GUIDELINES FOR THE MANAGEMENT OF COLORECTAL CANCER (2001)

Issued by
The Association of Coloproctology of Great Britain and Ireland

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BACKGROUND

i) Colorectal cancer in the United Kingdom

In 1995 there were over 32,000 new cases of colorectal cancer diagnosed in the United Kingdom, and in 1997 there were some 17,000 deaths (CRC 1999). Colorectal camcer is the second most common cause of cancer death after lung cancer, and the overall 5 year survival is less than 40% (CRC 1999). The high incidence of this disease, together with the fact that improvement in mortality in recent years has been modest, highlights the need for research into prevention, earlier diagnosis and better treatment.

Advanced disease at first presentation is still common, both the Trent\Wales and Wessex audits indicate that over 20% of patients present with distant metastases. This may improve with heightened awareness of the disease and its symptoms among the general public.

ii) Purpose

Following the Government white paper in 1991 "Working for Patients", 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 is possible to do so. In addition, they described the gold standard of good clinical care and were proscriptive of unacceptable clinical standards. The revised Guidelines have maintained these guiding principles and added newer evidence to support changes in clinical practice wherever possible.

It is important to stress, however, that guidelines are not intended to create a rigid framework where there is a reasonable difference of opinion. Thus, clinical freedom within limits defined by good practice is preserved.

iii) Development

An initial steering group set up by the Royal College of Surgeons of England in 1994 decided to develop the guidelines using the following three approaches: i) **literature review** in areas where unequivocal scientific bases for recommendations exist, ii) the results of contemporary **audits** of the management of all patients presenting with colorectal cancer in Trent, Wales and Wessex in order to define reasonable practice where appropriate and iii) **consensus** where no other approach is feasible or currently available. This has been complemented with the best results from the literature to provide "gold standards" at which to aim.

The original guidelines were drawn up by a small drafting committee, and revised by an expert advisory group composed of representatives of the main groups involved with the management of colorectal cancer. The revisions have followed a similar process of drafting and review by an expert advisory group.

Funding for the original guidelines was provided by a grant from the Department of Health to the Royal College of Surgeons of England. The revisions have been organised through the Association of Coloproctology of Great Britain and Ireland and funded by a charitable donation from Beating Bowel Cancer and by a donation from The Colon and Rectal Disease Research Foundation of Great Britain & Ireland.

Around the time the original guidelines were published two other documents appeared which had a significant impact on the provision of colorectal cancer care. These were the Calman Hine report and Guidance on Commissioning Cancer Services documents. (Department of Health 1995, NHS Executive 1997). These two documents have led to a significant change in the way in which

colorectal cancer care is provided. This has changed the pattern of delivery of colorectal cancer care from being predominantly organised and delivered by individual surgeons to a multidisciplinary team (MDT) based approach. These revised guidelines reflect this change in approach and changes in patients' demands for greater information and a greater role in determining their treatment. These radical changes towards a more patient centred delivery of care are welcomed as an opportunity to improve the quality of care for patients with colorectal cancer.

iv) Validity

The 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 which is not consistent with the evidence grading if the evidence is deemed to be unsatisfactory. Furthermore, some recommendations cover topics which are not amenable to formal studies but may represent good clinical practice (eg. informed consent). These items have been labelled as "good clinical practice" and highlighted in the recommendations by the insertion of the ✓ symbol.

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 and the guidelines revised. The next series of revisions for these guidelines are due to be published in 2006.

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 to routine clinics. Patients referred through such clinics should be investigated with either flexible or rigid sigmoidoscopy plus a high quality double contrast barium enema or colonoscopy, when appropriate. (p19) **B**

ii) Preoperative histology should be obtained from all rectal tumours. (p19) **C**

iii) Doctors carrying out colonoscopy should audit their results, and expect to achieve a high total colonoscopy rate with a low perforation rate. (p19) **B**

iv) It is acceptable for non-consultant staff to perform double contrast barium enemas, provided they have completed a recognised training programme, the examinations are performed to strict protocols and supervised by a consultant radiologist. (p19) **C**

v) All patients, particularly those with rectal cancer should have pre-operative staging to determine the local extent of the disease and the presence of lung and liver metastases. Endorectal ultrsound scanning should be performed to identify T1 rectal cancers, where local excision is being considered. CT or MRI scans should be undertaken to assess involvement of adjacent organs in more advanced tumours. (p20) **C**

vi) Surveillance and genetic testing should be offered to all FAP families and HNPCC families that either meet the Amsterdam criteria or have a confirmed mismatch repair gene mutation. (p 22) **A**

vii) First degree relatives of patients who develop colorectal cancer before the age of 45 years and members of families in which multiple cancers have occurred should be seen by a specialist, preferably with experience in genetic counselling, who can evaluate their risk of developing the disease and advise on appropriate investigations and surveillance. (p22) **B**

Access to Treatment

i) Patients should expect to receive initial treatment within 4 weeks between making a diagnosis of colorectal cancer and start of therapy. (p23) **B**

ii) Colorectal cancer should be treated by surgeons with appropriate training and experience and who work as part of a multidisciplinary team (p24) ✓

iii) All patients with colorectal cancer should have the benefit of a suitably informed surgical opinion and their management should be considered by the multidisciplinary team. (p24) ✓

iv) Patients with colorectal cancer should have access to a colorectal nurse specialist for advice and support during their treatment. (p24) ✓

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. (p25) **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. (p25) **C**

iii) Blood 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. (p26) ✓

iv) Mechanical bowel preparation prior to surgery is recommended. (p26) **C**

v) Subcutaneous heparin and/or intermittent compression should be employed as thromboembolism prophylaxis in surgery for colorectal cancer unless there is a specific contraindication. (p26) **A**

vi) All patients undergoing surgery for colorectal cancer should have antibiotic prophylaxis. It is impossible to be dogmatic as regards the precise regime, but a single dose of appropriate intravenous antibiotics appears to be effective. (p27) **A**

Elective Surgical Treatment

i) It is recommended that the term curative resection should be based on histological confirmation of complete excision or residual tumour. 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. (p27) **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. (p28) **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. (p29) **B**

iv) 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. 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. (p29) **B**

v) Cytocidal washout of the rectal stump should be undertaken prior to anastomosis. (p30) ✓

vi) The proportion of rectal cancers treated by abdomino-perineal excision of the rectum (APER) should be less than 40%, and, if distal clearance of 1 cm 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. (p30) **B**

vii) Local excision for cure in rectal cancer should be restricted to T1 cancers with well or moderate differentiation less that 3cm in diameter. It must be accepted that subsequent histopathological examination of cancers thought to be suitable for local excision will identify a small proportion which require more radical surgery. (p31) **B**

viii) Laparoscopic surgery for colorectal cancer should only be performed by experienced laparoscopic surgeons who have been properly trained in colorectal surgery and who are entering their patients into one of the national trials. (p31) **B**

Record Keeping

i) There are existing guidelines for the keeping of clinical records issued by the Royal College of Surgeons (RCS 1990), and these should be adhered to for patients with colorectal cancer. (p31) **C**

ii) A check-list should be used to construct an operation note for patients undergoing surgery for colorectal cancer. (p31 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. (p31) ✓

Emergency Treatment

i) Emergency surgery should be carried out during daytime hours as far as possible, by experienced surgeons and anaesthetists. (p32) **C**

ii) In patients presenting with obstruction, steps should be taken to exclude pseudo-obstruction before operation. (p32) **B**

iii) Stoma formation should be carried out in the patient's interests only, and not as a result of lack of experienced surgical staff. (p32) **B**

Adjuvant Therapy

i) Patients with Dukes C colon cancer should be considered for adjuvant chemotherapy. (p33) **A**

ii) Patients with Dukes B colon cancer should be considered for entry into randomised trials of adjuvant chemotherapy (p33) ✓

iii) Patients with high risk Dukes B colon cancer should be individually counselled about their level of risk and possible benefits of chemotherapy (p33) ✓

iv) There is no evidence to support the use of adjuvant chemotherapy in Dukes A cancers of colon or rectum. (p33) ✓

v) No definite recommendation can be made regarding adjuvant chemotherapy for patients with Dukes C rectal cancer. Patients may be either offered chemotherapy or be considered for clinical trials, in addition to appropriate adjuvant radiotherapy. (p34) **B**

vi) Systemic chemotherapy should only be administered by clinical staff with appropriate training and experience, according to JCCO guidelines. (p34) **C**

vii) Patients with a mobile rectal cancer should be considered for entry into clinical trials of pre-operative radiotherapy. (p36) **C**

viii) Patients with rectal cancer in whom the tumour is tethered or in whom local imaging indicates a high risk of incomplete resection should be selected for long course pre-operative radiotherapy to obtain tumour downstaging. (p36) **B**

ix) In patients with rectal cancer pre-operative radiotherapy using short course (25 Gy in 5 fractions in one week) or longer course (40-45 Gy in 20-25 fractions over 4-5 weeks) are both acceptable. (p36) **A**

x) In patients with rectal cancer who have not had pre-operative radiotherapy, post-operative radiotherapy and chemotherapy should be offered to patients with well established predictors of risk (e.g. evidence of tumour at the circumferential resection margins). (p36) **A**

xi) In patients with rectal cancer post-operative radiotherapy doses should be 40-50 Gy in 20-25 fractions or a suitable biological equivalent using a planned volume. (p36) **B**

xii) A planned radiotherapy volume using three or four fields is recommended for rectal cancers as this results in less morbidity and mortality. (p36) **B**

xiii) Patients with potentially operable rectal cancer should always be considered for entry into trials of adjuvant radiotherapy. (p36) **B**

Treatment of Advanced Disease

i) For fit patients with inoperable rectal carcinoma without evidence of metastatic disease, primary radiotherapy alone or in combination with chemotherapy should be considered. (p37) **B**

ii) Patients with metastatic disease who are fit for active therapy should be accurately staged with CT scans of abdomen and thorax. (p39) ✓

iii) Patients with evidence of unresectable metastatic disease should be referred to an oncologist for consideration of palliative chemotherapy as soon as the diagnosis of metastatic disease is made, but this may not be appropriate for elderly patients. (p39) **A**

iv) Chemotherapy for metastatic colorectal cancer should only be given after discussion at a Multidisciplinary Team meeting and under the direction of recognised clinical and medical oncologists within facilities conforming to JCCO guidelines. (p38) **C**

v) Entry into clinical trials evaluating the benefits of novel chemotherapy regimens in colorectal cancer should be encouraged. (p39) **C**

vi) Palliative treatment should be 5FU given by infusion combined with the use of irinotecan in the first line or on 5FU failure if the patient remains fit for chemotherapy. (p39) **A**

vii) Hepatic arterial infusional chemotherapy remains of unproven benefit. (p39) **A**

viii) Patients with metastatic disease limited to the liver which is potentially resectable should be considered for partial hepatectomy by an experienced liver surgeon. (p39) **B**

ix) Surgeons and oncologists who deal with colorectal cancer should make it a priority to build close links with palliative care specialists and units. (p40) **B**

x) All clinicians who deal with colorectal cancer should be trained in communication skills, in the control of pain and other cancer symptoms (p40) **C**

xi) 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 (p40) **C**

Outcome

Measurement of outcomes is an essential part of colorectal cancer care. In order to undertake measurement of outcomes manpower resources and IT facilities are required. These facilties are currently lacking in many hospitals.

