as a package and damage to the pelvic nerves is minimised. There is some debate as to whether a total mesorectal excision right down to the pelvic floor is necessary for all rectal cancers. It is generally agreed that for tumours of the upper third of the rectum it is safe to transect the mesorecum at 5 cm below the tumour, whereas for tumours of the lower two thirds of the rectum total mesorectal excision is necessary. Abdominoperineal excision of the rectum should only be necessary for very low tumours and should account for no more than 40% of all rectal cancer operations,[38] and indeed, in specialist centres this figure can be reduced further.[37] Providing a small rectal stump can be preserved an anastomosis is possible using stapling techniques. Unfortunately, however, this type of very low anastomosis is associated with a high anastomotic leakage rate (in the region of 20%)[39] and many surgeons advise the use of a defunctioning loop ileostomy in order to minimise the effects of leakage.[40]

If the principles in mesorectal excision are adhered to then overall local recurrence rates after rectal cancer surgery should be below 10%. As local recurrence is difficult to treat and ultimately fatal, good surgery also translates into better long term survival for patients with rectal cancer.

ADJUVANT THERAPY

Adjuvant therapy can be subdivided into adjuvant chemotherapy and adjuvant radiotherapy.

Adjuvant chemotherapy

As a result of many randomised trials it is now accepted that patients with Dukes's stage C carcinoma of the colon should be offered 5-fluorouracil based adjuvant chemotherapy if they are fit to receive it.[41] Other newer chemotherapy agents may be more effective but their use outside the setting of a randomised trial is not yet justifiable. There is some debate about the use of adjuvant chemotherapy in rectal cancer but it is generally agreed that the same rules apply as for colon cancer. It is more doubtful, however, whether or not patients with Dukes's stage B cancer should receive chemotherapy and this question is still being addressed by randomised studies.

Box 5: Adjuvant therapy

- Patients with stage C colorectal cancer should be considered for 5-fluorouracil based adjuvant chemotherapy.
- Preoperative radiotherapy for rectal cancer seems to be preferable to postoperative treatment.
- Preoperative radiotherapy reduces the risk of local recurrence of rectal cancer, but its role in conjunction with total mesorectal excision has yet to be fully established.

Box 6: Follow up

Follow up is carried out for:
- Early detection of metastases.
- Detection of metachronous polyps or cancers.
- Psychological support.
- Audit.

There is, however, little consensus as to how follow up should be conducted.

Currently, chemotherapy is not advised for patients with Dukes's stage A cancer.

Adjuvant radiotherapy

Adjuvant radiotherapy can only be recommended for rectal cancer as the morbidity associated abdominal radiotherapy is prohibitive. Within the pelvis, however, it has an important part to play. In North America the emphasis has been on postoperative radiotherapy and there is evidence that this is more effective when combined with 5-fluorouracil based chemotherapy.[42] However, in Europe emphasis has been on preoperative radiotherapy, and there is at least one randomised study indicating that preoperative treatment is associated with less morbidity and better disease control than postoperative radiotherapy.[43]

In general, preoperative radiotherapy can be divided into two categories. The first category is radiotherapy for the fixed rectal cancer in an attempt to render it operable. In these cases most radiotherapists would recommend 45 Gy in 25 fractions over five weeks followed by an interval of about a six weeks before surgery is attempted. While this can be effective, the results of this approach are often disappointing. The second strategy for preoperative radiotherapy is to use it on clearly operable disease in an attempt to reduce the risk of local recurrence. The most persuasive randomised trial examining this approach was the Stockholm 2 trial which demonstrated that 25 Gy in five fractions the week before surgery reduced local recurrence rates from 27% to 11% and was associated with improved survival.[44]

However, there was concern over the high local recurrence rate in the surgery only arm of this trial and for this reason a study based in the Netherlands randomised patients undergoing total mesorectal excision to preoperative radiotherapy or no preoperative radiotherapy.[45] This demonstrated a reduction in local recurrence from 8% to 2%, which was statistically significant. These results indicate that in order to benefit six patients it is necessary to treat 100 patients and it is known that this schedule of preoperative radiotherapy is associated with significant morbidity.[46] Thus, until the long term results of the Dutch trial are available, the precise role of radiotherapy in operable rectal cancer will remain unclear. In the meantime there is an ongoing Medical Research Council study (CR07) in which patients are randomised to have preoperative radiotherapy or postoperative radiotherapy only if the circumferential margins of the mesorectal excision are involved.[47] This study is steadily accruing patients and will inform this debate.

