Guidelines

for the Management of Colorectal Cancer

3rd edition (2007)

Issued by

The Association of Coloproctology of Great Britain and Ireland

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Background

i) Colorectal cancer in the United Kingdom

Colorectal cancer is the third commonest cause of cancer related death (after breast and lung cancer) in the United Kingdom and the second commonest in non smokers. Around 100 new cases of colorectal cancer are diagnosed each day in the UK. In 2002 there were 34,889 new cases of colorectal cancer diagnosed in the United Kingdom, and approximately 17,000 deaths (CRUK 2006), but there has been a substantial improvement in five year survival, from 22% to 50% over the last 10 years (CRUK 2006).

Many patients present with advanced disease; both the Trent/Wales and Wessex audits indicate that over 20% of patients present with distant metastases. This may improve with increased knowledge among the general public about the nature of the disease, its symptoms, and the potential for complete cure if treated early. The launch of the NHS National Bowel Cancer Screening Programme in late 2006 should facilitate education of the public and the healthcare community.

ii) Purpose

Following the Government white paper "Working for Patients" in 1991, the Department of Health approached the Association of Coloproctology of Great Britain & Ireland and the Royal College of Surgeons, to request the production of clinical practice guidelines for the management of, among other conditions, colorectal cancer. The original Guidelines were published in 1996, with the purpose of assisting clinicians in clinical decision-making and practice by removing uncertainty in areas where it was possible to do so. In addition, they described the gold standard of good clinical care and were proscriptive of unacceptable clinical standards. This, the third edition of the Association's Guidelines has maintained these guiding principles and added newer evidence, where available, to support changes in clinical practice.

Guidelines are not intended to create a rigid framework where there is a reasonable difference of opinion, but the range of opinion may be informed by participation in appropriate clinical trials and national audits, which can help to set standards of care. Furthermore, participation in national audits and clinical trials can help identify areas of best practice which can then be disseminated to improve patient care for all.

iii) Development

An initial steering group set up by the Royal College of Surgeons of England in 1994 decided to develop colorectal cancer guidelines using three approaches: i) carrying out a **literature review** in areas where there might be an unequivocal scientific basis for recommendations; ii) defining reasonable practice using the results of contemporary **audits** of the management of all patients presenting with colorectal cancer in Trent, Wales and Wessex; and iii) describing current **consensus** where there is no research evidence on which recommendations might be based. This has been complemented with information from the literature to provide "gold standards" at which to aim.

This edition of the guidelines follows the pattern of previous editions, using a small drafting committee to produce a document which is circulated to an expert advisory group composed of representatives of the main groups involved with the management of colorectal cancer. For the first time, anal cancer has been incorporated into these guidelines. This edition of the guidelines was organised and funded by the Association of Coloproctology for Great Britain and Ireland.

Around the time the original guidelines were published, two documents appeared which had a significant impact on the provision of colorectal cancer care. These were the Calman Hine report (Department of Health 1995) and Guidance on Commissioning Cancer Services (NHS Executive 1997). These two documents led to significant changes in the way in which care was provided, from being predominantly organised and delivered by individual surgeons, to a multidisciplinary team (MDT) based approach.

Since the last edition of these Guidelines in 2000, the delivery of colorectal cancer care has been changed further by introduction of national targets. The Department of Health introduced national urgent referral guidelines in 2000, based on higher risk symptoms and signs for colorectal cancer –" the Two Week rule". All units are now required to see at least 95% of patients who meet these criteria for urgent referral within two weeks. From the end of 2005, the NHS National Cancer Plan set a target that patients with colorectal cancer should be treated within 31 days (one month) from the decision to treat and 62 days (two months) from the date of urgent referral by a general practitioner. These revised guidelines reflect these changes. The move towards more patient-centred care is welcomed as an opportunity to improve the overall quality of care for these patients.

iv) Validity

These guidelines have been assessed using a system designed by the Health Services Research Unit, University of Aberdeen. This system is summarised below:

a) Grading of Evidence

Ia: Evidence obtained from meta-analysis of randomised controlled trials

Ib: Evidence obtained from at least one randomised controlled trial

IIa: Evidence obtained from at least one well-designed controlled study without randomisation

IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study

III: Evidence obtained from well-designed non-experimental descriptive studies such as comparative studies, correlation studies and case studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

Note: Every reference quoted in the text of the detailed version of the guidelines is graded according to this system.

b) Grading of Recommendations

A: Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation (levels Ia, Ib).

B: Requires the availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation (levels IIa, IIb, III)

C: Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable clinical studies of good quality (level IV)

Note: Every recommendation (given in bold type in each section of the detailed guidelines and summarised in the next section) carries a grading according to this system. However, the grade cannot be regarded as an absolute indication of the strength of the guideline; although poor research has been omitted or flagged as such in the text, the cited studies are of variable quality. Thus, a guideline may have a grading below that usually associated with the evidence grading if the research is considered to be of poor quality. Some recommendations cover topics which are not amenable to formal studies, but represent good clinical practice (e.g. informed consent). These items are labelled with ✔ symbols.

v) Review of Guidelines

The management of colorectal cancer is constantly evolving; new evidence becomes available at frequent intervals and guidelines must be updated accordingly. For this reason, a standing working party and a standing expert advisory committee have been charged with updating them every 5 years. A consensus conference for an expert advisory committee will be held at five yearly intervals to revise the guidelines. The next revision is due to be published in 2012.

3 Summary of Guidelines

Note: the page reference for the detailed, evidence-based guideline and the recommendation grading is given at the end of each summary guideline.

Investigation

i) It is recommended that patients with higher-risk symptoms should be fast-tracked either in special clinics or with urgent appointments in routine clinics. Patients so referred should be investigated with sigmoidoscopy (flexible or rigid) plus a high quality double contrast barium enema, or colonoscopy, or CT colonography. (p18) **B**

ii) Pre-operative histology must be obtained from all rectal tumours. (p18) **C**

iii) Colonoscopists should audit their results, and expect to achieve quality and safety standards consistent with British Society for Gastroenterology guidance. (p18) **B**

iv) With the exception of patients with peritonitis who require emergency surgery, all patients with colon or rectal cancer should have pre-operative staging by CT scan to determine the local extent of the disease and the presence of lung or liver metastases. Patients with rectal cancer should also have MRI scans of the pelvis to stage the tumour and assess involvement of adjacent organs. Endorectal ultrasound scanning should be performed to assess T1 rectal cancers when local excision is being considered. (p19) **B**

v) People with a greatly elevated personal risk of gastrointestinal malignancy should be identified on the basis of family history criteria and/or pathological criteria and/or presence of a pathogenic mutation in a gene known to be responsible for a colorectal cancer susceptibility syndrome. Lifetime cancer risk ranges from 10-100% for members of high risk groups. (p20) **B**

vi) Patients fulfilling family history and/or clinical criteria, or those with a relative known to have a mutation associated with susceptibility to colorectal cancer, should be referred to the Regional Genetics Centre for formal counselling and mutation analysis. (p20) **B**

vii) People with only one first degree relative affected by colorectal cancer aged <45yrs or only two affected first degree relatives fulfil criteria for moderate risk. Although the excess personal risk is modest, these patients should be offered a single colonoscopy at age 55yrs. Polyps must be snared and histologically characterised. If adenomatous polyp is confirmed, then adenoma surveillance guidance applies. If the colon is clear of neoplasia, the patient may be reassured and discharged with recommendations relevant to population risk (e.g. uptake of FOBT screening). (p21) **B**

ix) People with family histories that do not fulfil the criteria described above are considered low risk. These individuals should be reassured that their risk level is only marginally greater than the general population, and that they should avail themselves of population-based screening measures. (p24) **B**

Access to Treatment

i) Treatment should begin within 31 days of discussion with the patient of the decision to treat. (p26) B

ii) All patients with colorectal cancer should have the benefit of a suitably informed surgical opinion and their management should be discussed by the multidisciplinary team. (p27) **C**

iii) Patients with colorectal cancer should have access to a colorectal nurse specialist for advice and support from the time they receive the diagnosis. (p27) ✔

iv) It is important that patients with colorectal cancer are offered the opportunity to ask questions and to have important information repeated. Provision of information should be an essential part of every consultation (p30) **C**

Preparation for Surgery

i) All patients undergoing surgery for colorectal cancer should give informed consent. Informed consent implies being given information about the likely benefits and risks of the proposed treatment and details of any alternatives. Informed consent should be obtained by the operating surgeon where possible. (p30) **C**

ii) The patient who may require a stoma should be seen by a stoma nurse prior to surgery and the referral should be made at the earliest opportunity to allow adequate time for preparation. (p30) **C**

iii) Bowel preparation should not be used routinely before colorectal cancer resection. (p31) **B**

iv) A combination of graduated compression stockings and heparin should be used for thrombo-prophylaxis for patients undergoing colorectal surgery. (p31) **A**

v) All patients undergoing surgery for colorectal cancer should have antibiotic prophylaxis. A single dose of appropriate intravenous antibiotic is likely to be effective. (p31) **A**

Elective Surgical Treatment

i) It is recommended that the term curative resection should be based on surgical and histological confirmation of complete excision. Surgeons should expect to achieve an overall curative resection rate of 60%, but it is appreciated that this will depend at least in part on the stage at which patients present. (p32) **B**

ii) Any cancer whose distal margin is seen at 15 cm or less from the anal verge using a rigid sigmoidoscope should be classified as rectal. (p33) **C**

iii) It is recommended that total mesorectal excision should be performed for cancer in the lower two-thirds of the rectum, either as part of a low anterior resection or an abdomino-perineal resection (APER). In tumours of the upper rectum the mesorectum should be divided no less than 5 cm below the lower margin of the tumour. Care should be taken to preserve the pelvic autonomic nerves and plexuses, and perforation of the tumour during operation should be avoided. (p33) **B**

iv) If a surgeon has any doubt regarding the choice of operation between low anterior resection or abdomino-perineal excision of the rectum, an experienced second opinion should be sought. (p34) **B**

v) Surgeons should expect to achieve an operative mortality of less than 20% for emergency surgery and less than 7% for elective surgery for colorectal cancer. (p35) **B**

vi) Surgeons should carefully audit their leak rate for colorectal surgery, and should expect to achieve an overall leak rate below 8% for anterior resections and below 4% for other types of resection. Ultra-low pelvic anastomoses are associated with a higher leak rate, and the judicious use of a temporary defunctioning stoma is recommended. (p35) **B**

vii) Local excision for cure in rectal cancer should be restricted to T1 cancers less that 3cm in diameter with good or moderate differentiation. It must be accepted that subsequent histopathological examination of cancers thought to be suitable for local excision will identify a proportion which require more radical surgery. (p36) B

viii) All laparoscopic colorectal operations should be performed by surgeons properly trained in colorectal surgery. These surgeons should also have undergone preceptorship laparoscopic training, particularly in rectal procedures. Their results should be carefully audited in the local hospital multidisciplinary setting and should also be submitted to the Association of Coloproctology of Great Britain and Ireland colorectal cancer database. (p36) **A**

Record Keeping

i) Existing guidelines for the keeping of clinical records, issued by the Royal College of Surgeons (RCS 1990), should be adhered to. (p36) **C**

ii) A check-list should be used to construct an operation note for patients undergoing surgery for colorectal cancer. (p37 and Appendix 2) **C**

iii) All patients with colorectal cancer should be brought to the attention of the Colorectal Multidisciplinary Team. Records of these meetings, the cases discussed and the outcomes agreed must be recorded. (p37) ✔

Emergency Treatment

i) Emergency surgery should be carried out during daytime hours as far as possible, by experienced surgeons and anaesthetists who are members of a colorectal cancer MDT. (p37) **C**

ii) In patients presenting with obstruction, CT scanning should be carried out to exclude pseudo-obstruction before operation. (p37) **B**

iii) In patients with large bowel obstruction, the insertion of an expanding stent is an acceptable treatment option where adequate local expertise exists. Stenting may be used either for palliation or as a bridge to surgery. (p37) **C**

Adjuvant Therapy

i) Radiotherapy and chemotherapy for colorectal cancer should only be given after discussion at the Multi Disciplinary Team (MDT) Meeting and under the direction of recognised oncologists, within facilities conforming to National Guidelines. (p42) **C**

ii) All patients should be made aware of the common and serious short- and long-term side effects of radiotherapy and chemotherapy, the expected benefits, and the other options available, before treatment begins. (p42) ✔

iii) Patients with resectable rectal cancer should be considered for preoperative short-course radiotherapy (25Gy in 5 fractions in 1 week), with surgery performed within 1 week of completion of radiation. However, in certain cases the MDT may decide that the benefits of treating patients with lower-risk disease will not justify the additional toxicity of radiotherapy. (p42) **A**

iv) When the MDT decides that radiotherapy (with synchronous chemotherapy) would be appropriate to downstage the tumour, a dose of 45Gy in 25 fractions over 5 weeks, with or without a reduced volume boost dose of 5.4-9Gy in 3-5 fractions, is recommended. (p42) **B**

v) If the addition of radiotherapy to surgery is deemed necessary for rectal cancer, it should ideally be given pre-operatively. However, in cases with well established predictive factors for local recurrence (e.g. evidence of tumour at the circumferential resection margin, mesorectal lymph node involvement and extramural vascular invasion), post operative radiotherapy and chemotherapy should be considered for patients who did not receive pre-operative radiotherapy. A dose of 45Gy in 25 fractions over 5 weeks with a planned boost dose of 5.4-9Gy in 3-5 fractions is recommended. (p42) **A**

vi) A planned radiotherapy volume using three or four fields given pre-operatively is recommended for rectal cancers, as this results in less morbidity and mortality. (p42) **B**

vii) Fluoropyrimidine as monotherapy or oxaliplatin in combination with 5-fluorouracil and folinic acid should be considered as options for the adjuvant treatment of patients with node-positive colorectal cancer following potentially curative surgery. (p44) **A**

viii) In general, a higher risk but otherwise fit patient with colon cancer should be offered oxaliplatin-based adjuvant therapy. (p44) **A**

ix) Patients with high-risk node-negative colorectal cancer should be individually counselled by an oncologist with regard to their level of risk and the possible benefits of fluoropyrimidine-based chemotherapy. (p45) **A**

Treatment of Advanced Disease

i) In fit patients with inoperable but non-metastatic rectal carcinoma, primary chemo-radiation should be offered. When the course is completed, the tumour should be re-staged and potentially curative resection considered if appropriate. (p45) **B**

ii) Fit patients with operable or potentially operable liver or lung metastases should be reviewed in the MDT with a hepatobiliary (or thoracic) surgeon and colorectal oncologist, to evaluate operability and to decide on a combined plan of management to optimise the chance of successful resection of all metastatic disease. (p45) **B**

iii) Patients with evidence of unresectable metastatic disease should be discussed by the MDT as soon as possible after the diagnosis of metastatic disease is made and, if appropriate, referred to an oncologist for consideration of palliative chemotherapy. (p46) **C**

vi) Palliative treatment using fluoropyrimidines alone, or 5FU in combination with oxaliplatin or irinotecan, has been approved by NICE for the treatment of metastatic colorectal cancer. (p46) **A**

ix) Surgeons and oncologists should make it a priority to build close links with palliative care specialists and units. (p47) **B**

Follow-Up

i) It is reasonable to offer a single CT scan of the abdomen and thorax to asymptomatic patients during the first two post-operative years for the purpose of detecting operable metastatic disease. (p51) **B**

ii) Colonoscopic follow-up yields adenomatous polyps and cancers. It is recommended that a "clean" colon should be examined by colonoscopy at 5 yearly intervals. (p51) **B**

iii) Follow-up is necessary for audit, which should be structured to determine post-operative mortality, anastomotic leak rates, colostomy rates and 5-year survival. This should be regarded as a routine part of a Cancer Unit's work. (p51) **C**

iv) The Colorectal Cancer Multi-Disciplinary Team should audit the survival rates of patients who undergo surgery and share this information within the Cancer Network. Data from each hospital should also be submitted to the National Bowel Cancer Audit Programme (NBOCAP). Audit should include information on variables such as the socio-economic status of patients, which can lead to variation in outcomes from different centres. (p51) ✔

v) Adequate manpower resources and information technology facilities must be available for this essential part of colorectal cancer care. (p52) ✔

Histopathology

i) All resected polyps and cancers should be submitted for histopathological examination (p67) **B**

ii) Pathology reports should contain information on all of the data items contained in the Joint National Guidelines Minimum Data Set for Colorectal Cancer Histopathology Reports. (p67) **C**

iii) Pathology laboratories should store stained histology slides for a minimum of 10 years, and tissue blocks from specimens indefinitely, in order to facilitate future case review, clinical audit, and research (p67) **B**

iv) Pathological examination of colorectal cancer specimens should be carried out in laboratories which perform to high technical standards such as those required for Clinical Pathology Accreditation, and participate in external quality assessment schemes and regular audit of technical procedures and diagnosis (p67) **B**

Anal Cancer

i) Squamous anal cancer is rare and has a varied presentation. Any suspicious anal ulcer or lesion should be biopsied, if necessary under general anaesthetic. (p75) ✔

ii) Local staging of the disease should be carried out using a combination of examination under anaesthesia, anal ultrasound and MRI. CT should be used to determine the presence of distant metastases. (p75) **B**

iii) Small anal margin cancers (less than 2cm and well differentiated) can be locally excised, provided clear margins are obtained. (p75) **C**

iv) Anal canal lesions should usually be treated by concurrent chemo -radiotherapy. 5FU and Mitomycin C or Cisplatin are usually used, but there is some uncertainty as to the best regimen. (p75) **A**

v) All patients with anal cancer should be discussed by an Anal Cancer MDT. (p75) ✔

Detailed Guidelines

4 Investigations

The process of referral and investigation

i) Introduction

When a person is concerned about possible colorectal cancer and the GP feels investigation is appropriate, it is important that this is done promptly. Although there is little evidence that reducing delay before treatment improves survival, delay causes considerable psychological morbidity which makes it harder for patients and their families to cope with their disease, especially if it is incurable. It is important to develop management strategies which ensure that time lags before referral, diagnosis and treatment are kept to a minimum. Some delays, however, are unavoidable. These include the diagnostic process, which incorporates 'treat, watch-and-wait' strategies by both patients and GPs, the time taken for appointments to be arranged, the time for diagnostic investigations and staging of the cancer, optimising the patient's general health for surgery, and the time required to arrange for admission and operation, ensuring that adequate facilities (such as high dependency or intensive care beds) are available when necessary.

It should be possible to minimise delays after referral to hospital, but reducing delays before this may be difficult. Public awareness campaigns and referral guidelines over many years have not achieved earlier referral. The reasons for this include the biological nature of the cancer, which seems to be a dominant factor determining the speed at which patients and GPs recognise that the symptoms are significant (McSherry et al 1969 III, McDermott et al 1981 III, Wessex Colorectal Cancer Audit 1990-1993 IIb, Hackett et al 1973 III, MacArthur and Smith 1983 III, Byles at al 1992 III, Feinstein 1966 IIb).

The management of patients with low risk symptoms should aim to avoid unnecessary referral to hospital of patients with transient symptoms from benign disease. This will conserve diagnostic resources, so that they are available for more rapid investigation of patients who are more likely to have colorectal cancer (Thompson et al 2003).

ii) Clinical history

Most patients with rectal and sigmoid cancers present with a combination of rectal bleeding and change in bowel habit, usually to increased frequency of defaecation and/or looser stools. Smaller numbers present with only one of these symptoms (Shallow et al, 1995; Flashman K 2004 IIb). Rectal bleeding occurs without anal symptoms in over 60% of patients with cancer (Thompson et al 2007 IIb).

In contrast, patients with cancers proximal to the sigmoid colon are more likely to present as emergencies with intestinal obstruction, or with iron deficiency anaemia, with or without symptoms. Only a small number of patients with cancers proximal to the sigmoid present to Outpatient Departments without iron deficiency anaemia and/or an abdominal mass (Shallow et al 1995 IIb; Flashman K 2004 IIb). These patients are difficult to identify among the large numbers of patients with benign conditions.

The Department of Health Referral Guidelines for GPs aims to improve the selection process in primary care so that the majority of patients with higher risk symptoms are seen within two weeks (NICE Guidelines 2005 IV).

High risk criteria – NICE Guidelines (2005)

General recommendations

- A patient who presents with symptoms suggestive of colorectal or anal cancer should be referred to a team specialising in the management of lower gastrointestinal cancer, depending on local arrangements.
- In patients with equivocal symptoms who are not unduly anxious, it is reasonable to use a period of 'treat, watch and wait' as a method of management.
- In patients with unexplained symptoms related to the lower gastrointestinal tract, a digital rectal examination should always be carried out, provided this is acceptable to the patient.
- Only patients with new and persistent symptoms listed below should be referred to the fast-track system. These criteria should include over 80% of all colorectal cancers presenting to Outpatients.

Specific recommendations

- In patients aged 40 years and older, reporting rectal bleeding with a change in bowel habit towards looser stools and/or increased stool frequency persisting for 6 weeks or more, an urgent referral should be made.
- In patients aged 60 years and older, with rectal bleeding persisting for 6 weeks or more without a change in bowel habit and without anal symptoms, an urgent referral should be made.
- In patients aged 60 years and older, with a change in bowel habit to looser stools and/or more frequent stools persistent for 6 weeks or more without rectal bleeding, an urgent referral should be made.
- In patients presenting with a right lower abdominal mass consistent with involvement of the large bowel, an urgent referral should be made, irrespective of age.
- In patients presenting with a palpable rectal mass (intraluminal and not pelvic), an urgent referral should be made, irrespective of age. (A pelvic mass outside the bowel would warrant an urgent referral to a urologist or gynaecologist.)
- In men of any age with unexplained * iron deficiency anaemia and a haemoglobin of 11 g/100 ml or below, an urgent referral should be made.
- In non-menstruating women with unexplained * iron deficiency anaemia and a haemoglobin of 10 g/100 ml or below, an urgent referral should be made.

* 'Unexplained' in this context means a patient whose anaemia is considered on the basis of a history and examination in primary care not to be related to other sources of blood loss (for example, non-steroidal anti-inflammatory drug treatment or blood dyscrasia).

Low risk criteria

Screening studies show that the risk of having bowel cancer is never zero, even in patients without symptoms. Some cancers will be found incidentally in patients presenting with symptoms from benign disease, and symptomatic cancers can develop in patients who already have symptoms from functional bowel disease or piles. This means that patients with persistent low-risk symptoms which do not respond to treatment, or which recur after stopping treatment, should be referred to routine clinics. (Thompson et al 2003 III).

Criteria indicating that patients are at low risk of colorectal cancer are:

- Rectal bleeding with anal symptoms or with an obvious external visible cause such as prolapsed piles, rectal prolapse and anal fissures.
- Transient change in bowel habit for less than 6 weeks, particularly if to decreased frequency of defaecation and harder stools
- Abdominal pain without iron deficiency anaemia or an easily palpable abdominal mass, and not associated with loss of appetite causing weight loss or other higher risk symptoms.

When patients have persistent symptoms which would normally fit low-risk criteria, but there are other worrying factors such as a positive family history or a positive FOB, they should be seen on an urgent basis in a normal clinic.

Time lags in the process of referral, diagnosis and treatment

The time from first symptom to treatment has not changed in over forty years (McSherry et al 1969 III, McDermott et al 1981 III, Wessex Colorectal Cancer Audit (1990-1993 IIb). However, the delay before an outpatient appointment for some patients may have been reduced by the introduction of the Government's 'Two Week Standard' in July 2000 (Flashman et al 2004 IIb) although this did not reduce the time to treatment overall.

In the Wessex Audit, the mean total delays before elective surgery for patients with rectal and sigmoid (distal) or proximal cancers were 7.7 months and 6.6 months respectively. Patients who had emergency surgery had significantly shorter delays: 3.2 months for distal cancers and 2.5 months for proximal cancers. The difference in 5-year survival between the best and worst districts (52% versus 35.1%) did not appear to be due to delays in referral or access to treatment; median total delays were 3.5 versus 3.6 months. (Wessex Audit IIb).

The same audit found that 65% of the delay before surgery for rectal and sigmoid carcinomas occurred before referral to a hospital; waiting for an outpatient appointment accounted for 15%, and 20% occurred during the process of diagnosis and treatment. For patients with colon cancers proximal to the sigmoid, 35% of the delay was before GP referral, 19% waiting for outpatient appointments, and 46% was due to hospital delay in diagnosis.

iii) Clinical examination

There is a palpable rectal mass in 40-80% of patients with rectal cancer (McSherry et al 1969 III, Shallow et al 1955 III), and 82% of palpable rectal cancers may be detected by GPs (Dixon et al 1991 III). These patients can be identified by GPs for fast-track referral.

A digital rectal examination should therefore be an essential part of the examination of any patient presenting with lower GI symptoms above the age of 40 years, and of anybody below this age with persistent symptoms. A small cancer at the anorectal junction which may be missed by endoscopy can often be detected by rectal examination. Vaginal examination should be part of the assessment of suspected rectal cancer in women.

It is likely that a right-sided abdominal mass will be of greater diagnostic value than left-sided, in view of a higher prevalence of a palpable sigmoid colon. When there is uncertainty about the cause of an abdominal mass, the patient should be treated with laxatives and re-examined to establish whether the mass is persistent before referral.

iv) Investigations

Investigations can be tailored according to the symptoms. The majority of cancers in patients presenting with rectal bleeding and/or a change in bowel habit, without any other significant diagnostic factors, occur within 60 cm of the anal verge and can be diagnosed by flexible sigmoidoscopy. This allows the adoption of a selective policy for the investigation of the proximal colon, particularly in patients without mandatory reasons for this investigation, e.g. an iron deficiency anaemia, an abdominal mass, severe symptoms, a positive FOB test or a strong family history of bowel cancer.

If a potentially curable colorectal cancer is detected by sigmoidoscopy, it is important that complete visualisation of the colon is achieved either pre- or post-operatively, as the incidence of synchronous lesions is in the order of 4-5% (Finan et al 1987 III, Barillari et al 1990 III). In the future, CT colonography may be combined with CT scanning to both stage a primary tumour and to detect synchronous lesions. If complete colonic imaging is not possible before surgery, it is important this is done within six months, or as soon as possible after closure of a temporary ileostomy.

Methods of investigation

Complete examination of the large bowel can be achieved by colonoscopy, adequate endoscopic visualisation of the rectum plus a double contrast barium enema, or CT colonography. When imaging with barium enema or CT colonography is technically impossible or gives inconclusive results, colonoscopy may be appropriate (Fenlon 1998, IIa; Pappalardo 2000 IIa). Similarly, patients in whom colonoscopy has failed may need barium enema or CT colonography to examine the whole bowel. A barium enema should always be complemented by endoscopy, normally flexible sigmoidoscopy. Small polyps in the sigmoid colon may be missed on a double contrast barium enema, particularly in the presence of diverticular disease. However, the rectum can be visualised clearly, and radiologists should report on any abnormality in this area. A small anorectal carcinoma at the anorectal junction is easily missed without a careful digital rectal examination. For exclusion of synchronous lesions, there is some evidence that colonoscopy and CT colonography may be more accurate than barium enema (Barillari et al 1990 IIb, Winawer et al 2000 Ib; De Zwart et al 2001 IV); in a study of 389 patients, 50% of synchronous cancers were not detected on the initial barium study and the majority of these would not have been included in the planned resection specimen (Barillari et al 1990 IIb). In review of the literature from 1980 to 2000, De Zwart and colleagues found that colonoscopy had superior sensitivity for polyps in patients at high risk of colorectal neoplasia, but that the respective roles of endoscopy and radiology in average-risk screening populations was not known. For the detection of small polyps, colonoscopy has superior performance, whereas sensitivity is similar for colonoscopy and barium enema for the detection of larger (>1 cm) polyps and tumours. Overall, colonoscopy was associated with a higher complication rate.

CT colonography has higher sensitivity than barium enema for polyps, particularly in the proximal colon. (Rockley et al 2005 IIb; Taylor et al 2006 IIb). Meta-analysis for detection rates of polyps at CT colonography (Halligan et al 2005 Ia) has demonstrated that for polyps smaller than 6 mm, sensitivity ranges from 45%–97% and specificity from 26%–97%, for polyps between 6 and 9 mm average sensitivity is 86%, specificity 86% and for polyps 1 cm or larger, average sensitivity is 93%, specificity 97%. Meta-analysis was not possible for the smaller numbers of cancers but including all cancers the cancer detection rate is 96%. The "gold standard" used for comparison in this study was colonoscopy.

It must be accepted, however, that all investigations may vary in quality, and the choice between colonoscopy, barium enema and CT colonography for total colonic examination will also depend on local availability and expertise.

Colon cancer should ideally be confirmed by histology, but when an unequivocal lesion has been detected by a high quality double contrast barium enema or CT colonography in a patient with symptoms strongly suggestive of cancer and/or iron deficient anaemia, histology is not essential. On the other hand, histological confirmation of neoplasia should be considered mandatory in all rectal cancers when surgery might result in either a permanent stoma or an ultra-low anterior resection, or when pre-operative radiotherapy is being considered.

The rectum may be examined by either flexible or rigid sigmoidoscopy, but the flexible sigmoidoscope is to be preferred because it allows visualisation of more of the bowel (Winnan et al 1980 IIb). The J manoeuvre on flexible sigmoidoscopy is necessary to pick up small lesions at the anorectal junction. If an unprepared sigmoidoscopy is unsatisfactory, then it should be repeated after adequate bowel preparation, which can be carried out in the patient's home before the outpatient appointment (Lund et al 1998 Ib, Atkin et al 2000 Ib).

Quality of investigations

Regardless of whether colonoscopy, barium enema or CT colonography are employed, certain minimum levels of quality should be achieved by all three of these investigations.

- *Colonoscopy*

Colonoscopy should usually be performed as a day-case procedure after full bowel preparation, and the endoscopist should be prepared to biopsy or remove appropriate lesions and inject some form of permanent dye to mark the site of the polypectomy. Specialist units should be able to offer endoscopic placement of stents for obstructing lesions. Endoscopists should be able to deal with any bleeding that occurs following

polypectomy. The patient must give fully informed consent and this includes warning of possible discomfort and the risks of perforation and bleeding. Colonoscopy under a general anaesthetic may be associated with a greater risk of perforation. If sedation is used, care should be taken to avoid complications arising from excessive sedation. Guidelines have been issued by the British Society of Gastroenterology (Bell et al 1991 III).