Colorectal Cancer Units should carefully audit the outcome of treatment and achieve:

i) An operative mortality of 15-25% for emergency surgery and 4-7% for elective surgery with colorectal cancer. (p41) **B**

ii) Intensive care and high dependency care are an essential part of peri-operative colorectal cancer care and should be available in hospitals undertaking colorectal cancer surgery. (p41) ✓

iii) Wound infection rates after surgery for colorectal cancer should be around 10%. (p41) **A**

iv) A clinical anastomotic leak rate of around 8% for anterior resections and around 4% for other types of resection. However ultra low pelvic anastomoses will have higher leak rates (around 15%) and therefore the judicious use of a defunctioning stoma is recommended. (p42) **B**

v) Local recurrence rates after curative resection for rectal cancers should be around 10% within 2 years of follow up (p42) **B**

Follow-Up

i) Although there is no evidence that intensive follow up for the detection of recurrent disease improves survival, it is reasonable to offer liver imaging to asymptomatic patients during the first two post-operative years for the purpose of detecting operable liver metastases. (p45) **B**

ii) Although there is no evidence that colonoscopic follow-up improves survival, it has been shown to yield adenomatous polyps and cancers. If such a policy is pursued, it is recommended that a "clean" colon should be examined by colonoscopy at 3-5 year intervals. (p46) **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. (p46) **C**

iv) All patients with a stoma should have ready access to specialist nursing staff. (p46) **C**

Histopathology

i) All resected polyps and cancers should be submitted for histopathological examination (p55) **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. (p55) **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 (p55) **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 (p55) **B**

DETAILED GUIDELINES

INVESTIGATIONS

The process of referral and investigation

i) Introduction

When a patient is concerned they may have a colorectal cancer and their GP feels investigation is appropriate, it is an important aspect of the quality of their care that this is done promptly, even though there is little evidence that this will improve the survival of those with cancer. Delay in the treatment of cancer patients causes considerable psychological morbidity making it harder for them to cope with their disease, especially if it is incurable. It is important to develop management strategies, which ensure that time lags to referral, diagnosis and treatment are kept to a minimum. Some delays due to social and administrative reasons are unavoidable. This includes the diagnostic process, which incorporates 'treat, watch-and-wait' strategies by patients and General Practitioners, the time taken for the Outpatient appointment to be arranged, the time for investigations and staging of the cancer, optimising the patient's general health for surgery, pre-operative adjuvant therapy and the time taken to arrange for admission and operation ensuring that adequate Intensive Care Unit and high dependency facilities 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 for various reasons including the biological nature of cancer, which may be a dominant factor determining the speed at which patients and GPs recognise the significance of symptoms (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).

ii) Clinical history

Patients with cancers proximal to the splenic flexure do not usually present with the primary symptoms of bowel cancer. The dominant reasons for referral are an iron deficiency anaemia, an abdominal mass or signs and symptoms of intestinal obstruction (McSherry et al 1969 III, Shallow et al 1955 III, Ellis et al 1999 III). In contrast, most patients with rectal and sigmoid cancers present with rectal bleeding and a change in bowel habit, either as single symptoms or more commonly in combination (Shallow et al 1955 III, Ellis et al 1999III, Dodds et al 1999 III). The change in bowel habit is usually to increased frequency of defaecation and/or looser stools (Ellis et al 1999 III, Dodds et al 1999 III). Rectal bleeding in cancer patients occurs without anal symptoms in over 60% of patients (Ellis et al 1999 III, Dodds et al 1999 III).

The high prevalence of the symptoms of bowel cancer in the community and in general practice means that identifying the few with cancer can be very difficult. The recently introduced Department of Health Referral Guidelines for GPs aims to improve this selection process so that the majority of patients with higher risk symptoms are seen within two weeks.

Higher risk criteria

Only patients with new and persistent symptoms listed below should be referred to the fast-track system. These criteria should include 80-90% of all colorectal cancers presenting to Outpatients.

	Age Threshold
• Rectal bleeding WITH a change in bowel habit to increased frequency of defaecation and/or looser stools and persistent for at least 6 weeks	All ages
• Rectal bleeding persistently without anal symptoms	Over 60 years
• Change in bowel habit to increased frequency of defaecation and/or looser stools persistent for at least 6 weeks	Over 60 years
• Patients with an easily palpable right iliac fossa mass	All ages
• Patients with an easily palpable intraluminal rectal mass	All ages
• Patients with an unexplained iron deficiency anaemia: Hb below 11g/dl in men Hb below 10g/dl in women	All ages Post-menopausal

Low risk criteria

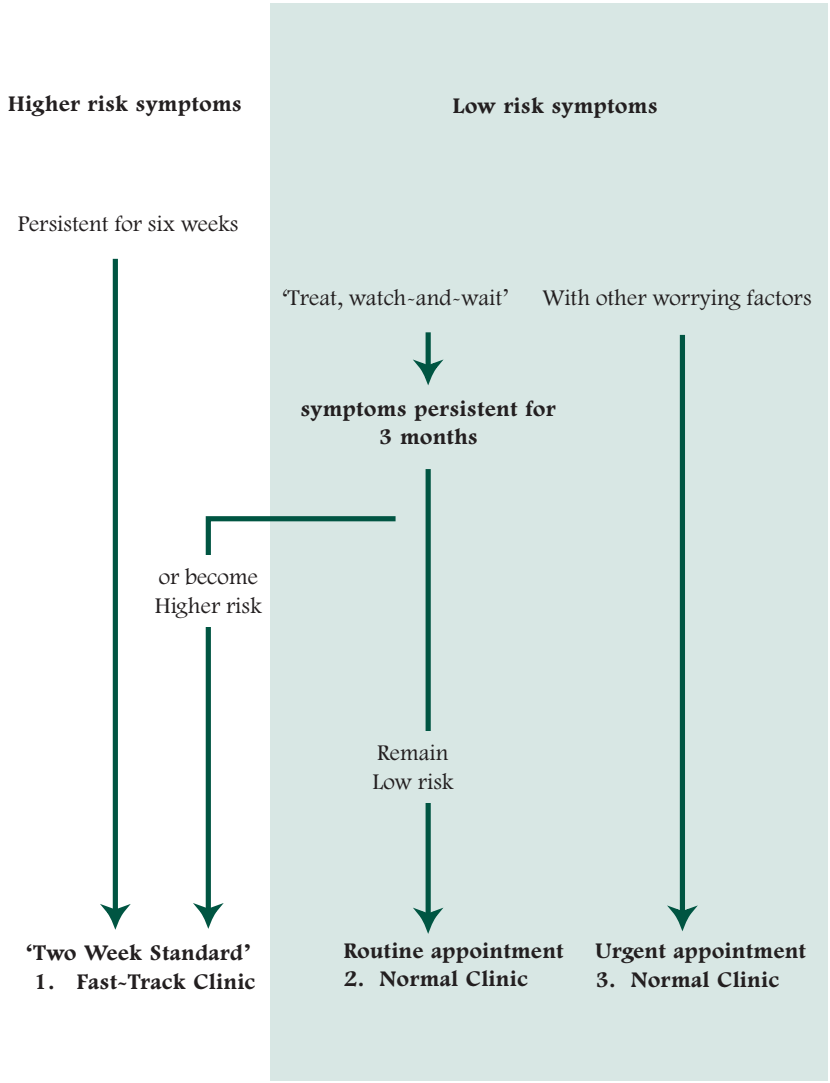
The risk of cancer is never zero even in patients with no symptoms as shown by screening studies. Some cancers will be diagnosed incidentally in patients being investigated for symptoms from benign disease. Others will have symptomatic cancers, which develop in patients already symptomatic from functional bowel disease or piles. This means that all low risk patients with persistent symptoms not responding to treatment or recurring after stopping treatment, should be referred to routine clinics.

Criteria indicating patients at very low risk of cancer are:

- **Rectal bleeding with anal symptoms**
- **Rectal bleeding with an obvious external visible cause such as prolapsed piles, rectal prolapse and anal fissures**
- **Transient changes in bowel habit for less than 6 weeks particularly if to a decreased frequency of defaecation with straining and harder stools**
- **Abdominal pain not associated with other high-risk symptoms, an iron deficiency anaemia, a palpable abdominal or rectal mass, or clearly due to intestinal obstruction**

Patients with persistently low risk symptoms, but with other worrying factors, such as a positive family history, can be seen on an urgent basis in a normal clinic, the third route for referral.

THE THREE ROUTES OF REFERRAL



Time lags in the process of referral, diagnosis and treatment

In the Wessex Audit (IIb) 65% of the delay in patients having elective surgery for rectal and sigmoid carcinomas occurred before referral to a hospital, 15% waiting for an outpatient appointment and 20% during the process of diagnosis and treatment. The figures for colon cancers proximal to the sigmoid were 35% before GP referral, 19% waiting for outpatient appointment and 46% due to hospital delay in diagnosis.

In the Wessex Audit (IIb) the 15% of patients initially referred to physicians had a significantly longer delay to treatment than the 85% referred directly to surgeons. In the Trent\Wales Audit (IIb) there was a similar longer time to treatment for patients initially referred to physicians even when those presenting with anaemia were excluded.

The time to referral, diagnosis and treatment has not changed over the last twenty years (McSherry et al 1969 III, McDermott et al 1981 III, Wessex Colorectal Cancer Audit (1990-1993 IIb). However the delay waiting for an Outpatient appointment may now be affected by the introduction of the Government's 'Two Week Standard' (July 2000).

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). 82% of palpable rectal cancers may be detected by GPs (Dixon et al 1990 III), and may help to categorise a patient for fast-track referral who otherwise has low risk symptoms.

A rectal examination should be an essential part of the examination of any patient presenting with lower GI symptoms above the age of 40 years and anybody below this age with persistent symptoms. A small cancer at the anorectal junction may be missed by endoscopy, and the simplest way of being alerted to this situation is a rectal examination. Vaginal examination should be considered a part of the assessment of rectal cancer in women.