FOLLOW UP

There is little consensus regarding the follow up of patients treated for colorectal cancer, which varies from no follow up at all to lifelong scrutiny with regular carcinoembryonic antigen estimations, cross sectional imaging, and colonoscopy. In essence there are four reasons for follow up.[4] The first is to detect the development of metastatic disease at an early stage when treatment may be more effective. This is particularly true of liver metastases which may be suitable for resection. The second reason is to detect metachronous polyps or cancers, and it is generally agreed that patients should undergo colonoscopy at three years after a successful bowel resection. If this colonoscopy is negative then colonoscopy every five years is indicated. The third reason to follow up patients with colorectal cancer is to facilitate audit, and the fourth is to provide psychological support for the patients. Previously there was no evidence of any benefit accruing from intensive follow up but a recent meta-analysis of randomised trials has indicated that intensive follow up with computed tomography and carcinoembryonic antigen estimation does result in improved survival,[48] presumably by picking up those patients who are suitable for liver resection for metastatic disease (see next section). Unfortunately, it is not clear how often these investigations should be performed and further intensive research is necessary in this area.

MANAGEMENT OF ADVANCED DISEASE

Surgery for metastatic disease

There is now good evidence, although not from randomised studies, that survival may be prolonged by liver resection in patients with operable hepatic metastases.[49] The precise indications for surgical resection are not clear but it is generally accepted that if all disease can be removed while retaining sufficient functioning liver then resection should be attempted providing the patient is fit enough to withstand the surgery. If the disease is not resectable then it may be possible to destroy metastases using in situ techniques such as cryoablation and radiofrequency ablation.[50] Again there is evidence that this may prolong survival, although it is weaker than that for liver resection. Pulmonary resection for isolated lung metastases has also been reported but opportunities to carry out this surgery are infrequent.[51]

Surgery for locally advance disease

When considering the treatment of locally advanced disease, either primary or recurrent, it must be remembered that surgical excision provides the only realistic hope of cure. Thus when the primary tumour is invading adjacent structures such as the duodenum, stomach, kidney, ureter, or bladder consideration should be given to en-bloc resection of the tumour with an adequate portion of the adjacent organ. As far as advanced rectal cancers are concerned, a prolonged course of preoperative radiotherapy as described above should be considered prior to attempting resection.

Treatment of inoperable advanced disease

When colonic cancer is truly inoperable then surgical defunctioning or bypass may alleviate symptoms. Palliative radiotherapy is worth considering in patients with advanced rectal cancer as this may reduce symptoms. Recently there has been interest in stenting rectal and left sided inoperable cancers in order to alleviate obstructive symptoms but this will do little to reduce bleeding and mucus discharge. Palliative chemotherapy is the mainstay of the treatment of inoperable advanced colorectal cancer and the Mayo regimen of bolus 5-fluorouracil and folinic acid has been widely used. However, this regimen appears to be the least effective and most toxic of the regimens that have been widely tested in randomised trials. The De Gramont regimen of intermittently infused

Box 7: Management of advanced disease

- Patients with isolated liver metastases should be considered for liver resection.
- Systemic chemotherapy can prolong survival, but is palliative.
- Although chemotherapy is still largely based on 5-fluorouracil, newer agents, notably capecitabine and irinotecan, are showing significant promise.

5-fluorouracil and folinic acid and the Lokich regimen of continuously infused 5-fluorouracil appear to be more effective.[52] Raltitrexed is also an effective treatment but there have been recent concerns regarding toxicity with this drug.[53] A promising new approach is the use of oral capecitabine, and this also appears to be more effective than the Mayo regimen.[54] Two randomised trials have shown that patients who do not respond to or relapse on treatment with 5-fluorouracil and folinic acid may respond to the topoisomerase inhibitor irinotecan.[55 56] There is also some less robust evidence that adding irinotecan to 5-fluorouracil and 5-folinic acid as primary treatment increases the response rate and may produce modest improvements in survival.[57 58] It has to be stressed, however, that chemotherapy can only be viewed as a palliative measure and median survival advantage can only be measured in months.