National quality standards for endoscopy have been established by the Department of Health using a Global Rating Scale (GRS) (www.grs.nhs.uk) and by the British Society for Gastroenterology (www.BSG.org.uk). These standards set the quality for the whole of the patient journey through endoscopy, with particular emphasis on quality and training.

Complete colonoscopy to the caecum can be achieved in 90% of cases with a perforation rate of 0.1% (Cotton & Williams 1990 III), but these figures have not been achieved for the whole country (Bowles et al 2004 IIb). The Trent/Wales audit showed that total colonoscopy was achieved in less than 50% of cases, whereas the BSG Colonoscopy Audit of 9,000 colonoscopies had an adjusted completion rate of 57% (Bowles et al 2004 IIb). There is clearly a great discrepancy between the best published results and the experience of most colonoscopists in the United Kingdom (Bowles et al 2004 IIb, Trent/Wales Audit IIb).

It is important that the endoscopist can recognise when a total colonoscopy has been achieved, and this can only be guaranteed when the terminal ileum has been biopsied (Cotton & Williams 1990 III). This is generally not practicable. A printed picture of the ileo-caecal valve may be a reasonable compromise.

It is important to audit the completeness and safety of colonoscopy on a regular basis, which, in addition to the GRS process, can be done by taking part in the National Bowel Cancer Audit Programme (NBOCAP; www.nbocap.org.uk).

- *Barium enema*

Barium enemas should be double contrast examinations (Laufer 1979 III). Increasingly, radiographers are performing barium enemas. Such examinations should be double-read, with one observer being a consultant radiologist, to reduce errors in interpretation. A designated consultant radiologist should be responsible for the supervision of radiographer-performed studies. The radiographers concerned should be specially trained and work to an agreed protocol.

Every attempt should be made to examine the whole of the large bowel and particular attention should be paid to the sigmoid colon and caecum, as failure to display these areas properly can lead to lesions being missed (Lauer et al 1965 III). In addition, inexperience combined with failure to distend the caecum can produce misleading appearances, which can be misinterpreted as malignancy and can result in unnecessary laparotomy.

It is not always possible to be certain of the radiological findings in barium enemas for reasons including the state of the preparation and physical considerations such as the mobility of the patient and colonic anatomy including diverticular disease and overlapping loops, but non-committal reporting of barium enemas by radiologists reduces the efficiency of this examination, which then requires further colonic imaging, usually by colonoscopy. For a barium enema to be of use in reaching a clinical decision, a firm opinion as to the most likely process giving rise to the radiological appearances should be given on the report. The aim should be to keep to a minimum the number of 'uncertain' reports.

A survery of radiologists examined the complications of barium enema over a two year period 1992 -94. During this period 738,216 barium enema examinations were included in this study (50% barium enemas performed in the United Kingdom). There was a ratio of one serious complications for every 9000 examinations, perforation of the rectum occurred once in every 25,000 examinations, one death attributed to the barium enema was reported to occur in every 60,000 examinations (Blakeborough et al 1997 III).

Teams carrying out barium enema should audit their results and should expect to achieve a false negative rate of less than 10%. Despite good radiological techniques, however, it may be impossible to be sure of always excluding neoplasia (Thomas et al 1995 IIb), particularly where there is severe diverticular disease of the sigmoid colon. In such cases, supplementary endoscopy by flexible sigmoidoscopy or colonoscopy is mandatory.

- *CT colonography*

CT colonography is increasingly being used in symptomatic patients who require total colonic imaging, and it is regarded as a robust examination for cancer detection. (Taylor et al 2003 III). There is evidence that patients prefer CT colonography to equivalent investigations (Taylor et al 2003 III; Gluecker et al 2003 III). Mechanical insufflation with CO_2 reduces patient discomfort and improves colonic distension and assessment of segments.

A designated consultant radiologist should be responsible for the supervision of radiographer-performed studies. The radiographer concerned should be specially trained and work to an agreed protocol. Ideally this should be a radiographer with prior training in barium enema work and so possessing many of the skills required to perform the examination. The perforation rate is low (0.06 to 0.08 per cent) (Sosna et al 2006 III; Burling et al 2006 III) and may be asymptomatic but demonstrated, due to the sensitivity of CT for detection of intramural and free air. The symptomatic perforation rate is reported to be 0.03%. Perforation can usually be managed successfully with conservative treatment.

IV contrast media may be given to aid in the assessment of extraluminal organs in symptomatic individuals. Antispasmodics may be given but are not essential. Ideally, the patient should be scanned both supine and prone, but a lateral decubitus position is an option if the patient is unable to lie prone. The milliamps (mA) should be reduced for prone scanning as only luminal information is required (Iannaccone et al 2003 III).

Image interpretation requires an expert reader. Currently there are no standards as to the number of supervised examinations required to achieve competency (Taylor et al 2004 III). The examinations should be double read. Computer Aided Diagnosis (CAD) is increasingly available as a second read of the data set, but is currently controversial. Faecal tagging may reduce the false positive rate for the reporting of small and medium sized polyps.

CT colonography is increasingly used for investigation of suspected bowel cancer, but its results should be audited with particular regard to false negative rates. CT colonography may be considered as part of the staging examination of patients with left-sided tumours, to assess the right colon at the same time.

In summary, it is recommended that patients with higher-risk symptoms should be fast-tracked either in dedicated 2-week clinics or with urgent appointments in routine clinics. Patients so referred should be investigated with sigmoidoscopy (flexible or rigid), and when appropriate by high quality double contrast barium enema, or colonoscopy or CT colonography. A barium enema should always be complemented by sigmoidoscopy.

Recommendation grade B

Pre-operative histology must be obtained from all rectal tumours.

Recommendation grade C

Colonoscopists should audit their performance and achieve quality and safety standards consistent with British Society for Gastroenterology guidance published in "Quality and Safety Indicators in Endoscopy".

Recommendation grade B

It is acceptable for non-consultant staff to perform double contrast barium enemas, colonoscopy and CT colonography, provided they have completed a recognised training programme and the examinations are performed to strict protocols and supervised by a consultant with appropriate training and experience.

Recommendation grade C

Pre-operative assessment of the stage of disease

Pre-operative staging is becoming increasingly important, both because of the improvement in imaging techniques and a greater choice of adjuvant and surgical treatments, particularly in rectal cancer.

Survival and clinical outcomes following treatment of colorectal cancer are markedly affected by the local extent of the disease, whether the lymph nodes are involved, whether the disease is disseminated, and surgical technique.

- *Assessment of the rectum: Local extension and peri-rectal lymph nodes*

The Royal College of Radiologists recommended high resolution MRI (1.5 Tesla) should be undertaken to assess circumferential resection margin and pelvic nodal involvement. (Padhani 1999 III, Kumar & Scholefield 2000 III, Heriot et al 1999 III). The degree of local extension determines whether a curative excision is possible, and whether preoperative radiotherapy should be offered (Brown et al 1999 IIb and Beets-Tan et al 2001 IIB). When local excision is being considered, staging by endorectal ultrasound scanning is recommended to determine the depth of tumour penetration.

MRITumour involvement in small perirectal lymph nodes can be identified using MRI (Brown et al 1999a IIb). It is important to consider the morphology of such nodes; size alone is an unreliable guide to tumour involvement. Lymph nodes > 1cm in diameter are more likely to contain tumour (Padhani 1999 III, Kumar & Scholefield 2000 III, Heriot et al 1999 III), and the majority of involved lymph nodes in colorectal cancer specimens measure >5mm (Dworak 1991 III); however, currently there is no reliable imaging method that allows these to be differentiated from reactive nodes. MRI with ultra-small particles of iron oxide (USPIO) may have a role in identification of malignant nodes (Koh et al 2004 III) in the future.

The value of MRI lies not so much in staging early tumours (where rectal endosonography is currently more accurate) but in assessing the tumour extent, particularly in the lateral and anterior planes. Involvement of the mesorectum is easily demonstrated on MRI and a histological clearance of less than 1mm may be predicted. The corresponding MRI measurement for predicting tumour involvement has been reported to be 1mm (88% sensitivity) (Brown et al 2003 III) and more cautiously 5mm (Beets Tan 2001 III). Rectal distension should not be used as this may impact on the preoperative prediction of involvement of the resection margin. (Slater et al 2006 III).

- *Assessment of the chest and liver for metastases*

A chest X-ray will identify most pulmonary metastases, but it is not as sensitive as CT. Although up to 25% of patients who develop a recurrence will have pulmonary metastases, only 2-4% will be identified with isolated metastases in the lung (Sugarbaker et al 1987 III).

Pre-operative staging using a CT scan of the thorax, abdomen and pelvis should be normal practice except in cases where information on cancer stage and metastatic spread would have no influence on management. The Royal College of Radiologists suggests that 18 FDG PET-CT is accurate for detecting hepatic and extra-hepatic disease. When CT imaging of the abdomen and pelvis reveals no liver metastases, a chest x-ray may be acceptable to assess the lungs.

With the exception of patients with peritonitis who require emergency surgery, all patients with colon or rectal cancer should have pre-operative staging using CT scanning of the thorax and abdomen and pelvis to determine the local extent of the disease and the presence of lung or liver metastases. Patients with rectal cancer should also have MRI scans of the pelvis to assess tumour stage and involvement of adjacent organs. Endorectal ultrasound scanning should be performed to assess early rectal cancers when local excision is being considered.

Recommendation grade B

vi) The significance of family history

It is now established that heritable factors make a significant contribution to an individual's risk of colorectal cancer. A twin study from Scandinavia found that heritable factors accounted for 35% of the risk of developing colorectal cancer (Lichtenstein et al 2000 IIa). The heritable factors can be considered in two broad groups. First, high penetrance (usually autosomal dominant) inherited syndromes, notably FAP and HNPCC, which account for fewer than 5% of all colorectal cancers (Cancer Research Campaign 1999 III). Second, heritable risk for colorectal cancer identifiable clinically through clustering of colorectal cancers within families (Lovett 1976 III). The mode of inheritance in this second, larger cohort, is likely to be multifactorial and is as yet incompletely understood. Several genes are likely to be involved, and they appear to predispose to adenomatous polyp formation as well as colorectal cancer (Ponz de Leon et al 1987 III, Burt 1985 IIa). The

likely mode of inheritance is autosomal dominant but with low penetrance and such genes may be carried by up to 20% of the population (Cannon-Albright et al 1988 III). A low-penetrance genetic pre-disposition of this kind is likely to be modified by a range of different genetic and environmental factors.

High penetrance autosomal dominant disease

People recognized at increased risk of colorectal cancer due to high penetrance genetic disorders are identified in the following ways: recognition of a family history of colorectal cancer that fulfils empiric criteria; presence of pathognomonic clinical/pathology features; identification of a molecular genetic defect in an affected proband or relative. Collectively, such cases account for a small proportion (3-5%) of all cases of colorectal cancer. However, the absolute cancer risk is very high and so surveillance is necessarily intensive. Guidance on the management of people in these high-risk categories is qualitatively distinct from that recommended for people fulfilling low-moderate risk criteria, and this is reflected in the recommendations for the two risk categories.

Although there are other, very rare, syndromes associated with excess colorectal cancer risk, this guidance is restricted to discussion of hereditary nonpolyposis colorectal cancer (HNPCC), familial adenomatous polyposis (FAP), MYH associated polyposis (MAP), juvenile polyposis syndrome (JPS) and Peutz-Jeghers syndrome (PJS). The syndromes are defined and summarised in Online Inheritance in Man (OMIM). All, except MAP, are due to germline transmission of a dominant gene defect associated with bowel cancer susceptibility and an excess of other cancer types. MAP is an autosomal recessive disorder, and so there are important issues around cancer risk in relatives and who should be offered surveillance within such families. Genes responsible for these syndromes have been identified and large numbers of mutations characterized. Because penetrance is incomplete, not all people who carry pathogenic mutations have cancer themselves and some may not have a particularly striking family history. Furthermore, mutations in causative genes have not been identified for all high-risk families. Hence, identification of at-risk individuals may be through family history criteria and/or pathological criteria and/or presence of a pathogenic mutation in one of the genes listed in the appendix.

People with a greatly elevated personal risk of gastrointestinal malignancy should be identified on the basis of family history criteria and/or pathological criteria and/or presence of a pathogenic mutation in a gene known to be responsible for a colorectal cancer susceptibility syndrome.

These patients, and those with a relative who is known to have such a mutation, should be referred to the Regional Genetics Centre for formal counselling and mutation analysis.

Recommendation grade B

Surveillance is not required for individuals who do not carry the mutation that has been shown to be causative in affected relatives. Hence, a negative gene test from an accredited genetics laboratory in families with characterised mutations means that GI surveillance should cease.

Recommendation grade B

Hereditary non-polyposis colorectal cancer (HNPCC)

HNPCC can be defined empirically by family history or by demonstration of a pathogenic gene mutation. HNPCC was previously defined using the following criteria: >3 family members affected by colorectal cancer or >2 with CRC and one with endometrial cancer in >2 generations; one affected relative must be age <50 at diagnosis; one of the relatives must be a first degree relative of the other two (Vasen et al 1991 IV, Vasen et al, 1999 IV, Rodriguez-Bigas et al, 1997 IV). Lifetime GI cancer risk associated with HNPCC is variously reported as around 80% for colorectal cancer and 13-20% for gastric cancer in studies that have selected families by HNPCC criteria (Vasen et al, 1995 III, Aarnio et al 1995 III).

Since the causative DNA mismatch repair (MMR) genes have now been identified (Papadopoulos 1997 IIb, Peltomaki et al, 1997 IIb)), fulfilment of these criteria is not required. Lesser degrees of family history are associated with a lower proportion of cancer cases carrying mutations in one of the known genes. However, an appreciable proportion of early onset colorectal cancer is due to MMR gene mutations (Farrington et al 1998 IIb). This should be borne in mind when managing young patients with colorectal cancer who do not

have an obvious family history, as they may be obligate gene carriers. A web-based model has been developed and validated (http://www1.hgu.mrc.ac.uk/Softdata/MMRpredict.php) that predicts the likelihood that a cancer patient carries a mutation. The algorithm uses age at diagnosis, tumour location and cancer family history to define those who merit tumour immunohistochemical assessment of MMR gene expression and subsequent genetic analysis.

Large bowel surveillance and surgery for HNPCC family members and MMR gene carriers

Total colonic surveillance (at least biennial) should begin at age 25 years, or 5 years younger than the age at diagnosis for the first cancer case in the family, whichever is the earlier. Surveillance should continue to age 75 years or until it has been demonstrated that the individual does not carry the causative mutation.

Recommendation grade B

Any patient with a colorectal malignancy who is a member of a family which is known to carry a mutation in an MMR gene should be counselled and offered a surgical procedure that includes both a cancer control element and prophylaxis. At present there are no data supporting, or against, offering primary prophylactic surgery for patients who do not yet have cancer.

Recommendation grade C

People with MMR gene mutations or those from Amsterdam positive HNPCC families who have cancer will require resectional surgery unless treatment is deemed as palliative. The risk of metachronous colorectal cancer is high. For patients with proximal tumours, colectomy and ileorectal anastomosis facilitates surveillance of the retained rectum (Lynch et al, 1993 III, Church 1996 IV). The risk of cancer in the retained rectum is 3% every 3 years for the first 12 years after abdominal colectomy, so endoscopic surveillance of the rectum is mandatory (Rodriguez Bigas et al, 1997, III).

Surveillance does not completely prevent cancer development, and interval cancers may occur. There are insufficient data to recommend for or against primary prophylactic surgery in MMR gene carriers, so if this considered, it must be on the basis of discussion between a fully informed patient and clinicians. Prophylactic surgery should not be offered to at-risk HNPCC family members who are not proven gene carriers, since the maximum colorectal cancer risk is 40% for males and 15-30% for females.

Upper gastrointestinal surveillance for HNPCC family members and MMR gene carriers

Some HNPCC families have a particular propensity for gastric cancer (Lynch et al 1993, III). There are no studies of gastric surveillance in HNPCC and no reported observational data. However, it appears reasonable to offer upper GI endoscopy contemporaneously with colonoscopy after the age of 50 years, when the greatest increase in risk occurs.

In families with HNPCC where there have been cases of gastric cancer, biennial upper GI endoscopy should commence at age 50 years, or 5 years earlier than the first gastric cancer case in the family, whichever is the earlier. Surveillance should continue to 75yrs or until the causative mutation in that family has been excluded.

Recommendation grade C

Familial adenomatous polyposis (FAP)

Familial adenomatous polyposis is an autosomal dominant syndrome with very high penetrance, characterised by the presence of more than 100 adenomatous polyps in the colon and rectum (Bussey 1975, IV; Bulow 1989 III). The condition is usually due to truncating mutations of the APC gene on chromosome 5q and causative mutations can be identified in ~60% of families (Wallis et al 1999 , IIb; van der Luijt et al, 1997 IIb). Some APC mutation negative cases are due to MYH mutations. The risk of developing large bowel cancer is >90% by age 70 years without prophylactic surgery (Bulow 1989 III), although as more mutations are discovered, it is clear that penetrance is lower than previously thought. The risk of gastroduodenal cancer is ~7% (Sieber et al, 2003 IIb). Around 25% of all cases are due to new (sporadic) mutations and consequently there is no family history in such cases.

Large bowel surveillance for FAP family members

In a minority of FAP families a mutation cannot be identified, and so annual flexible sigmoidoscopy should be offered to at-risk family members from age 13-15 years until age 30, and 3-5 yearly thereafter until age 60 years. Surveillance may be offered as a temporary measure for people with documented APC gene mutations who wish to defer prophylactic surgery for personal reasons. Such individuals should be offered 6 monthly flexible sigmoidoscopy and annual colonoscopy, but surgery should be strongly recommended before they reach the age of 25 years. After colectomy and ileorectal anastomosis, the rectum must be kept under review at least annually for life, because the risk of cancer in the retained rectum is 12-29% (de Cosse et al, 1992 III; Nugent 1992 III). The anorectal cuff after restorative proctocolectomy should also be kept under annual review for life.

In cases where a mutation is identified, surgery is recommended (see below) but some patients may wish to defer surgery. The patient must be counselled about cancer risk and offered intensive surveillance. These recommendation are based on indirect data collected prior to widespread mutation testing (Morton et al, 1993, III). It is clear that large numbers of polyps are associated with high risk of cancer (Debinski et al, 1996 IIb) and patients who develop large numbers of polyps early in life should be dissuaded from delaying surgery.

Prophylactic colorectal surgery

Identification of cases and prophylactic surgery has improved survival in FAP (Bulow et al, 2000 III; Vasen et al 1998 IIb). Patients with proven FAP require surgery to remove the majority of at-risk large bowel epithelium. Because of the significant risk of cancer in the retained rectum, the optimal procedure is proctocolectomy with ileoanal pouch.

Patients with FAP should be advised to undergo prophylactic colectomy between the age of 16 and 20 years. The operation of choice is proctocolectomy and ileoanal pouch, but colectomy and ileorectal anastomosis may be appropriate for patients with relatively few polyps.

Recommendation grade C

Upper gastrointestinal surveillance in FAP

To combat the substantial risk of upper GI malignancy in FAP after prophylactic colectomy, upper GI surveillance is recommended. While the presence of gastroduodenal polyposis is well recognised, there are few published studies on which to gauge the potential benefit of surveillance. However, the approach seems reasonable and 3 yearly upper GI endoscopy is recommended from age 30 years with the aim of detecting early curable cancers. Patients with large numbers of duodenal polyps should undergo surveillance yearly.

Peutz-Jeghers Syndrome (PJS)

Peutz-Jeghers Syndrome is a rare autosomal dominant syndrome with high penetrance, defined by the presence of hamartomatous polyps of the small intestine, colon and rectum, in association with muco-cutaneous pigmentation . The risk of colorectal cancer is 10-20% (Tomlinson et al 1997 III). In 20-63% of cases, inactivating mutations can be identified in the gene STK11(LKB1), but there is evidence for genetic heterogeneity (Boardman et al 2000 IIb).

Large bowel surveillance by colonoscopy or flexible sigmoidoscopy with barium enema is recommended 3 yearly from age 18 years.

Recommendation grade C

Juvenile Polyposis Syndrome (JPS)

Juvenile polyposis is a rare condition, defined by the presence of multiple hamartomatous polyps of the colon and rectum that develop during childhood. It is associated with a colorectal cancer risk of around 10-38% and a gastric cancer risk of 21%. In around 50% of cases, mutation of the SMAD4 gene is found (Roth et al, 1999 IIb; Yoon et al, 2000, IIb, Huang et al, 2000, IIb), but there is some evidence for genetic heterogeneity. .

Isolated juvenile polyps are relatively common and do not appear to be associated with excess cancer risk. Because juvenile polyposis is rare, experience is limited. Many polyps are located in the right colon and so the whole colon should be visualised (Howe et al, 1998 IIb). There is particular risk of malignancy in cases where there is adenomatous element to the polyps. Hence, polyps should be snared and sent for histology. Consideration should be given to prophylactic surgery in cases with multiple polyps that cannot be controlled by snaring, those with symptoms, those with adenomatous changes, and those where colorectal cancer is a feature of the family history.

Colorectal surveillance for JPS

Surveillance of the whole of the large bowel by colonoscopy or flexible sigmoidoscopy with double-contrast barium enema is recommended 1 - 2 yearly for individuals believed to have JPS from age 15-18 years, or even younger if the patient has presented with symptoms. Screening intervals could be extended at age 35 years in at-risk individuals, but documented gene carriers or affected cases should be kept under surveillance until age 70 years and prophylactic surgery discussed.

Recommendation grade C

Lower risk groups

People with a family history of colorectal cancer but who do not have a recognisable high risk genetic disorder may still have an increased personal risk of the disease. This section addresses the cancer risk of asymptomatic individuals who have affected relative(s).

Colorectal cancer is common, so many people have an affected relative by chance. In various studies, 4-10% of control subjects report at least one affected first degree relative. The greater the number of affected relatives and the younger the age at onset, the greater the personal risk (St John et al, 1993 IIb; Slattery et al, 1994 IIb; Houlston et al, 1994 III).

There are no pathognomonic features of this category of familial clustering of colorectal cancer and so, outwith HNPCC, FAP and other cancer susceptibility syndromes, at-risk groups are currently defined by empiric family history risk criteria. This guidance aims to define the level of empiric risk at which it is appropriate to consider clinical surveillance and specifically excludes people with a family history that fulfils criteria for HNPCC or other autosomal dominant genetic syndrome associated with colorectal cancer susceptibility.

Although the aggregate risk of colorectal cancer for groups of people can be defined by family history parameters, it is important to emphasise that the risk is heterogeneous for individuals within such risk categories. Furthermore, some people will develop colorectal cancer who have a family history that does not fulfil these criteria, and it is essential that this residual risk is made explicit.

Family history and personal colorectal cancer risk

Risk of colorectal cancer can be estimated empirically from the current age of the at-risk individual, age-at-onset of affected relatives, and the number and relationship of those affected. While there is an excess risk to people with any affected family member, only those with a first degree relative who has developed colorectal cancer at a young age, or those with at least two first degree relatives with colorectal cancer, have sufficiently high relative risk to merit consideration for invasive surveillance.

It is important to emphasise that the absolute population risk for younger age groups is low, and so even relatively high relative risks do not necessarily reflect high absolute risk, nor do they show that surveillance should be recommended. The current age of the individual is an important determinant of the absolute risk of colorectal cancer in the next ten years. Risk estimations derived from population data (http://www.isdscotland.org/isd/1425.html) show that people aged 70 years have a 4% chance of developing colorectal cancer in the next 10 years, which is substantially greater than the 10-year risk for people aged 40-60 years with a relative risk (RR) of 5 (Butterworth et al, 2006 IIa; Dunlop 1997 IIb). It is inconsistent to offer intensive surveillance to people with a family history if their absolute risk is less than the population risk for those aged 70 years.

The risk of future colorectal neoplasia in individuals with close relatives who have developed colorectal cancer should be estimated using family history information.

Recommendation grade B

High-moderate risk

High-moderate risk criteria relate to people who report a family history of three or more first-degree relatives affected by colorectal cancer (none aged <50yrs), where germline transmission to the at-risk individual is possible. People in this category are at sufficient risk to merit low-intensity surveillance between the ages of 55 and 75 years.

Individuals who meet high-moderate risk criteria should be offered 5 yearly colonoscopy from age 55 until 75 years if the colon is clear of neoplasia. If polyps are found, they should be removed by snare polypectomy and histologically characterised. Patients with adenomas should have 3 yearly colonoscopy.

Recommendation grade B

Moderate risk

People with only one first degree relative affected by colorectal cancer aged <45yrs, or with only two affected first degree relatives, fulfil criteria for moderate risk. Observational and case/control data indicate a modest excess personal risk (Table 1).

There is some potential benefit of surveillance for people in this group over the age of 55 yrs. Between 4% and 21% of 55-year old people have been reported to have adenomas, but only 2-6% have significant neoplasia (Winawer et al, 1997 IIb; Dove Edwin et al, 2005 IIb). A single colonoscopy at the age of 55 years will both identify any cancers, and permit the removal of polyps. If affected patients are then enrolled on adenoma surveillance programs, colorectal cancer incidence may be expected to fall by 66% (Guillem et al 1992 Ib). Thus colonoscopy at the age of 55 years for people fulfilling these family history risk criteria may be expected to produce an appreciable reduction in cancer-related mortality. Surveillance before the age of 45years is not justified, because only 1.6-2% carry a significant adenoma (Guillem et al 1992 Ib), and the 10 year risk of cancer is less than 1%.

Individuals who meet moderate risk criteria should be offered a single colonoscopy at age 55 years. Any polyps must be snared and histologically characterised. If adenomatous polyp is confirmed, then adenoma surveillance guidance applies. If the colon is clear of neoplasia, the individual should be reassured and discharged with recommendations relevant to population risk (eg uptake of FOBT screening).

Recommendation grade B

In all cases where surveillance is appropriate, total colonoscopy is to be preferred, because of the risk of proximal colonic lesions and the opportunity for snare polypectomy. When complete colonoscopy cannot be achieved, the patient should be offered a double contrast barium enema on the same day. Flexible sigmoidoscopy and barium enema (with targeted follow-up colonoscopy) is an acceptable alternative to colonoscopy.

Recommendation grade B

Low risk

People with family histories that do not fulfil high, high/moderate, or moderate risk criteria are classified as low risk.

People at low risk should be reassured. It should be emphasised that their risk level is only marginally greater than that of the wider population, and that they should avail themselves of population-based screening measures.

Recommendation grade B

Referrals made solely on the basis of family history are best centralised to facilitate audit. This has resource implications, and might be done through the Regional Genetics Service. Audit should include documentation of family history, level of risk assigned and correlation with outcome measures including: proportion of consultands offered screening, screening-related complications, and long term cancer incidence/mortality in screened and unscreened groups through NHS flagging.

Recommendation grade C

Table 1 Risk of developing colorectal cancer in relation to family history

Risk group	ISD# Scotland RR (absolute 10yr risk)	Butterworth (lifetime risk of CRC death)*	Houlston (OR)	St John
Population	Lifetime 5.1%#	(At age 40 <0.5%)§ (At age 55 1.0%)§ (At age 75 2.5%)§	1:50	N/A
Any FH	N/A	2.14 (At age 40 <1.0%) (At age 55 1.8%)	1:17	1.8
One young relative affected <45yrs**,<50yrs†	N/A	3.55 (At age 40 <1.0%†) (At age 55 3.5%†)	1:10	3.7**
Two or more affected relatives	N/A	3.97 (At age 40, <1.0%) (At age 55, 3.8%)	1:6	5.7

http://www.isdscotland.org/isd/1425.html
† Meta-analysis includes all papers in this table and document.
§ Office of National Statistics data 2004. Series MB1 no 23 Table 3.
* Derived from data collected in 1970.
** Affected relative aged <50yrs

5 Treatment

Access

i) Waiting times

Between 1990 and 1993, the Trent/Wales Audit revealed an overall median waiting time of 20 days (mean 26 days), with a range of 0 – 330 days. In the Wessex audit the median waiting time was 18 days (mean 27 days), with a range of 0 – 400 days. However, the Department of Health introduced national urgent referral guidelines in 2000 based on high risk symptoms and signs for colorectal cancer – the so-called "Two Week rule". All units are now required to achieve in excess of 95% of these patients seen within the specified time.

From the end of 2005, the NHS National Cancer Plan has aspired to the target that patients with colorectal cancer should be treated within 31 days (one month) from the decision to treat and 62 days (two months) from urgent general practitioner referral. There are two exceptions to this rule; if a patient wishes to defer treatment, and when a patient is medically unfit and requires specific medical treatment prior to cancer surgery. This is referred to as 'stop the clock', and the Cancer Waiting Time clock may be suspended for the duration of the delay (Department of Health 2005 IV).

Treatment should begin within 31 days of discussion with the patient of the decision to treat.

Recommendation grade B

ii) The multidisciplinary team (MDT)

A colorectal cancer MDT in a relatively small district general hospital (DGH) serving a population of 200,000 can expect to deal with about 120 new patients per year, and would include two or three surgeons. Larger centres may be able to form teams with more specialised members, such as hepatobiliary surgeons.

The core team should include the following members:

- At least two specialist surgeons who have been trained in, and maintain a special interest in, techniques relevant to colorectal cancer, and who can demonstrate a high level of skill in this area. Each surgeon in the MDT should carry out a minimum of 20 colorectal resections with curative intent per annum. Sub-specialisation should be specifically encouraged among surgeons who treat patients with rectal cancer.
- Oncologist. Whenever elective surgery is considered for patients with rectal cancer, a clinical oncologist should be involved in discussion about each patient before surgery is scheduled. In view of the current shortage of clinical oncologists in the NHS, teleconferencing may be appropriate to enable this discussion to be held. A medical oncologist may also be included in the MDT if available.
- Diagnostic radiologist with gastro-intestinal expertise.
- Histopathologist.
- Skilled colonoscopist of any discipline (surgeon, physician, or specialist nurse).
- Clinical nurse specialists (CNSs). In many respects, the role of CNSs for colorectal cancer is similar to that of breast care nurses. A CNS should be available to provide support, assistance, information and advice to every patient. She/he should have specific expertise in colorectal cancer and in addition, should be trained in communication skills and counselling. These nurses should ensure that patients' non-clinical needs – for example, for information and support – are met.
- Palliative care specialist (doctor or nurse), who should work with palliative care services in the community.
- Meeting co-ordinator, who should take responsibility for organising MDT meetings. The co-ordinator should have the authority to ensure that extended team members such as social workers and psychologists are available when required. The co-ordinator should also be responsible for feedback about patients referred to more specialised teams, and the return of such patients to the local colorectal cancer MDT.