It is likely that a right-sided abdominal mass will be of greater diagnostic value than left 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 that the mass is persistent before referral.

iv) Investigations

Investigations can be tailored according to the symptomatic presentation. The majority of cancers in patients presenting with rectal bleeding or a change in bowel habit without any other significant diagnostic factors occur within 60 cms of the anal verge and can be diagnosed by flexible sigmoidoscopy, which means that a selective policy for the investigation of the proximal colon by a barium enema or colonoscopy can be safely adopted. Patients presenting with an iron deficiency anaemia, an abdominal mass or abdominal pain indicating incipient intestinal obstruction will require full colonic imaging by barium enema or colonoscopy.

If a 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). If this is done pre-operatively and the patient is shown to have disseminated disease at operation, the examination will have been unnecessary, and in patients with a stenosing lesion, the proximal examination can be either impossible or less effective in excluding small lesions. However if complete colonic imaging is not achieved pre-operatively in patients subsequently having curative surgery, it is important this is done within six months of surgery or as soon as possible after closure of a temporary ileostomy.

Methods of investigation

Complete examination of the large bowel can be achieved either by total colonoscopy or adequate endoscopic visualisation of the rectum plus a double contrast barium enema. It may be appropriate to perform CT colography in the small number of patients in whom colonoscopy and barium enema have been technically impossible or have given inconclusive results (Fenlon 1998, IIa; Pappalardo 2000 IIa).

The rectum may be examined by flexible or rigid sigmoidoscopy. A small anorectal carcinoma at the anorectal junction is easily missed, and in patients having an examination of the rectum by flexible sigmoidoscopy a J manoeuvre may reduce the risks of missing these lesions. If an unprepared sigmoidoscopy is unsatisfactory, then it should be repeated after an enema, which can be achieved on a domiciliary basis before the outpatient appointment (Lund et al 1998 Ib, Atkin et al 2000 Ib). It is important that a barium enema should always be complemented by endoscopy, ideally flexible sigmoidoscopy should be combined with a double contrast barium enema. The sigmoid colon is the area where polyps may be missed on a double contrast barium enema, particularly in the presence of diverticular disease. The rectum is clearly visualised on a double contrast barium enema and radiologists should report on any abnormality in this area.

For exclusion of synchronous lesions there is some evidence that colonoscopy may be more accurate than barium enema (Barillari et al 1990 IIb, Winawer et al 2000 Ib); 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 al1990 IIb). It must be accepted, however, that both investigations may vary in quality, and the choice between colonoscopy and barium enema for total colonic examination will depend on local availability and expertise.

Although histological confirmation of a colon cancer is ideal, if an unequivocal lesion has been detected by a high quality double contrast barium enema in a patient with symptoms strongly suggestive of cancer or an iron deficient anaemia, it is acceptable to dispense with histology. On the other hand, histological confirmation of neoplasia should be considered mandatory in rectal cancers, which might result in either a permanent stoma formation or an ultra low anterior resection, or when pre-operative radiotherapy is being considered.

Quality of investigations

Regardless of whether colonoscopy or barium enema is employed, certain minimum levels of quality should be achieved with both of these investigations.

- **Colonoscopy**

Colonoscopy should usually be done as a day-case procedure after full bowel preparation, and the endoscopist should be prepared to biopsy or remove appropriate lesions (i.e. areas of inflammation, sessile and pedunculated polyps). The patient should be warned 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).

Complete colonoscopy to the caecum can be achieved in 90% of cases with a perforation rate of 0.1% (Cotton & Williams 1990 III), but whether or not these are realistic figures for the whole country is debatable. The Trent/Wales audit showed that total colonoscopy was achieved in less than 50% of cases, whereas the BSG Colonoscopy Audit of 9000 colonoscopies had a completion rate of 83% (Bowles et al 2001 IIb) and there is clearly a great discrepancy between the best published results and the experience of most colonoscopists in the United Kingdom (Bowles et al 2001 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.

- **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 this area 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 resulting in an 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.

Despite good radiological technique, 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.

In summary, it is recommended that patients with higher-risk symptoms should be fast-tracked either in special clinics or with urgent appointments to routine clinics. Patients referred through such clinics should be investigated with either flexible or rigid sigmoidoscopy plus a high quality double contrast barium enema or colonoscopy when appropriate.

Recommendation grading: B

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

Recommendation grading: C

Doctors carrying out colonoscopy should audit their results, and expect to achieve a high total colonoscopy rate with a low perforation rate.

Recommendation grading: B

It is acceptable for non-consultant staff to perform double contrast bariumenemas, provided they have completed a recognised training programme, the examinations are performed to strict protocols and supervised by a consultant radiologist.

Recommendation grading: C

v) Pre-operative assessment of the stage of disease

This is becoming increasingly important, both because of the improvement in imaging techniques and a greater choice of adjuvant and definitive surgical treatments, particularly in rectal cancer based on the presence or absence of both local and distant disease.

Clinical outcomes including survival following treatment of colorectal cancer is markedly affected by the local extent of the disease, whether the lymph nodes are involved and whether the disease is disseminated.

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

Where possible MRI rather than CT, should be undertaken when rectal cancers are being considered for resection as it is important to determine whether adjacent organs are involved (Padhani 1999 III, Kumar & Scholefield 2000 III, Heriot et al 1999 III). The degree of local extension may determine whether a curative excision can be achieved, and whether preoperative adjuvant radiotherapy should be given (Brown et al 1999 IIb and Beets-Tan et al 2001 IIB). In patients with rectal cancer where

local excision is being considered (T1 lesions), staging by endorectal ultrasound scanning to determine the depth of penetration is recommended .

MRI can identify small perirectal lymph nodes by virtue of their morphology (Brown et al 1999a IIb). The use of size criteria alone for defining lymph node involvement is unreliable and must be used with great caution. Lymph nodes > 1cm in diameter are more likely to be involved (Padhani 1999 III, Kumar & Scholefield 2000 III, Heriot et al 1999 III). The majority of involved lymph nodes in colorectal cancer specimens measure <5mm (Dworak 1991 III) and there is currently no method for differentiating these from reactive nodes.

The value of MRI lies not so much in early T1/T2 staging (where rectal endosonography is currently more accurate) but in assessing the tumour extent (particularly in the lateral and anterior planes) to predict tumour free extension. Involvement of the mesorectum is easily demonstrated on MRI. A histological clearance of less than 1 mm may be predicted when this appears to be less than 5 mm on MRI (Beets Tan, 2001 III). The high soft tissue differentiation, multiplanar imaging and improved resolution of current scanners dictate that MRI is fast becoming the investigation of choice for rectal cancer regardless of position (Brown 1999 IIb).

- **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).

The sensitivity of ultrasound for identifying liver metastases >1 cm varies from 53%-82% (Padhani 1999 III, Kumar & Scholefield 2000 III, Heriot et al 1999 III). CT and MRI are more sensitive (Padhani 1999 III). Contrast enhanced CT scanning in the portal phase represents the most cost effective option for examining the liver and a complete abdominal examination can be performed at the same time.

A routine pre-operative intravenous urogram in patients with rectal cancer to detect involvement of the ureters has been advocated in the past, but this has been shown to be of little value (Phillips et al 1983 III)

Although there are some patients that will benefit from open surgery regardless of whether there is disseminated disease, the avoidance of pre-operative staging should now be the exception rather than the rule.

It is recommended that all patients, particularly those with rectal cancer should have pre-operative staging to determine the local extent of the disease and the presence of lung and liver metastases. Endo rectal ultrasound scanning should be performed to identify T1 rectal cancers, where local excision is being considered. CT or MRI scans should be performed to assess involvement of adjacent organs in more advanced tumours.

Recommendation grading: C

vi) The significance of a family history

It is now established that heritable factors make a significant contribution to an individual's risk of colorectal cancer. A recent study of 45,000 twin pairs 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 autosomal dominantly inherited syndromes, namely FAP and HNPCC, which account for less than 5% of all colorectal cancers (Cancer Research Campaign 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, some may predipose to adenomatous polyp formation (Ponz de Leon et al 1986 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). It is clear, however, that such a low-penetrance genetic pre-disposition, is likely to be modified by a range of different genetic and environmental factors.

High penetrance autosomal dominant disease

Direct mutation analysis is available for any family with FAP and should be offered to all relatives once they have reached the age for surveillance. This is usually around the age of 12 years. Direct mutation analysis will give positive results in approximately 80% of families (Wallis et al 1996 IIa). In the absence of identifying a mutation in the family, surveillance should be offered to all 'at risk' relatives on an annual follow up. Except in atypical families, surveillance by flexible sigmoidoscopy is sufficient. In the presence of an identified mutation in an FAP family, any family member identified as not carrying the mutation should be withdrawn from the surveillance programme. In HNPCC five different genes have been shown to cause this condition, making direct mutation analysis a more complex and lengthy process. Nonetheless, it should be made available to all families in which the Amsterdam criteria are met. Between 40 and 60% of presumed HNPCC families have identifiable mutations at the present time, depending on the clinical criteria used. Surveillance for HNPCC is by full colonoscopy because of the propensity for right-sided lesions. This should be offered two to three yearly to 'at risk' individuals from 25 years (Burke et al 1997 IIb).

The impact of pre-symptomatic diagnosis in FAP and HNPCC has been demonstrated to reduce the mortality and incidence of colorectal cancer in these families substantially (Morton et al 1992 III, Jarvinen et al 2000 IIb).

Lower risk groups

Two large prospective cohort studies have identified the empiric risk for first degree relatives in which there is clustering of colorectal cancer (St John et al 1993, Fuchs et al 1994 IIA). These studies were consistent in their findings. The key determinants of risk are the youngest age of onset of colorectal cancer within the family, and the number of individuals who are first degree relatives of each other. First degree relatives of one individual in whom colorectal cancer has developed at 45 years of age or younger have three times the lifetime risk of colorectal cancer above that of the general population. Any individual with two affected first degree relatives aged less than 75 years at diagnosis has over twice the lifetime risk of colorectal cancer as compared to the general population.

There are no national guidelines for surveillance in this cohort and no randomised, controlled study has been carried out to attempt to demonstrate the benefit. It is known, however, that these family members develop polyps more frequently than the general population, as has been demonstrated in a population based screening trial (Lieberman et al 2000 IIa). Polypectomy does lead to a substantial reduction in cancer incidence (Atkin 1992 IIb). In many areas of Great Britain surveillance is currently offered to individuals with an empiric risk of more than twice that of the general population risk for colorectal cancer. This type of surveillance is usually offered on a five yearly

basis (Neugut et al 1995, Winawer et al 1997 IIb). Despite the resource implications of this type of surveillance, the impact of such surveillance in cancer incidence and mortality in these families is as yet poorly documented.