CONCLUSION

Significant advances in the treatment of colorectal cancer have been made in recent years and in terms of improved survival the most important areas appear to be early detection and high quality surgery, particularly in the pelvis. The role of adjuvant therapy has been partially clarified but the treatment of advanced disease remains inadequate; as our understanding of the genetic and biochemical basis of cancer improves it is hoped that new biological modifiers and gene therapy may have a part to play in the future.

Authors' affiliations

A Leslie, R J C Steele, Department of Surgery and Molecular Oncology, University of Dundee, Ninewells Hospital and Medical School, Dundee, UK

REFERENCES

1 **Cancer Research Campaign**. *CRC cancer stats: large bowel-UK*. London: CRC, November 1999.
2 **Michels KB**, Giovannucci E, Joshipura KJ, *et al*. Prospective study of fruit and vegetable consumption and incidence of colon and rectal cancers. *J Natl Cancer Inst* 2000;**92**:1740–52.
3 **Sandhu MS**. Systematic review of the prospective cohort studies on meat consumption and colorectal cancer risk: a meta-analysis approach. *Cancer Epidemiol Biomarkers Prev* 2001;**10**:439–46.
4 **Association of Coloproctology of Great Britain and Ireland**. *Guidelines for the management of colorectal cancer*. London: Royal College of Surgeons of England, 2001.
5 **United Kingdom Committee for Co-ordination of Cancer Research**. *Handbook for the clinico-pathological assessment and staging of colorectal cancer*. London: UKCCCR, 1997.
6 **NHS Executive**. *Guidance on commissioning cancer services: improving outcomes in colorectal cancer*. London: Department of Health, 1997.
7 **Fijten GH**, Starmans R, Muris JW, *et al*. Predictive value of signs and symptoms for colorectal cancer in patients with rectal bleeding in general practice. *Fam Pract* 1995;**12**:279–86.
8 **McSherry CK**, Cornell GN, Glenn F. Carcinoma of the colon and rectum. *Ann Surg* 1969;**169**:502–9.
9 **Stellon AJ**, Kenwright SE. Iron deficiency anaemia in general practice: presentations and investigations. *Br J Clin Pract* 1997;**51**:78–80.
10 **Rex DK**, Rahmani EY, Haseman JH, *et al*. Relative sensitivity of colonoscopy and barium enema for detection of colorectal cancer in clinical practice. *Gastroenterology* 1997;**112**:17–23.
11 **Rex DK**, Cutler CS, Lemmel GT, *et al*. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. *Gastroenterology* 1997;**112**:24–8.
12 **Waye JD**, Kahn O, Auerbach ME. Complications of colonoscopy and flexible sigmoidoscopy. *Gastrointest Endosc Clin N Am* 1996;**6**:343–77.
13 **Thoeni RF**, Laufer IG. In: Gore R, Levine MS, eds. *Gastrointestinal radiology*. Philadelphia: WB Saunders, 1994.
14 **Bishop DT**, Hall NR. The genetics of colorectal cancer. *Eur J Cancer* 1994;**30A**:1946–56.
15 **Hodgson S**, Bishop D, Dunlop M, *et al*. Suggested screening guidelines for familial colorectal cancer. *J Med Screen* 1995;**2**:45–51.
16 **Vasen HF**, Mechlin JP, Khan PM, *et al*. The International Collaborative Group on Hereditary Non-Polypsis Colorectal Cancer (ICG-HNPCC). *Dis Colon Rectum* 1991;**34**:424–5.
17 **Aaltonen LA**, Salovaara R, Kristo P, *et al*. Incidence of hereditary nonpolyposis colorectal cancer and the feasibility of molecular screening for the disease. *N Engl J Med* 1998;**338**:1481–7.
18 **Bond JH**. Colorectal cancer update. *Advances in Gastroenterology* 2000;**5**:1163–82.
19 **Mandel JS**, Church TR, Bond JH, *et al*. the effect of faecal occult blood screening on the incidence of colorectal cancer. *N Engl J Med* 2000;**343**:1603–7.
20 **Winawer SJ**, Fletcher RH, Miller L, *et al*. Colorectal cancer screening: clinical guidelines and rationale. *Gastroenterology* 1997;**112**:594–642.
21 **Gillen CD**, Walmsley RS, Prior P, *et al*. Ulcerative colitis and Crohn's disease: a comparison of the colorectal cancer risk in extensive colitis. *Gut* 1994;**35**:1590–2.
22 **Eaden JA**, Abrams KR, Mayberry JF. The risk of colorectal cancer in ulcerative colitis: a meta-analysis. *Gut* 2001;**48**:526–35.