- Team secretary who will provide clerical support for the MDT, recording all decisions made by the team and communicating appropriate information promptly to all those (such as GPs) who may require it. In smaller teams, the co-ordinator may take the role of team secretary.

MDTs should maintain close contact with other professionals who are actively involved in supporting the patient or carrying out the treatment strategy decided by the core team (the extended team). Extended teams should include the following members:

- Gastroenterologist
- Liver surgeon who is a member of a liver resection MDT and can advise the colorectal cancer MDT
- Thoracic surgeon with expertise in lung resection
- Interventional radiologist with expertise in insertion of lower intestinal stents
- GPs/primary care teams
- Dietician
- Liaison psychiatrist/clinical psychologist
- Social worker
- Clinical geneticist/genetics counsellor
- Clinical trials co-ordinator or research nurse

Selected individuals from the extended team may be included in the core team.

Each Network should ensure that nominated individuals are available to fill each role in every extended team and should carry out regular audits to check that they do, in fact, fulfil the function of that role when required. Trusts may pool resources so that individuals with specific expertise work with more than one colorectal cancer team. Teams based in Cancer Units must work closely with colleagues in the associated Cancer Centre.

For details of Anal Cancer and Liver Resection MDTs, see Improving Outcomes in Colorectal Cancer (NICE, 2004 IV).

All patients with colorectal cancer should have the benefit of a suitably informed surgical opinion and their management should be discussed by the multidisciplinary team.

Recommendation grade ✔

Patients with colorectal cancer should have access to a colorectal nurse specialist for advice and support from the time they receive the diagnosis.

Recommendation grade ✔

iii) Surgical specialisation

There is considerable variability between outcomes achieved by individual surgeons. In a prospective study carried out between 1974 and 1979, McArdle and Hole (1991 IIb) found wide variations between surgeons in rates of curative resection, operative mortality, anastomotic leak, local recurrence and survival, even when hazard rate ratios were adjusted for patient-related risk factors. Three major population audits, Trent/Wales, Wessex, and Lothian; all give similar figures for operative mortality, but more recent data from NORCCAG show an improving operative mortality rate; this probably reflects the trend to sub-specialisation and changes in surgical training. Fewer surgeons now operate on patients with colorectal cancer; each surgeon is more specialised and has a higher case load. Anonymised audits such as these are particularly valuable because they reveal changes over a long time period.

There is now a substantial body of research assessing the effects of surgical specialisation and patient throughput (both the number of cases treated per surgeon and per hospital) on outcomes in colorectal cancer. The review carried out to inform the NICE guidance on the management of colorectal cancer identified 6 systematic reviews and 28 other studies dealing with these issues. Considered as a whole, this evidence shows that surgical specialisation is associated with better outcomes, particularly in rectal cancer.

As a general rule, the more complex the operation, the greater the surgical skill required; such skill is acquired and developed through specialised training and experience and maintained by regular practice. A surgical training programme for rectal cancer in Stockholm reduced the permanent stoma rate and local recurrence rates, and 5 year cancer-specific survival rates increased as a result of the total mesorectal excision project (Martling A 2000 IV). It is not, therefore, surprising that in surgical oncology as a whole, the benefits of higher volume practice and greater specialisation would be particularly apparent in outcomes for types of cancer for which surgery is more challenging; and this is indeed the pattern with colorectal cancer.

Surgery for rectal cancer, which is more difficult to do well, shows volume and specialisation effects much more clearly than surgery for colon cancer. A study of 3200 patients in Scotland who underwent resection for colorectal cancer between 1991 and 1994 reported that differences in outcome following apparently curative resection for colorectal cancer among surgeons appeared to reflect the degree of specialisation rather than case volume, and concluded that it was likely that increasing specialisation would lead to further improvements in survival (Mc Ardle and Hole 2004 III). A survey in Australia of all new cases of colorectal cancer registered at each Australian State Cancer Registry reported that patients seen by low volume surgeons were most likely to be given a permanent stoma and that patients with rectal cancer who were operated on by high volume surgeons were significantly more likely to receive a colonic pouch (McGrath 2005 III). Similar results were reported from California, where a study of 7257 patients with rectal cancer treated between January 1994 and December 1997 showed that patients with rectal cancer who underwent surgery at high volume hospitals were less likely to have permanent colostomy and had better survival rates than those who were treated at low volume hospitals (Hodgson D, 2003 III).

In rectal cancer, 11 of 13 studies assessing surgical specialisation reported that more specialised surgeons achieved better outcomes. Greater specialisation tends to be associated with higher patient throughput, so it is difficult to separate these issues. Six out of eight good quality studies of specialisation in rectal cancer showed significant effects on one or more of the following measures of outcome; survival rates (up to five years); quality of surgery (assessed by complication rates or tumour-free excision margins); and local recurrence rates. Greater specialisation is also associated with shorter in-patient stay and less frequent use of stomas (Improving Outcomes in Colorectal Cancer, NICE 2004 IV).

Recommendations

Surgery for colorectal cancer should only be carried out by surgeons with appropriate training and experience, working as part of a multidisciplinary team.

Recommendation grade B

Process

i) Preparation for surgery

Surgery for colorectal cancer should be avoided if the hazards are deemed to outweigh the potential benefits, i.e. when the patient is medically unfit for surgery or has advanced disease which is not amenable to surgical therapy. One study suggested that poor outcomes result when the patient is of advanced years, there are multiple sites of metastases or greater than 25% hepatic replacement, and when haemoglobin is less than 10 (Kuo et al, 2003 III). As the decision not to operate depends on highly individual factors, it is impossible to provide specific guidelines; but in making such a decision it is important to involve the patient and/or close relatives so that the underlying reasoning is clear and acceptable to all concerned.

There is increasing evidence supporting the use of models which take patient co-morbidity into account, such as the P-POSSUM and Cleveland Clinic scoring systems (Senagore et al 2004 IIb; Poon et al 2005 IIb; Fazio et al 2004 IIb), to help predict surgical outcome. A review of the accuracy of evaluating operative risk in colorectal cancer surgery using ASA and POSSUM-based models and based, in part, on the ACPGBI Colorectal Cancer Database, concluded that post-operative death could be predicted using simple numerical tables. This method can be used in everyday practice for pre-operative counselling of patients and their carers, as a part of the process of informed consent. The tables may also be used to compare the outcomes achieved by multidisciplinary colorectal cancer teams (Al-Homoud, 2004 III).

Social deprivation has an adverse impact on cancer-specific outcome (Hole and McArdle 2002 IIb; Wrigley et al 2003 IIb), and presentation with obstruction, perforation or as an emergency is associated with social deprivation (Rabeneck et al 2006 IIb). The impact of the combination of social deprivation and an ageing population on trends in surgical outcomes should be recognised.

When it is decided that surgery is to proceed, certain fundamental aspects of preparation should be considered. These are listed below:

a) Informed consent

b) Preparation for stoma formation

c) Cross-matching

d) Bowel preparation

e) Thrombo-embolism prophylaxis

f) Antibiotic infection prophylaxis

g) Enhanced recovery

a) Informed consent

Valid consent to treatment for colorectal cancer is essential and reflects patients' fundamental legal and ethical right to determine what happens to their own body. Valid consent requires that the patient must be competent to take decisions about treatment options, must have received sufficient information in an understandable form to make this decision, and must not be acting under duress. Informed consent is therefore a process of discussing options and coming to a joint decision with the patient by providing information about:

- Benefits and risks of the proposed treatment
- What the treatment will involve
- What the implications of not having the treatment are
- What alternatives may be available
- What the practical effect on their life of having, or not having, the treatment will be

The information will be gathered from a number of sources including the responsible Consultant, Specialist Colorectal Nurse, Stoma Therapist, Patient Support Groups and other information sources such as the Internet. This process would allow a patient time to reflect on the options and agree treatment with the responsible clinician. The health professionals carrying out a procedure are ultimately responsible for ensuring that the patient is genuinely consenting to what is being done as it is they who would be held responsible in law if this were challenged later. In most circumstances, the surgeon who is undertaking an operative procedure will signal completion of the consent process by completing a written consent form with the patient.

The risks attached to operative treatment should be discussed and documented, in particular, the risk of bleeding, infection, DVT, PE, anastomotic leak, the risk of an unplanned stoma and, in pelvic surgery, urinary and sexual dysfunction. Functional outcome should form part of the general discussion about the outcomes of treatment. It may be appropriate to discuss mortality risk and, increasingly, risk models are available to offer validated predictions to patients requiring this level of information.

Adult patients are always assumed to be competent to give consent unless demonstrated otherwise. Competent adult patients are entitled to refuse treatment. Practitioners should be aware that no one can give consent on behalf of an incompetent adult, who should be treated in their "best interest". "Best interests" go wider than "best medical interests", to include factors such as the wishes and beliefs of the patient when competent, their current wishes, their general well being and their spiritual and religious welfare. People close to the patient may be able to give information on some of these factors. Where the patient has never been competent, relatives, carers and friends may be best placed to advise on the patient's needs and preferences. Clinicians are wise to document carefully the reasons for their decision in delivering a particular treatment when acting on behalf of a patient without written consent.

The Human Tissue Act 2004 makes consent the fundamental principle underpinning the lawful retention and use of body parts, organs and tissues from the living or the deceased for specific health related purposes and public display. The Act regulates the removal, storage and use of human tissue, referred to in the Act as "relevant material". The legislation will be brought into force during 2006 under the guidance of the Human Tissue Authority which will issue codes of practice covering consent; donation of solid organs, tissue, and cells for transplantation; post mortem examination; anatomical examination; removal storage and disposal of human organs and tissue; donations of allogenic bone marrow, peripheral blood stem cells and donor lymphocytes for transplantation. Clinicians are referred to information available from the Department of Health website and that of the Human Tissue Authority itself for further guidance (www.hta.gov.uk IV).

It is important that patients with colorectal cancer are offered the opportunity to ask questions and to have important information repeated. Provision of information should be an essential part of every consultation

Recommendation grade B

All patients undergoing surgery for colorectal cancer should give informed consent. Informed consent implies being given information about the likely benefits and risks of the proposed treatment and details of any alternatives. Informed consent should be obtained by the operating surgeon where possible.

Recommendation grade C

b) Preparation for stoma formation

If a patient may require a stoma, the nature and consequences of this should be carefully explained. It is also important that the site of the stoma be marked prior to surgery to ensure optimum fitting of the appliance (Devlin 1982 IV). **The patient should be seen by a stoma nurse prior to surgery** (Saunders 1976 IV)**, and the referral should be made at the earliest opportunity to allow adequate time for preparation.** It is recognised that this may not be possible in some emergency situations and in this case the stoma site should be marked by an experienced surgeon.

Recommendation grade C

c) Cross-matching

There is evidence that blood transfusion may increase the likelihood of recurrence of colorectal cancer, and immunological mechanisms have been invoked (Burrows & Tartter 1982 III). This has not been unequivocally proven, however, (Bentzen et al 1990 III), and a trial comparing the use of autologous and allogeneic blood in patients undergoing resection of colorectal cancer showed no difference in prognosis (Busch et al 1993 Ib). **Blood transfusion should not be withheld if there is a clinical indication to give it, and preparations for blood transfusion should be made in all patients undergoing surgery for colorectal cancer except where an individual patient refuses.** For an uncomplicated right hemicolectomy, group and save serum may be sufficient, but formal cross-matching is recommended for more extensive operations, especially rectal resections.

Recommendation grade C

d) Bowel preparation

In the previous edition of these Guidelines, mechanical bowel preparation was recommended despite the conflicting evidence in the Trent/Wales audit and in Irving et al 1987 (III). The Cochrane Review, last updated in 2004 (Guenaga et al 2005 Ia), stated that prophylactic mechanical bowel preparation before colorectal surgery has not been proven valuable for patients. Controversially it seems that bowel preparation might lead

to more anastomotic leakage and thus the procedure should be omitted. There is good evidence to suggest that mechanical bowel preparation using polyethylene glycol (PEG) should not be used before elective colorectal surgery (Slim 2004 Ia). In addition, bowel preparation with a phosphate enema was associated with an increased risk of anastomotic leakage requiring re-operation, compared with oral PEG (Platell 2006 Ib). A randomised trial of sodium picosulphate (Picolax) versus no preparation showed that bowel preparation did not influence outcome after colorectal surgery (Burke 1994 1b). The rationale for avoiding bowel preparation prior to low anterior resection is less compelling than for colonic resection.

Bowel preparation should not be used routinely before colorectal cancer resection.

Recommendation grade B

e) Thromboembolism prophylaxis

Patients undergoing surgery for colorectal cancer are at risk of deep vein thrombosis (DVT) and pulmonary embolism (PE) (Salzman and Davies 1980 III). The most widely studied prophylactic measure against these complications is the use of subcutaneous heparin, and although there have been no studies confined to patients with colorectal cancer, a meta-analysis of appropriate trials has indicated that the rates of DVT, PE and death from PE can all be significantly reduced in general surgical patients (Collins et al 1988 Ia, Mismetti 2001 Ia). Low molecular weight heparin (LMWH) has attracted recent attention, and although a large randomised trial in patients undergoing abdominal surgery has shown it to be of similar efficacy to standard heparin, bleeding related complications were less common (Kakkar et al 1993 Ib). Other measures which can be taken are intravenous dextran, the use of intermittent pneumatic compression devices and the use of graduated compression stockings. Dextran does not appear to be as effective as heparin (Salzman & Davies 1980 III), but there has been one trial indicating that intermittent compression is equivalent to heparin in reducing the incidence of DVT at least (Persson et al 1991 Ib). Graduated stockings alone are less effective than other measures (Persson et al 1991 Ib). All surgeons in Trent/Wales used heparin and/or intermittent compression.

Patients undergoing pelvic surgery for malignancy may be considered "high risk" for thromboembolic disease, particularly after pre-operative adjuvant therapy. In these "high risk" cases the use of self administered LMWH for 2-3 weeks following surgery is recommended by the Cochrane review.

A combination of graduated compression stockings and heparin should be used for thrombo-prophylaxis for patients undergoing colorectal surgery.

Recommendation grade A

f) Antibiotic prophylaxis

There is now very good evidence that prophylactic administration of antibiotics can decrease morbidity, shorten hospital stay and reduce infection-related costs after general surgical operations (Page et al 1993 Ib). In the United Kingdom, perioperative intravenous administration is favoured for colorectal surgery (Keighley 1988 Ib), but the oral route may also be satisfactory (Page et al 1993 Ib). Various antibiotics and combinations of antibiotics have been shown to be effective; in Trent/Wales the most favoured regime was a combination of a cephalosporin and metronidazole. Gentamicin with metronidazole and augmentin alone were also used. If intravenous cephalosporin and metronidazole are used, there is evidence from a randomised, controlled trial that a single dose immediately before surgery is as efficacious as a three dose regimen in preventing wound infection (Rowe-Jones et al 1990 Ib).

With modern antibiotic prophylaxis, the rates of wound infection (presence of wound discharge with positive microbiology) should be less than 10% (Page et al 1993 Ib, Rowe-Jones et al 1990 Ib). It should be noted, however, that a rate of 2% for elective colorectal surgery has been reported (Matheson et al 1985 III).

All patients undergoing surgery for colorectal cancer should have antibiotic prophylaxis. It is not clear which regime is most appropriate, but a single dose of an appropriate intravenous antibiotic given shortly before surgery is normally effective.

Recommendation grade A

Wound infection rates after elective surgery for colorectal cancer should be less than 10%.

Recommendation grade A

e) Enhanced Recovery

With the development of Enhanced Recovery Programmes (ERP) optimising peri-operative care, there is a growing body of evidence which shows that hospital stays can be reduced without an increase in morbidity, deterioration in quality of life or increased cost (King et al 2006 III).

ii) Rates of curative resection

Curative resection can be defined as removal of all macroscopic disease at the time of operation, backed up by histological evidence that the resection margins of the specimen submitted to the pathologist are clear of tumour (Phillips et al 1984 IV). If the surgeon is in doubt as to whether this has been achieved, this should be stated. If residual tumour is thought to remain, it should be biopsied where it is safe to do so (UKCCCR 1989 IV).

The rate of curative resection achieved by an individual surgeon will, to some extent, depend on the stage of the tumours seen in his or her practice. The Trent/Wales and Wessex audits have shown that this varies across districts, with the percentage of tumours presenting at Dukes' stage A varying from 6 to 18% and the percentage with distant metastases varying from 19 to 39%. The rate of curative resection varied from 31% to 72%, and was inversely correlated with the percentages of cases with distant metastases.

The ACPGBI audit report based on data from 10194 patients between April 2002 and March 2003 showed that overall, approximately 30% of patients have incurable disease at presentation. This total was made up of 14% who had no operation (advanced cancer, co-morbid disease or patient choice), 4% who had an operative procedure that did not include cancer resection and a minimum of 12% who had metastatic disease at surgery.

Curative resection also depends on good surgical technique, especially for rectal cancers. As this is a subjective intra-operative assessment, surgeons vary as to the proportion of their operations which are classified as curative (McArdle and Hole 1990 IIb). In the Trent/Wales audit, the overall rate of curative resection was 60% and in Wessex it was 53%, figures very similar to those reported by two large prospective studies involving around 150 surgeons in the UK. (Phillips et al 1984 IIb, McArdle et al 1990 IIb). Better results are described in the literature, however; an overall curative resection rate for low rectal tumours of 77% has been reported (Karanjia et al 1994 III), and other specialist centres describe similar results (Whittaker and Goligher 1976 III, Lockhart-Mummery et al 1976 III, Dixon et al 1991 III, Karanjia et al 1990 III, Michelassi et al 1990 III). Although it is tempting to ascribe this finding purely to the skill and experience of specialist surgeons, particularly good results such as these may be the result of selective referral patterns to specialist units.

The term curative resection should be based on surgical and histological confirmation of complete excision. Surgeons should expect to achieve an overall curative resection rate of 60%, but it is appreciated that this will depend at least in part on the stage at which patients present.

Recommendation grade B

iii) Definition of rectal tumour

In 1999, representatives of the American Society of Colon and Rectal Surgeons and the Association of Coloproctology met with the Australian Societies to define the rectum and the procedures used to treat cancer of the rectum.

As the treatment of rectal cancer differs from the treatment of colonic cancer in some important respects, particularly in the areas of surgery and radiotherapy, it is important to have a clear anatomical definition of the rectum. Strictly, the rectum is that part of the large bowel distal to the sigmoid colon and its upper limit is indicated by the end of the sigmoid mesocolon. Standard anatomical texts put this at the level of the third sacral vertebra (Williams and Warwick 1980 IV), but it is generally agreed by surgeons that the rectum starts at the sacral promontory (UKCCCR 1989 IV). This is not particularly helpful pre-operatively, however, and it has been agreed by the Expert Advisory Committee that **any tumour whose distal margin is seen at 15cm or less from the anal verge using a rigid sigmoidoscope should be classified as rectal.**

Recommendation grade C

iv) Surgical technique

a) Resection

There is little controversy regarding the resection of colonic tumours. There has been a tendency to move away from segmental resection for tumours of the transverse colon and splenic flexure in favour of extended right hemicolectomy, and although there have been no randomised trials, this is widely accepted as being safer. The no-touch isolation technique in which the vascular supply to a tumour is divided before the tumour is handled has been tested in a randomised controlled trial and shown to confer no significant advantage (Wiggers et al 1988 Ib).

In rectal cancer, however, resection technique is of great importance. Although most local recurrences after resection of colonic cancer occur alongside disseminated disease (Abulafi and Williams 1994 III), local recurrences after rectal excision are often isolated, and the reported rate of recurrence after curative rectal resection varies from 2.6% (Karanjia et al 1990 III) to 32% (Hurst et al 1982 III). Individual surgeons vary greatly in this respect, with two studies showing a variation of 0 to 21% in recurrence rate among the participating surgeons (Phillips et al 1984 IIb, McArdle and Hole 1990 IIb).

The reasons for this variation are not entirely clear, although there is good evidence that surgical technique is a critical factor. Complete excision of the mesorectum is associated with a low rate of local recurrence (Heald et al 1982 III, Heald and Ryall 1986 III), and a pathological study has shown that distal mesorectal spread often extends further than intramural spread, with secondaries being found up to 3cm distal to the primary cancer (Scott et al 1995 IIb). Evidence from Europe has shown that education of established surgeons can lead to improvements in technique which result in a reduction in local recurrence and a reduction in the abdomino-perineal resection rate (Martling et al 2000 IV). It is recommended that lymph node clearance should extend for 5cm beyond the distal margin of a rectal cancer, and in tumours of the middle and lower thirds of the rectum the only practical way of achieving this is by total mesorectal excision. When this is done, care must be taken to preserve the autonomic nerves and plexuses on which sexual potency and bladder function depend.

There was a concern that a tendency to avoid abdomino-perineal excision (APER) in favour of anterior resection might account for high local recurrence rates (Phillips et al 1984 IIb, Neville et al 1987 III), but several series have shown no difference between the operations (Dixon et al 1991 III, Morson et al 1963 III, Patel et al 1977 III, Williams et al 1984 III, Holm et al 1995 IIa). Recurrence rates are higher after APER than anterior resection, and whether this is due to involved circumferential margins (Radcliffe 2006 IV) or technical problems is not clear. Randomised controlled studies comparing APER and anterior resection are not available, but where differences in local recurrence rates for the two operations exist, it has been suggested that they may be explained by the plane of dissection being nearer the rectum in anterior resection – a problem which can be avoided by total mesorectal excision (Heald 1988 III).

A study of surgical technique by Marr et al (2005 III) describes the perineal approach to the abdomino-perineal excision with the patient in the prone position. The anus and levator muscles are excised allowing a cylinder of tissue to be removed. This results in the surgical resection margin being farther away from the muscularis propria and sphincters and a lower rate of CRM involvement. The resulting perineal deficit is covered by surgical flaps.

Perforation of the tumour during resection is also an important factor, as it is associated with local recurrence (Phillips et al 1984 IIb, Patel et al 1977 III, Zirngibl et al 1990 III). This phenomenon appears to be independent of tumour stage or fixity (Wiggers et al 1988 IIb).

The role of pre-operative radiotherapy is discussed under the section on Adjuvant Radiotherapy.

In summary, it is recommended that total mesorectal excision should be performed for tumours in the lower two-thirds of the rectum, either as part of a low anterior resection or an APER. In tumours of the upper rectum the mesorectum should be divided no less than 5cm below the lower margin of the tumour. Care should be taken to preserve the pelvic autonomic nerves and plexuses, and perforation of the tumour during operation should be avoided.

Recommendation grade B

b) Anastomosis

Anastomotic dehiscence is a major source of operative morbidity and mortality after resection for colorectal cancer. Its rate is known to vary greatly from one surgeon to another and it is known to be more common after anterior resection of the rectum than after colonic resection (Fielding et al 1980 IIb, McArdle and Hole 1990 IIb). In the Trent/Wales audit (IIb) the overall leak rate was 4.9%, and the associated mortality was 20%. For anterior resection, however, the leak rate was 7.4%, compared with 3.7% for other types of resection. The Wessex audit (IIb) revealed very similar figures, with an overall leak rate of 3.4% (6.9% for anterior resection, 2.6% for others), and an associated mortality of 23.2%. The NORCCAG study (IIb) similarly showed a colonic leak rate of 4.1% and a leak rate of 6% for anterior resection.

Things have moved on since the 13% leak rate seen in the Large Bowel Cancer project in 1980. Review of the literature indicates that even better results can be achieved by individual surgeons, some of whom report rates below 5% (Matheson et al 1985 III, Staib et al 2002 III, Brannigan & Finnis 2005 IIb).

It is not possible to be dogmatic as regards method of anastomosis. Although the best published results involved the use of a single layer interrupted serosubmucosal technique (Matheson et al 1985 III, Carty et al 1991 III), this may have been due to the skill of the surgeon and/or case selection rather than the technique itself. A Cochrane review has not shown any advantage of stapled over hand-sewn anastomosis (Lutosa et al 2006 Ia), but a Scandinavian study did report a significant difference in leak rates between two types of stapling device (Folkesson et al 2004 III).

Stapling has, however, made the performance of the ultra-low anastomosis after anterior resection much more feasible. As it is known that distal intramural spread rarely extends more than 1cm beyond the palpable edge of the tumour (Williams et al 1983 IIb), the ability to obtain distal clearance of 1cm or more should therefore allow an anterior resection which is oncologically sound so long as it is combined with total mesorectal excision (vide supra).

Unfortunately, such anastomoses are associated with a high leakage rate, even when the same surgeon has very acceptable leakage rates from other types of resection (Karanjia et al 1994 III). Anastomotic leakage is associated with poorer survival (up to a five-fold increase in 30-day mortality) and a significant increase in the local recurrence rate (Brannagan and Finnis 2005 Ib; Bell et al 2003 III and Branagan 2005 III Walker et al 2004 III, McArdle et al, 2005 III). This desire for more distal anastomoses is based on the perception that quality of life is better with a low anastomosis than with a permanent colostomy. This is not, however, supported by a review of 11 trials including 1412 patients, which identified no differences in quality of life differences between the two treatment modalities (Pachler and Wille-Jorgensen 2006 Ib).

Cochrane reviews have shown no difference in leak rates in patients where bowel preparation has been omitted and whose anastomoses have not been drained (Guenaga et al 2006 Ia, Jesus et al 2006 Ia).

There is evidence that a defunctioning stoma can ameliorate the consequences of leakage, decreasing the risk of death and need for a permanent stoma (Karanjia et al 1994 III). A number of trials have compared a defunctioning ileostomy with defunctioning colostomy with mixed outcomes. There are advantages and disadvantages for each type of stoma. The balance of evidence slightly favours a defunctioning ileostomy over transverse colostomy (Williams et al 1996 Ib, Gooszen et al 2000 Ib).

Other problems associated with the low anastomosis are functional; many patients have urgency and increased frequency of bowel action (Williams and Johnston 1984 IIb) after low anterior resection, and this has been attributed to loss of the reservoir function of the rectum. Formation of a colonic J-pouch may overcome this difficulty (pouch limbs should be no more than 5-6cm long), and several studies now attest the efficacy of this procedure (Seow-Choen and Goh 1995 Ib, Mortensen et al 1995 IIb).

Finally, as large numbers of viable tumour cells can be demonstrated in the lumen of the colon at the time of operation (Umpleby et al 1984 IIb), the use of a cytocidal washout prior to anastomosis is generally accepted as a sensible precaution to reduce the risk of anastomotic recurrence.

Although no definite recommendations can be made regarding anastomotic technique, the interrupted serosubmucosal method has the lowest reported leak rate and stapling facilitates ultra-low pelvic anastomoses.

Recommendation grade B

Cytocidal washout of the rectal stump should be used prior to anastomosis.

Recommendation grade ✔

Surgeons should carefully audit their leak rate for colorectal surgery, and should expect to achieve an overall rate below 8% for anterior resections and below 4% for other types of resection.

Recommendation grade B

Surgeons should expect to achieve an operative mortality of less than 20% for emergency surgery and less than 7% for elective surgery for colorectal cancer.

Recommendation grade B

After anterior resection and total mesorectal excision, the judicious use of a temporary defunctioning stoma is recommended, and the formation of a colonic pouch should be considered.

Recommendation grade B

v) Rates of permanent stoma formation

The lowest rate of permanent stoma formation for rectal cancer in the literature is 9% in a unit routinely employing a stapled anastomotic technique for low anterior resection (Karanjia et al 1994 III), other specialist units have reported rates of 10% (Williams et al 1985 III) and 19% (Matheson et al 1985 III). In the Trent/Wales audit, the figure was 37%.

There seems to have been a general reduction in the proportion of rectal cancer treated by APER with the passage of time, but there is still marked individual variation. Case mix and an increasingly elderly population may explain some of this variation. As stated above, distal intramural spread rarely extends more than 1cm beyond the palpable edge of the tumour (Williams et al 1983 IIb), and it is possible that failure to recognise this finding results in an inappropriate number of APERs being performed by non-specialist surgeons.

In low rectal cancers, a surgeon may be unsure of the feasibility of anterior resection. In such a case, it is strongly recommended that a second opinion from an experienced rectal surgeon is obtained.

It is difficult to determine what the ideal ratio of anterior resection to APER should be, but it is recommended that the overall proportion of resectable rectal cancers treated by APER should be less than 30%. If distal clearance of 1cm can be achieved, a low rectal cancer may be suitable for anterior resection. If a surgeon has any doubt regarding the choice between these two operations, an experienced second opinion should be sought.

Recommendation grade ✔

vi) Local excision

Occasionally, small pT1 rectal cancers can be safely treated by a local excision, and some polyps excised by snare diathermy will contain invasive carcinoma. Careful studies have shown that cancers fulfilling histological criteria defined elsewhere can be regarded as curable by local excision (Whiteway et al 1985 IIb) whereas sm3 and pT2 tumours are associated with a higher risk of lymph node involvement and of local recurrence without further treatment (Kikuchi et al, 1995 IIb, Graham et al 1990 IIb). Follow up after local excision using MR scanning is recommended.

Local excision of rectal adenomas using transanal endoscopic microsurgery has become popular over the last five years. Published data suggest that this is at least as good as traditional transanal resection and may offer advantages for patients with polyps in the middle third of the rectum (Steele et al 1996 IIb).

Local excision in rectal cancer is appropriate only for pT1 cancers which are graded well or moderately well differentiated and less than 3cm in diameter. Subsequent histopathological examination of cancers treated by local excision may, however, identify a proportion which require more radical surgery.

Recommendation grade B

vii) Laparoscopic surgery

Laparoscopic surgery offers a range of potential benefits for patients, and is being used increasingly for colorectal cancer. As with all new surgical techniques, extensive practice is required to develop the necessary skills.