Surveillance and genetic testing should be offered to all FAP families and HNPCC families that either meet the Amsterdam criteria or have a confirmed mismatch repair gene mutation.

Recommendation grading: A

It is recommended that first degree relatives of patients who develop colorectal cancer before the age of 45 years and members of families in which multiple cancers have occurred should be seen by a specialist, preferably with experience in genetic counselling, who can evaluate their risk of developing the disease and advise on appropriate investigations and surveillance.

Recommendation grading: B

TREATMENT

Access

i) Waiting times

The Trent/Wales Audit (IIb) has revealed an overall median waiting time of 20 days (mean 26 days) with a range of 0-330 days. In the Wessex audit (IIb), the median waiting time was 18 days (mean 27 days) with a range of 0-400 days.

From this data it is recommended that surgeons should expect to achieve waiting times of 4 weeks or less between making a diagnosis of colorectal cancer and start of therapy.

Recommendation grading: B

ii) The multidisciplinary team (MDT)

Colorectal cancer care should now be delivered through a multidisciplinary team based approach. It is axiomatic that doctors and nurses who decide on therapeutic strategy and implement that strategy should have sufficient experience in the management of colorectal cancer. Core members of the Multidisciplinary team are:

Surgical specialist: it is difficult to be precise as to what constitutes sufficient experience, and there are few data to support the contention that all patients with colorectal cancer should be treated by specialists in coloproctology. This is compounded by the current lack of accreditation procedures, so that there is no way of assessing the experience of a surgeon who professes to be a coloproctologist. However, a colorectal surgeon is expected to attend the MDT meeting, to be a member of the specialist association and to contribute to local and national audit of their colorectal cancer work.

Oncologist with an interest in gastrointestinal cancer, either a clinical oncologist who can offer radio- and chemo-therapy, or a medical oncologist who works closely with a clinical oncologist.

Nurse specialist in colorectal cancer. This individual should be able to provide a point of patient contact and also be a source of information for patients. In addition he/she should liaise on the patients behalf with the different specialties and disciplines involved in the total care of the colorectal cancer patient.

Radiologist with a gastrointestinal interest

Histopathologist with a gastrointestinal interest

It has been suggested that the core team should meet weekly or once every two weeks depending on the workload in each unit. These meetings should be part of each consultant's job plan and should occur during the normal working day.

The core team must maintain close contact with the other professionals involved in caring for the cancer patient. This must include prompt communication with the patient's General Practitioner and the palliative care team. At any one time there should be a lead clinician to whom each patient relates. Written and verbal information must be provided for patients about their disease and information given to them about transfer of care from one member of the team to another e.g. from a surgeon to an oncologist ((Improving Outcomes in Colorectal Cancer Nov. 1997, NHS Executive, Department of Health IV,).

Although surgery is the mainstay of the treatment of colorectal cancer, total management should be overseen by a multidisciplinary team (Improving Outcomes in Colorectal Cancer Nov. 1997, NHS Executive, Department of Health IV,).

There is evidence that considerable variability exists between individual surgeons. In a six-year prospective study, McArdle and Hole (1991 IIb) found wide variation 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. Similar findings have been reported by other groups (Carter 1995 III , Hermanek et al 1995 IIb). In none of these studies, however, has it been possible to demonstrate a correlation between outcome with number of cases of colorectal cancer treated by the individual consultant. See Outcomes section (page 41).

Audit of all aspects of the care provided for colorectal cancer patients is also a function of the Multi Disciplinary Team.

Although it is not yet possible on scientific grounds to specify a minimum number of cases which should be performed each year, it is recommended that colorectal cancer should be treated by surgeons and oncologists with appropriate training and experience working in multidisciplinary teams, which audit outcomes of treatment.

Recommendation grading: ✓

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

Recommendation grading: ✓

Access to a specialist colorectal nurse is recommended for all patients with colorectal cancer.

Recommendation grading: ✓

Process

i) Preparation for surgery.

In general terms, surgery for colorectal cancer should be avoided if the hazards are deemed to outweigh the potential benefits, i.e. in the patient who is medically unfit for surgery or who has advanced disease which is not amenable to surgical therapy. 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.

Given that surgery is to proceed, there are certain fundamental aspects of preparation which deserve consideration, and 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

a) Informed consent:

All patients undergoing surgery for colorectal cancer should give informed consent unless they are unable to do so in which case it may be necessary to obtain consent from a relative. The consent should be obtained by a doctor who fully understands the nature of the operation, ideally the surgeon who is undertaking the procedure and is therefore able to answer any pertinent questions the patient or relatives may have. The risks of death and morbidity must be carefully explained; in particular, the likelihood of requiring a stoma and developing urinary problems and impotence after rectal surgery should be discussed. In addition, patients should be warned of the increased stool frequency that may be experienced after subtotal colectomy and the risk of a poor functional result after a low anterior resection.

In the light of recent cases, the General Medical Council has published guidelines for seeking patients' informed consent to investigations, treatment, screening or research. (www.gmc-uk.org/standards/consent.htm IV,)

The use of human tissue and biological samples in research has been summarised by the Medical Research Council (Human Tissue and Biological Samples for use in Research, Report of the Medical Research Council Working Group to develop Operational and Ethical Guidelines, November 1999 and Interim Operational and Ethical Guidelines issued by the Medical Research Council, consultation document, November 1999 (IV). The need for informed consent is essential so that research can proceed according to the principles of the Declaration of Helsinki, which are currently under revision (World Medical Association, Declaration of Helsinki, Ethical principles for medical research involving human subjects, 1964 - last amended October 2000 IV). The use of human tissue requires the following; informed consent, the research should only proceed if the potential benefits are proportional to associated risks, the need to ensure confidentiality is maintained and finally that the interests of the participants should outweigh those of science or society.

The legal position of the ownership/custodianship of samples is not resolved. At the present time, tissue samples for research should be treated as gifts for moral and ethical reasons. Scientists obtaining new samples donated specifically or partly for research must make it clear to participants that this is the case. However, in the case of archived tissue samples left over from treatment or diagnosis, **it might be acceptable to assume abandonment if a legal basis for transfer of control of the samples was needed**. Some authorities, for example the Nuffield Council on Bioethics, have favoured the position that tissue samples for research had been abandoned by the donor. The sale of human tissue or biological samples for use in research is not ethical. The human body and its parts shall not, as such, give rise to financial gain (European Convention on Human Rights and Biomedicine 1997 IV).

The outcome of public consultation to determine an acceptable balance between individual confidentiality and data protection and the legitimate use of patient identifiable data without consent is awaited (Al-Shahi & Warlow 2000 IV).

Recommendation grading: 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 grading: 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). **Thus it is recommended that blood 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 grading: ✓

d) Bowel preparation:

Mechanical bowel preparation is generally regarded as mandatory before elective colorectal surgery, and all surgeons in Trent/Wales (Ib) used some form of such preparation. However, not all surgeons hold this view (Irving et al 1987 III), and a randomised study showed no benefit from sodium picosulphate preparation when compared with no preparation in left colonic or rectal resection (Burke et al 1994 Ib). No definite recommendations can be given therefore, but **the consensus view is still in favour of mechanical bowel preparation**.

Recommendation grading: C

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 IIb). All surgeons in Trent/Wales used either **heparin and/or intermittent compression, and it is recommended that either of these strategies should be employed in surgery for colorectal cancer unless there is a specific contraindication**.

Recommendation grading: 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, and in Trent/Wales (IIb) 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).

It is therefore recommended that all patients undergoing surgery for colorectal cancer have antibiotic prophylaxis. It is impossible to be dogmatic as regards the precise regimen, but a single dose of appropriate intravenous antibiotics appears to be effective.

Recommendation grading: A

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). The term is imprecise, if a surgeon is in doubt 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 (IIb) have shown that this is variable 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 this was inversely correlated with the percentages of cases with distant metastases.

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 & Hole 1991 IIb). In the Trent/Wales audit the overall rate of curative resection was 60% and in Wessex it was 53% (IIb), 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 & 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.

It is therefore recommended that the term curative resection should be based on histological confirmation of complete excision or residual tumour. 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 grading: 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 3rd sacral vertebra (Williams & 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 15 cm or less from the anal verge using a rigid sigmoidoscope should be classified as rectal**.

Recommendation grading: 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 resections 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 & 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 & 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, Heald & 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 IIa). It is recommended that lymph node clearance should extend for 5 cm 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 show 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). 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).

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 (p35).

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 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.

Recommendation grading: 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 & Hole 1991 IIb).

It is not possible, however, 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. Stapling methods have been compared with manual suturing techniques in several randomised trials (Beart et al 1981 Ib, Brennan et al 1982 Ib, Everett et al 1986 Ib, McGinn et al 1985 Ib, West of Scotland and Highland Anastomosis Group 1991 Ib), and overall there is no observable difference in leak rates for colorectal surgery.

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 1 cm beyond the palpable edge of the tumour (Williams et al 1983 IIb), the ability to obtain distal clearance of 1 cm of 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). However, 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 & Johnston 1983 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, and several studies now attest the efficacy of this procedure (Seow-Choen & 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. After anterior resection and total mesorectal excision the judicious use of a temporary de-

functioning stoma is recommended, and the formation of a colonic pouch should be considered.

Recommendation grading: B

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

Recommendation grading: ✓

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). However, in a report from the West Midlands Cancer Registry the proportion of rectal tumours treated by abdomino-perineal excision (APER) between 1957 and 1981 was 68% (Allum et al 1994 IIb). In the Large Bowel Cancer Project, 56% of patients undergoing curative resection of the rectum had an APER (Phillips et al 1984 IIb), and in the Trent/Wales audit the figure was 37% (IIb).

It is not clear exactly why these differences exist. 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 1 cm 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 rectal cancers treated by APER should be less than 40% depending on stage of disease at presentation and if distal clearance of 1 cm 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 grading: B

vi) Local excision:

Occasionally small pT1 rectal cancers are technically suitable for a local excision and some polyps excised by snare diathermy will contain invasive carcinoma. Careful studies have shown that cancers fulfilling the histological criteria defined on page 47 can be regarded as cured by a local excision (Whiteway et al 1985 IIb) whereas pT2 tumours are associated with a higher risk of lymph node involvement and of local recurrence without further treatment (Graham et al 1990 IIb). 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 polyps in the middle third of the rectum (Steele et al 1996 IIb).