23 **Towler B**, Irwig L, Glasziou P, *et al*. A systematic review of the effects of screening for colorectal cancer using the faecal occult blood test, haemoccult. *BMJ* 1998;**317**:559–65.
24 **Steele RJC**, Parker R, Patnick J, *et al*. A demonstration pilot for colorectal cancer screening in the United Kingdom: a new concept in the introduction of healthcare strategies. *J Med Screen* 2001;**8**:197–202.
25 **Knol JA**, Marn CS, Francis IR, *et al*. Comparisons of dynamic infusion and delayed computed tomography, intraoperative ultrasound and palpation of liver metastases. *Am J Surg* 1993;**165**:81–7.
26 **Beets-Tan RGH**, Beets GL, *et al*. Accuracy of magnetic resonance imaging in prediction of tumour-free resection margin in rectal cancer surgery. *Lancet* 2001;**357**:497–504.
27 **Kwok H**, Bissett IP, Hill GL. Preoperative staging of rectal cancer. *Int J Colorectal Dis* 2000;**15**:9–20.
28 **Finan PJ**, Ritchie JK, Hawley PR. Synchronous and "early" metachronous carcinomas of the colon and rectum. *Br J Surg* 1987;**74**:945–7.
29 **Burke P**, Mealy K, Gillen P, *et al*. Requirement of bowel preparation in colorectal surgery. *Br J Surg* 1994;**81**:907–10.
30 **Miettinen RP**, Laitinen ST, Makela JT, *et al*. Bowel preparation with oral polyethylene glycol electrolyte solution vs. no preparation in elective open colorectal surgery: prospective, randomised study. *Dis Colon Rectum* 2000;**43**:669–75.
31 **Scottish Intercollegiate Guidelines Network (SIGN)**. *Prophylaxis of venous thromboembolism: a national clinical guidelines*. Edinburgh: SIGN, 2002 (under review).
32 **Glenny AM**, Song F. Antimicrobial prophylaxis in colorectal surgery. *Quality in Health Care* 1999;**8**:132–6.
33 **Scotia Study Group**. Single-stage treatment for malignant left-sided colonic obstruction: a prospective randomised clinical trial comparing subtotal colectomy with segmental resection following intraoperative irrigation. *Br J Surg* 1995;**82**:1622–7.
34 **MacRae HM**, McLeod RS. Handsewn vs stapled anastomoses in colon and rectal surgery: a meta-analyis. *Dis Colon Rectum* 1998;**41**:180–9.
35 **Matheson NA**, McIntosh CA, Krukowski ZH. Continuing experience with single layer appositional anastomosis in the large bowel. *Br J Surg* 1985;**72**(suppl):S104–6.
36 **Pye G**, Steele RJC. Anastomoses involving the colon and rectum; an 8-year experience. *J R Coll Surg Edinb* 1996;**41**:95–6.
37 **Heald RJ**, Moran BJ, Ryall RD, *et al*. Rectal cancer: the Basingstoke experience of total mesorectal excision, 1978–1997. *Arch Surg* 1998;**133**:894–9.
38 **Mella J**, Biffin A, Radcliffe AG, *et al*. Population-based audit of colorectal cancer management in two UK health regions. *Br J Surg* 1997;**84**:1731–6.
39 **Rullier E**, Laurent C, Garrelon JL, *et al*. Risk factors for anastomotic leakage after resection of rectal cancer. *Br J Surg* 1998;**85**:355–8.
40 **Dehni N**, Schlegel RD, Cunningham C, *et al*. Influence of a defunctioning stoma on leakage rates after low colorectal anastomosis and colonic J pouch-anal anastomosis. *Br J Surg* 1998;**85**:1114–17.
41 **Dube S**, Heyden F, Jenicek M. Adjuvant chemotherapy in colorectal carcinoma; results of a meta-analysis. *Dis Colon Rectum* 1997;**40**:35–41.
42 **Colorectal Cancer Collaborative Group**. Adjuvant radiotherapy for rectal cancer: a systematic overview of 8507 patients from 22 randomised trials. *Lancet* 2001;**358**:1291–304.
43 **Frykholm GJ**, Glimelius B, Pahlman L. Preoperative or postoperative irradiation in adenocarcinoma of the rectum: final treatment results of a randomised trial and an evaluation of late secondary effects. *Dis Colon Rectum* 1993;**36**:564–72.
44 **Swedish Rectal Cancer Trial**. Improved survival with preoperative radiotherapy in resectable rectal cancer. *N Engl J Med* 1997;**336**:980–7.
45 **Kapiteijin E**, Marijnen CA, Nagtegaal ID, *et al* Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *N Engl J Med* 2001;**345**:638–46.
46 **Dahlberg M**, Glimelius B, Graf W, *et al*. Preoperative irradiation affects functional results after surgery for rectal cancer: results from a randomised study. *Dis Colon Rectum* 1998;**41**:543–9.