Several recent randomised studies have compared short and long term results of laparoscopic colorectal cancer surgery with open surgery. Three trials involving 750 patients undergoing laparoscopic surgery showed that there was no difference in the rates of overall survival, disease-free survival and tumour recurrence compared with open resection (Lacey et al 2002 Ib, COST study group 2004 III, Leung et al 2004 Ib). Furthermore, the study from Barcelona suggested that survival for stage III disease may be better after laparoscopic surgery (Lacey et al 2002 Ib) but long term results from the MRC-CLASSIC (Guillou et al 2005 Ib) and the European COLOR (Veldkamp et al 2005 Ib) studies may yield more information. One meta-analysis (Abraham et al 2004 Ia) and other randomised studies (Lacey et al 2002 Ib, COST study group 2004 III, Leung et al 2004 Ib, Guillou e al 2005 Ib, Veldkamp et al 2005 Ib) have demonstrated that lymph node harvest is no different between laparoscopic and open surgery. Completeness of resection margins is also similar, and although circumferential margin positivity in the MRC-CLASSIC study was greater in laparoscopic than in open anterior resection (12% vs 6% respectively), this was not statistically significant (Guillou et al 2005 Ib). However, there may be a tendency towards male sexual dysfunction after laparoscopic rectal excisions (Jayne et al 2005 Ib).

Early reports of laparoscopic colorectal cancer surgery led to concern about port-site metastases. Subsequent studies have demonstrated that these were due to poor techniques rather than inherent problems with laparoscopic cancer surgery, and that the incidence is less than 1% - similar to open surgery (Silecchia et al 2002 III). Laparoscopic colorectal resection takes longer to perform than open procedure, but operative duration falls with increasing experience. Blood loss and blood transfusion requirements are less in patients undergoing laparoscopic colorectal surgery (Schwenk et al 2005 IV). Short term complications, particularly wound infections, are reduced in laparoscopic surgery, whilst anastomotic leakage and mortality rates are similar to those for open procedures. There is also a tendency for less long term morbidities, expecially in the rates of incisional herniation and small bowel obstruction (Duepree et al 2003 III). Hospital stay is 20% shorter for laparoscopic surgery (Abraham et al 2004 Ia). Laparoscopic colorectal resection results in less post-operative pain and in less need for analgesia compared with open surgery, as well as short term improvements in quality of life (Schwenk et al 2005 IV). Although laparoscopic colorectal surgery is more costly to the healthcare providers, the overall cost to society is the same (Janson et al 2004 Ib). The addition of an enhanced recovery programme with laparoscopic colorectal cancer surgery may further improve short term recovery and reduce hospital stay (King et al 2006 Ib).

All laparoscopic colorectal operations should be performed by properly trained surgeons in colorectal surgery. These surgeons should have undergone preceptorship laparoscopic training, particularly in rectal procedures. Their results should be carefully audited both in the local hospital multidisciplinary setting and also submitted to the Association of Coloproctology of Great Britain and Ireland colorectal cancer database.

Recommendation grade C

viii) Record keeping

There are existing guidelines issued by the Royal College of Surgeons (RCS 1990 IV), and it is recommended that these should be adhered to for patients with colorectal cancer. In the Trent/Wales audit, scrutiny of operation notes revealed absence of information on anastomotic technique, on the extent of resection and the presence or absence of liver metastases.

Recommendation grade C

A check-list should be used to construct an operation note for patients undergoing surgery for colorectal cancer. See Appendix 2

Recommendation grade C

Meetings of the Multidisciplinary Team should be on a regular basis to allow timely decision making on all colorectal cancer patients. Meetings should include a register of attendance. Records of cases discussed and decisions made must also be recorded.

Recommendation grade C

ix) Management of patients presenting as emergencies

Patients with colorectal cancer frequently present as emergencies and this is associated with higher operative mortality. In the Trent/Wales audit, 20% of all operations were emergency/urgent procedures, and the operative mortality was 20%, compared with 5% for scheduled/elective operations. In the Wessex audit, 14% of operations were classified as emergencies, and the operative mortality was 21% compared with 6% for elective operations. The commonest emergency presentation of colorectal cancer is obstruction; in the Trent/Wales audit this accounted for 16% of all colorectal cancer presentations, and in the Wessex audit this figure was 12%. Bleeding and perforation are much less common. A clinical diagnosis of obstruction should be confirmed by CT scan, contrast enema or CT colonography to exclude pseudo-obstruction.

In patients presenting with apparent obstruction, CT scanning should be carried out before operation to exclude pseudo-obstruction.

Recommendation grade C

The ACPGBI audit (Tekkis et al 2005 III) reported on 8728 patients, of whom 20% were recorded as having an urgent operation within 24 hours (10.4%) and an emergency operation within 2 hours (9.6%). Following apparently curative resection for colorectal cancer, there is an excess of both cancer-related and intercurrent deaths in patients who present as an emergency (McArdle and Hole 2004 III and Jestin 2005 III). The Swedish study confirmed that there was a stage-specific difference in survival, with poorer survival of patients at all stages after emergency surgery compared with elective.

In the absence of perforation or life-threatening bleeding, operation for large bowel obstruction can be regarded as an urgent rather than emergency procedure, and every effort should be made to operate during the day with experienced surgeons and anaesthetists. An exception to this may be the situation where the ileo-caecal valve is competent, and the caecum is in danger of perforation.

The patient with obstruction should be carefully prepared for surgery, with adequate fluid resuscitation, monitored by blood pressure and urine output measurements at the very least. Antibiotic and DVT prophylaxis should be administered. Centres undertaking this type of surgery should have an intensive care unit or a high dependency unit, and these should be used for postoperative and preoperative care when appropriate.

The type of surgery which should be undertaken for large bowel obstruction is to some extent controversial; However, a Cochrane review reported no difference in outcomes between staged surgery or primary resection (De Salvo et al, 2006 Ib)

For right-sided lesions, primary resection and ileocolic anastomosis is usually feasible (Deans et al 1994 III). For left sided lesions, the use of a simple defunctioning colostomy is not generally favoured except in extreme circumstances, where the patient is not considered fit for a more extensive procedure. Rather, immediate resection of the obstructing cancer should be carried out, either as a Hartmann's procedure with end colostomy, or, when conditions are favourable, as a primary resection with anastomosis (Deans et al 1994 III). If the latter option is chosen, this can be done either as a segmental resection (Koruth et al 1985 IIb), or as a subtotal colectomy with ileorectal anastomosis (Dorudi et al 1990 III). A recent randomised trial has indicated that these two procedures are roughly equivalent, although long-term bowel habit is better with the former (SCOTIA 1994 Ib).

A systematic review of the efficacy and safety of colorectal stents suggests that colorectal stents offer good palliation and are safe and effective as "a bridge" to surgery with low rates of mortality and morbidity (Khot et al 2002 IIa, Watson et al 2005 III).

Emergency surgery should be carried out during daytime hours as far as possible, by surgeons and anaesthetists who are members of a colorectal cancer MDT. Stoma formation should be carried out in the patient's interests only.

Recommendation grade C

The overall mortality for emergency/urgent surgery should be less than 25%.

Recommendation grade ✔

In patients with large bowel obstruction the insertion of an expanding stent is an acceptable treatment option, where adequate local expertise exists, either as palliation or as a bridge to surgery.

Recommendation grade B

x) Adjuvant Radiotherapy in resectable rectal cancer

Many randomised controlled trials have compared the addition of radiotherapy (preoperative or postoperative) to surgery with surgery alone in rectal cancer, reporting varying results. A meta-analysis examining the addition of radiotherapy to standard surgery identified 22 randomised controlled trials (14 giving radiotherapy preoperatively and 8 postoperatively), with a total of 8507 patients included (Colorectal Cancer Collaborative Group 2000). This showed a reduction in isolated local recurrence for both preoperative (from 22.5% to 12.5%; p<0.00001) and postoperative radiotherapy (25.8% to 16.7% p=0.00001). The benefit of adding radiotherapy to surgery was marginal for overall survival (62% vs 63% deaths; p=0.06).

Preoperative Radiotherapy

Preoperative radiotherapy is usually delivered either by conventional fractionation or short course preoperative radiotherapy (SCPRT). The former method is used to shrink the tumour before resection, whilst the latter is used to reduce the risk of local recurrence.

Conventional fractionation consists of doses ranging from 45-50 Gy in 25 daily fractions over 5 weeks followed by surgery 4-8 weeks after completion of radiotherapy, allowing maximal tumour shrinkage. This is more effective with the addition of synchronous 5FU-based chemotherapy, which is given either on the first and fifth week of radiotherapy or as a continuous infusion throughout the duration of radiotherapy, otherwise known as chemoradiotherapy (CRT).

SCPRT delivers a lower dose, 25 Gy, but within a short duration of 5 daily fractions over 1 week. Surgery is performed on the following week, before the onset of acute side-effects of radiotherapy. The short interval between commencing radiotherapy and surgery (usually less than 10 days) means that SCPRT does not achieve any significant tumour shrinkage prior to surgical resection. It is therefore appropriate only for patients with rectal cancers which are clinically and radiologically assessed to be resectable.

There is consistent evidence that local recurrence can be reduced by adequate dose preoperative radiotherapy. Another meta-analysis of 14 randomised controlled trials (6426 patients) which compared preoperative radiotherapy followed by surgery with surgery alone showed a halving in the rate of local recurrence (OR 0.49; p<0.001; 95% CI 0.38-0.62) and a small improvement of overall survival (OR 0.84; p=0.03; 95% CI 0.72-0.98) (Camma et al 2000 Ia).

The trial which influenced surgical and oncological practice in the late 1990's was the Swedish Rectal Cancer Trial. One thousand one hundred and sixty eight patients with resectable rectal cancer were randomised to receive SCPRT followed by surgery or surgery alone (Swedish Rectal Cancer Trial 1997). The use of SCPRT reduced the risk of local recurrence from 27% to 11% at 5-years (p<0.001) and improved the 5-year overall survival from 48% to 58% (p=0.004). These benefits were maintained for a prolonged period (median follow-up 13 years) (Folkesson et al 2005 Ib).

Since publication of the Swedish Rectal Cancer Trial results, significant progress has been made in the multidisciplinary management of rectal cancer. Firstly, the observation that achieving wide circumferential resection margins (CRM) around the tumour improves local control and overall survival has been widely accepted (Quirke et al 1986, Dahlberg et al 1999). Secondly, the practice of total mesorectal excision (TME) surgery has become the standard of care in the UK. As a result, local recurrence following surgery has fallen

significantly, with single centre series reporting figures as low as 3%-6% after TME alone (Heald et al 1986 IIb, Martling et al 2000 IIb). This has raised the question of whether or not there was a role for SCPRT in addition to optimal TME surgery.

In response to this question, the Dutch Colorectal Cancer Group randomised 1861 patients to SCPRT followed by TME surgery or TME surgery alone. Patients who were found to have an involved CRM following TME alone were to receive postoperative radiotherapy. This trial showed that the addition of SCPRT to TME reduced the risk of local recurrence from 8.2% to 2.4% at 2-years ($p<0.001$) (Kapiteijn et al 2001 III) and from 11.4% to 5.8% at 5-years (Marijnen et al 2005 III). There was no difference in overall survival (63.5% vs 64.3% at 5-years; $p=0.87$).

The UK MRC CR07 trial was similar in design to the Dutch TME trial, but differed in several respects. Firstly, although TME surgery was not a protocol requirement, it was performed in 93% of the patients randomised. Secondly, the control arm was not surgery alone but selective postoperative CRT (45 Gy in 25 fractions with synchronous 5FU) in CR07, compared with post-operative radiotherapy alone in the Dutch trial. A total of 1350 patients were entered between March 1998 and August 2005. The early data from CR07 confirms than the addition of SCPRT to TME reduces local recurrence from 11.1% to 4.7% at 3 years and improves disease free survival from 74.9% to 79.5% ($p=0.031$) (Sebag Montefiore et al 2006 Ib).

In the event of a patient being found to have an involved CRM following SCPRT and TME surgery, further radiotherapy given postoperatively is contraindicated. The risk of long-term radiation toxicity associated with this approach is considerable (84% at 5-years) (Svoboda et al 1999 IIb).

Differential efficacy of SCPRT

By adopting a policy of offering SCPRT to all patients with resectable rectal cancer, the major concern is that for a relatively low percentage absolute reduction of local recurrence rate (approximately 6%), many patients have been exposed to the risk of long-term toxicity associated with the addition of radiotherapy. Is it possible to select specific sub-groups of patients who may have a greater probability of benefiting and to avoid treating sub-groups who may not benefit?

Data from both Dutch TME and CR07 trials suggest that the greatest benefits of SCPRT were in patients with mid rectal tumours (5-10 cm from the anal verge) (1.0 vs 10.1%; $p<0.001$ and 4.9% vs 9.9%; $p=0.017$ respectively) and those with lymph node involvement (4.3% vs 15.0%; $p<0.001$ and 9.0% vs 17.4%; $p=0.008$) (Kapiteijn et al 2001 III; Marijnen et al 2003 III; Sebag Montefiore et al 2006 Ib). The numbers needed to treat in order to prevent one local recurrence varies from 9-20 patients.

The relative reduction in local recurrence for patients undergoing abdominoperineal resection (APER) (4.9% vs. 10.1%; $p=0.02$ and 8.3% vs 9.3%; $p=0.397$ for the Dutch TME and CR07 respectively) was smaller than those undergoing anterior resection (1.2% vs. 7.3%; $p<0.001$ and 2.4% vs 12.0%; $p<0.0001$ respectively). However, this would have been confounded by the fact that a significant percentage (29% and 17% respectively) of APER patients had an involved CRM, leading to a high risk of local recurrence (Nagtegaal et al 2002 Ib). The use of SCPRT did not influence the risk of local recurrence if the CRM was involved (1mm or less), 9.3% vs 16.4%; $p=0.08$ and 17% vs 10%; $p=0.360$ for the Dutch and CR07 trials respectively (Marijnen et al 2003 III, Sebag-Montefiore et al 2006 Ib). Postoperative radiotherapy or CRT has not been shown to compensate adequately for an involved CRM in either trial.

In the Dutch TME trial, no benefit from SCPRT was seen in upper rectal tumours (10-15 cm from the anal verge) (1.3% vs 3.8%; $p=0.170$) but CR07 reported a significant reduction of local recurrence (1.4% vs 16.5%; $p=0.002$). In CR07, the vast majority of tumours in this group were between 10 and 12 cm. It is recognised that the quality of TME surgery as defined by an intact mesorectal fascia is predictive of local recurrence risk (Nagtegaal et al 2002; Quirke et al 2006) and this appears independent of CRM status. The CR07 trial showed that despite good quality TME (grade 3), the addition of SCPRT virtually eliminated the risk of local recurrence (1.3% vs 6.1%; $p=0.0005$) (Quirke et al 2006).

Other Recent Randomised Trials of Resectable Rectal Cancer

The EORTC 22921 trial randomised 1011 patients with resectable (clinically staged T3-4) mid and lower rectal cancers to receive preoperative 5FU-based CRT or conventional radiotherapy alone with or without 4 further cycles of adjuvant 5FU chemotherapy postoperatively in a 2x2 trial design (Bosset et al 2005). TME was not a

protocol requirement. The results show a significant reduction in local recurrence (p=0.0016) for patients who received chemotherapy (either synchronously or as an adjuvant) in addition to preoperative radiotherapy. Local recurrence at 5 years in patients not receiving chemotherapy was 17.1%. Patients receiving adjuvant chemotherapy subsequent to preoperative radiotherapy had a similar rate of local recurrence to those receiving CRT with no subsequent adjuvant chemotherapy (8.7% vs 9.6%).

The FFCD 9203 trial randomised 733 patients with resectable palpable (clinically staged T3-4) rectal cancers to preoperative CRT or conventional radiotherapy alone. TME was not a protocol requirement. All patients were to receive 4 cycles of 5FU chemotherapy postoperatively (Gerard et al 2005 Ib). The results are similar to the corresponding arms of the EORTC trial (local recurrence of 8% vs 16.5% at 5-years).

The German GAO/ARO/AIO-94 trial randomised 421 patients with resectable T3-4 rectal cancers to CRT given either preoperatively or postoperatively. All patients were to have TME surgery. Patients receiving preoperative treatment had fewer local recurrences (6% vs 13%; p=0.006) and a lower risk of late toxicity (12% vs 24%; p=0.01) (Sauer et al 2004 Ib).

The Polish trial randomised 312 patients with resectable palpable T3-4 rectal cancers to SCPRT or CRT followed by TME surgery. Unlike the other trials, the primary endpoint of this trial was not local recurrence but sphincter preservation rate. Initial results showed that the use of CRT did not appear to improve sphincter sparing (58% vs 61%; p=0.57) despite the fact that the tumours were on average almost 2 cm smaller (p<0.001) as a result of CRT (Bujko et al 2004 Ib).

In summary, these trials show that there are two strategies that have been proven to produce local recurrence rates in the region of 5-10% in resectable rectal cancer. These are short course preoperative radiotherapy followed by TME surgery (Dutch TME and CR07); or preoperative long course chemoradiotherapy followed by surgery (EORTC 22921; FFCD 9203; GAO/ARO/AIO-94). Inferior results (local recurrence rates in excess of 10%) are achieved by surgery alone, even though TME is performed (Dutch TME, CR07) or long course preoperative radiotherapy without either concurrent or postoperative chemotherapy (EORTC 22921) or post-operative chemoradiotherapy (GAO/ARO/AIO-94). The best results of all arise from the combination of very high quality TME surgery preceded by short course preoperative radiotherapy (CR07 subset analysis) (Sebag Montefiore et al, 2006 Ib).

The least intrusive of these strategies is the use of short course pre-operative radiotherapy followed by TME surgery. It remains to be proven whether the long-term complications of this approach outweigh the benefits in terms of the reduction in local recurrence and marginal effect on disease–free and overall survival.

Postoperative Radiotherapy

Meta-analysis of the postoperative radiotherapy trials also shows an effect on local recurrence, but the size of benefit is smaller (18.6% vs 13.3%) than for preoperative radiotherapy (Colorectal Cancer Collaborative Group 2001). No significant effect on either cancer specific survival or overall survival has been confirmed.

Two randomised trials have specifically examined the question of the optimal timing of radiotherapy. The Uppsala trial randomised 471 patients to either SCPRT or postoperative radiotherapy (60 Gy in 30 fractions over 7-8 weeks). Preoperative radiotherapy resulted in patients at lower risk of local recurrence (13% vs 22%; p=0.02) and fewer long-term complications (Frykholm et al 1993). The German GAO/ARO/AIO-94 trial has convincingly shown that postoperative CRT is less effective and more toxic than preoperative radiotherapy. Therefore the routine use of postoperative radiotherapy with or without chemotherapy cannot be recommended.

If a patient has a resection where the circumferential margin is involved (less than or equal to 1mm), and they have not received preoperative radiotherapy, then postoperative CRT is an acceptable salvage approach.

Developments in Radiology

Since the design of the trials described above, the increasing use of MRI for locoregional staging has significantly improved the ability of the Colorectal Multidisciplinary Team (MDT) to predict the T and N stage of newly diagnosed rectal cancers with greater accuracy. More importantly, most patients at risk of an involved CRM can be identified by measuring the distance of the tumour to the nearest mesorectal margin (Beets-Tan 2001; Brown et al 2003). A decision can then be made by the MDT whether to proceed to surgery, to offer SCPRT or to recommend downstaging/sizing CRT. For low lying rectal tumours arising below the origin of the levator ani, the risk of an involved CRM is increased (Nagtegaal et al 2005 III; Marr et al 2005 III), and therefore long course chemoradiotherapy tends to be selected for lower stage tumours.

Limitations of the Evidence

The evidence to support the use of preoperative CRT in resectable rectal cancer remains controversial. In the German GAO/ARO/AIO-94 trial, preoperative CRT did not appear to improve the curative resection rate when compared with those who had immediate surgery (91% vs 90%; p=0.69) (Sauer et al 2004 IIb). However, the Polish trial showed that patients receiving CRT had a lower risk of an involved CRM when compared with SCPRT (4% vs 13%; p=0.017) (Bujko et al 2004 IIb). Whether or not this translates to improved locoregional control remains to be seen.

Toxicity

Using an appropriate 3 or 4 field radiotherapy delivery technique, postoperative mortality is not increased with the use of SCPRT or preoperative CRT (Kapiteijn et al 2001; Sebag-Montefiore et al 2006; Gerard et al 2005). For SCPRT, surgery should be performed within 7 days of completion of radiotherapy (Marijnen et al 2001; Hartley et al 2002). SCPRT is associated with delayed perineal wound healing and subsequently, a higher risk of impotence in men (Marijnen et al 2002). CRT is associated with more diarrhoea when compared with RT alone (Gerard et al 2005). Data from the Dutch TME study suggests that despite optimisation of radiotherapy technique for SCPRT, long-term effects on bowel functioning will still be seen. Of 597 patients from this study analysed for late effects, there was a significant higher rate of incontinence compared with patients undergoing surgery alone (62% vs 38%, p=0.001) (Peeters et al 2005 IIb). Data on toxicity and late bowel function following CRT from the randomised trials are awaited.

xi) Radiotherapy in unresectable rectal cancer

The MRC Second Rectal Cancer Trial randomised 279 patients with clinically fixed or tethered cancers to long course radiotherapy (40 Gy in 20 fractions over 4 weeks) followed by surgery 4 weeks later or surgery alone. Radiotherapy made no difference to the proportion of curative resections (47% vs 40%; p=0.21) performed but reduced the risk of subsequent local recurrence (hazard ratio 0.68; p=0.04; 95% CI 0.47-0.98) (MRC 1996).

The use of preoperative synchronous CRT has been extensively studied in both resectable and unresectable rectal cancers, but rarely in the context of a randomised controlled trial. In locally advanced disease classified as fixed on palpation or involving or threatening the CRM on MRI scanning, non randomised studies have reported the outcomes of patients treated with preoperative CRT followed by radical surgery. In a collated series of 677 UK patients treated with 5FU plus preoperative long course radiotherapy, complete resection with clear CRM was achieved in 57% and pathological complete responses in 13% (Sebag-Montefiore et al 2005). Several phase II trials in the same patient group incorporating irinotecan or oxaliplatin with 5FU-based CRT have reported CRM clear resections in 70-80% and pathological complete responses in 15-20%. A large randomised trial to evaluate this group of patients is in development.

Summary

Significant improvements in the locoregional control of resectable rectal cancer have been achieved by an MDT approach which includes accurate preoperative staging, TME surgery and proforma pathology reporting, particularly the recognition that achieving a clear CRM is the primary aim of the team. The addition of radiotherapy or CRT further improves locoregional control. However the benefits of SCPRT are modest and must be balanced against the risk of acute and long-term toxicity. The use of routine MRI staging can identify patients who are more likely to benefit from SCPRT (Dukes' B and C) and those who may not benefit (Dukes' A and involved CRM).

Lower rectal cancers are the most difficult to manage as the ability of MRI to predict the CRM is less accurate and the quality of surgical resection is more unpredictable. These patients are at considerable risk of under-treatment and yet at the same time, risk being over-treated.

Radiotherapy and chemotherapy for colorectal cancer should only be given after discussion at the Multi Disciplinary Team (MDT) Meeting and under the direction of recognised oncologists, within facilities conforming to national guidelines.

Recommendation grade C

All patients should be made aware of the common and serious short and long term side effects of radiotherapy and chemotherapy, the expected benefits and the other options available, before treatment begins.

Recommendation grade ✔

Patients with resectable rectal cancer should be considered for preoperative short course radiotherapy (25Gy in 5 fractions in 1 week) with surgery performed within 1 week of completion of radiation. However, in certain cases the MDT may decide that the benefits of treating patients with lower risk disease will not justify the additional toxicity of radiotherapy.

Recommendation grade A

When local staging indicates that radiotherapy (with synchronous chemotherapy) would be appropriate to downstage the tumour, a dose of 45Gy in 25 fractions over 5 weeks, with or without a reduced volume boost dose of 5.4-9Gy in 3-5 fractions, is recommended

Recommendation grade B

If the addition of radiotherapy to surgery is deemed necessary for rectal cancer, it should ideally be given pre-operatively. However, in cases with well established predictive factors of local recurrence (e.g. evidence of tumour at the circumferential resection margin, mesorectal lymph node involvement and extramural vascular invasion), post operative radiotherapy and chemotherapy should be considered for patients who did not receive pre-operative radiotherapy. A dose of 45Gy in 25 fractions over 5 weeks with a planned boost dose of 5.4-9Gy in 3-5 fractions is recommended.

Recommendation grade A

A planned radiotherapy volume using three or four fields given pre-operatively is recommended for rectal cancers as this results in less morbidity and mortality.

Recommendation grade B

MDTs should prospectively audit the outcomes of all patients with rectal cancer managed by the team in terms of curative resection rate (R0), postoperative morbidity and mortality, locoregional recurrence and overall survival.

Recommendation grade B

Summary chart of recommended treatment options for rectal cancer

NB This table is meant as a guide; management decisions for individual patients will be determined by patient factors.

Prospective audit within each MDT will provide invaluable evidence on the effectiveness of the treatment selection policies adopted

MRI STAGING	Upper rectum	Mid rectum	Lower rectum
EARLY STAGE T1-2N0 CRM clear	Surgery	Surgery	Surgery[1]
INTERMEDIATE STAGE Early T3N0 or N1 CRM clear Discuss with patient:	Discuss with patient: SCPRT+Surgery or Surgery	Discuss with patient: SCPRT+Surgery or Surgery	Discuss with patient: SCPRT+Surgery or CRT + surgery
ADVANCED STAGE CRM threatened by tumour or involved nodes or tumour beyond CRM or involved internal iliac/obturator nodes	CRT + surgery	CRT + surgery	CRT + surgery

[1] Consider endoluminal ultrasound for detailed T stage and use surgery alone for T1 and non full thickness T2 lesions

Chemotherapy for colorectal cancer

Chemotherapy has an increasing role in the management of colorectal cancer and has been a major contributing factor to the significant improvements in prognosis over the last two decades. It should be given as part of a management plan agreed following discussion at a specialist colorectal Multi Disciplinary Team (MDT) Meeting. Systemic therapy is optimally administered under the direction of a recognised clinical or medical oncologist, within facilities conforming to national guidelines. Entry into clinical trials evaluating new treatments and strategies for colorectal cancer should be actively encouraged.

xii) Adjuvant chemotherapy

a General Recommendations

The choice of adjuvant treatment should be made jointly by the patient and the clinician responsible for treatment. Decisions should be taken after a detailed discussion between these individuals taking into account the patient's risk factors for relapse, their co-morbidities, performance status, any specific contraindications, and the side-effect profile of the agent(s). The method of administration and preferences of the individual are also important considerations.

b Node positive disease

Large meta-analyses of historical data from randomised trials have demonstrated that post-operative systemic single-agent chemotherapy improves survival for patients with Dukes' C tumours. The standard regimens were based on 5-flourouracil (5-FU) modulated by folinic acid (FA), and given for 6 months. Pooled data suggest that 5-FU/FA regimens can increase disease-free survival at 5 years from 42% to 58%, and overall survival by as much as 13%, from 51% to 64%, when compared with surgery alone (NICE 2004 Ia) Current national guidance makes no distinction between colon and rectal cancer, and recommends that all patients with node positive disease be offered chemotherapy, if they are deemed fit enough to tolerate its side effects.

More recently, oral forms of 5-FU (uracil- tegafur and capecitabine) have been licensed for this indication, on the basis of the results of two large randomised trials comparing their efficacy and safety with bolus 5-FU/FA (Mayo Clinic regimen) in the postoperative adjuvant setting (Twelves et al 2005 Ib, Lembersky et al 2006 Ib). Both confirmed that the oral drugs were at least as effective as the standard intravenous treatment. For example in the X-ACT study, after a median follow-up of 3.8 years, 35% of patients in the capecitabine arm had experienced disease recurrence or died, compared with 39% in the 5-FU/FA arm. With regard to survival, 80% and 77% of patients were alive in the capecitabine and 5-FU/FA arms, respectively, with no apparent differences in quality of life (Twelves et al 2005 Ib). These agents are also associated with less toxicity and greater patient convenience. In April 2006 they received approval by NICE for adjuvant use.

There is also now overwhelming evidence of additional benefit from the use of combination therapy, specifically regimens based on oxaliplatin and 5-FU. Two phase III, randomised controlled trials that compared oxaliplatin containing regimens with standard treatment have been published (Wolmark et al 2005 Ib, Andre et al 2004 Ib). The first was the Multicenter International Study of Oxaliplatin/5-fluorouracil and leucovorin in the Adjuvant Treatment of Colon Cancer (MOSAIC) trial. This study included 2246 participants, 60% with stage III and the remainder with stage II colon cancer. The second was the National Surgical Adjuvant Breast and Bowel Project (NSABP C-07) trial, involving 2492 patients, 71% with stage III and the remainder with stage II colon cancer. In both trials the addition of oxaliplatin to 5-FU/FA, albeit administered via different regimens, led to a statistically significant reduction in rate of relapse when compared with 5-FU/FA monotherapy. Analysis of disease-free survival at 3 years showed a hazard ratio for recurrence of 0.77 (95% CI, 0.65 to 0.91) in the MOSAIC trial (median follow-up 37.9 months), and 0.79 (95% CI, 0.67 to 0.93) in C-07 (median follow-up 34 months). Additional analyses on MOSAIC showed a 24% reduction in the rate of relapse (improved disease-free survival) at a median follow-up of 4 years (hazard for recurrence 0.76; 95% CI, 0.65 to 0.90). Toxicity was acceptable with low rates of persistent severe (greater than grade1) neuropathy (<1%) and no excess of treatment associated fatality in the oxaliplatin containing arms. Oxaliplatin has also recently been approved by NICE for this indication.

The challenge is now to determine for the individual patient which of these alternative approved treatments is the more appropriate for use as adjuvant therapy in node positive colorectal cancer. The benefit in terms of improved likelihood of disease free survival from the use of oxaliplatin should be set against the side effects and acceptability of the regimen. In general, a higher risk, otherwise fit patient should be offered oxaliplatin based adjuvant therapy as their risk of death from cancer significantly outweighs their risk of death from other causes.

Fluoropyrimidines as monotherapy or oxaliplatin in combination with 5-fluorouracil and folinic acid should be considered as options for the adjuvant treatment of patients with node positive colorectal cancer following potentially curative surgery.