In summary local excision for cure in rectal cancer should be restricted to pT1 cancers with well or moderate differentiation and less that 3cm in diameter. It

must be accepted that subsequent histopathological examination of cancers thought to be suitable for local excision will identify a small proportion which require more radical surgery.

Recommendation grading: B

vii) Laparoscopic surgery:

Laparoscopic and laparoscopic-assisted surgery for colorectal cancer have been advocated recently by several groups, but the advantages of this type of surgery over conventional approaches are not clear (Wexner et al 1993 III). The initial concerns over the frequency of port site recurrence appear to be associated with poor laparoscopic technique (Nduka et al 1994 III, Wexner & Cohen 1995 III). Although laparoscopic resection of colorectal cancer is technically possible, the long term benefits will only be identified as a result of large clinical trials, such trials have not yet been completed (NICE 2000 IV). These concerns must be adequately explained to patients before consent to laparoscopic surgery for colorectal cancer is obtained. It is also very important that the clinical results and the pathology of resected specimens should be very carefully audited.

It is recommended that laparoscopic surgery for colorectal cancer is only performed by experienced laparoscopic surgeons who have been properly trained in colorectal surgery and who are entering their patients into one of the national trials.

Recommendation grading: B

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 (IIb), 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 grading: C

It is therefore recommended that a check-list is used to construct an operation note for patients undergoing surgery for colorectal cancer (See Appendix 2).

Recommendation grading: 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 grading: ✓

ix) Management of patients presenting as an emergency:

Colorectal cancer frequently presents as an emergency, and when it does so it is associated with a higher operative mortality. In the Trent/Wales audit (IIb), 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 (IIb), 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 (IIb) this accounted for 16% of all colorectal cancer presentations, and in the Wessex audit (IIb) this figure was 12%. Bleeding and perforation are much less common. A clinical diagnosis of obstruction should be confirmed by a plain abdominal radiograph and a water soluble contrast enema or sigmoidoscopy to exclude pseudo-obstruction (Koruth et al 1985 IIb).

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 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 occasionally, preoperative care when appropriate.

The type of surgery which should be undertaken for large bowel obstruction is to some extent controversial, but broad guidelines can be given. 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 with on-table colonic lavage (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).

In summary, emergency surgery should be carried out during daytime hours as far as possible, by experienced surgeons and anaesthetists.

Recommendation grading: C

In patients presenting with obstruction, measures should be taken to exclude pseudo-obstruction before operation and stoma formation should be carried out in the patient's interests only ~ not as a result of lack of experienced surgical staff. The overall mortality for emergency/urgent surgery should be less than 25%.

Recommendation grading: B

x) Adjuvant chemotherapy:

Colon cancer

There is evidence that in patients who have had a curative resection for Dukes C carcinoma of the colon, adjuvant systemic chemotherapy has a significant impact on population survival (Moertel et al 1995 Ib, IMPACT, 1995 Ib, Zaniboni et al 1998 Ib). Two recent meta-analyses have been performed. In the colorectal cancer collaborative group meta-analysis 12,000 patients in 33 RCTs were included. This concluded that prolonged use of a 5FU based regimen for greater than three months can improve survival in colorectal cancer. The size of the benefit for Dukes C colon cancer was estimated at about 6% (range 2-10%)(NHS Executive 1997 IV). A different meta-analysis of 39 trials indicates the size of the benefit is about 5% absolute improvement in 5 year survival in those receiving chemotherapy (Dube et al 1997 Ia). The side effects of the treatment have been shown to cause only minor psychological distress (Norum 1997 IIb). However, in individual patients the survival benefit is small and there will be some patients for whom systemic chemotherapy will be inappropriate in view of age or comorbidity.

Patients with Dukes C colon cancer should be considered for adjuvant chemotherapy

Recommendation grading: A

In node negative colon cancer (Dukes B), there remains uncertainty of the value of adjuvant chemotherapy. A pooled analysis of 1,116 patients with B2 (Astler Coller)colon cancer randomised to chemotherapy versus observation showed no significant improvement in overall survival (OR 0.86, CI 0.72-1.07), 5 year survivals were 80% for control and 82% for chemotherapy patients, (IMPACT B2 1999 Ib). In contrast, a grouped analysis of the National Surgical Adjuvant Bowel Project (NSABP) trials C-01-04, which included 1,565 Dukes B patients, concluded that a 30% proportional reduction in mortality resulted from the use of chemotherapy (Mamounas et al 1999 Ia) consistent with a 5% absolute reduction in death at 5 years. This data together suggests a small (perhaps 2-5%) absolute increase in survival for Dukes B cancer patients from adjuvant chemotherapy. Given the toxicity of treatment, this is inadequate justification for routine use of chemotherapy in these patients. The size of benefit and its balance with toxicity needs further clarification in clinical trials.

Some poor risk features can be identified in Dukes B cancers (serosal involvement, perforated tumours, extramural vascular invasion, poorly differentiated histology, and in rectal cancer, involvement of the circumferential resection margin). These patients may have as poor a prognosis as node positive patients. Individual patients should be assessed for their specific risk on this basis and counselled regarding the relative lack of evidence to support adjuvant chemotherapy. However, it may be appropriate to offer chemotherapy to such patients on the basis of the proportionate reduction in risk observed in the clinical trials.

Patients with Duke B colon cancer should be considered for entry into randomised trials of adjuvant chemotherapy

Recommendation grading: ✓

Patients with high risk Dukes B colon cancer should be individually counselled about their level of risk and possible benefits of chemotherapy.

Recommendation grading: ✓

There is no evidence to support the use of adjuvant chemotherapy in Dukes A cancers of colon or rectum.

Recommendation grading: ✓

Rectal cancer

The impact of adjuvant chemotherapy alone has been difficult to identify because many trials have assessed the combination of chemotherapy and radiotherapy together. Combined chemotherapy and radiotherapy has been associated with a survival benefit in patients with Dukes B and C rectal cancer, when compared with radiotherapy alone (Krook et al 1991 Ib). The meta-analysis of adjuvant chemotherapy of colorectal cancer (Dube et al 1997 Ia) showed a greater benefit for rectal cancer than for colon cancer (OR for mortality 0.64 95% CI 0.48 - 0.85) and estimated the size of benefit to be a 9% increase in survival for rectal cancer patients. NSABP R-02 evaluated chemotherapy with or without post-operative radiotherapy and showed no advantage for survival in adding radiotherapy to adjuvant chemotherapy (Wolmark et al 2000 Ib). Conversely, early data from the Dutch study of adjuvant therapy in rectal cancer shows no advantage for adjuvant chemotherapy and they conclude it is acceptable to continue randomising into the ongoing trial (Kapiteijn et al, 2001 Ib), QUASAR 1 trial will provide further information. However, the indirect evidence suggests that there is a benefit for post-operative adjuvant chemotherapy in rectal cancer.

No definite recommendation can be made regarding adjuvant chemotherapy for patients with Dukes C rectal cancer. Patients may be either offered chemotherapy or be considered for clinical trials, in addition to appropriate adjuvant radiotherapy.

Recommendation grading: B

Adjuvant chemotherapy regimens

Certain statements can now be made regarding the schedule and duration of adjuvant chemotherapy if it is used. 5FU remains the basis for all adjuvant regimens. There is no advantage to high dose versus low dose folinic acid (QUASAR 2000 Ib, Haller et al 1998 Ib). Levamisole does not add any further benefit in place of or in addition to folinic acid (QUASAR 2000, Ib, Haller et al 1998 Ib, Wolmark et al 1998 Ib). Using a standard 5FU and folinic acid regimen, there is no advantage in a longer duration of therapy over 6 months (O'Connel et al 1998 Ib, Haller et al 1998 Ib). The toxicity of a weekly bolus 5FU and folinic acid regimen is less than the conventional 5 day fractionated regimen but a non randomised comparison in the QUASAR trial showed no reduction in effectiveness (QUASAR, 2000, Ib).

There is no consensus view beyond the above comments as to the optimum chemotherapy regimen. All 5FU based regimens are associated with a risk of toxicity notably diarrhoea, stomatitis and leucopenia. A higher incidence of severe infections has been observed in older patients, but in spite of increased toxicity, patients over 70 are equally likely to complete treatment as younger patients (Moore & Haller 1999 IIb).

Systemic chemotherapy should only be administered by clinical staff with appropriate training and experience, according to Joint Council for Clinical Oncology guidelines.

Recommendation grading: C

The role of portal vein infusion (PVI) of chemotherapy remains uncertain. The meta-analysis of 4000 patients in 10 studies showed a possible survival advantage of about 5% (Liver Infusion Meta-analysis Group 1997 Ia). Since then the EORTC study has been negative (Rougier et al 1998 Ib). The UKCCCR AXIS trial, which was powered to look for an overall survival benefit of 5%, showed no overall advantage for PVI 5FU in the initial analysis (James 1999 Ia). However, the estimated 5 year survival benefit in curatively resected colon cancer group was 5% compared with 0% for curatively resected rectal cancer patients. Similar trends were seen in the meta-analysis, although at present it is not possible to say conclusively that any benefit to PVI 5FU is confined to colon cancers. It is reasonable to conclude at this stage that the overall, absolute benefit to PVI 5FU is unlikely to be greater than 5%. However, molecular analysis of the curatively resected colon cancers in AXIS (a

group chosen before the main AXIS results were available) showed significantly larger treatment effects in those with certain molecular markers on genetic testing, compared to those without these markers. (Barratt et al 1999 IIb).

Therefore following full evaluation with large scale trials around the world the level of benefit from a one week infusion of PVI 5FU does not indicate it should be routinely applied. However, its role is not yet finally resolved.

xi) Adjuvant radiotherapy

There is no established role for radiotherapy in the management of colonic carcinoma. The following applies to carcinomas of the rectum and rectosigmoid. A systematic overview has been undertaken by the colorectal cancer collaborative group and was published in the NHS executive research evidence on colorectal cancer in 1997. This includes 13 pre-operative radiotherapy studies and 8 post operative radiotherapy studies.

Pre-operative radiotherapy

There is consistent evidence that local recurrence of rectal cancer can be reduced by about 50% by adequate dose pre-operative radiotherapy given over one week or five weeks. The proportional reduction is not influenced by stage of tumour or fixity. In the earlier trials, parallel opposed treatment fields were used, and an increased post-operative mortality from cardiovascular causes was observed. This effect was not present in other trials when improved radiotherapeutic technique employing three or four fields was used.