47 **Steele RJC**, Sebag-Montefiore D. Adjuvant radiotherapy for rectal cancer. *Br J Surg* 1999;**86**:1233–4.
48 **Jeffrey GM**, Hickey BE, Hider P. Follow-up strategies for patients treated for non-metastatic colorectal cancer (Cochrane Review). The Cochrane Library, Issue 1, 2001. Oxford: Update Software.
49 **Scheele J**, Stang R, Altendorf-Hofmann A, *et al*. Resection of colorectal liver metastases. *World J Surg* 1995;**19**:59–71.
50 **Seifert JK**, Junginger T, Morris DL. A collective review of the world literature on hepatic cryotherapy. *J R Coll Surg* 1998;**43**:141–54.
51 **Shirouzu K**, Isomoto H, Hayashi A, *et al*. Surgical treatment for patients with pulmonary metastases after resection of primary colorectal carcinoma. *Cancer* 1995;**76**:393–8.
52 **Lokich JJ**, Ahlgren JD, Gullo JJ, *et al*. Prospective randomised comparison of continuous infusion fluorouracil with a conventional bolus schedule in metastatic colorectal carcinoma: a mid-Atlantic oncology programme study. *J Clin Oncol* 1989;**7**:425–32.
53 **Zalcberg J**. Overview of the tolerability of "Tomudex" (raltitrexed): collective clinical experience in advanced colorectal cancer. *Anticancer Drugs* 1997;**8**(suppl 2):517–22.
54 **Hoff PM**, Ansari R, Batist G, *et al*. Comparison of oral capecitabine versus intravenous fluorouracil plus leucovorin as first-line treatment in 605 patients with metastatic colorectal cancer: results of a randomised phase III study. *J Clin Oncol* 2001;**19**:2282–92.
55 **Cunningham D**, Pyrhonen S, James RD, *et al*. Randomised trial of irinotecan plus supportive care versus supportive care alone after fluorouracil failure for patients with metastatic colorectal cancer. *Lancet* 1998;**352**:1413–18.
56 **Rougier P**, Cutsem E, Bajetta E, *et al*. Randomised trial of irinotecan versus fluorouracil by continuous infusion after fluorouracil failure in patients with metastatic colorectal cancer. *Lancet* 1998;**352**:1407–12.
57 **Saltz LB**, Cox JV, Blanke C, *et al*. Irinotecan plus fluorouracil and leucovorin for metastatic colorectal cancer. *N Engl J Med* 2000;**343**:905–14.
58 **Douillard JY**, Cunningham D, Roth AD, *et al*. Irinotecan combined with fluorouracil compared with fluorouracil alone as first-line treatment for metastatic colorectal cancer: a multicentre randomised trial. *Lancet* 2000;**355**:1041–7.

BEST PRACTICE

Upcoming articles

The following articles have been commissioned for the "Best practice" series and will appear over the coming months:

- Motor neurone disease
- Liver failure in children
- Diabetes in adults
- Acute glomerular nephritis
- Osteoporosis
- SLE in adults
- Colorectal cancer
- Parkinson's disease
- Paediatric tuberculosis
- Irritable bowel syndrome
- Adult asthma
- Inflammatory bowel disease
- Stroke
- Rheumatoid arthritis in children
- Rheumatoid arthritis in adults
- Viral suppression in HIV therapy
- Lung cancer
- Angina
- End stage renal failure in children
- End stage renal failure in adults
- Hypertension