Recommendation grade A

In general a higher risk, otherwise fit, patient should be offered oxaliplatin based adjuvant therapy

Recommendation grade A

c Node negative disease

The magnitude of benefit for adjuvant chemotherapy in Dukes' B tumours is smaller. Some studies of 5-FU based treatment have failed to demonstrate any benefit at all. Examples include the IMPACT B2 study, a pooled analysis of 1,116 patients with stage B2 colon cancer randomised to chemotherapy versus observation which showed no significant improvement in overall survival (OR 0.86, CI 0.72-1.07) (IMPACT 1999 Ib) In contrast, a grouped analysis of the National Surgical Adjuvant Bowel Project (NSABP) trials C-01 and 04, which included 1,565 Dukes' B patients, concluded that a 30% proportional reduction in mortality resulted from the use of chemotherapy consistent with a 5% absolute reduction in death at 5 years (Wolmark et al 1999 Ib) The more recently reported UK QUASAR 1 study has also shown a modest benefit with bolus 5-FU/FA of around a 4% improvement in overall survival, and confirmed that this was cost-effective, especially in the under 70 age group. This data together suggests a small (5% or less) absolute increase in survival for patients with Dukes' B cancers from adjuvant single agent chemotherapy. The MOSAIC trial (q.v.) included node negative patients, and a smaller but statistically significant incremental benefit to the addition of oxaliplatin was demonstrated, although a licence has not been sought in this indication

A number of poor risk features can be identified in Dukes' B cancers: serosal involvement (T4), perforated or obstructed tumours, poorly differentiated or mucinous histology and perineural or extramural vascular invasion. A combination of these features may confer a worse prognosis in a node negative tumour than in an otherwise favourable lesion with one or two positive lymph nodes. Individual patients should be assessed for their specific risk on this basis by the MDT and counselled regarding the pros and cons of treatment.

Patients with high risk node negative colorectal cancer should be individually counselled by an oncologist with regard to their level of risk and the possible benefits of flouropyrimidine based chemotherapy.

Recommendation grade A

xiii) Chemotherapy for Advanced Disease

a Locoregional recurrence

This is most often observed following surgery for rectal cancer, but with modern staging techniques (i.e. MRI) and selective pre-operative treatment strategies it is anticipated that it will become a much less frequent event. Pre-operative chemoradiation prior to surgical resection of recurrent disease has increased resectability rates to 60% but remains unproven in Phase III trials (Rodel et al, 2000 IIb). Patients with locoregional recurrence in the absence of metastatic disease should be reviewed by the multi-disciplinary team for consideration of radical salvage combined modality treatment.

b Inoperable primary disease

Inoperable primary disease is most commonly seen with rectal cancers, and is associated with a poor prognosis. Combined chemoradiation to downstage or downsize such tumours prior to attempted resection is the current standard approach. The potential for additional neo-adjuvant systemic therapy prior to chemo-radiation to improve resectability rates is currently the subject of investigation in a number of clinical trials.

For patients unfit for such an approach, palliation is the objective of therapy. Palliative radiotherapy or systemic chemotherapy can offer useful symptom control, and the choice of regimen is the same as for metastatic disease (see 2d below).

In fit patients with inoperable but non-metastatic rectal carcinoma primary chemo-radiation should be offered, prior to re-staging and potentially curative resection considered if appropriate.

Recommendation grade B

c Operable Metastatic disease

It has been known for many years that patients with operable metastases in the liver or lung may benefit from resection, and with careful patient selection, hepatectomy for colorectal metastases is associated with a 5 year survival of around 33% (Garden et al, 2006 Ia, Scheele et al, 1990 III). It is currently unclear whether patients with operable metastatic disease benefit from pre-operative chemotherapy, and if the temporal development of metastases (synchronous or metachronous) has any influence on the role of systemic therapy. The results of a UK-led international phase III trial investigating the magnitude of benefit for pre- and post-operative chemotherapy in this setting are awaited with interest (EORTC/GITCCG 40983). There is also some evidence to support the use of the same approach for patients with resectable pulmonary metastases, but there is no evidence that resection of nodal metastatic disease is beneficial.

Non-randomised evidence exists to support the use of pre-operative combination chemotherapy prior to resection in patients with potentially operable liver metastases (Giacchetti et al 2000 III). Such patients should be discussed in the multidisciplinary team meeting in the presence of a hepatic surgeon. If appropriate following radiological and surgical review, pre-operative combination chemotherapy should be delivered for at least 8 weeks prior to re-imaging.

Fit patients with resectable or potentially resectable liver or lung metastases should be reviewed in the MDT with a hepatobiliary (or thoracic) surgeon and colorectal oncologist, to evaluate operability and to decide on a combined plan of management to optimise the chance of achieving complete resection of all metastatic disease.

Recommendation grade B

d Inoperable metastatic disease

Selection of patients for chemotherapy requires the opinion of an oncologist experienced in colorectal cancer chemotherapy. A large number of factors including performance status, serum biochemistry and overall tumour burden influence the patient's ability to tolerate treatment. These can also independently predict progression and survival Performance status is a particularly potent indicator. In a meta-analysis of patients treated in trials of 5-FU based chemotherapy, median survival times were 4, 10 and 14 months for patients with ECOG performance status scores of 2, 1 and 0 respectively (Thirion et al, 1999 Ia).

Patients with unresectable metastatic disease should be discussed by the MDT and should be referred to the palliative care team. If appropriate, they should also be referred to an oncologist for consideration of palliative chemotherapy.

Recommendation grade C

A number of meta-analyses of palliative chemotherapy have shown improved survival with chemotherapy compared with best supportive care. The evidence indicates that early single agent chemotherapy prior to clinical deterioration for advanced disease improves survival by 3 to 6 months and either improves or maintains quality of life (Simmonds 2000 Ia). In patients with stable or responding disease after 12 weeks therapy, a rest from treatment with close observation until disease progression was not shown to be detrimental to survival and contributed to improved quality of life in one UK study (Maughan et al, 2003 Ib). The oral 5FU prodrugs UFT and capecitabine have shown equivalent survival and increased ease of administration compared to bolus 5FU and low dose folinic acid, and are NICE approved as single agents for first line treatment.

Palliative treatment using fluoropyrimidines alone or 5FU in combination with oxaliplatin or irinotecan are NICE approved for the treatment of metastatic colorectal cancer.

Recommendation grade A

More recently combination chemotherapy with intravenous 5-FU plus either irinotecan or oxaliplatin has been shown to offer survival benefits in both first and second line situations. Current NICE guidance supports the use of all three of the active drugs (a fluoropyrimidine, oxaliplatin and irinotecan) and as such has deemed them cost effective. As always, however, therapeutic decisions should be taken at the discretion of the treating oncologist, bearing in mind the fitness of the individual and other criteria as above. Improved results have been reported in studies in which all three of these agents are used in the majority of patients (Grothey 2005 III).

The most recent developments are with targeted monoclonal antibodies used in conjunction with chemotherapy bevacizumab (Avastin), an antibody to the vascular endothelial growth factor, has been shown to confer an additional benefit of 4.7 months in median survival compared to irinotecan and 5-FU alone in the first line setting (Hurwitz et al, 2004). Cetuximab (Erbitux), an epidermal growth factor receptor inhibitor, appears capable of overcoming drug resistance in second and third line situations (Cunningham et al, 2004 III). Both these agents are licensed and at the time of writing are subject to a NICE appraisal. The preliminary guidance suggests that they are unlikely to be approved on the grounds of cost-effectiveness. It is hoped that the results of the numerous ongoing clinical trials with these and other molecularly targeted drugs will demonstrate sufficient benefit to overcome such hurdles.

Treatment for Advanced Disease

xiv) Palliative care

The diagnosis and treatment of cancer can have a devastating impact on the quality of patients' lives and that of their families and carers. Patients with cancer face uncertainty and may have to undergo unpleasant and sometimes debilitating treatments. Patients, families and carers need access to support from the time that cancer is first suspected through to death and into bereavement (NHS Cancer Plan 2000 IV).

Good communication between health professionals and patients is essential for the delivery of high quality care. It is also central to empowering patients to be involved in decision making. All patients, but particularly those with advanced or incurable disease, need to receive high quality information, symptom control, psychological, social and spiritual support.

In the past, patients tended to be referred for palliative care only when they were in the terminal phase of their illness. Increasingly, palliative care is being seen as an integral part of care, often being delivered alongside cancer treatment. Careful control of symptoms is important aspects of the quality of care.

All patients should have access to specialist palliative care advice and services appropriate to their needs. Services should be provided in the community and in hospitals as well as in specialist palliative care units. The overall management plan agreed with the patient and family should include an understanding of the extent to which the patient wishes to be informed and involved in decision making, how far active treatment should be pursued, and where the patient would prefer to die.

Surgeons and oncologists who deal with colorectal cancer should make it a priority to build close links with palliative care specialists and units.

Recommendation grade B

All clinicians who deal with colorectal cancer should be trained in communication skills, in the control of pain and other cancer symptoms

Recommendation grade C

It is important that patients with colorectal cancer are offered the opportunity to ask questions and to have important information repeated. Information giving should be seen as an essential part of every consultation.

Recommendation grade C

6 Follow up

Reasons for Follow-up

The debate continues on the subject of patient follow up after curative treatment for colorectal cancer. Further evidence in the literature has failed to clarify the issue since publication of the last guidelines. Possible benefits from long-term follow up are:

i) Detection of potentially curable recurrent or metastatic disease.
ii) Detection of asymptomatic recurrence when early chemotherapy may improve quality of life and prolong survival.

iii) Detection of metachronous tumours.

iv) Provision of psychological support by patient / doctor contact.

v) Facilitation of audit, clinical governance and continuing professional development.

vi) Survival rates

i) Detection of potentially curable recurrent disease

Four well conducted systematic reviews are supportive of clinical follow up, but three of them conclude that there is a lack of evidence to either confirm or refute the premise that follow-up detects potentially recurrent disease (Jeffery et al, 2002, Ia Renehan et al, 2002 Ia, Richards & McLeod 1997 Ia, Edelman et al 1997 Ia). However, one of these systematic reviews suggests that intensive follow up can improve survival after colorectal cancer (Renehan et al, 2002 Ia). Interestingly this latter study largely relies upon the same trials as the other reviews but reaches a different conclusion.

Of five prospective randomised trials, those from Sweden (Ohlsson et al 1995 Ib), Finland (Mäkelä et al 1995 Ib), Denmark (Kjeldsen et al 1997 Ib) and Australia (Schoemaker et al 1998 Ib) failed to show a survival benefit at 5 years between patients subjected to intensive, compared with minimal, or no, follow up. An Italian trial (Pietra et al 1998 Ib) found benefit for an intensive group. However these 5 studies do not provide a definitive answer to possible survival benefit from follow up for a variety of reasons:

- All published trials are of low statistical power due to small numbers and the fact that only a small proportion of patients with metastatic disease are potentially curable. The authors of the largest trial, including almost 600 patients, concluded that their study was too small to demonstrate a reduction in mortality rate of less than 20% by intensive follow up (Kjeldsen et al 1997 Ib).
- There is no agreement as to what constitutes a "minimal" follow up regimen. In one study this included regular appointments every 3 months for 2 years then 6 monthly. Each visit included clinical examination, LFT, FOB, CEA and colonoscopy at 5 years (Schoemaker et al 1998 Ib). In contrast another study carried out no follow up in the "minimal" group (Ohlsson et al 1995 Ib).
- There is no uniform definition of "intensive" follow up. For example liver scanning was not included in one study (Kjeldsen et al 1997 Ib).

In the Italian trial, which found in favour of intensive follow up, CEA was the most effective indicator of recurrent disease and the authors conclude that frequent CEA assays should be part of an optimum follow up plan. They failed to show that any of the other clinical or instrumental tests were cost efficient in screening for local recurrence. However, their conclusion about CEA results are at variance with those of a substantial non randomised study (|Secco et al, 20002 IIa) and of the only randomised trial of CEA-prompted second-look surgery (Lennon et al 1994 Ib).

Bruinvels and colleagues (1994 Ia) set out to perform a meta-analysis of published studies to determine whether intensive follow-up is associated with increased 5-year survival rates. At the time they were unable to identify a single randomised trial with patients allocated to follow-up or no follow-up groups. They therefore looked at non-randomised studies in which controls were either historical or self-selected (defaulted from

follow-up). There were only seven such studies in the literature and after analysis the authors were unable to draw definite conclusions. Their suggestions included regular follow up and monthly CEA measurements for the first two or three years, combined with aggressive hepatic surgery as indicated. Others do not support CEA based follow up and results from the only major randomised trial also suggest a lack of survival benefit from regular CEA measurement (vide supra). A more recent meta-analysis (Rosen et al 1998 Ia) included the data from the only two published randomised trials at the time of the analysis with a total of 213 patients (Ohlssen et al 1995 Ib, Mäkelä et al 1995 Ib). In order to increase the power of their analysis the authors included non-randomised studies but their conclusion, in favour of follow up, is thus weakened.

Many centres have now adopted a policy of CT scanning to look for liver metastases at one and two years. This has happened largely as a result of data from liver resection specialists showing that patients with resectable liver disease have a 30% 5 year survival, compared with a very small prospect of five year survival if left untreated (Renehan et al, 2002, Ia, Jeffrey et al 2002 Ia, Simmonds et al 2006 IIb).

No study directly addresses the place of postoperative liver scanning and guidance for its use in asymptomatic patients is limited. However, there is little doubt that a small number of patients found to have metastatic liver disease may be cured by liver resection (Rees et al 1997 IIb). A very large trial will be necessary to resolve this issue.

Inclusion of an annual liver CT scan for patients in the intensive arm of the Australian randomised trial of intensive versus standard follow up (vide supra) resulted in 3 liver resections in 157 patients who underwent 674 liver scans. One patient was alive and disease free at 2 years. These data are consistent with other studies, which show that up to 40% of patients will develop liver metastases despite apparently curative surgery and, of these, 2 - 3 % are suitable for liver resection. The 5-year survival in this selected group is 30% and the role of routine postoperative liver scanning, for a large population, is therefore uncertain.

In summary, despite a substantial number of new publications since the initial guidelines (Renehan 2005 III, SHPIC report 1999 IV, NICE Guidance 2004,Ia, Desch et al 1999 IV) the recommendations remain essentially unchanged. There is no evidence that intensive follow-up has a significant effect on survival, but neither is there evidence to the contrary. It is possible that liver imaging by ultrasound or CT may improve the likelihood of being able to offer a potentially curative hepatic resection in <5% of patients. It is therefore reasonable to undertake a CT scan in asymptomatic patients at some time in the first two post-operative years after curative resection.

It must be stressed that many issues around the values of follow up scans remain unresolved: the optimal timing and frequency of this investigation has not been determined, the role of adjuvant chemotherapy and its timing in relation to hepatic surgery and more information on which to base the recommendation is urgently required. Current trials in the UK and Europe are in progress (FACS and GILDA).

Polyp cancers

Population screening for colorectal cancer will lead to the detection of more polyp cancers. Completeness of excision is easier to determine for those with a stalk than for sessile lesions (see Histopathology section). If there is doubt about completeness of the original excision, repeat endoscopic examination is recommended within three months of the index procedure, if the previous polypectomy site is identifiable at this examination biopsy of the polypectomy site and tattooing of the area are recommended. A further endoscopic examination of the area is recommended after a further 6 months. If the area appears healthy at this time the patient should revert back to adenoma surveillance (Atkin et al 2002 III).

ii) Detection of asymptomatic recurrence when early chemotherapy may improve quality of life and prolong survival.

Two small randomised trials have shown that early systemic chemotherapy for asymptomatic metastatic colorectal cancer improves time to symptomatic deterioration, compared with delaying chemotherapy until symptoms develop (The Nordic Gastrointestinal Tumour Adjuvant Therapy Group (NGTATG) 1992 Ib, Scheithauer et al 1993 Ib). Quality of life measurements in these studies also favour early chemotherapy for asymptomatic disease.

iii) Detection of metachronous cancers

Patients with colorectal cancer are at increased risk of developing adenomas and a second primary (metachronous) cancer in the remaining large bowel (Heald & Lockhart Mummery 1972 IIb, Tornqvist et al 1981 IIb). Surveillance colonoscopy after the initial resection results in a substantial yield of such tumours, many of which were probably synchronous with the index cancer (Cali et al 1993 III, Winawer et al 1993 Ib). On this basis patients who did not have complete colonic visualization/imaging preoperatively should undergo early (within 12 months of operation) colonoscopy. Once complete colonoscopy has been achieved and the patient found to be free of cancers and polyps ("clean colon"), further colonoscopy should be repeated at five yearly intervals (Brady et al 1990 III, Winawar et al 1993 Ib, Kronberg et al 1983 IV, Barlow & Thompson 1993 IV Atkin 2002 III). If adenomatous polyps are found follow up should be arranged in accordance with the guidelines from the British Society for Gastroenterology (see Appendix 5*).

There is considerable debate and no evidence about when to stop offering endoscopic surveillance. It is suggested that colonoscopic surveillance should cease when patient and doctor have discussed and agreed that the likely benefits no longer outweigh the risks of further examinations (usually around age 75 years), or when the patient is clearly unfit for further intervention. It must be stressed that there is no evidence that colonoscopic follow-up has a significant impact on survival following surgery for colorectal cancer. Guidance for adenoma surveillance is included in Appendix 5*.

iv) Provision of psychological support

The social and psychological morbidity associated with anorectal excision can be minimised by a combination of attention to surgical technique, the provision of community services and support from a stoma specialist (Devlin et al 1971 III). However surgery for colorectal cancer gives rise to considerable morbidity from impaired bowel, psychological and sexual function (Sprangers et al 1993 III).

A study of patients with various cancers, including colorectal, found that the majority were in favour of regular follow up and thought that the advantages outweighed the disadvantages (Kiebert et al 1993 IIb). Patients with breast cancer prefer follow up and hospital visits do not increase stress and anxiety (GIVO 1994 IIb, Morris et al 1992 IIb). However a more recent UK study of patients with breast cancer in remission found that general practice follow up was not associated with increase in time to diagnosis of recurrence, increase in anxiety or deterioration in health related quality of life (Grunfield et al 1996 Ib).

There are a limited number of studies in colorectal cancer. The Danish trial above included an evaluation of the effect of follow up examinations on health-related quality of life in patients undergoing either intensive or minimal fallow up. The authors concluded that the relatively small benefit did not justify intensive follow up after surgery for colorectal cancer (Kjeldsen et al 1999 Ib). A Dutch study also failed to show an effect of the follow up visit on quality of life (Stiggelbout et al 1997 Ib). However patients expressed a strong preference for follow up and the majority would prefer regular appointments even if it did not lead to earlier detection of recurrence.

v) Facilitation of audit, quality assurance and clinical governance

Audit is the only means by which clinical outcomes can be measured and it underpins clinical governance. Accurate, relevant, reliable data in which clinicians have confidence, is an absolute prerequisite for audit and demands organised and disciplined methods of collection. The Association of Coloproctology of Great Britain and Ireland has produced a minimum data set which may help to overcome some, but not all, of the pitfalls in data collection for colorectal cancer audit (Stamatakis et al 2001 IV). Fundamental to the data set is a data dictionary, which precisely defines each field to ensure conformity of interpretation. The data set and data dictionary are freely available on the internet at www.canceruk.net. Data collection forms are included in Appendix 4. It is only by audit that surgeons can evaluate their results against professional standards. Information from audit provides the stimulus to investigate and perhaps modify personal practice.

If guidelines are to be of value, surgeons must audit their results, and for this some form of follow-up is essential. This might be by regular surgeon / patient contact or through review by clinical nurse specialists (MacBride & Whyte 1998 IV), primary care (Florey et al 1994 Ib) or postal contact. In the absence of supportive evidence local circumstances may dictate local practice.

Evidence to support or refute any survival value for regular follow up is not available. In the absence of hard evidence it is reasonable to offer a single CT scan of the abdomen and thorax to asymptomatic fit patients at sometime during the first two years after resection for the purpose of detecting resectable liver metastases.

Recommendation grade B

Colonoscopic follow-up yields treatable adenomatous polyps and cancer. If such a policy is pursued, it is recommended that a "clean" colon should be examined by colonoscopy at 5 yearly intervals. Patients should be counselled about the potential complications of colonoscopy.

Recommendation grading B

In the absence of evidence from randomised trials, the most persuasive arguments for routine follow-up are patient support and audit. Evidence suggests that patients' preference is for follow up, but by whom and where may depend on local circumstances. All patients should have ready access to specialist nursing staff throughout the period of follow up.

Recommendation grade C

Follow up should cease in elderly or frail patients by agreement between the patient and their treating clinician.

Recommendation grade ✔

vi) Survival rates

Thirty years ago, the overall 5 year survival rate for colorectal cancer in the UK was in the region of 38% (CRC 1993 III). Data from the Birmingham Cancer Registry between 1977 and 1981 indicated that after curative resection, 5-year age-adjusted relative survival rates for colon cancer were 85%, 67% and 37% for Dukes' stage A, B, and C respectively. For rectal cancer, the equivalent figures were 80%, 55% and 32% (Slaney et al 1991 IIb).

More recent figures show that the overall age-standardised survival rates for colon and rectal cancer for 1986-1990 were 40 and 38% respectively. For 1996-99, these figures were 48 and 49% respectively (CRUK 2006 III). These data do not separate out the patients whose cancer is so far advanced that curative resection is not possible, and whose life expectancy is therefore short (about 50% of the total), nor do they allow for stage. Comparative data with either mainland Europe or North America should be viewed with some care since all the variables involved in audits are not always taken into account.

A study of 2269 patients undergoing resection for colorectal cancer in hospitals in central Scotland between 1991 and 1994 showed that cancer-specific survival was lower in socially deprived patients. This difference was not accounted for by the stage of disease at presentation and type of operation. This excess mortality was confined to patients undergoing apparently curative resection (Hole and McArdle, 2002 III). In another study of 3200 patients undergoing surgery between 1991 and 1994 in Scotland, an excess of both cancer-related and intercurrent death was found in men (McArdle et al, 2003 III).

More than a quarter of patients over 90 died within 30 days of their surgery compared with just over 10% of those aged between 80 and 89. Clearly these outcomes also relate to co-morbidity which increases with age. These figures are very similar to those reported from Holland between 1987 and 2000 where the 30 day post-operative mortality increased from 8% for the age group 80 – 84 to 13% for those 85 – 89 and 20% for nonagenarians (Damhuis, 2005 III).

Each MDT should audit the survival rates of the patients they manage. Data from each hospital should be submitted both to Cancer Registries and to the National Bowel Cancer Audit Programme (NBOCAP).

Audit should include both clinical information and non-clinical variables such as socio-economic status.

Recommendation grade ✔

Adequate staff and information technology facilities must be available for this essential part of colorectal cancer care.

Recommendation grade ✔

Audit should be structured with particular reference to outcome measures, and should be regarded as a routine part of a consultant's work. It may be facilitated by the use of a database such as that promoted by the Association of Coloproctology. If other "local" databases are used, field definitions should match those of the Association's data dictionary, to ensure conformity of data collection (see Appendix 4).

Recommendation grade C

7 Histopathology reporting

Access

i) Indications

Accurate, detailed and consistent pathology reporting is important for estimating prognosis and planning further treatment. When applied to groups of patients it is also an index of any shift towards earlier diagnosis which may result from screening programmes. Unfortunately, the quality of pathology reporting has been found to be highly variable (Bull et al 1997 III), and this has important implications for the interpretation of differences in outcomes in different areas of the country. The use of structured proformas has been demonstrated to improve the informational content of pathology reports (Cross et al 1998 IIb).

The structure of a pathology report depends on whether the tissue submitted is a locally resected carcinoma or a full resection specimen. Such reporting should be available for all patients, and it is the surgeon's responsibility to ensure that all resection specimens, including polyps, are sent for histological examination.

Process

Careful and accurate pathology reporting of colorectal cancer resection specimens is vital because pathology reports are used to:

- confirm the diagnosis
- inform prognosis
- plan the treatment of individual patients
- audit pathology services
- evaluate the quality of other clinical services, notably radiology, surgery and oncology
- collect accurate data for cancer registration and epidemiology
- facilitate high quality research
- plan service delivery

In colorectal cancer, some of the key reasons for high quality pathology reporting include:

1) To confirm that radical surgery was necessary, and to place the patient in a correct disease stage for an accurate prognosis to be given and appropriate post-operative therapy to be advised.
2) Patients who have lymph node involvement (Dukes C1 & C2 or pN1 and pN2) are likely to be offered adjuvant chemotherapy, if age and co-morbidity allow, which is of probable benefit, mildly toxic and costly (Quasar 2007 Ib, Andre et al 2004; Ib). Those without lymph node metastases but with adverse pathological features (extramural vascular invasion, perforation, serosal involvement and incomplete resection) may also be offered adjuvant therapy for small but definite probability of benefit.
3) Patients with rectal adenocarcinoma and involvement of the non-peritonealised (circumferential) resection margin are at high risk of local recurrence (Quirke et al, 1986 III, Ng et al, 1993 III) and may receive post-operative radiotherapy +/- chemotherapy which is toxic and costly but may decrease the likelihood of this unpleasant and nearly uniformly fatal complication. The frequency with which circumferential margin involvement is found may indicate the quality of rectal cancer surgery being performed (Quirke et al 2006 Ib).
4) To determine the effects of pre-operative neoadjuvant therapy (Rodel et al, 2005 III).
5) To allow audit of diagnostic and surgical procedures in relation to clinical outcomes avoiding selection bias, to identify good surgical practice and the comparison of patients in clinical trials (Quirke et al, 1997 III, Nagtegaal et al,2002 III).

6) To facilitate improvements in the quality of rectal cancer surgery by grading the plane of surgical excision and recording the frequency of abdomino-perineal excisions (Nagtegaal et al, 2002 III).

Communication of pathology information to the patient and the multidisciplinary team is essential for quality clinical management. Pathologists should attend multidisciplinary team meetings and provide pathology reports that are accurate, complete, understandable, timely and transferable. The use of proformas has been demonstrated to facilitate these requirements and their use is strongly recommended, supplemented as necessary by the use of free text (Branston et al, 2002 Ib; Cawthorn et al, 1990 III).

This dataset has been revised in the light of recent new knowledge to present recommendations on core data items that should be consistently recorded, to provide advice on how information on these items can best be obtained from the resection specimen, and to include an example template proforma for reporting that is amenable to incorporation within laboratory information management systems. It has been approved by the Royal Colleges of Pathologists, the Association of Coloproctology of Great Britain and Ireland, The NCRI Colorectal Cancer Committee and the Pathology Section of the British Society of Gastroenterology. The proformas for resection specimens and local excision specimens can be found in Appendix 6.

The main changes in this edition are the addition of a small number of core data items, the provision of more detailed practical guidance on optimal methods for obtaining the maximum information from a resection specimen, the inclusion of a dataset for reporting local excision specimens and the introduction of standards against which pathologists can audit their practice. The intention is to build further on the major quality improvements that followed the introduction of the original dataset.

Only a small number of additions to the core items for major colorectal cancer resections have been made. These comprise:

1. Measurement of the extent of extramural spread beyond the muscularis propria. There is some evidence to show that this is related to prognosis in rectal cancer (Quirke et al, 2006 Ib, Branston et al, 2002 Ib) but the main reason for adding this item is to facilitate audit of preoperative imaging of extramural spread, (Mercury 2006 III) an increasingly important factor in selecting patients with rectal cancer for neoadjuvant therapy.
2. Recording of tumour involvement of the non-peritonealised resection margin (previously known as the circumferential resection margin) in colonic tumours when this is appropriate, in addition to rectal tumours. This will facilitate the selection of patients with colonic tumours for postoperative adjuvant therapy (Petersen et al, 2002 III).
3. Grading of the surgical plane of resection in rectal cancer specimens. Evidence from two large prospective randomised trials (Quirke et al, 2006 Ib Nagtegaal et al 2002 III), has demonstrated that this predicts local recurrence and survival. Its continual feedback to multidisciplinary teams may lead to improved quality of surgery and clinical outcomes (Quirke et al, 2006 Ib)
4. Recording of marked or complete tumour regression in patients with rectal cancer who have received preoperative neoadjuvant chemoradiotherapy. There is emerging evidence that this is predictive of outcome when resection margins are clear (Rodel et al, 2005 III) but there is uncertainty over the best way for it to be assessed. It is therefore recommended that only complete regression or the presence of minimal residual tumour is recorded at present.

A revision (the 6th edition) of TNM staging of colorectal cancer (Sobin et al 2002 IIb) has been published since the first edition of this Dataset was published. It recommended major changes to the definitions of lymph node involvement that were given in the previous (5th) edition, (Sobin et al 1997 IIb) particularly in relation to the rules governing whether an extramural tumour mass was considered to be a lymph node that had been replaced by tumour. The changes were not evidence-based and cannot be interpreted reproducibly (Howarth et al 2004 III). For these reasons it is recommended that the criteria used in the 5th edition of TNM are retained for colorectal cancer reporting nationally (although pathologists may choose to provide an additional TNM stage according to 6th edition rules if this is desired locally).

Audit

There is compelling evidence that the introduction of the original Colorectal Cancer Dataset improved the standard of colorectal cancer reporting with regard to the completeness of information within pathology reports (Cross et al 1998 IIb, Branston et al 2002 Ib). However, audits show that significant differences remain in the frequencies with which important adverse prognostic features are found between individual pathologists and multidisciplinary teams (Pheby et al 2004 III, Maughan et al, 2003 III). When these features are used as the basis for offering adjuvant therapies and giving prognostic information to patients, the extent of the differences is a cause for concern. Most prominent among these are the number of lymph nodes that are examined and the demonstration of serosal involvement and extramural vascular invasion. Some of the differences, for example in the number of lymph nodes retrieved from a resection specimen, may be related to factors such as the extent of the resection undertaken or the use of neoadjuvant therapy, but it is likely that the way that the pathologist examines the specimen is most important. There is good evidence to show that the prognosis of Dukes B colorectal cancer is directly related to the number of lymph nodes examined pathologically (Swanson et al, 2003 III), with the implication that some of these patients are 'understaged' and that if more lymph nodes had been examined, metastases would have been found.

It is therefore recommended that pathologists audit their reports at regular intervals (perhaps yearly) to ensure that their overall results are not significantly different from what might expected. Three standards are recommended for this purpose, namely that in a series of at least 50 resection specimens,

a) the median number of lymph nodes examined is 12

b) the frequency of serosal involvement is at least 20% for colonic cancers and 10% for rectal cancers

c) the frequency of extramural vascular invasion is at least 25%

We believe there is a reasonable evidence base to suggest that the median harvest of lymph nodes should be at least 12 in centres but accept that the evidence base is weaker for the two other outcome measures. Nevertheless, we believe that this is a start at setting such standards and evidence will follow to allow us to adjust these levels in the future.

In order to facilitate this, proposals for the optimum dissection and blocking of resection specimens are given in the section of Macroscopic Features below.