However, in all these trials local recurrence rates in the surgery alone arm were in the region of 20-30%. With improvements in surgical technique, including total mesorectal excision, local recurrence rates are falling to less than 10% in many specialists' practice. Preliminary results from the Dutch rectal cancer trial show that local recurrence rates were reduced from 8.2% with TME surgery alone to 2.4% with the addition of a one-week course of pre-operative radiotherapy (Kapiteijn at al, 2001 Ia). This was at a cost of increased perineal infection rates of 26% versus 18% in the abdomino-perineal group (n = 485, p = 0.05) and increased sexual difficulties (impotence and dyspareunia) in the irradiated group. No survival benefit is apparent at this time. There remains uncertainty as to whether this level of reduction in local recurrence rates in the absence of a survival advantage and in view of the side effects, is sufficient to use pre-operative radiotherapy in all cases of mobile rectal cancer. Continued entry into the UK radiotherapy study (CR07) is encouraged.

Post-operative radiotherapy

Meta-analysis of the post-operative radiotherapy trials also shows an effect on local recurrence, but the evidence is less consistent and the size of benefit is smaller (33% reduction SD 11%, p=0.003) than for pre-operative radiotherapy. No effect on survival has been confirmed. The combination of chemotherapy with radiotherapy has been shown to improve survival (Krook et al 1991 III) and has been the standard American pattern of care for Dukes B and C rectal cancer since the 1990 NIH consensus statement (IV). This has evolved into a combination of 5FU by infusion during radiotherapy with improvement in relapse and overall survival (O'Connell et al 1994 Ib). The question remains as to whether the improved survival was due to the synergy of 5FU and radiotherapy or simply an effect of improved chemotherapy. The NSABP R-02 trial shows that the addition of post-operative radiotherapy to chemotherapy only reduced local recurrence (13% to 8%, p=0.02) but had no effect on relapse free survival or overall survival. However, the more effective 5FU + LV (leucovorin) chemotherapy did improve survival (Wolmark et al 2000 Ib). Thus the evidence for the benefit of adjuvant chemotherapy in rectal cancer is increasing, while the evidence for post-operative radiotherapy seems to indicate that it only has an effect on local recurrence.

The toxicity of post-operative radiotherapy is significant. There is an increased likelihood of small bowel being in the radiation field. Grade 3/4 toxicities are seen in over 70% of patients with leucopenia (23-33%), and diarrhoea (37-49%) being most frequently reported (Tepper et al 1997 Ib).

Pre or post operative radiotherapy

The weight of evidence is that pre-operative radiotherapy in rectal cancer has a greater effect on local recurrence than post operative radiotherapy. Pre-operative radiotherapy also has a small effect on overall survival which is not the case for post-operative radiotherapy as distinct from chemotherapy. The additional argument for using pre-operative radiotherapy is that it results in a separation in time between the pre-operative radiotherapy and the post-operative adjuvant chemotherapy and thereby a reduction in toxicity.

Patients with mobile rectal cancer should be considered for entry into clinical trials of pre-operative radiotherapy.

Recommendation grading: C

Patients in whom the tumour is tethered or in whom local imaging indicates a high risk of incomplete resection should be selected for long course pre-operative radiotherapy to obtain tumour downstaging.

Recommendation grading: B

Pre-operative radiotherapy using short course (25 Gy in 5 fractions in one week) or longer course (40-45 Gy in 20-25 fractions over 4-5 weeks) are both acceptable.

Recommendation grading: A

In patients who have not had pre-operative radiotherapy, post operative radiotherapy and chemotherapy should be considered for patients with well established predictors of risk for tumour recurrence (e.g. evidence of tumour at the circumferential resection margins or radial margins of less than 1mm).

Recommendation grading: A

Post-operative radiotherapy doses should be 40-50 Gy in 20-25 fractions or a suitable biological equivalent using a planned volume.

Recommendation grading: B

A planned radiotherapy volume using three or four fields is recommended as this results in less morbidity and mortality.

Recommendation grading: B

Patients with potentially operable rectal cancer should always be considered for entry into trials of adjuvant radiotherapy.

Recommendation grading: B

xii) Treatment of Advanced Disease

a) Locoregional recurrence
b) Inoperable primary disease
c) Metastatic disease
d) Palliative care

a) Locoregional recurrence

The three-year survival of patients with locoregional recurrence of colorectal cancer is in the region of 10% (Nicholls 1986 III). There is some evidence that resection of locally recurrent disease may improve survival (Schiessel et al 1986 III, Pollard et al 1989 III), but this has not been proven in a randomised trial. Pre-operative chemoradiation prior to surgical resection of recurrent disease has increased resectability rates to 60% (Rodel et al 2000 III) but remains unproven in Phase 3 trials. A systematic review of the literature has been performed to attempt to define the optimal radiotherapy dose for symptomatic treatment of recurrent disease (Wong et al 1998 IIa). No randomised trials were identified. Symptom relief occurred in around 70-80% of patients after radiotherapy but the median duration of relief was only 3 months with between 25 and 50% being symptom free at 6 months in different series.

b) Inoperable primary disease

Inoperable primary disease is commonest in the rectum, and is associated with a very poor prognosis (Baigrie & Berry 1994 III). There is no evidence that palliative resection improves survival (Baigrie & Berry 1994 III). In a group of patients, clinically irresectable tumours may be rendered operable by radiotherapy (Brierley et al 1995 IIa, MRC Rectal Cancer Working Party Ib 1996, Marsh et al 1994 Ib), and such patients have a much better prognosis than those whose tumours remain in-situ (Påhlman & Glimelius 1992 III). Currently, trials are underway investigating the role of combined chemoradiation schedules to downstage such patients prior to attempted resection.

For patients unfit for such an approach, palliation is the objective of therapy. In the patient with an inoperable obstructing rectal cancer, a defunctioning colostomy, preferably in the form of a Hartmann's procedure, may provide useful palliation. Transanal tumour ablation using laser, electrocoagulation or resectional techniques may provide better palliation, and should be considered in these cases (Baigrie & Berry 1994 III). Radiotherapy is useful for relieving pelvic pain (Sischy et al 1982 III); side effects can occur (Puthwala et al 1982 III) and duration of relief is relatively short lived. Chemotherapy alone may be useful in the presence of metastatic disease (see next section), but local treatments for the primary tumour may still need to be considered.

For fit patients with inoperable rectal carcinoma without evidence of metastatic disease, primary radiotherapy alone or in combination with chemotherapy should be considered

Recommendation grading: B

c) Metastatic disease

The liver followed by the lung are the commonest sites for metastatic colorectal cancer. In most instances, systemic treatment is the only therapeutic option, although in a small number of cases surgical excision of metastases or in-situ destructive therapy may be feasible.

Patients with a small number of metastases in the liver or lung may benefit from appropriate resection, and with careful patient selection, hepatectomy for colorectal metastases can be associated with a 5 year

survival of around 33% (Scheele et al 1990 III). The hypothesis that this approach prolongs life has not been tested by a randomised trial, but a retrospective review of 2040 patients with metachronous isolated hepatic metastases compared the outcome of those who did not undergo resection with those who did. After resection of hepatic metastases mean survival was 31 months (projected 5 year survival 26%) compared with those (887) who did not have resection whose mean survival was 11 months (projected 5 yr survival 2%, p<0.001) (Wade et al 1996 III). Non-randomised evidence exists to support the use of pre-operative chemotherapy prior to resection in those with potentially operable liver metastases (Giachetti et al 1999 III). It is important to note that good results from this type of intervention depend on a low operative mortality, and it should only be attempted where this can be achieved.

In-situ destructive therapies (interstitial laser ablation, cryotherapy, radiofrequency ablation) have been in use over the last decade for colorectal liver metastases. In Phase 2 trials in excess of 50% of patients are alive at two years, which compares favourably with systemic chemotherapy (Seifert & Morris 1998 III, Curley et al 1999 III, Rossi et al 1996 IIb). However, patient selection for fitness to travel for invasive therapy and metastases limited to the liver will affect this. There is no Phase 3 evidence of benefit. These therapies require further evaluation in the context of Phase 3 trials.

A meta-analysis of 5 trials of palliative chemotherapy (3 systemic, 2 regional chemotherapy, Sheithauer et al 1993 Ib, NGTATG 1992 Ib, Beretta et al 1994 III, Allen-Mersh et al 1994 IIb) has demonstrated an improved survival with chemotherapy compared with best supportive care (p=0.0002). The evidence indicates that early chemotherapy prior to clinical deterioration for advanced disease improves survival by 3 to 6 months without any adverse impact on quality of life (NHS Exec 1997 IV, CCCG 2000 Ia). In patients with stable or responding disease after 12 weeks therapy, a rest from treatment with close observation until disease progression is not detrimental to survival and contributes to improved quality of life (Maughan 2001Ib).

Selection of patients for chemotherapy requires the opinion of an oncologist experienced in colorectal cancer chemotherapy. Poor performance status, low serum albumin, high alkaline phosphatase and liver involvement were independent predictors of progression, and low serum albumin, high glutamyl transferase and high CEA predicted for poor survival (Fontzilas et al 1996 III). Performance status is a particularly potent indicator. In a meta-analysis of patients treated in trials of 5FU based chemotherapy, median survivals were 4, 10 and 14 months for patients with ECOG performance status scores of 2,1 and 0 respectively (Thirion et al 1999 Ia). However, whilst these variables may help in identifying patients with an overall poor prognosis, they do not necessarily predict who will or will not benefit from chemotherapy.

The mainstay of treatment is still 5 fluorouracil. The following conclusions can be drawn regarding 5FU therapy in metastatic colorectal cancer:

1. Infusional regimens (at least 24h duration) of 5FU doubles response rate (23% v 13% P<0.003) compared with bolus regimens with a small improvement in median survival (Meta-Analysis Group in Cancer (MGC), 1998 Ib) and reduced toxicity (MGC, 1998, IIa).

2. Hepatic arterial infusion (HAI): HAI with 5FU or FUDR increases response rate for isolated hepatic metastatic disease from 14% to 41% (p< 0.0001) compared with IV regimens (MGC 1996 IIa). No survival advantage is proven at present.

3. Biomodulation is the use of a second agent to modulate the cellular response to 5FU therapy. Biomodulation of 5FU with Folinic Acid doubles response rates and has become a standard component of therapy (23% v 11% p< 0.0001.) (ACCMP 1992 IIa). Low dose folinic acid has been shown to be as effective as high dose when used in combination with bolus regimens of 5FU.