Clinical information required on specimen forms

While the nature of the resection and the site of the tumour are usually obvious to the pathologist from the specimen that is submitted to the laboratory, it is good practice for him/her to confirm this with the specimen request form. A diagram of the surgical procedure can be extremely valuable in complex specimens. It is also important for the pathologist to be told:

- the type of tumour if known (with details of the previous biopsy)
- if there is a history of inflammatory bowel disease or familial cancer
- the stage of the tumour recorded before surgery
- whether neoadjuvant therapy has been given. It is particularly important for the pathologist to know the precise site of the tumour when neoadjuvant therapy has apparently led to disappearance of the tumour.

Specimen handling and dissection

Specimens should be received fresh and unopened as soon as possible after resection. If submitted outside laboratory hours, they can be refrigerated at 4°C overnight without risk of appreciable autolysis, but if there is likely to be a longer delay before handling they should be placed unopened in a large volume of formalin-based fixative (Burroughs et al, 2000 III, Quirke et al, 2007 III).

The fresh intact surgical specimen is first inspected to locate the tumour and the presence of any macroscopically obvious perforation through the tumour recorded. The non-peritonealised surgical resection margin in the vicinity of the tumour is then inked or painted with a suitable marker, to enable the subsequent identification of margin involvement. This margin represents the 'bare' area in the connective tissue at the surgical plane of excision that is not covered by a serosal surface. Its extent varies greatly according to the site of the tumour. Low rectal tumours will be completely surrounded by a non-peritonealised margin (the circumferential margin), while upper rectal tumours have a non-peritonealised margin posterolaterally (which is inked) and a peritonealised (serosal) surface anteriorly that is not inked (Figure 1).

Tumours of the ascending and descending colons will usually also have a non-peritonealised margin posterolaterally (which is inked) and a peritonealised (serosal) surface anteriorly (which is not) (Figure 2). The sigmoid and transverse colons are usually on a narrow mesentery, so tumours here often have no non-peritonealised margin to speak of. The peritoneal covering of the caecum is prone to individual variation, so tumours here may have a small or large non-peritonealised area.

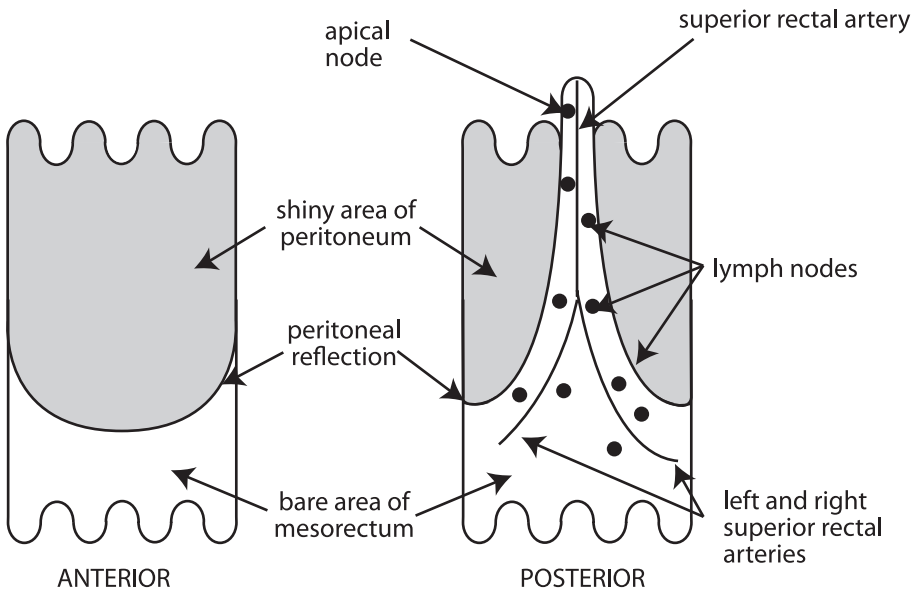

Figure 1. Diagrammatical representation of a resected rectum. Anteriorly the specimen is covered by peritoneum down to the peritoneal reflection and only the unshaded area below this is the non-peritonealised (circumferential) margin that is at risk of tumour involvement. Posteriorly the non-peritonealised margin extends upwards as a triangular shaped bare area containing the main vessels that continues as the sigmoid mesocolon.

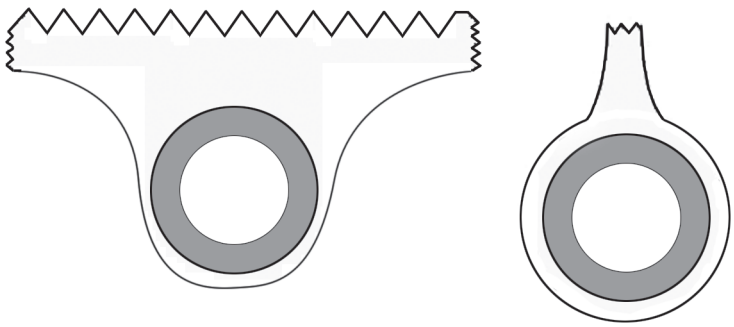

Figure 2. Diagrammatic cross sections of the ascending colon (right) and sigmoid colon (left). The ascending colon has a broad non-peritonealised (jagged) margin posteriorly while the sigmoid colon is suspended on a narrow mesentery and has a narrow non-peritonealised margin.

After inking the margins, many pathologists open the unfixed specimen anteriorly, apart from a segment extending 1–2 cm above and below the tumour, which is left intact to avoid any subsequent confusion over whether the serosal surface or non-peritonealised margin is involved. A paper towel "wick" is then passed through the residual lumen at the tumour site to aid fixative permeation. Some pathologists prefer to open the bowel at the level of the tumour also, especially when the lesion is small, and this is acceptable provided care is taken to ensure that it does not compromise a proper assessment of the key data items, notably involvement of the serosa and the non-peritonealised margin. The opened specimen is pinned to a cork board and immersed in an adequate volume of formalin. It is recommended that resections should be allowed to fix for at least 48 hours before further dissection and block taking; this facilitates subsequent thin transverse slicing through the tumour and the identification of lymph nodes (Richards et al 1998 III Specimens can be unpinned from the board after 24 hours and allowed to float free so as to avoid the risk of suboptimal fixation of tissue previously adjacent to the cork surface.

After the specimen is fixed, the macroscopic data items (described below) are recorded and the segment of bowel including the tumour, the intestine proximally and distally for some 30mm, and the attached mesentery are sectioned transversely at 3–4 mm intervals with a sharp knife to produce slices that include the tumour, the adjacent lymph nodes, and the serosal and non-peritonealised resection margins. It is recommended that these slices be laid out sequentially for photography, enabling a permanent record of the macroscopic appearances to be kept for presentation at the multidisciplinary team meeting if required.

Tissue Sampling

The following blocks of tissue are recommended as a minimum sampling:

- At least four blocks of the tumour to show
  - the deepest tumour penetration into or through the bowel wall
  - involvement of the serosal surface
  - invasion of extramural veins
  - involvement of any adjacent organs

- A block to show the closest approximation of tumour to the non-peritonealised resection margin (either in continuity with the main tumour mass or a separate extramural deposit or tumour in a lymph node, whichever is closest)

- If macroscopic tumour is <30mm from the proximal or distal margin, appropriate blocks to show the closest approximation to that margin (including stapling device doughnuts, if they are submitted, and tumour reaches the end margin of the main specimen)

- A block of tumour and the adjacent mucosa

- A block of normal-appearing background mucosa

- All lymph nodes identified

- The highest node should be submitted separately

- Any other macroscopic abnormalities

Appropriate selection of blocks from the transverse slices is crucial if the maximum amount of information is to be obtained. Serosal involvement is best identified in blocks that are taken from areas that are dulled, fibrotic, or haemorrhagic and is particularly prone to occur where the peritoneum is reflected at an acute angle from the bowel surface on to the adjacent mesentery or in deep crevices or clefts between fat lobules (Ludeman et al, 2005 III). Two blocks taken from where the tumour is closest to the serosa are recommended. Extramural vascular invasion can sometimes be identified macroscopically; blocking areas where the base of the tumour has been sectioned tangentially in tumour slices has been shown to improve its recognition (Sternberg et al, 2006 III).

Rectal tumours that have undergone neoadjuvant therapy may regress to the point that no definite residual tumour can be recognised. In such cases at least five blocks from the site of the original mass should be taken in the first instance (Quirke et al 2007 III). If these do not show residual tumour on microscopic examination, then the whole of the tumour site should be blocked.

The identification of lymph nodes should begin with the highest (apical) lymph node. This is the first node identified by sectioning serially and distally from the sutured vascular margin, regardless of the actual distance between node and tie (Figure 1); it should be identified and blocked separately. Whereas only one vascular "high tie" is present in rectal resections, several vessels might drain colonic resections; if the tumour lies between two major arteries it is appropriate to examine both high tie nodes. The remaining lymph nodes can most easily be identified in the transverse slices of the mesentery, especially if it is sufficiently fixed (see above). Care must be taken to ensure that all of the mesentery between the tumour and the highest lymph node is serially sliced if it has not already been included in the initial slicing. Lymph nodes that are situated very close to a non-peritonealised resection margin should be blocked in such a way as to allow measurement of the distance of any tumour that they may contain from the margin.

It is recommended that lymph nodes should be blocked in their entirety for histological examination, using multiple 3mm slices if appropriate, except when large lymph nodes contain macroscopically overt metastases (van Wyk et al, 2000 III)

Core data items

Macroscopic

- Site of tumour
- Maximum tumour diameter
- Distance to the nearer end resection margin
- Tumour perforation
- Relation of the tumour to the peritoneal reflection (rectal tumours only)
- Grade of the plane of surgical excision (rectal tumours only)
- Distance of the tumour from the dentate line (for abdominoperineal excisions only)

Microscopic

- Histological type
- Histological differentiation
- Maximum extent of local invasion (pT stage) and extramural spread
- Resection margins (end margins and non-peritonealised margins)
- Lymph node status (number present, number involved, apical lymph node)
- Extramural vascular invasion
- Evidence of significant tumour regression (following neoadjuvant therapy)
- Histologically confirmed distant metastases
- Background abnormalities

Other

- TNM stage (5th edition)
- Dukes stage
- Completeness of resection
- SNOMED codes

Non core data items

Macroscopic

- Specimen dimensions
- Precise anatomical location of non-peritonealised margin involvement (rectal tumours)
- Quality of the surgical resection plane in abdominoperineal excisions

Microscopic

- Separate identification of mucinous tumours
- Nature of advancing margin (infiltrative vs. expansive)
- Tumour budding
- Extramural tumour nodules less than 3mm in diameter
- Submucosal vascular invasion
- Immunohistochemical data

Other

- Molecular data

Macroscopic assessment

Measurements made on the gross specimen are recorded in millimetres. They are confirmed or amended, where appropriate, by subsequent microscopy.

Data recorded for all Colorectal Tumours

Site of Tumour

This will usually be stated on the request form. However if examination of the specimen suggests that the stated site is incorrect this should be queried with the surgeon and corrected if necessary.

Maximum tumour diameter

This is measured from the luminal aspect of the bowel. The thickness of the tumour is ignored for this measurement.

Distance of tumour to nearer cut end

This is the measurement from the nearer cut end of the specimen, and not the non-peritonealised or circumferential margin. It is only necessary to examine the margins histologically if tumour extends macroscopically to within 30mm of one of these (Cross et al, 1989 III). For tumours further than this it can be assumed that the cut ends are not involved. Exceptions to this recommendation are adenocarcinomas that are found on subsequent histology to have an exceptionally infiltrative growth pattern, show extensive vascular or lymphatic permeation or are pure signet ring carcinomas, small cell carcinomas or undifferentiated carcinomas.

Presence of tumour perforation

Perforation through the tumour into the peritoneal cavity is a well established adverse prognostic factor in colorectal cancer (Petersen et al 2002, III) and should be recorded. Such cases are always regarded as pT4 in the TNM staging system (see below). It is important to appreciate that localised perforation into the mesentery, mesorectum or retroperitoneum does not count as tumour perforation in this context; neither does perforation of the proximal bowel as a result of a distal obstructing tumour.

Data recorded for Rectal Tumours only

Relationship to the Peritoneal Reflection

The crucial landmark for recording the site of rectal tumours is the peritoneal reflection. This is identified from the exterior surface of the anterior aspect of the specimen (see Figure 3 below).

Rectal tumours are classified according to whether they are:

a entirely above the level of the peritoneal reflection anteriorly

b astride (or at) the level of the peritoneal reflection anteriorly

c entirely below the level of the peritoneal reflection anteriorly

Tumours below the peritoneal reflection have the highest rates of local recurrence (Quirke et al, 2006 Ib)

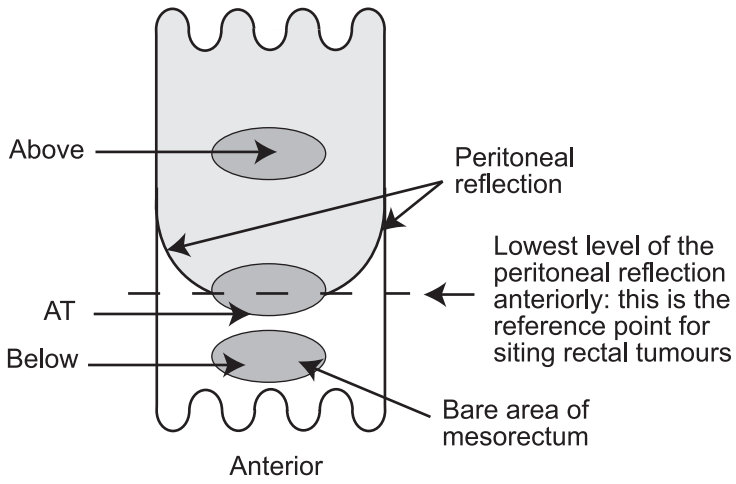

Figure 3

Plane of Surgical Excision

Recently published prospective randomised control trials (Quirke et al, 2006 Ib; Nagtegaal et al, 2002 III) have demonstrated that a macroscopic assessment of the plane of excision of rectal cancers predicts not only margin positivity but also local recurrence and survival. Excision in the mesorectal plane has the best outcome while that extending into the muscularis propria has the worst. The plane of resection can also be used as a marker of the quality of surgery and feedback to the surgical team has been demonstrated to reduce the frequency of resections through the muscularis propria plane with time (Quirke et al, 2007 III) Descriptions of the three planes of excision are given below; illustrations of each have been published and are available at www.rcpath.org/.....

Mesorectal fascial plane

The mesorectal surface is smooth with only minor irregularities of its surface such that no defect is deeper than 5mm. The mesorectum itself is of good bulk anteriorly and posteriorly and there is no 'coning' near the tumour.

Intramesorectal plane

The mesorectum is of moderate bulk but the mesorectal surface is irregular. The muscularis propria of the rectal wall is not visible except at the area of insertion of the levator muscles. Moderate coning of the specimen is present distally.

Muscularis propria plane

There is little bulk to the mesorectum and its surface is irregular with deep cuts and tears, some of which extend on to a visible muscularis propria.

Distance from dentate line

This can only be measured for low rectal tumours in abdominoperineal excision of rectum (APER) specimens. This measurement is important to make as it identifies patients who have lost their internal sphincter.

Microscopic assessment

Tumour Type

Virtually all colorectal cancers are adenocarcinomas. Other rare forms worthy of special mention are:

- adenosquamous carcinomas
- true squamous carcinomas (not including upwardly spreading anal tumours)
- signet ring cell carcinomas
- adenocarcinoid (goblet cell carcinoid) tumours
- small cell carcinomas
- totally undifferentiated carcinomas

Mucinous carcinomas (where >50% of the tumour is composed of extracellular mucin pools) are recorded as adenocarcinomas. Whether they have a different prognosis from conventional adenocarcinomas that is independent of other prognostic factors, or respond differently to certain chemotherapeutic agents, is controversial (Purdie et al, 2000 III). There is also some evidence that neoadjuvant therapy may 'induce' a mucinous phenotype (Nategaal et al, 2004 III). For these reasons their separation cannot be justified as a core item. However, because right sided mucinous adenocarcinomas are well recognised to occur in hereditary non-polyposis colorectal cancer (HNPCC), it would be prudent for pathologists to identify such tumours at the MDT meeting when they occur in young individuals.

Differentiation by Predominant Area

Poorly differentiated carcinomas should be separated from other types but only if this forms the predominant area of the tumour (Halvorsen et al 1988 III). The criteria for poorly differentiated tumours are either irregularly folded, distorted and often small tubules or the absence of any tubular formation. Small foci of apparent poor differentiation are not uncommon at the advancing edge of tumours but these are insufficient to classify the tumour as poorly differentiated.

There is considerable recent interest in the phenomenon of tumour budding at the advancing margin of colorectal cancers, with accumulating evidence that it might have prognostic significance (Prail 2007 III). However, this is not yet considered sufficient to justify its inclusion as a core data item.

Local Invasion

The maximum degree of local invasion into or through the bowel wall is recorded. This is based on the criteria for pT staging in the TNM staging system, which is shown in Appendix A. It should be noted that the pT4 stage encompasses either tumour involvement of the serosal surface (pT4a) or infiltration of an adjacent organ (pT4b). Because these two features may have different implications (for instance invasion of a lower rectal tumour into the levators is staged as pT4b but there would be little chance of the same tumour having serosal involvement) and therapeutic connotations they are recorded in separate boxes. Accordingly, pT4 tumours may have either or both the pT4 boxes marked.

Involvement of the serosal (peritoneal) surface is defined as tumour breaching of the serosa with tumour cells visible either on the peritoneal surface or free in the peritoneal cavity (Shepherd et al, 1997 IIb). It is important that blocks are taken to optimise recognition of this feature (see above) and that further sections

are cut from blocks whose initial sections show tumour cells that are close to the surface or localised peritoneal inflammation, erosion or mesothelial hyperplasia. Serosal involvement through direct continuity with the primary tumour (pT4) is recorded differently from peritoneal tumour deposits that are separate from the primary that are regarded as distant metastases (pM1). It is very important to appreciate the difference between involvement of the serosal surface and involvement of a non-peritonealised (sometimes referred to as 'circumferential') surgical resection margin, which is recorded separately. The first is a risk factor for intraperitoneal metastasis while the latter is a risk factor for local recurrence.

TNM conventions recommend that direct invasion of an adjacent organ by way of the serosa is always recorded as pT4 while intramural (longitudinal) extension into an adjacent part of the bowel (e.g. extension of a caecal tumour into the terminal ileum or of a rectal cancer into the anal canal) does not affect the pT stage (TNM 2001 IIb). Extramural extension of a rectal cancer into the skeletal muscle of the levator ani is classified as pT4. The conventions also state that tumour entirely within vessels does not qualify as local spread in pT staging.

The maximum distance of tumour spread beyond the bowel wall is recorded in millimetres from the outer margin of the muscularis propria, as illustrated in Figure 4. For pT1 and pT2 tumours this will be zero.

Response to Neoadjuvant Therapy

There is preliminary evidence that completely excised rectal carcinomas that have received pre-operative neoadjuvant chemoradiotherapy that has resulted in complete or marked regression have a better prognosis than those without significant regression (Rodel et al 2005 III). However, there is no consensus over how lesser degrees of regression are estimated histologically. While this evidence alone may not be sufficient to warrant recording of response to therapy as a core data item, the fact that it is also regularly sought by oncologists at multidisciplinary team meetings has led to the recommendation that the most obvious degrees of regression are documented. Accordingly, the following categories are included:

- No residual tumour cells or mucus
- Mucus lakes (surrounded by a host response) without tumour cells
- Minimal residual tumour, i.e. only occasional microscopic tumour foci are identified with difficulty
- No marked regression

For tumour staging following neoadjuvant therapy, only the presence of tumour cells in the surgical specimen is taken to determine the stage. Fibrosis, haemorrhage, necrosis, inflammation and acellular mucus are ignored. Cases with complete regression are therefore recorded as pT0 (or more precisely ypT0 – see below).

Resection Margins

Doughnuts

It is not necessary to examine doughnuts from stapling devices histologically if the main tumour is >30 mm from the cut end of the main specimen (Cross et al 1989 III) or in other rare cases described above. If doughnuts are not sectioned or if no doughnuts are submitted for examination, this item should be recorded as not applicable.

Margin (cut end)

When cut ends are examined histologically (see criteria above) the presence or absence of tumour should be recorded. If margins are not examined histologically they should be recorded as not applicable.

Non-Peritonealised ('Circumferential') Resection Margin

This margin has been defined in detail above. Its involvement is predictive of local recurrence and poor survival in rectal tumours (Quirke et al 1986 III, Ng et al 1993 III) and in those that have not received neoadjuvant

therapy it may be an indication for postoperative adjuvant therapy. The importance of non-peritonealised margin involvement in colonic tumours, particularly those of the caecum and ascending colon, has been recognised more recently (Petersen et al 2002 III, Bateman et al, 2005 III, Quirke et al, 2006 III)

The minimum distance between the tumour and the circumferential margin in millimetres is also recorded from the histological slides (see Figure 4 below). If this is <1 mm then the circumferential margin is regarded as involved in the assessment of completeness of resection later on in the proforma. Such involvement may be through direct continuity with the main tumour, by tumour in veins, lymphatics or lymph nodes or by tumour deposits discontinuous from the main growth.

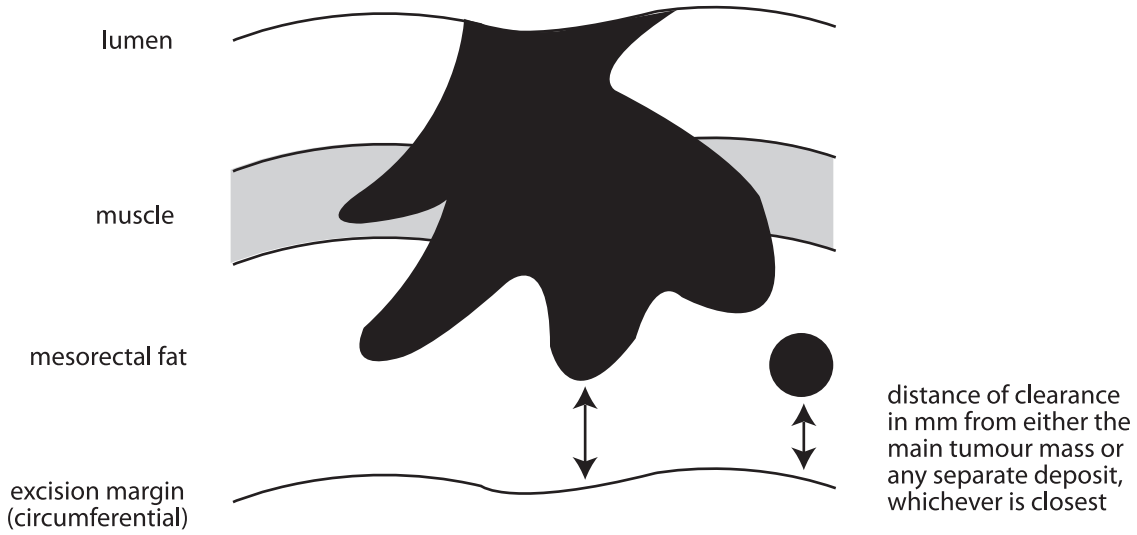

Figure 4.

One study has suggested that the definition of an involved non-peritonealised margin should be increased to 2mm for rectal tumours (Nagtegaal et al 2002 III). This issue will be kept under review.

Metastatic Spread

Lymph Nodes

All of the lymph nodes that have been retrieved from the specimen should be examined histologically as described above. Multiple or serial sections from lymph node blocks are not recommended for routine reporting; neither is the use of immunohistochemistry or molecular techniques. Extracapsular invasion is not recorded specifically.

Extramural deposits of tumour that have no lymph node structure are regarded as lymph node deposits that have completely effaced the original lymph node if they measure >3mm in diameter, according to the recommendations of the 5th edition of the TNM classification (Sobin 1997 IIb). Smaller deposits are regarded as apparent discontinuous extensions of the main tumour. Any tumour involvement of a lymph node, no matter how small, is regarded as significant.

pN1 corresponds to involvement of 1-3 nodes and pN2 to involvement of 4 or more nodes.

Apical node positive

For proper Dukes staging the pathologist will need to identify separately the apical lymph node closest to the main vascular tie(s). This is not defined by any measure of distance, but is simply the first node identified by slicing the mesentery serially and distally from each main vascular tie.

Extramural vascular invasion

This is recorded when tumour is present within an extramural endothelium-lined space that is either surrounded by a rim of muscle or contains red blood cells. It is also strongly suspected when a rounded or elongated tumour profile is identified in the extramural tissues adjacent to an artery and especially when no separate accompanying vein can be identified. The selection of tumour blocks to optimise the identification of venous invasion (see above) is encouraged; the routine use of special stains or immunohistochemistry is not (Sternberg et al 2006 III).

The prognostic significance of extramural vascular invasion is well established (Talbot et al 1980 III). Some studies have also found independent prognostic significance for involvement of submucosal veins while others have not. Only extramural venous involvement is recommended for recording at present.

Histologically confirmed distant metastases

The presence of histologically confirmed distant metastases, and their site, is recorded. It should be noted that disease classifiable as distant metastasis may sometimes be present within the primary tumour resection specimen, for example a serosal or mesenteric deposit that is distant from the primary mass. Metastatic deposits in lymph nodes distant from those surrounding the main tumour or its main artery in the specimen, which will usually be submitted separately by the surgeon (e.g. in para-aortic nodes or nodes surrounding the external iliac or common iliac arteries), are also regarded as distant metastases (pM1) (TNM 2001 IIb).

Background Abnormalities

The presence of any pathological abnormalities in the background bowel should be recorded. The following are particularly of note:

- adenoma(s), including their number
- synchronous carcinoma(s) (each of which will require a separate proforma)
- ulcerative colitis
- Crohn's disease
- familial adenomatous polyposis
- diverticulosis

Pathological staging

Complete resection at all margins

This includes the ends of the specimen, the non-peritonealised resection margin and the doughnuts. Tumours that are completely excised are classified as R0, those with microscopic (but not macroscopic) margin involvement are classified as R1 and those with macroscopic margin involvement as R2.

When doughnuts and the ends of the specimen are not examined histologically because the tumour is >30mm away these are assumed to be tumour-free.

Non-peritonealised margins are regarded as involved if tumour extends histologically to <1 mm from this margin.

Peritoneal (serosal) involvement alone is not a reason to categorise the tumour as incompletely excised.

TNM Staging

The TNM Staging definitions are shown in Appendix 4.

The prefix 'p' is used to indicate pathological staging. If neoadjuvant preoperative chemotherapy or radiotherapy has been given, the prefix 'yp' should be used to indicate that the original p stage may have been

modified by therapy. Accordingly, when there has been complete regression of the tumour, the TNM stage is ypT0, ypN0, ypMx.

The following are worth re-stating:

i In determining the pT stage, tumours that have perforated into the peritoneal cavity are regarded as pT4, irrespective of other factors.

ii Direct intramural spread of caecal carcinomas into the terminal ileum or rectal cancers into the anal canal does not affect the pT stage. However direct extramural spread (across the serosa) of a colorectal carcinoma into another part of the large or small intestine corresponds to pT4.

iii Extramural deposits of tumour that are not obviously within lymph nodes are regarded as discontinuous extensions of the main tumour if they measure <3mm in diameter but as lymph nodes if they measure >3mm in diameter.

iv The difference between stage pN1 and pN2 is the number of lymph nodes involved (pN1 = 1-3 nodes, pN2 = 4+ nodes), irrespective of their site in the resection specimen.

v Pathological M staging can only be based on distant metastases that are submitted for histology by the surgeon and will therefore tend to underestimate the true (clinical) M stage. Pathologists will therefore only be able to use M1 (distant metastases present) or MX (distant metastases unknown). Note that metastatic deposits in lymph nodes distant from those surrounding the main tumour or its main artery in the specimen are regarded as distant metastases.

Dukes Classification

The Dukes & Bussey modification of the original Dukes classification of resection specimens is recommended:

Dukes A: Tumour limited to the wall of the bowel, lymph nodes negative

Dukes B: Tumour spread beyond muscularis propria, lymph nodes negative

Dukes C1: Lymph nodes positive but apical node spared

Dukes C2: Apical lymph node involved

SNOMED Coding

Colorectal carcinomas should be coded according to the SNOMED system.

Reporting of local excision for colorectal cancer

Local excision of colorectal cancer is usually undertaken in one of two situations:

a) as a curative procedure for early (T1) colorectal cancer

b) as a palliative procedure in debilitated patients.

While the principles of pathological reporting are the same as in major resections, a number of features require special attention in local excisions of (presumed) early cancers with curative intent because they are used to determine the necessity for more radical surgery. In addition to the assessment of completeness of excision, these include the recording of parameters that predict the presence of lymph node metastasis in early tumours, namely poor differentiation, the depth of invasion into the submucosa and the presence of submucosal lymphovascular invasion (Coverlizza et al 1989 III, Cooper et al 1995 III, Volk et al 1995, III, Haggitt et al 1985 III).

Local excisions are undertaken endoscopically or, in the case of early rectal tumours, under direct vision. The majority of such tumours arise within pre-existing adenomas that may be polypoid, sessile or flat, and the best pathological information is derived when lesions are excised in their entirety to include both the invasive and preinvasive components (Burroughs et al 2000 III). Polypoid lesions on a narrow stalk can be fixed intact, while sessile lesions should be pinned out, mucosal surface upwards, on a small piece of cork or other suitable material, taking pains to identify the narrow rim of surrounding normal tissue, before fixing intact. Piecemeal removal of tumours, entirely acceptable for palliative resections, should be avoided because it precludes a reliable assessment of completeness of excision.

After fixation, polypoid lesions may be bisected through the stalk if they measure <10mm; larger polyps are trimmed to leave a central section containing the intact stalk, and all fragments embedded for histology. It is recommended that at least three sections are taken from blocks containing the stalk. The margins of larger, sessile lesions should be identified with appropriate coloured markers (inks or gelatine) and the whole of the specimen transversely sectioned into 3 mm slices and submitted for histology in sequentially labelled cassettes. In cases where the margin of normal tissue is less than 3 mm, a 10 mm slice containing the relevant margin should be made and further sectioned at right angles.