4. Combined therapy with established drugs. The combination of protracted venous infusion of 5FU with mitomycin C (1 RCT) has shown improved response rate, progression free survival and survival compared with 5FU alone (Ross et al 1997 Ib). Biomodulation of 5FU with Methotrexate doubles response rate (19% v 10% p< 0.0001) with a small improvement in survival. (Median survival 10.7 v 9.1 mo p 0.02) (NHS Exec 1997 IV). It has not been shown to be superior to folinic acid modulation. Neither cisplatin nor interferon have been shown to be beneficial when combined with 5FU (NHS Exec 1997 IV).

Patients with metastatic disease who are fit for active therapy should be accurately staged with CT scans of abdomen and thorax.

Recommendation grading: ✓

Patients with evidence of unresectable metastatic disease should be referred to an Oncologist for consideration of palliative chemotherapy as soon as the diagnosis of metastatic disease is made

Recommendation grading: A

Chemotherapy for metastatic colorectal cancer should only be given after discussion at the Multi Disciplinary Team Meeting and under the direction of recognised Clinical and Medical Oncologists within facilities conforming to JCCO guidelines

Recommendation grading: C

Entry into clinical trials evaluating the benefits of novel chemotherapy regimens in colorectal should be encouraged

Recommendation grading: C

On current evidence, standard therapy should include an infusional 5FU regimen combined with the use of irinotecan (see below) in first line or on 5FU failure if the patient remains fit for chemotherapy (Performance Score 0~1)

Recommendation grading: A

Hepatic arterial infusional chemotherapy remains of unproven benefit

Recommendation grading: A

Patients with metastatic disease limited to the liver which is potentially resectable should be considered for partial hepatectomy by an experienced liver surgeon

Recommendation grading: B

New chemotherapy agents.

A number of new chemotherapy agents have been evaluated in the last five years.

1. *Thymydilate synthase (TS) targeted chemotherapy.*
   A number of new agents have been evaluated which also target TS. These include 5FU prodrugs (e.g.UFT, Capecitabine) and agents using the reduced folate pathway (raltitrexed). No evidence of increased efficacy over optimal usage of 5FU has been demonstrated for any of the agents to date. Equivalent survival benefit with increased ease of administration has been documented for capecitabine and UFT with respect to bolus 5FU and low dose folinic acid (Pazdur et al 1999 Ib, Carmichael et al 1999 Ib, Twelves et al 1999 Ib, Cox et al 1999 Ib). For raltitrexed, equivalent survival and response rates have been demonstrated (Cunningham et al 1996 Ib, Cocconi et al 1998 Ib, Pazdur & Vincent 1997 Ib, Maughan et al 1999 Ib) but with increased toxicity when compared with infusional 5FU schedules (Maughan et al 1999 Ib). Treatment related deaths range from 3~6% in the trials and particular attention to renal function, patient selection and supervision is required for safe usage of this agent.

2. *Irinotecan.*
   Irinotecan is a topoisomerase~1 inhibitor. In second line therapy, two RCTs show improved survival for chemotherapy with single agent irinotecan in 5FU refractory patients versus best supportive care

(Cunningham et al 1998 Ib) and versus alternative F5U regimens (Rougier et al 1998 Ib) with maintained quality of life. In first line therapy, two RCT's show improved response rate, progression free and overall survival using irinotecan in combination with 5FU for metastatic disease (Douillard et al 2001 Ib, Saltz et al 2001 Ib). Side effects of irinotecan include diarrhoea, myelotoxicity, alopecia and anticholinergic syndrome.

3. *Oxaliplatin*
Oxaliplatin is a novel platinum agent which acts by DNA cross linking. In second line therapy: Phase 2 trials show activity in 5FU refractory colorectal cancer by the addition of Oxaliplatin to a 5FU regimen (Raymond et al 1998 Ib). In first line therapy, two RCTs show improved response rate and progression free survival using oxaliplatin in combination with 5FU in first line treatment versus 5FU alone, but no overall survival benefit has been documented, though a high proportion of patients crossed over to the combination therapy on progression (de Gramont et al 2000 Ib, Giacchetti et al 1997 Ib). Side effects of oxaliplatin include some enhanced 5FU toxicity (diarrhoea, mucositis, hand foot syndrome, myelotoxicity), nausea, vomiting and a reversible cold induced sensory neuropathy.

d) 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. Cancer patients 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 cancer 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 and expert control of symptoms are 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 grading: B

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

Recommendation grading: 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.

Recommenation grading: C

Outcome

i) Operative mortality

Operative mortality for operations for colorectal cancer varies according to whether the operation category is elective or emergency, and whether it is curative or palliative. Even so, there is considerable variability amongst surgeons for curative resection, with 30-day mortality ranging from 0 to 20% (McArdle & Hole 1990 IIb). Overall, the Trent/Wales audit (Ib) revealed an operative mortality of 7.6%; this was 19.9% for emergency surgery and 5.1% for elective surgery. The Wessex audit figures (Ib) were almost identical. A very similar overall operative mortality of 8.6% was reported from the Birmingham Cancer Registry despite going back to 1957 (Allum et al 1994 IIb). Even specialist centres report operative mortality rates in the region of 4% for elective resections, although it can be as low as 1.5% (Matheson et al 1985 III). Patient factors such as age, urgency of operation and Dukes' stage have a major effect on mortality and risk models to adjust for such factors should be taken into account when assessing outcomes (Stamatakis et al, 2000 IIb).

Surgeons and others should be wary of over-interpreting small datasets as it is well documented that wide variations in outcome may occur (Poloniecki 1998 IIb; Marson 1997 IIb; Parry 1998 IIb). This may lead to considerable differences in outcomes achieved by different surgeons within a single year. In many cases these variations will disappear with time or as increasing numbers of patients are audited, as shown in the Lothian audit (Marson 1997 IIb). The minimum number of colorectal cancer cases required for reliable individual comparisons will depend on the frequency of the adverse event of interest. For example, to accurately assess inter-surgeon variation in peri-operative mortality around 150 cases for each surgeon will be required.

It is recommended that surgeons should expect to achieve an operative mortality of 15-25% for emergency surgery and 3-7% for elective surgery for colorectal cancer.

Recommendation grading: B

In an increasingly elderly population access to Intensive Care and High Dependency Care facilities in hospitals undertaking colorectal cancer resections is necessary.

Recommendation grading: ✓

ii) Wound Infection

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).

It is therefore recommended that wound infection rates after elective surgery for colorectal cancer should be less than 10%.

Recommendation grading: A

iii) Anastomotic dehiscence

Anastomotic dehiscence is a major source of operative morbidity and mortality after resection for colorectal cancer. 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%. It is of interest that the leak rate seen in the audits was better than the 13% rate seen in the Large Bowel Cancer project in 1980, but review of the literature indicates that even better results can be achieved by individual surgeons, with overall rates as low as 1.5% having been reported (Matheson et al 1985 III). It must be stressed, however, that ultra low stapled anterior resection tends to be associated with leakage rate in the region of 10-20%, even when the same surgeon has very acceptable leakage rates from other types of resection (Karanjia et al 1994 III). A defunctioning stoma can ameliorate the consequences of leakage (Karanjia et al 1994 III), and its use is recommended in such operations (vide supra).

On the basis of the Trent/Wales and Wessex audits, therefore, it is recommended that 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. However, surgeons performing appreciable numbers of ultra low pelvic anastomoses can expect a higher leak rate for this procedure, and the judicious use of a defunctioning stoma is recommended.

Recommendation grading: B

iv) Recurrence rates:

As indicated in the sections on surgical technique and adjuvant therapy, local recurrence after resection of rectal cancer may be influenced by stage of disease and surgical technique and the use of radiotherapy (vide supra). Current evidence suggests that, with the use of optimal surgical techniques and preoperative radiotherapy for tethered or fixed tumours, local recurrence rates of less than 10% should be achieved after curative resections.

It is therefore recommended that surgeons should audit their results, and aim to achieve local recurrence rates after curative resection of less than 10% within two years.

Recommendation grading: A

v) Survival Rates

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

It is recommended that the survival rates of patients with colorectal cancer should be audited locally by the Multi Disciplinary Team and Cancer Networks, national audit may be possible in the future.

Recommendation grading: ✓

Manpower resources and information technology facilities are required to allow this essential part of colorectal cancer care.

Recommendation grading: ✓

FOLLOW-UP

Access

Reasons for Follow-up

There is continuing debate on the subject of patient follow up after curative treatment for colorectal cancer despite a substantial new literature since publication of the last guidelines. Possible benefits from long-term follow up are:

a) Detection of potentially curable recurrent disease.
b) Detection of asymptomatic recurrence when early chemotherapy may improve quality of life and prolong survival.
c) Detection of metachronous tumours.
d) Provision of psychological support by patient / doctor contact.
e) Facilitation of audit, clinical governance and continuing professional development.

a) Detection of potentially curable recurrent disease

Two substantial literature reviews conclude that there is a lack of evidence to either confirm or refute the premise that follow-up detects potentially recurrent disease (Richard & McLeod 1997 Ia, Edelman et al 1997 Ia). 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 (Kejeldsen 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 (Moertel et al 1993 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.

A minority of surgeons include liver scans as part of routine follow up (Mella et al 1997 IIb, Virgo et al 1995 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 the issue. Inclusion of an annual liver CT scan for patients in the intensive arm of the Australian randomised trial of intensive vs 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 very 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 (SHPIC report 1999 IV, Haward 1997 IV, 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 1-3% of patients. It is therefore reasonable to maintain the initial guideline, to suggest such a scan in asymptomatic patients at some time in the first two post-operative years after curative resection. It must be stressed, however, that the optimal timing and frequency of this investigation has not been determined and more information on which to base the recommendation is urgently required.

b) 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, prolongs survival compared with delaying chemotherapy until symptoms develop The Nordic Gastrointestinal Tumour Adjuvant Therapy Group 1992 Ib, Scheithauer et al 1993 Ib). Quality of life measurements in these studies also favour early chemotherapy for asymptomatic disease. A further study found that hepatic intra arterial chemotherapy prolonged survival and improved quality of life compared with best supportive care (Allen-Mersh et al 1994 Ib).

These innovative studies should encourage future trials of follow up for colorectal cancer to address the issues of early or delayed chemotherapy to prolong and improve quality of life, in addition to the usual but more restricted question of achieving a cure from further surgery.

c) 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 preoperatively should undergo early (within 6 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 three to five yearly intervals (Brady et al 1990 III, Winawar et al 1993 Ib, Kronberg et al 1983 IV, Barlow & Thompson 1994 IV). If adenomatous polyps are found, the examination should be repeated sooner. 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.

d) 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.

e) Facilitation of audit, quality assurance and clinical governance

Audit is the only means by which clinical outcomes can be measured and it is likely to underpin the new initiative of 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 2000 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 on 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.