An example template proforma for reporting local excision specimens is included in this dataset. The core data items to be recorded are:

- Specimen type, whether a polypectomy, an endoscopic mucosal resection or a transanal endoscopic microsurgical (TEM) excision
- Tumour site
- Maximum tumour diameter in millimetres
- Histological type
- Histological differentiation
- Extent of local invasion
- Lymphovascular invasion
- The presence of a background adenoma
- Margin involvement
- The minimum clearance of the invasive carcinoma (in millimetres)
- A pT stage (it is inappropriate to use Dukes classification because this requires assessment of the nodal status)

Some of these require special consideration:

Histological Differentiation

This is assessed by the same criteria as in major resection specimens. Poor differentiation (including signet ring cell adenocarcinoma) is regarded by most as an indication for radical surgery.

Extent of Local Excision

Tumours that invade the muscularis propria usually require further surgery. The frequency of lymph node metastasis in sessile tumours that involve the superficial, middle, and deep thirds of the submucosa (so-called Kikuchi levels sm1, sm2 and sm3 respectively (Kikuchi et al 1995 III) has been reported to be 2%, 8% and 25%. Accordingly, tumours invading the deepest third of the submucosa should be recorded separately for consideration of further therapy. In polypoid lesions, Haggitt identified the level of invasion into the stalk of the polyp as being important in predicting outcome and found that 'level 4' invasion, in which tumour extended beyond the stalk of the polyp into the submucosa but did not invade the muscularis propria, was an adverse factor (Haggitt et al 1985 III).

Lymphovascular invasion

Definite invasion of endothelium-lined vascular spaces in the submucosa is generally regarded as a significant risk for lymph node or distant metastasis. Sometimes retraction artefact around tumour aggregates can make assessment uncertain, in which case this uncertainty should be recorded and the observation interpreted by the MDT in the light of any other adverse histological features.

Margin involvement

It is important to record whether the deep (intramural) resection margin is involved by invasive tumour (which may be an indication for further surgery) and whether the mucosal resection margin is involved by carcinoma or the pre-existing adenoma (in which case a further local excision may be attempted).

There has been considerable discussion and controversy in the literature over what degree of clearance might be regarded as acceptable in tumours that extend close to the deep submucosal margin. It is important that this is measured and recorded in the report. It is likely that most would regard a clearance of <1mm as an indication for further therapy. Some would use <2mm and a few <5mm.

There is also emerging evidence that identification of the phenomenon of tumour budding may be of prognostic importance in predicting outcome following local excisions (Ueno et al 2004 III). While this is not yet considered to be sufficient to warrant inclusion as a core data item, local MDTs may wish to receive this information if they will use it in a therapeutic decision-making process.

All resected colorectal tumours should be submitted for histopathological examination, which should reach acceptable quality standards as outlined above.

Recommendation grade B

Pathology reports should contain information on all of the data items contained in the Joint National Guidelines Minimum Data Set for Colorectal Cancer Histopathology Reports.

Recommendation grade C

Pathology laboratories should store stained histology slides for a mimimum of 10 years, and tissue blocks from specimens indefinitely, in order to facilitate future case review, clinical audit, and research.

Recommendation grade B

Pathological examination of colorectal cancer specimens should be carried out in laboratories which perform to high technical standards such as those required for Clinical Pathology Accreditation, and that participate in external quality assessment schemes and regular audit of technical procedures and diagnosis.

Recommendation grade B

8 Guidelines for the management of anal cancer

Background

Anal cancer is a rare disease, accounting for 1 – 2 % of gastrointestinal malignancies. The annual incidence is 1 per 100,000, or approximately 500 new cases in the UK per year. Squamous cell carcinoma or epidermoid carcinoma is the commonest form. Rarer types of anal malignancy include adenocarcinoma of the anal glands, small cell and undifferentiated carcinoma, which should be treated as low rectal carcinomas. Conversely there is no evidence that rectal excision is of benefit for anal melanoma.

Squamous cell cancer may affect the mucosa of the anal canal or the skin of the anal margin. Distal anal cancers have a large cell keratinising morphology. Cloacogenic (basaloid transitional cell tumours) are non-keratinising and usually occur in the upper anal canal. The behaviour and treatment of these types is similar. Squamous cell cancers of anal canal have different pathological spread to low rectal adenocarcinoma and are staged differently. Squamous cell cancers of the anal margin, which are distal to the anal verge and involve the hair-bearing area, are classified and treated as skin tumours.

Predisposing factors for anal squamous carcinoma have been identified as HPV infection (subtypes 16,18 and 31), HIV and immunosuppression.

Investigations

The process of referral and investigation

(i) Presentation & Diagnosis

Anal cancer usually presents as a mass or ulcer, and suspicious lesions should be biopsied. Patients may also present with groin lymphadenopathy. Anal cancer may be detected as a finding following Histopathological examination of an anal lesion, making a high index of clinical suspicion an essential prerequisite for diagnosis of these lesions.

HIV testing should be considered in homosexual males and those at risk of contracting HIV. HIV status has implications relating to sepsis, toxic effects of chemoradiotherapy and future management.

Risk factors

Sexually transmitted infection appears to be a significant cause of anal cancer. (Frisch M et al 1997 IIb) Human papilloma virus (Serial type 16 and 18) is associated with anal intraepithelial neoplasia (AIN). (Chawla et al 2001 III, Zbar et al 2002 III). This may proceed to invasive cancer although the risk is not known.

Others with immuno-suppression, particularly HIV infection, are also at risk; among HIV positive homosexual men, the incidence of AIN is over 36 % (Clark et al 2004 III).

Smoking is a risk factor for anal cancer. (Ryan et al 2000 III, Frisch M et al 1997 IIb)

(ii) Staging

Tumours of the anal margin, which are distal to the anal verge and involving the hair-bearing area, are classified in the same way as skin tumours.

Anal cancer spreads via the lymphatic system and to a lesser extent by the blood stream. Tumours of the distal anal canal (below the dentate line and anal verge) drain to the inguinal nodes; femoral nodes and thus to the external iliac system. The lymphatics of the proximal anal canal drain to the mesorectal nodes, then along relevant branches of the inferior mesenteric artery and thus to para aortic nodes. They also drain to the internal iliac and obturator nodes (Hill J et al 2003 IIb).

TNM staging for anal cancer has a different basis from low rectal cancers. It is based on size (T1-T3) and in the case of T4 lesions, invasion of the adjacent organs. The N stage (regional lymph nodes) reflects the pattern of lymphatic spread. The AJCC-TNM staging system is used. (Appendix 6)

Pre-treatment staging

- Clinical. It is often necessary to perform an examination under anaesthetic to assess the stage of the anal cancer and to biopsy it. Assessment can be documented in a diagrammatic form. An accurate assessment of size is required for staging (TNM) and to determine prognosis.

- Endo-anal ultrasound has been used to assess the anal sphincters for benign disease and in low rectal cancers. It stated advantage is an accurate assessment of the depth of tumour in relation to the anal sphincter. (Magdeburg et al 1999 III, Giovannini et al 1992 IIb, Bartram et al 1991 IV).

  Endo-anal techniques can be painful; the imaging field of view is limited and mesorectal lymph nodes may be missed.

  It is most likely to be accurate in early disease (T1 and T2) that has not spread beyond the external anal sphincter. There are claims that 3D endosonography improves nodal detection. Ultrasound may improve the accuracy of clinical staging.

- MR imaging. Anal carcinoma may be assessed using a pelvic-phased array MR coil, similar to that used to assess rectal adenocarcinoma of the anorectal junction. The ability to demonstrate sphincter anatomy using either endo-anal coils or high spatial resolution external surface pelvic phased array coils have been described (Laghi et al 2002 III, Stoker et al 2000 III, Salerno G et al 2004 III).

  Imaging is increasingly employed to define disease extent to aid treatment planning, for the follow up of patients undergoing chemoradiation, and in the surveillance of patients to detect relapse. Clear pre-treatment delineation of pelvic disease enables optimal planning of radiotherapy to the target volume. Post treatment assessment can be useful to document tumour regression and, in patients that fail to show a response or have recurrent disease, the technique enables delineation of disease for possible salvage surgery.

- Distant metastases can be detected by using CT scanning. 40% of patients develop distant disease in the chest and abdomen.

- Enlarged groin lymph nodes can be assessed by fine needle aspiration (or biopsy), if necessary under ultrasound guidance. A high proportion of enlarged groin nodes in patients with anal cancer will show reactive changes only.

(iii) Residual / recurrent disease

Patients being considered for salvage surgery should be restaged with:

- Pelvic MRI for the extent of local disease. There may be difficulties in differentiating disease from radiation effects, even using a combination of ultrasound and MRI.
- CT chest/abdomen for distant metastases.

Approximately 10% of patients who undergo chemo-radiotherapy do not respond fully, and most local treatment failures are apparent within 18 months of starting combined therapy. Local persistence or recurrence of disease is usually digitally palpable even before it becomes symptomatic. However, differentiation between complications of radiation and recurrence can be difficult and it may be necessary to perform a biopsy under anaesthetic, although this may precipitate radio necrosis.

- Following chemoradiotherapy, MRI is able to demonstrate tumour regression and document sustained response but this finding is based on a relatively small series of patients. However, since the imaging experiences in low rectal cancer staging can be readily applied to anal tumours and relationship of

tumour to the anal sphincter complex can be defined more clearly by imaging than by clinical examination, it is proposed that patients with anal cancers should be imaged using high resolution MRI at baseline and following chemoradiotherapy. (Laghi et al 2002, Stoker et al 2000, Salerno G et al 2004 III)

- PET scanning may be of value for detecting distant metastases or local spread after chemo-radiotherapy.

Treatment

(i) Chemoradiotherapy

Standard treatment for most patients with anal cancer is chemoradiotherapy. Currently, the radiotherapy schedule used is 45 Gy in 25 fractions plus a boost or as per the ACT II protocol i.e. 50.4 Gy in 28 fractions.

Until the late 1980's, surgical excision was used to treat primary anal cancer in the UK. Chemoradiotherapy was adopted as standard after its effectiveness was demonstrated in the first UK trial of treatment for anal cancer (ACT I). By the early 1990's the results of this trial and separate trials run by the EORTC (European Organisation for Research and Treatment of Cancer) and RTOG (Radiation Therapy Oncology Group) were available. ACT I was the largest of the 3 trials and, like the EORTC trial, compared radiotherapy to the same radiotherapy with 5-fluorouracil (5-FU) and mitomycin C (MMC) during the first and final week of the first radiotherapy course. The trial established chemoradiation as the treatment of choice for the majority of patients with the disease, (Arnott et al 1996 Ib, Bartelink et al 1997, Flam et al 1996 Ia), even though there was no significant difference in overall survival at 3 years (58% with RT vs 65% for chemo radiotherapy ($p = 0.25$).

Ongoing studies and current practice

Following the closure of these trials, several pilot studies were conducted to test alternative treatment schedules and dose escalation of either chemotherapy or radiotherapy, with the aim of improving prognosis in anal cancer.

When designing the second UK trial (ACT II), a primary aim was to avoid the 6-week radiotherapy gap in the previous trial, to unify UK practice. This trial uses a continuous 2 phase schedule of 50.4Gy in 28 fractions, and compared 5-FU/MMC with 5-FU/CDDP (Bartram et al 1991 IV, Bowman et al IIb). Chemotherapy is given during the first and fifth weeks of radiotherapy.

Patients receive whole pelvic radiotherapy to include the tumour and involved nodes with a 3 cm margin to include inguinal, internal and external iliac nodes using an opposed parallel pair field arrangement. They then receive a second phase with a shrinking field to include tumour and involved nodes with a 3 cm margin only. The whole pelvic dose is 30.6 Gy and the dose to the second phase treatment field is 19.8Gy.

Patients are randomised to 2 additional courses of chemotherapy or follow up alone following chemo radiation. Irrespective of the drug combination given during chemo radiation, 5-FU & CDDP are given as maintenance.

It is recommended that outside of the trial patients receive the same radiotherapy treatment using either the 5FU/MMC or 5FU/CDDP at the clinician's discretion, but without any additional chemotherapy following radiotherapy.

Frail & Elderly patients

EXTRA, a phase II trial which closed in September 2006 combined oral chemotherapy (capecitabine, mitomycin C and the ACT II radiotherapy schedule. It is hoped that the oral schedule will reduce hospitalisation and be simpler for patients, particularly the elderly. This group of patients might also be adequately treated with a reduced radiation dose (Charnley et al 2005 IIb). Further studies are required to determine whether these encouraging results can be maintained (Chawla et al, 2001 III).

Current Treatment for Relapse

In ACT I, approximately 30% of patients relapsed after primary treatment with chemoradiation. Of these relapsed patients, approximately half were suitable for surgery. The other half therefore might have benefited from further palliative chemotherapy. The choice of mitomycin or cisplatin depends on which drugs were used in the initial therapy.

For inoperable patients who have had 5-FU/CDDP or 5FU/MMC, there is no data on alternative treatment schedules.

(ii) Surgery

a. Local excision

T1 tumours within 2cm of the anal margin can be treated by local excision. Local control and survival rates are high with clear margins (Mendenhall et al 1996 IV).

Local excision is not recommended for any other anal tumours.

b. Primary anorectal excision

Before 1980, abdominoperineal resection (APER), with or without inguinal block dissection, was the standard treatment, achieving 5-year survival rates of 38-70%. (Frisch et al 1993 III, Bowman et al 1984 IIb, Pintor et al 1989 III). Nigro et al introduced combined chemotherapy and radiotherapy in 1974 (Nigro 1974 IIb), and by the mid-1980s, achieved a 5-year survival rate of 80%, (Nigro et al 1984 IIa). Subsequently, chemoradiotherapy has become the treatment of choice for anal squamous cancers for which local excision is not appropriate.

c. Defunctioning Stoma

Chemoradiation offers the prospect of successful local control without a permanent stoma. Potentially temporary stomas may be appropriate for patients with either:

a) advanced tumours with loss of sphincter function before chemo radiotherapy, or

b) recto vaginal fistulas, or are at risk of developing such fistulas during treatment.

The reversal rate of temporary stomas is low, reflecting the frequency with which they are used for patients with advanced disease.

The ACT 1 trial shows a 65% permanent stoma rate with radiotherapy alone and 61% with combined therapy. (Arnott et al 1996 Ib).

d. Groin lymph node dissection

30% of patients presenting with anal cancer will have palpable inguinal nodes (Pintor et al 1989 III). Up to half of these are inflammatory. Fine needle aspiration is appropriate, possibly with ultrasound guidance. Inguinal lymph node involvement is a prognostic factor for local recurrence and impaired cancer-related survival. (Bartelink et al 1997 Ib).

There are no trials of prophylactic block dissection. Many radiotherapy protocols include the groins in their treatment fields. Radiation dose to clinically uninvolved inguinal lymph nodes has been lowered in the trial protocols of the current UK ACT II study and RTOG-9811 trials.

Although treatment doses have been reduced, relapse after prophylactic radiotherapy can usually be salvaged by groin dissection (Gerard et al 2001 III,Clark et al 2004 III). Later presentation of groin involvement can be treated by radiotherapy or surgical block dissection; the latter having significant morbidity and impaired

wound healing even if a myocutaneous flap is used. Block dissection may be hazardous after radiotherapy or not feasible. Sentinel node biopsy is under assessment.

e. Salvage surgery

The main purpose of follow up after chemoradiotherapy is to detect local failure, be it residual or recurrent disease. Before proceeding to excisional surgery, tumour recurrence or persistence should be established by biopsy under anaesthesia. The patient should be restaged (preferably with MRI and / or CT) to determine whether ano-rectal excision is likely to result in disease-free margins and whether there is no detectable distant disease, which would make excisional surgery ill-advised. The failure rate after chemotherapy is in the order of 10-30 %; half of these can be staged as potentially operable for local control, but only 50 % are potentially long term survivors. (Longo et al 1994 III,Ellenhorn et al 1994 III, van der Wal et al 2001 IIb)

Though anorectal excision is essentially the same as for low rectal adenocarcinoma (the mesorectal nodes are excised) the skin incision should be modified according to the configuration of the tumour. Because of the differences in spread of squamous as compared to rectal adenocarcinoma there should be wide removal of the ishiorectal fossa fat. Delayed wound healing is common (42%) and consideration should be given to reconstruction with a myocutaneous flap although there is significant morbidity even after this. (Clark et al 2004 III, Renehan 2005 IIb, van der Wal et al 2001 IIb, Radice E et al 1999). Without flap reconstruction, there are significant delays in wound healing and some never heal.

Anal Cancer MDT

Anal cancer is a rare disease and specific expertise in management is necessary to optimise outcome. The NICE Guidelines "Improving Outcomes in Colorectal Cancer" recommended that each network should have an 'Anal Cancer MDT' based within the Cancer Centre Colorectal MDT.

This would ensure the necessary range of expertise for the management of these patients and allow the team to obtain specific experience in this rare disease. As the primary treatment is chemo-radiation, the Multi Disciplinary Team should be led by not more than two oncologists. This would ensure the necessary expertise for the management of these patients and allow the team to obtain specific experience in this rare disease.

- There should be one, preferably two members of the MDT who specialise in the surgery of anal cancer.
- All cases of anal cancer within the network should be reviewed by the anal cancer MDT .
- The network should define appropriate referral guidelines and ensure review by the anal cancer MDT after initial diagnosis.
- All patients being considered for surgery (including local excision) within the network should be discussed by the Anal Cancer MDT, and the surgery should be undertaken by designated surgeons who are members of the MDT and have a special interest in anal cancer.
- Pathology should be reviewed by the nominated Anal Cancer MDT pathologist.
- The MDT may occasionally need to seek advice from a gynaecological oncologist with experience in vulval cancer (HPV conditions), and a plastic surgeon.
- Persistent disease, recurrence or relapse should be discussed by the Anal Cancer MDT. Clinical staging should be undertaken by the MDT oncologists and surgeons at the meeting (according to protocol) and reviewed by the MDT radiologists.
- Management of anal cancer within a designated network Anal Cancer MDT should improve the quality of treatment. It will allow the audit of short and long-term effects of treatment in comparison with results between networks.
- Registration of cases through the network's pathologists with the Anal Cancer MDT for each network will allow the necessary data to be collected.
- Significant deficiencies of clinical staging, imaging and pathology have been demonstrated by national audit (Karandikar et al 2006 III).

- Proforma reporting will improve quality of information available for audit.
- Inclusion in clinical trials should be encouraged.

Follow up

The aim of follow up for anal cancer is:

1. To detect local failure after local excision or chemoradiotherapy that might be amenable to further surgery or chemoradiation.
2. To detect the occurrence of distant metastases, which may be asymptomatic for which early chemotherapy may improve the prognosis or long-term survival.

There is little evidence to suggest an ideal protocol.

Local failure is most common in the first eighteen months. This can be monitored by digital examination to assess regression of the tumour following chemo-radiotherapy. Imaging by endosonography has the advantage of being able to assess the depth and penetration in relation to the sphincter. It has been suggested that it helps to differentiate fibrosis from recurrence. MRI can demonstrate extrasphincteric spread. CT is usually used to detect distant spread although there are problems with the detection of groin and iliac lymph modes. Monitoring of lymph nodes is usually performed clinically but FNA or ultrasound may help.

The outpatient follow up protocol outlined in The ACT 1 and ACT 2 trials are widely adopted i.e. outpatient follow up two monthly for a year, three monthly for a second year and then every six months. Digital examination of the anus should be performed at each review appointment.

Suggested imaging recommendations:

- Careful evaluation of the primary site following initial treatment should include clinical examination with examination under anaesthesia and or MRI scanning where there is concern that residual disease remains. If residual disease is demonstrated full staging including CT or chest and abdomen is required before proceeding to salvage abdomino-perineal resection.
- CT surveillance to detect distant metastases based on clinical suspicion. 40% of patients will develop distant disease in the chest and abdomen.
- MRI surveillance if clinically suspicious of residual disease. 10% fail to respond to preoperative chemo radiotherapy and most local relapses are detected within the first 2 years after treatment.

Prognosis

Survival

Randomised trials have not shown any overall survival advantage of chemoradiotherapy (CRT) over RT alone. Overall three-year survival was 65% with anal cancer related mortality of 39% (Arnott et al 1996 Ib). The 5 year survival was 50% and the 5 year local failure rate was 46%. Of the local failures in the ACT I study only 58% were suitable for salvage surgery. The EORTC (Bartelink et al IIb) reached a similar conclusion although with a smaller number of patients (110 compared with 577).

There is a significant relationship of tumour depth to 5 year and overall survival. When the disease was confined to sphincter muscles, the local and overall recurrence rate was 23%, but when the tumour invaded through the sphincters, the local and overall recurrence rates were 48% and 53% respectively. Depth of invasion increased with larger lesions and nodal involvement was uniformly frequent in lesions > 2cms. After adjustment for stage, tumour diameter failed to remain a significant independent prognostic variable. (Bowman et al 1984 IIb).

For patient information and illustrative purposes, the findings of Cummings et al 2003, in a non randomized

studies of radiation 5FU and mitomycin, can be used to give indicative rates of local recurrence in a 5 year survival as follows (Cummings et al 2003 IIb);

	Local control	5 year survival
T1	90-100%	80%
T2	65-75%	70%
T3/T4	40-55%	45-55%

Histopathology Reporting

This section should be read in conjunction with Section 7 (Histopathology) of these Guidelines.

Process

The Welsh audit of anal cancer demonstrated poor documentation overall (Karandikar et al 2006 III). Use of structured performas has been shown to improve histopathology reporting.

Local resections

The size of the lesion (usually anal margin) should be documented together with lateral and deep resection margins. One possible role of the pathologist is to register anal cancers with the local cancers surveillance unit. Specimens, which do not have clear margins, should be brought to the attention of the network anal cancer MDT.

Resection Specimen

This will usually be an anorectal excision for persistent disease following chemoradiotherapy, recurrence or complications.

Cut up of the specimen should concentrate on size, depth of invasion (in relation to sphincters), involvement of adjacent organs and circumferential resection margins.

Histology type

Usually squamous but other varieties should be recorded.

TNM staging

Is different compared to rectal adenocarcinoma invading the anal canal. Pathological T staging essentially relates to size; and on clinical staging to invasion of adjacent organs and pattern of lymph node spread.

i) pT1 to pT3 relates to size

ii) pT4 is any size that invades adjacent organs. Note that the invasion of the sphincter muscle is not classified as pT4.

iii) Regional Lymph Nodes. N1 is a nodal involvement in the meso rectum; N2 is unilateral internal iliac/inguinal lymph nodes on; N3 is involvement of the mesorectal/inguinal, bilateral internal iliac and / or inguinal lymph nodes.

If the patient has had neoadjuvant treatment the staging should therefore show the prefix “yp”.

The pathological findings should be reported using a proforma.

Recommendations

Squamous anal cancer is rare and has a varied presentation. Any suspicious anal ulcer or lesion should be biopsied, if necessary under general anaesthetic.

Recommendation grade ✔

Local staging of the disease should be carried out using a combination of examination under anaesthesia, anal ultrasound and MRI. CT should be used to evaluate the possibility of distant metastases.

Recommendation grade B

Small anal margin cancers (less than two cm and well differentiated) can be locally excised provided clear margins are obtained. Larger lesions up to 5cm i.e. T2 or less can also be considered for excision by the anal cancer MDT.

Recommendation grade C

Anal canal lesions should usually be treated by concurrent chemo radiotherapy. 5FU and Mitomycin C or Cisplatin are usually used but there is some uncertainty as to the best regimen. Wherever possible, patients should be considered for randomisation within one of the ongoing trials.

Recommendation grade A

Anorectal excision should be reserved for residual or recurrent disease and for severe complications of radiotherapy. Patients may prefer primary anorectal excision. The data suggest that the outcome is the same for early lesions.

Recommendation grade A

There is no agreed follow up protocol. Its aims should be: - Identification of local failure, detection of metastases, to provide data for audit etc

Recommendation grade ✔

Consideration should be given to surveillance in high-risk groups, i.e. those with HPV, HIV or other forms of immunosuppression.

Recommendation grade B

All patients with anal cancer should be discussed by a specialist Anal Cancer MDT which should include at least one surgeon who specialises in surgery for anal cancer, a clinical oncologist with specific expertise in the management of anal cancer, histopathologist, radiologist, clinical nurse specialist, etc, as outlined in the NICE guidelines. This allows access to the necessary expertise in all disciplines and allows comparison of outcomes between centres.

Recommendation grade ✔

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Appendix 1

The Trent/Wales Audit

In order to decide on the information to be collected for the audit of colorectal cancer management in Trent and Wales, an expert working party was set up by the Royal College of Surgeons, and a data collection proforma was designed. When this was complete, letters were sent to all surgeons who treat patients with colorectal cancer in Trent Region and Wales requesting consent to collect data on their patients. All agreed. Letters were also sent to all physicians, geriatricians, oncologists, pathologists and hospital chief executives to inform them of the study.

Data was collected on all patients presenting with a diagnosis of colorectal cancer to all hospitals in Trent Region between July 1992 and June 1993, and in Wales between January and December 1993 by six specially trained research assistants. Hospitals were visited in rotation by the research assistants, and all patients presenting since the previous visit were identified using a number of avenues including the hospital records systems, histopathology records, audit clerks etc. The pertinent case records, operation notes and histopathology reports were then reviewed, and the data collection proformas filled out. After completion the form was checked by a single research fellow and the data was transferred to a microcomputer by means of an optical reading scanner. The data was stored and analysed using the Statistical Package for the Social Sciences (SPSS for Windows). All data was coded for security reasons.

At the beginning of the study, the data collectors in both regions were given specimen patient records from which to abstract data to check on uniformity of interpretation. The quality of the data throughout was maintained by regular meeting between the data collectors and the research fellow. Validation procedures consisted of a 10% rate of random checks in which the data collected was compared with the original patient records.

In addition, a questionnaire was sent to all surgical consultants in the two study areas, to establish their policies for pre-operative management, follow up and referral for radiotherapy and chemotherapy. The surgeons were also asked to indicate their areas of special interest.

The Wessex Audit

The Wessex audit arose from the observation that, in 1990, the 5 year crude survival rates for colon cancer varied between 24% and 39%, and for rectal cancer from 28% to 38% throughout Wessex. A retrospective study on patients from three districts revealed that the variation was not due to stage at diagnosis, and therefore probably due to treatment. Medical notes were not sufficiently complete to identify which types of treatment were influencing outcome. An Expert Working Group discussed the findings and decided to set up a prospective audit of the total population of patients with colorectal cancer in Wessex co-ordinated by the Wessex Cancer Intelligence Unit.

Standards of Care were set and endorsed by the Regional Medical Advisory Committee. It was planned to revise these on an annual basis as the medical audit progressed. The audit has three objectives:

1. To identify the indicators most closely associated with outcome of the disease in terms of overall survival, symptom free survival, recurrence and basic quality of life.
2. To facilitate the setting of appropriate audit Standards to promote optimum clinical practice in relation to the outcome indicators above.
3. To develop methods of monitoring the Standards so ensuring that they are practical, appropriate and valid.

The Cancer Intelligence Unit co-ordinates data collection, data analysis and dissemination of the audit information on behalf of the clinicians in Wessex. The clinicians are represented by the working group, a panel of colorectal cancer experts who meet regularly with the Cancer Intelligence Unit to review the progress of the audit and formulate the next steps in the audit process.

The audit has collected information on all cases of colorectal cancer diagnosed in Wessex residents from September 1991 to August 1994, and is following up each case annually for 5 years. This time period ensures that the audit will have sufficient statistical power to identify significant variation in survival between Districts and thus sufficient data on clinical management to identify the factors which influence outcome. This is the defined end point of the audit.

Data collected on aspects of the patient's referral, diagnosis, clinical management and follow up is entered on a form designed by the working group and sent to the Cancer Intelligence Unit on a monthly basis. Three whole time equivalent data clerks are employed to minimise extra work for participating clinicians. A booklet has been produced describing and interpreting the data collection form. Accuracy and validity of data is ensured by: regular meetings between clerks and the Cancer Intelligence Unit, double entry of randomly selected samples of data, internal audit and finally, validity checks within the database.

At annual intervals the data is reviewed and a report published. The ascertainment of the Standards is reviewed both for the Region and Districts. All participating surgeons, physicians and pathologists receive feedback on the information collected on their cases anonymously compared with other individuals throughout the Region.

The NORCCAG Audit

This audit was set up in 1992 as a result of discussions between three Consultant Surgeons and one Clinical Oncologist. The purpose of the working group was to identify the practicality of commencing a prospective audit along the lines of the Trent/Wales and Wessex audits. The group was able to generate interest in all of the colorectal units in the (then) Northern Region. The audit was financed such that data could be collected independently by two data clerks reviewing case notes. Subsequently the funding has been provided courtesy of the Northern Cancer Network and contributions from the hospitals within the region.

As with the other audits, data is verified by meeting between the data clerks and the local cancer information departments in each hospital and regular audit trails are constructed. An annual report is presented with the data anonymised but each surgeon and unit are aware of their own identity in the audit.

The catchment population comprises 3.1 million from 17 hospitals, with 86 participating surgeons. The data from 1997/8 was used for the first report and data has subsequently been forwarded to the ACGB&I database for the annual audit.

Definitions

For the purposes of all the audits, the data definitions used were those of the Association of Coloproctology of Great Britain and Ireland (see Appendix 4).

Appendix 2

Colorectal cancer operation note

Any operation note must provide sufficient information to allow a clear understanding of the operative findings, the procedure carried out and the personnel involved. The essential requirements are contained in the Royal College of Surgeons' Guidelines for Clinicians on Medical Records and Notes (RCS, 1990), but in colorectal cancer, there is specific information which is important both for audit purposes and for planning further treatment (NBOCAP report 2005 Ib).

A suggested proforma for a colorectal cancer operation note

Surname _____ Forenames _____ Date of Birth_____

Hospital No _____ Consultant _____ Hospital _____

Ward _____

Surgeon _____ Anaesthetist _____

Date of Operation _____

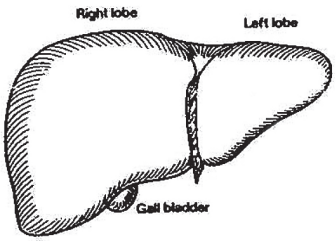
Time Start _____ Time End_____

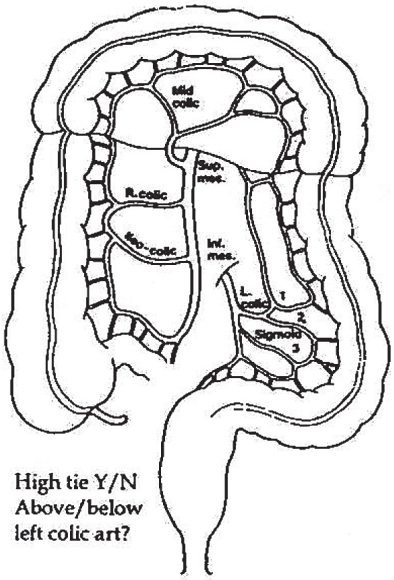
Operation Title

Curative / palliative / uncertain, due to liver / local extension / other_____

Elective / Emergency due to perforation / obstructed / bleeding

ASA grade I / II / III / IV / V (see over for definition)





Splenic flexure mobilised ☐ Y ☐ N Tumour is mobile / tethered / fixed to _____

Presence of abscess / perforation / ascites No_____ Blood transfused _____ units

Stoma ☐ Y ☐ N ileostomy / colostomy : temporary / permanent

Operative Severity

☐ Minor	Gastroscopy, wedge excision nail	☐ Complex Major D	Elective aortic aneurysm (AAA)
☐ Intermediate	Ingunial hernia, excision of breast lump	☐ Complex Major C	Anterior resection of rectum
☐ Major	Cholecystectomy, partial thyroidectomy	☐ Complex Major B	Ruptured AAA, oesophagogastrectomy
☐ Major +	Parotidectomy, colonic resection	☐ Complex Major A	Cardiac surgery entailing bypass

Multiple procedures

☐ 1
☐ 2
☐ >2

Blood loss

☐ <= 100ml
☐ 101-500 ml
☐ 501-999 ml
☐ >=1000 mls

Presence of Malignancy

☐ None
☐ Primary only
☐ Nodal metasases
☐ Distant metastases

Peritoneal Soiling

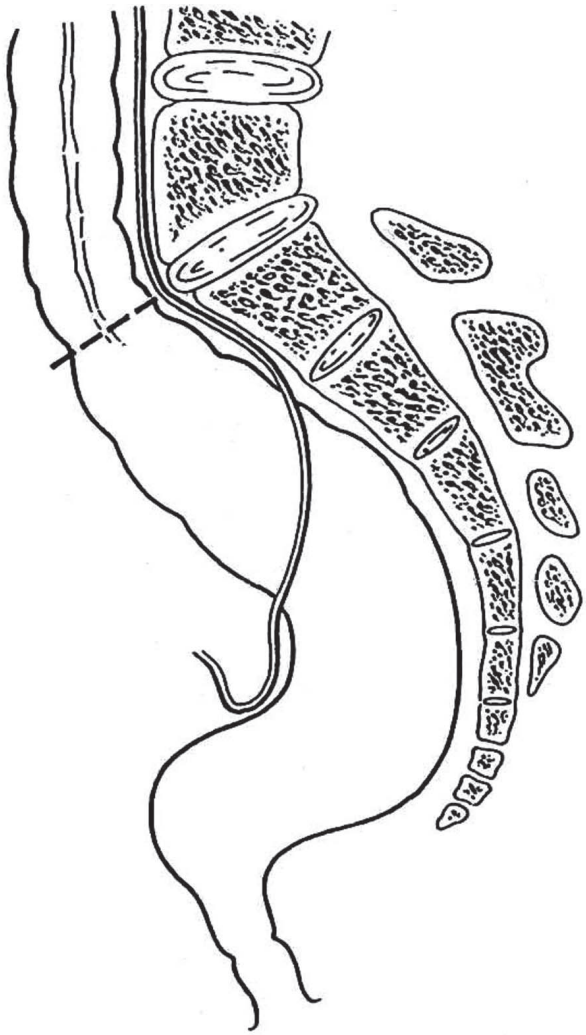
☐ None
☐ Minor (serious fluid)
☐ Local pus
☐ Free bowel contents, bile or pus

Mode of Surgery

☐ Elective
☐ Urgent (requiring surgery within 24 hours of admission, at least 2 hrs) available for resuscitation - even if this period was not used
☐ Emergency (requiring surgery within 2 hrs of admission)

Colorectal cancer operation note proforma continued

For rectal and distal sigmoid tumours



Height of tumour	cm
Anastomosis to anal verge	cm
Distal irrigation	☐ Y ☐ N
TME / PME ? (estimate of % age)	%
Distance of lesion to distal cut margin	cm
Distance to dentate line (if AP resection)	cm

ASA Grade Definitions

Grade I: Fit and well

Grade II: Mild systemic disease (including smoking, obesity, treated hypertension); not necessarily the cancer

Grade III: Disease which restricts activity

Grade IV: Life threatening disease

Grade V: Not expected to survive for 24 hours

NB In an emergency situation, the suffix E is added to the ASA grade. In general, the risk attached is equivalent to the next group lower, i.e. IE equates to II, IIE equates to III etc.

Appendix 3

Clinicopathological staging of colorectal cancer

i) Dukes' staging (based on histological examination of the resection specimen)

A - invasive carcinoma not breaching the muscularis propria B - invasive carcinoma breaching the muscularis propria, but not involving regional lymph nodes C1 - invasive carcinoma involving the regional lymph nodes (apical node negative) C2 - invasive carcinoma involving the regional lymph nodes (apical node positive).

Note: Dukes' stage D has come to mean the presence of distant metastases.

ii) TNM staging

T - primary tumour

TX Primary tumour cannot be assessed T0 No evidence of primary tumour T1 Tumour invades submucosa T2 Tumour invades muscularis propria T3 Tumour invades through muscularis propria into subserosa or into non-peritonealised pericolic or perirectal tissues T4 Tumour perforates the visceral peritoneum or directly invades other organs or structures

Note: i) Direct invasion in T4 includes invasion of other segments of the colorectum by way of the serosa, eg. invasion of the sigmoid colon by a carcinoma of the caecum. ii) Tumours which have received pre-operative irradiation should be identified in the histopathology staging by the prefix "y"; e.g. ypT3.

N - Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastasis in 1 to 3 pericolic or perirectal lymph nodes
N2 Metastasis in 4 or more pericolic or perirectal lymph nodes

M - Distant Metastasis

M0 No distant metastases
M1 Distant metastases

pTNM Pathological Classification:

The pT, pN and pM categories correspond to the T, N, and M categories.

iii) Histological types of colorectal carcinoma (WHO classification)

- adenocarcinoma
- mucinous adenocarcinoma
- signet ring carcinoma
- squamous carcinoma
- adenosquamous carcinoma
- small cell carcinoma
- undifferentiated carcinoma

NB: It is strongly recommended that the staging of colorectal cancer be recorded according to the Joint National Guidelines for a Minimum Data Set for Colorectal Cancer Histopathology Reporting.

Appendix 4

Association of Coloproctology of Great Britain and Ireland Colorectal Cancer Minimum Dataset

Data Definitions

For future upgrades of data definitions please refer to http://www.canceruk.net/clinit/ products_acp.htm

Unit Details

Unit name

The name of the Hospital or other organisation that provides the services and employs the staff involved in the management of the services.

Unit ID number

This number identifies the site uniquely. Each copy of the database should have it's own Unit ID number. If you do not know what this identifier is contact Clatterbridge Centre for Oncology at the address above and they will provide you with the correct number.

If you are running more than one copy of the database you will require more than one ID number, contact the helpdesk for additional numbers.

Usual address

Unit's full postal address. The text of the address is divided into several lines for road, town, area or county.

Usual postcode

Full postcode for the Unit.

Phone number

Phone number for the Unit/Department. e.g. (0151) 334 4000 Ext. 4294. Text and numbers can be entered.

Fax number

Fax number for the Unit/Department.

Name of the lead Clinician for Colorectal Cancer

The name of the Unit's lead Clinician for Colorectal Cancer.

Patient Details

Colorectal Unit ID code (hidden)

This is assigned automatically and identifies the Unit or organisation against each record. A Clinician who practices at various organisations over time is able to compile the dataset without losing the facility to identify the organisation at which services were provided.

Unit Patient Number (Hospital number)

The number or code assigned by the unit to identify the patient uniquely throughout the unit/organisation. This may also be known as the hospital number, case-sheet number, case number or registration number.

The patient number is normally assigned on first registering with the unit, is often used as the reference number for filing the patient's medical notes and is the key field for identifying the patient in a computerised records system. The number may be assigned automatically by a computer system or through a manual procedure.

Date of birth

The date of the patient's birth. If unknown, the user would need to enter an approximate date or a pseudo-date such as 01/01/1800 rather than leaving the item blank.

Sex

- 1 Male
- 2 Female

Postcode of patient's usual address

Full postcode of patient's usual address. Patients with no fixed abode should be assigned a pseudo-postcode of ZZ99 3VZ.

Patient's NHS Number

The patient's (new) NHS number if known. The existing alphanumeric codes of varying formats have been replaced by a ten-digit number. Introduction began in 1995/96 and the NHS Executive intended the new number to be used in the exchange of data throughout the health service from April 1997. This is not a mandatory field because some units may not have access to this data item at point of entry.

Forename / Surname

Used as an alternative identifier. The program is not intended to be used as a patient management system so these fields are not mandatory.

Family History

Has a family history been taken y/n.

Consultant/Surgical Firm

The Surname of the Consultant with overall responsibility of the patient. In some cases this will be after an internal referral.

Follow ups ceased

Have follow up visits ceased for this patient y/n.

Death

Is the patient dead ?

- 1 Yes
- 2 No
- 3 Unknown

Date of death

Date patient died.

Cause of death

Cause of death.

- 1 Died of cancer
- 2 Died of other cause (cancer present)

- 3 Died of other cause (no evidence of cancer)
- 4 Unknown

Post-Mortem

Was there a post-mortem y/n

Other Hospital Casesheet number/s

If patient has been seen or is being seen at other hosptial multiple casesheet numbers for the patient can be recorded.

Other Hospital name

If patient has been seen or is being seen at any other hospital the hospitals/other identifiers can be recorded along with the foreign/other casesheet number/s.

Tumour Details

Date of Diagnosis

The date on which cancer was diagnosed at operation, histology, colonoscopy, barium enema or other means.

Referral type

To identify the source of the referral

- 1 GP Emergency/elective referral by GP
- 2 A/E Patient self referral to A/E
- 3 Internal From another consultant

Date of receipt of referral

The date of receipt by the hospital of the referral

Date of first hospital contact

Date of the first outpatient attendance/emergency admission

Was this the first referral to a member of the Multi Disciplinary Team

Was this the first referral to a member of the Multi Disciplinary Team y/n.
If the patient was not originally referred to a member of the MDT then this should be set to NO

Was this the first appointment offered

To identify if the delay in patient outpatient appointment Is due to patient choice y/n

Urgent appointment

To identify whether the patient was deemed by the Colorectal surgeon to have a substantial risk of colorectal cancer based on their primary care referral y/n

Major Tumour Site / ICD10 Site code

The major site as identified by the clinician at presentation. There is no need to record all of the sites if multiple tumours at presentation

- 1 Caecum C18.0
- 2 Appendix C18.1
- 3 Ascending colon C18.2
- 4 Hepatic Flexure C18.3

- 5 Transverse colon C18.4
- 6 Splenic flexure C18.5
- 7 Descending colon C18.6
- 8 Sigmoid colon C18.7
- 8 Recto-Sigmoid C19
- 9 Rectum C20

Synchronous tumour ?

Def: Lower margin of tumour
15cm or less from anal verge.
Is there a synchronous tumour y/n.
If the patient presents with more than one new site at clinic then this identifier should be set to yes.
If it is set to YES then the user can record a second site.

Synchronous Tumour Site / ICD10 Synchronous Site code

A second site as identified by the clinician at presentation. There is no need to record all of the sites if multiple tumours at presentation. (List as above for Major Tumour site).

Height above anal verge (cm)

Height above the anal verge for rectal cancer.

Colonoscopy

Result of colonoscopy.

- 1 Normal (no evidence of tumour, true negative or false negative)
- 2 Abnormal (tumour or polyp)
- 3 Inadequate (bowel not fully visualised)
- 4 Not done
- 5 Not known

Date of colonoscopy

The date on which colonoscopy carried out.

Colonoscopy complications: Over sedation, Bleeding, Perforation, Other complication

Over sedation y/n, Bleeding y/n, Perforation y/n, Other complication y/n.

If 'Other Complication' exists, specify

If other colonoscopy complication, record the 'other' complication here.

Reason for incomplete colonoscopy

The reason for an incomplete colonoscopy.

- 1 Obstructing tumour
- 2 Poor bowel presentation
- 3 Patient intolerance / technical reasons
- 4 Other

Barium enema

Result of barium enema.

- 1 Normal (no evidence of tumour)
- 2 Abnormal (tumour or polyp)
- 3 Inadequate (bowel not fully visualised)
- 4 Not done
- Not known

Date of barium enema

The date on which barium enema carried out.

Flexi-Sigmoidoscopy

Result of flexible-sigmoidoscopy.

- 1 Normal (no evidence of tumour)
- 2 Abnormal (tumour or polyp)
- 3 Inadequate (bowel not fully visualised)
- 4 Not done
- 5 Not known

Date of Flexi-Sigmoidoscopy

The date on which flexi-sigmoidoscopy carried out.

Distant Metastases: Liver, Lung, Bone, Other

Does patient have liver, lung, bone, other metastases y/n.

If 'other' metastases, specify

If patient has presented with Distant Metastases, specify where.

Was this a screened case ?

Was this a screened case y/n.

If screened, specify

- 1 FOB
- 2 Colonoscopy
- 3 Other

Modified Dukes' Stage

Final clinicopathalogical staging. A, B, C, D, Not known. (Not known is included as the staging is a mandatory field).

Dukes D = metastatic spread distant/local ie all incurable disease

Primary Surgery: Pre-operative Details

ASA Grade

- 1 Fit
- 2 Relevant disease
- 3 Restrictive disease

- 4 Life threatening disease
- 5 Moribund

No surgery carried out

No surgery carried out on this tumour y/n. Record YES if no surgery at all was carried out on this tumour site.

Reason no surgery performed

If no surgery was carried out record the reason.

- 1 Patient unfit
- 2 Patient refuses treatment
- 3 Advanced disease
- 4 Other treatment given, specify

If '4 other treatment given', specify

If reason no surgery performed is "other" specify the treatment.

Previous operation related to this tumour?

Is there a previous operation related to this tumour site y/n. The default for this field for all new surgery records is set to NO.

This field identifies a small group of patients in the following category: Occasionally patients will have surgery eg stoma, before having chemo/RT, and will subsequently then have a laparotomy/resection. In order to identify that this new surgery is in fact the primary surgery (for the tumour site) you must replace the surgery record (in the example above -stoma) with the subsequent surgery (example - laparotomy/resection). You can either DELETE the record and reenter it from scratch OR just edit and update the details of the existing record. When the second operation is carried out, you must return to the question "Previous operation related to this tumour" and change to YES.

Previous procedure

- 1 Laparotomy (+/- biopsy)
- 2 Stoma (either at laparotomy or trephine)

Date of start of first definitive procedure

Date of the start of the first definitive procedure (may mean definitive surgery, radiotherapy or chemotherapy but not examination under anaesthetic) for this tumour.

Thrombo prophylaxis y/n

Antibiotic prophylaxis y/n

Date referred to colorectal nurse or stoma therapist

Date seen by colorectal nurse or stoma therapist

Primary Surgery: Operation Details

Curative resection

The surgeons opinion of the completeness of the excision at the time of operation which should not be revised in the light of subsequent histopathology reporting.

- Curative
- 2 Palliative
- 3 Uncertain

If palliative, due to:

If the item recorded in Curative resection is 'palliative' then is it due to:

- 1 Local disease
- 2 Liver disease
- 3 Other (please specify)

Other, please specify (palliative)

Free text field.

If uncertain, due to:

If the item recorded in Curability ? is 'uncertain' then is it due to:

- 1 Local
- 2 Distant
- 3 Other (please specify)

Other, please specify (uncertain)

Free text field.

Surgeon

Name of surgeon that performed procedure.

GMC code

GMC national code for surgeon. The consultant code is an eight character alphanumeric code based on the GMC registration number: the first character will be the letter 'C': characters 2-7 will be the doctors GMC number; character 8 is a check digit. The default code for Consultant Code 'not known' is C9999998.

Grade

Grade of surgeon.

- 1 Consultant
- 2 Associate specialist
- 3 Staff grade/Clinical Assistant
- 4 SPR
- 5 SHO
- 6 HO
- 7 Other

Assistant

Name of the assistant that assisted with procedure.

GMC code

General Medical Council national code for assistant.

Grade

Grade of the assistant (list as above)

2nd Assistant

Name of 2nd assistant that assisted with procedure IF APPROPRIATE.

GMC code

GMC national code for 2nd assistant.

Grade

Grade of 2nd assistant (list as above)

Date of surgery

Date of surgery including any definitive surgery for this tumour and may be a palliative procedure such as Stent insertion.

Start time of Surgery

Time of day at which the procedure began (24 hour clock).

Mode of operation

CEPOD classifications.

- Elective (Operation at a time to suit both patient and surgeon e.g. after an elective admission)
- Scheduled (An early operation but not immediately life-saving. Operation usually within 3 weeks)
- Urgent (as soon as possible after resuscitation. Operation within 24 hours)
- Emergency (Immediate and life-saving operation, resuscitation simultaneous with surgical treatment. Operation usually within 1 hour)

Procedure type

- 1 Closed without procedure
- 2 Stoma only
- 3 Bypass/Stent
- 4 Excision
- 5 EUA

Procedure name / OPCS4 code

- 1 EUA only H44.4 With/without biopsy
- 2 Laparotomy only T30.9 No other procedure except with or without biopsy
- 3 Laparoscopy only T43.8 Can include with/without biopsy
- 4 Loop stoma only H15.1 Large or small bowel
- 5 End stoma only H15.2 Either at laparotomy or trephine method
- 6 Right hemicolectomy H07.8 Any right hemicolectomy to include extended right hemicolectomy

To include ileo-rectal or ileo-sigmoid Excision of transverse colon Excision of the descending and/or sigmoid colon with colorectal anastomosis Excision of the sigmoid colon with colorectal anastomosis

- 7 Subtotal colectomy H11.8
- 8 Transverse colectomy H08.8
- 9 Left hemicolectomy H09.8

• 10 Sigmoid colectomy	H10.8	
• 11 Anterior resection	H33.4	Carried out for tumours with less than 15cm from anal verge
• 12 APER	H33.1	Abdomino-perineal excision of rectum
• 13 Hartmann's procedure	H33.5	Excision of part of left colon with end colostomy and closure or exteriorisation of the distal remnant
• 14 TART	H41	Trans-anal resection of tumour (by any method except TEMS)
• 15 TEMS		Trans-anal endoscopic micro-surgery
• 16 Stent		Stent placed across tumour by any means
• 17 Polypectomy		Excision of a malignant polyp (endoscopic or open)

Local complications

Did local complications exist y/n.

If tumour complications exist, specify

- 1 Pericolic abscess
- 2 Free perforation
- 3 Intestinal obstruction
- 4 Other, specify

If Complications "4 Other, specify", specify

If other Tumour complication, describe.

Anaesthetist grade

Grade of most senior anaesthetist present in theatre during the operation (list as above).

Was anastomatosis done

Was anastomotosis done y/n.

Primary Surgery: Post-operative Details

Date Discharged

Date patient discharged from ward.

Postoperative death within 30 days

Did patient die within 30 days of the surgical procedure y/n.

Death due to cardiovascular causes ?

Was death was due to cardiovascular causes y/n.

Stoma

Stoma exists y/n.

Stoma type

- 1 Permanent
- 2 Temporary with intent to close

Date of closure of stoma

Date on which temporary stoma closed.

Minor complication: leak / abscess / bleed / other

Minor complication: a complication that did not require re-operation y/n.

Major complication: leak / abscess / bleed / other

Major complication: a complication that required re-operation y/n.

Histopathology Details

Pathological Dukes Staging

A, B, C, Not known. (Not known is included as the staging is a mandatory field).

Date of report

Date of the histopathology report.

TNM Staging

Summary of TNM staging:

Tx Minimum requirements for tumour assessment not met pT0 No evidence of primary tumour pT1 Tumour extends into the sub-mucosa pT2 Tumour extends into the muscularis propria pT3 Tumour extends through muscularis propria into subserosa on into nonperitonealised pericolic or perirectal tissues pT4Tumour extends directly into the other organs or tissues, or tumour perforates the visceral peritoneum of the specimen y Prefix indicating pre-operative radiotherapy was given to this tumour

Nx Minimum requirements for lymph node assessment not met

pN0 No lymph node mets

pN1 Metastatic tumour in 1 to 3 pericolic or perirectal lymph nodes

pN2 Metastatic tumour in 4 or more pericolic or perirectal lymph nodes

Mx Minimum requirements to assess distant metastasis cannot be met

M0 No distant metastases

M1 Distant metastasis present

From:CANCER Principles and Practice of Oncology 5th Edition, Vincent T.DeVita Jr, Samuel Hellmann, Steven A.Rosenberg; Lippincott-Raven

Positivity of distal margins

- 1 Yes
- 2 No

Positivity of proximal margins

- 1 Yes
- 2 No

Positivity of circumferential margins

- 1 Yes
- 2 No
- 3 N/A

Circumferential margins refer to the completeness of the surgeon's resection margin in the opinion of the histopathologist. In parts of the colon where it is completely surrounded by peritoneum, recording of the

circumferential (surgical resection) margin is not appropriate. This should be recorded as Not Applicable (N/A).

Positivity of margin: When the tumour is 1mm or less from the surgical resection circumferential margin.

Histological grade

The histological grade of the invasive component of the lesion as reported by the pathologist.

- 1 Poor
- 2 Other

Histological type

- 1 Adenocarcinoma
- 2 Mucinous tumour (>50%)
- 3 Other

Number of lymph nodes found

Indicate here the number of lymph nodes recovered from the pathology specimen

Number of positive lymph nodes found

Indicate here the number of lymph nodes in the pathology specimen found to contain malignant tumour

Extramural vascular invasion y/n

Perforations or serosal involvement for tumours at sites with serosal cover y/n

Distance between lower end of tumour and resection margin in rectal and recto-sigmoid tumours

Distance should be measured in the fixed specimen (mms).

Distance between lower end of tumour and dentate line in APER specimen

Distance should be measured in the fixed specimen (mms).

NOTE: Definitions relating to the Joint National Guidelines Minimum Dataset for Colorectal Cancer Histopathology Reporting (only) data items are not included in this document although those data items are included within the structure of the database.

Oncology Details

Radiotherapy y/n

RT given

- 1 Pre-op
- 2 Post-op

Radiotherapy trial y/n

Purpose of RT

- 1 Adjuvant
- Palliative

Chemotherapy y/n
Chemotherapy given

- 1 Pre-op
- 2 Post-op

Purpose of Chemotherapy

- 1 Adjuvant
- 2 Palliative

Chemotherapy trial y/n

Follow Up Details

Date of Follow-Up Visit

The date on which the patient was seen in clinic for follow-up.

Date of Closure of temporary stoma

The date on which a temporary stoma was closed.

Permanent stoma

Any stoma that has not been closed within 3 years y/n.

Local Recurrence (within field of operation)

Local/regional recurrence occurring within the field of the operation y/n.

Date of diagnosis of local recurrence

Date of diagnosis of local recurrence.

Local recurrence diagnosed by

Local recurrence diagnosed by:

- 1 Clinical
- 2 Imaging
- 3 Histology
- 4 Other

Distant spread

Regional/metastatic disease occurring outside the field of operation y/n. If distant spread, specify:

Date of diagnosis of distant spread

Date of the diagnosis of distant spread.

Distant spread: Liver / Lung / Bone / Other y/n

If Distant spread 'Other', then specify

Specify other distant spread.

Referral to Palliative Care

Patient referred to palliative care y/n

Date referred to Palliative Care

Date patient referred to palliative care

For future upgrades of data definitions please refer to: http://www.canceruk.net/clinit/ products_acp.htm

Appendix 5: Histopathology Reporting

National Dataset for Colorectal Cancer Resection Histopathology Reports

Surname _____ Forenames _____ Date of Birth_____

Hospital_____ Hospital No_____ NHS No _____

Date of receipt _____ Date of reporting _____ Report No_____

Pathologist _____ Surgeon _____ Sex _____

Specimen Type:

Total colectomy / Right hemicolectomy / Transverse colectomy / Left hemicolectomy / Sigmoid colectomy / Anterior Resection / Abdominoperineal Excision / Other (state)

Gross Description

Site of Tumour

Maximum tumour diameter _____mm

Distance of tumour to nearer cut end _____mm

Tumour perforation (pT4) Yes ☐ No ☐

For rectal tumours:

Relation of tumour to peritoneal reflection (tick one):

Above ☐ A stride ☐ Below ☐

Plane of surgical excision (tick one):

Mesorectal fascia ☐

Intramesorectal ☐

Muscularis propria ☐

For abdominoperineal resection specimens:

Distance of tumour from dentate line _____mm

Histology

Type

Adenocarcinoma Yes ☐ No ☐

If No, Other type _____

Differentiation by predominant area

Well/moderate ☐ Poor ☐

Local Invasion

No carcinoma identified (pT0) ☐

Submucosa (pT1) ☐

Muscularis propria (pT2) ☐

Beyond muscularis propria (pT3) ☐

Tumour invades adjacent organs (pT4a) ☐

AND/OR

Tumour cells have breached the serosa (pT4b) ☐

Maximum distance of spread beyond muscularis propria _____mm

Response to Neoadjuvant Therapy

Neoadjuvant therapy given Yes ☐ No ☐ NK

If yes,

No residual tumour cells or mucus lakes only ☐

Minimal residual tumour ☐

No marked regression ☐

Tumour involvement of margins

	N/A	Yes	No
Doughnuts	☐	☐	☐
Margin (cut end)	☐	☐	☐
Non-peritonealised "circumferential" margin	☐	☐	☐

Histological measurement from tumour to non-peritonealised margin _____mm

Metastatic Spread

No of lymph nodes present _____

No of involved lymph nodes_____

(pN1 1-3 nodes, pN2 4+ nodes involved)

Apical node involved (Dukes C2) Yes ☐ No ☐

Extramural vascular invasion Yes ☐ No ☐

Histologically confirmed distant metastases (pM1): Yes ☐ No ☐

If yes, site: _____

Background Abnormalities: Yes ☐ No ☐

If yes, type: (delete as appropriate)

Adenoma(s) (state number_____)

Familial adenomatous polyposis / Ulcerative colitis / Crohn's disease / Diverticulosis / Synchronous carcinoma(s)

(complete a separate form for each cancer)

Other _____

Pathological Staging

Complete resection at all surgical margins

Yes (R0) ☐ No (R1 or R2) ☐

TNM (5th edition)

(y) pT_____ (y) pN_____ (y) pM_____

Dukes

Dukes A ☐ (Tumour limited to wall, nodes negative)

Dukes B ☐ (Tumour beyond M. propria, nodes negative)

Dukes C1 ☐ (Nodes positive and apical node negative)

Dukes C2 ☐ (Apical node involved)

Signature: _____ Date _____ SNOMED Codes T _____ / M _____

National Dataset for Colorectal Cancer Local Excision Histopathology Reports

Surname _____ Forenames _____ Date of Birth_____
Hospital_____ Hospital No_____ NHS No _____
Date of receipt _____ Date of reporting _____ Report No_____
Pathologist _____ Surgeon _____ Sex _____

Specimen Type:

Polypectomy / Endoscopic Mucosal Resection / Transanal Endoscopic Microsurgical (TEM) Excision /

Other _____

Comments: _____

Gross Description

Site of Tumour _____

Maximum tumour diameter (if known) _____mm

Histology

Tumour Type

Adenocarcinoma Yes ☐ No ☐

If No, Other

Differentiation

Well/moderate ☐ Poor ☐

Local Invasion

Confined to submucosa (pT1) ☐

Into muscularis propria (pT2) ☐

Beyond muscularis propria (pT3) ☐

For pT1 tumours:

Maximum thickness of invasive tumour from muscularis mucosae _____mm

Haggitt level (polypoid tumours) 1 / 2 / 3 / 4

Kikuchi level (for sessile/flat tumours,) sm1/ sm2/ sm3

Lymphatic or vascular invasion:

None ☐

Possible ☐

Definite ☐

Background Adenoma:

Yes ☐ No ☐

Margins

Not involved ☐

Involved by adenoma only ☐

Deep margin Involved by carcinoma ☐

Peripheral margin Involved by carcinoma ☐

Histological measurement from carcinoma to nearest deep excision margin _____mm

Pathological Staging

Complete resection at all margins

Yes (R0) ☐ No (R1 or R2) ☐

pT stage _____

Signature: _____ Date _____ SNOMED Codes T _____ / M _____

APPENDIX 6 Anal Cancer Staging

The following is a staging system for anal cancer described by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer.

TNM definitions

Primary tumor (T)

TX: Primary tumor cannot be assessed

T0: No evidence of primary tumor

Tis: Carcinoma in situ

T1: Tumor 2 cm or less in greatest dimension

T2: Tumor more than 2 cm but not more than 5 cm in greatest dimension

T3: Tumor more than 5 cm in greatest dimension

T4: Tumor of any size that invades adjacent organ(s), e.g., vagina, urethra, bladder*

[Note: *Direct invasion of the rectal wall, perirectal skin, subcutaneous tissue, or the sphincter muscle(s) is not classified as T4.]

Regional lymph nodes (N)

NX: Regional lymph nodes cannot be assessed

N0: No regional lymph node metastasis

N1: Metastasis in perirectal lymph node(s)

N2: Metastasis in unilateral internal iliac and/or inguinal lymph node(s)

N3: Metastasis in perirectal and inguinal lymph nodes or bilateral internal iliac and/or inguinal lymph nodes

Distant metastasis (M)

MX: Distant metastasis cannot be assessed

M0: No distant metastasis

M1: Distant metastasis

AJCC stage groupings

Stage 0

Tis, N0, M0

Stage I

T1, N0, M0

Stage II

T2, N0, M0

T3, N0, M0

Stage IIIA

T1, N1, M0

T2, N1, M0

T3, N1, M0

T4, N0, M0

Stage IIIB

T4, N1, M0

Any T, N2, M0

Any T, N3, M0

Stage IV

Any T, any N, M1

References

1. Anal canal. In: American Joint Committee on Cancer. AJCC Cancer Staging Manual. 6th ed. New York, NY: Springer, 2002, pp 125-130.