The 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 liver imaging to asymptomatic fit patients during the first two years after resection for the purpose of detecting operable liver metastases.

Recommendation grading : B

There is no evidence that colonoscopic follow-up improves survival, but it has been shown to produce a high yield of treatable adenomatous polyps and cancer. If such a

policy is pursued, it is recommended that a "clean" colon should be examined by colonoscopy at 3~5 year intervals. Patients should be counselled as to the risks from 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. 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 use of a database, such as that promoted by the Association of Coloproctology. If other "local" databases are used it is recommended that field definitions should match those of the Association's data dictionary to ensure conformity of data collection (see Appendix 4).

Recommendation grading : **C**

All patients should have ready access to specialist nursing staff throughout the period of follow up.

Recommendation grading : **C**

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

i) Local resections

This includes polyps excised endoscopically which are found to be malignant on subsequent histological examination and sessile tumours which are electively treated by formal surgical transanal excision. In each case it is essential that the pathologist assesses all excision lines. For polypectomy specimens this requires careful examination of the stalk and the base of the polyp, usually requiring multiple sections. For formal excisions it is important to assess the whole of the deep resection plane, and for the pathologist to be able to do this adequately the surgeon should pin the specimen out on a cork mat before fixation, so that multiple properly orientated blocks can be taken for histological examination.

When invasive malignancy is identified in a polypectomy or formal excision specimen, more radical surgery is indicated if:

- there is doubt about completeness of excision of the carcinoma
- there is invasion of the muscularis propria
- the invasive tumour is poorly differentiated (criteria of Morson 1985 IIb)

The pathology report of a locally resected carcinoma must therefore make specific mention of each of these parameters.

There is considerable evidence to suggest that lymphatic or vascular invasion in the submucosa (including the polyp stalk) is also an indication for further surgery (Coverlizza et al 1989, IIb), but this has not been confirmed in other studies (Geraghty et al 1991 IIb). There is also some controversy over the management of locally excised pT1 tumours in which the carcinoma invades the full thickness of the submucosa (so-called Kikuchi type Sm3 tumours), some authorities also regard this as an indication for further surgery (Kikuchi et al 1995 IIB)

ii) Full Resection Specimens

It is important to know if a tumour has been completely excised and how advanced it is, as both of these parameters may affect further treatment. In order to provide this information, there must be proper fixation of the specimen and careful pathological dissection prior to selecting tissue blocks for histology. In order to assess the circumferential resection margin in rectal cancers, it is strongly recommended that this margin is painted with ink before sectioning and slicing at 3-4mm transversely through the whole of the tumour and the entire mesorectum distally and proximally. Dukes staging requires the separate identification of the "apical" lymph node, i.e. the node closest to the main vascular ligature.

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 as set out below.

Joint National Guidelines Minimum Dataset for Colorectal Cancer Histopathology Reporting

These proposals for reporting of colorectal cancer should be implemented for the following reasons:

1. Patients who have lymph node involvement (Dukes stages C1 & C2, TNM stages pN1, pN2) are likely to receive adjuvant chemotherapy which is of possible benefit, mildly toxic and costly (Moertel et al 1995 Ib, IMPACT 1995 Ib).

2. Patients with rectal adenocarcinoma and circumferential margin involvement are at high risk of local recurrence (Quirke et al 1986 IIb, Adam et al 1994 IIb, Ng et al 1993 IIb) and may receive post-operative radiotherapy +/- chemotherapy which is toxic and costly but may decrease the likelihood (MRC Rectal Cancer Working Party 1996 Ib, Thomas & Linbald 1988 Ib) of death from this unpleasant and nearly uniformly fatal complication. The frequency of circumferential margin involvement found may indicate the quality of rectal cancer surgery being performed (Quirke 1997 IIb).

3. To confirm that radical surgery was necessary and to place the patient in the appropriate stage so that the individual can be given a prognosis and surgeons can accurately audit their outcomes avoiding case mix selection bias.

4. To identify whether the anal sphincter has been lost. The frequency of abdomino-perineal resections may be an indicator of the quality of surgery.

5. To allow the equitable comparison of surgeons in colorectal cancer audits (McArdle & Hole 1991 IIb, Hermanek et al 1995 IIb) to identify good surgical practice (Quirke 1997 IIb) and the comparison of patients in clinical trials.

The form reproduced on the next page has been devised to include the minimum amount of data required for a careful assessment of a colorectal cancer specimen. It is evidence based and has been widely discussed. It has been approved by the Royal Colleges of Pathologists and Surgeons (England), the Associations of Coloproctology and Clinical Pathologists, The United Kingdom Coordinating Committee for Cancer Research Colorectal Cancer Subcommittee, the Scottish Intercollegiate Guidelines Network, the Welsh CROPS Project, the UK Association of Cancer Registries and the Pathology Section of the British Society of Gastroenterology. We strongly recommend its use as a minimum dataset.

JOINT NATIONAL GUIDELINES MINIMUM DATA SET
COLORECTAL CANCER HISTOPATHOLOGY REPORT

Surname _____ Forenames _____ Date of birth _____ Sex ____

Hospital _____ Hospital No. _____ NHS No _____

Date of receipt _____ Date of reporting _____ Report No _____

Pathologist _____ Surgeon _____

Gross Description

Metastatic Spread

Site of tumour _____

Maximum tumour diameter _____

Distance of tumour to nearer margin (cut end) ____

Presence of tumour perforation (pT4) [ ] Yes [ ] No

For rectal tumours

Tumour is [ ] above [ ] at [ ] below
the peritoneal reflection

Distance from the dentate line _____

Yes No

Histology

Type

Adenocarcinoma [ ] Yes [ ] No
(to include mucinous and signet ring adenocarcinomas)

If No, other _____

Differentiation by predominant area
[ ] Well/moderate [ ] Poor

Local Invasion
[ ] Submucosa (pT1)
[ ] Muscularis propria (pT2)

[ ] Beyond muscularis propria (pT3)
[ ] Tumour cells have breached the peritoneal surface
or invaded adjacent organs (pT4)

Margins

Tumour involvement	N/A	Yes	No
Doughnut	[ ]	[ ]	[ ]
Margin (cut end)	[ ]	[ ]	[ ]
For rectal tumours	[ ]	[ ]	[ ]
Circumferential margin involvement	[ ]	[ ]	[ ]

Histological measurement from tumour to circumferential margin .....mm

No of lymph nodes examined _____

No of positive lymph nodes _____

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

	Yes	No
Apical node positive (Dukes C2)	[ ]	[ ]
Extramural vascular invasion	[ ]	[ ]

Background Abnormalities

Adenoma(s)	[ ]	[ ]
Synchronous carcinomas(s) (Complete a separate form for each cancer)	[ ]	[ ]
Ulcerative colitis	[ ]	[ ]
Crohn's disease	[ ]	[ ]
Familial adenomatous polyposis	[ ]	[ ]

Other comments _____

Pathological Staging

Complete resection at all margins [ ] Yes [ ] No

TNM

[ ] T [ ] N [ ] M

Dukes

[ ] Dukes A (Growth limited to wall, nodes negative)

[ ] Dukes B
(Growth beyond muscularis propria, nodes negative)

[ ] Dukes C1
(Nodes positive and apical node negative)

[ ] Dukes C2 (Apical node positive)

Histologically confirmed liver metastases [ ] Yes [ ] No

Signature _____ Date ____/____/____ SNOMED Codes ____/____

NOTES ON RECORDING OF DATA ITEMS

Please record data items for all primary colorectal cancers as follows, with all measurements in mm.

GROSS DESCRIPTION

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

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

Distance of tumour to nearest margin

Measured from the nearest cut end of the specimen, not the circumferential margin. It is only necessary to examine the margins histologically if tumour extends macroscopically to within 30mm of one of these. 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

If the tumour has perforated into the peritoneal cavity this should be recorded. Such cases are always regarded as pT4 in the TNM staging system (page 54). If perforation does not involve the tumour the "No" box should be marked.

FOR RECTAL TUMOURS

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 Fig. 1).

Rectal tumours are classified according to whether they are:

a) entirely above the level of the peritoneal reflection anteriorly

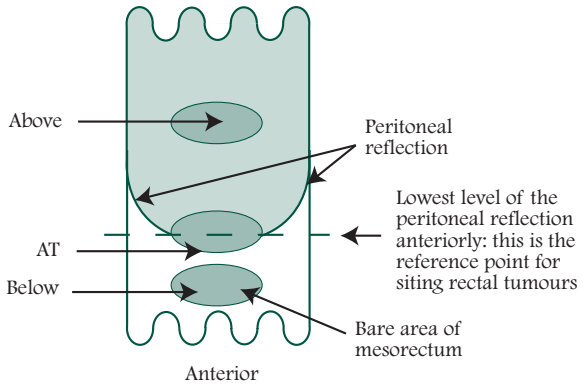
b) astride (or at) the level of the peritoneal reflection anteriorly

c) entirely below the level of the peritoneal reflection anteriorly

Tumours below the peritoneal reflection have the highest rates of local recurrence.

Fig. 1

Site of tumour in relation to the anterior level of the peritoneal reflection:



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.

HISTOLOGY

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)
- adenocarcinoid (composite carcinoma/carcinoid) tumours
- small cell carcinomas
- totally undifferentiated carcinomas

Mucinous carcinomas and signet ring carcinomas are recorded as adenocarcinomas.

Differentiation by Predominant Area

Poorly differentiated carcinomas should be separated from other types, but only if this forms the *predominant* area of the tumour. 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.

The criteria for poorly differentiated tumours are either irregularly folded, distorted and often small tubules or the absence of any tubular formation.

Invasion

The *maximum* degree of local invasion into or through the bowel wall is recorded, so only one of the four boxes should be marked.

Sufficient blocks of the tumour should be taken to assess this carefully. It is recommended that the whole tumour and attached mesentery (or mesorectum) are serially sliced at 3-4 mm intervals with a sharp knife in order to identify macroscopically the areas of deepest invasion, which should be blocked for histological confirmation.

Involvement of the serosal (peritoneal) surface is defined as the presence of tumour cells on the peritoneal surface. Thus tumour cell penetration of the serosa needs to be seen by penetration or ulceration. Note that this does not constitute circumferential margin involvement since there is no involvement of a retroperitoneal margin.

Margins

Doughnuts

Strictly speaking, it is not necessary to examine doughnuts histologically if the main tumour is >30mm from the cut end of the main specimen or in other rare cases described above but this is a decision to be made locally.

When doughnuts from stapling devices are examined histologically the presence or absence of tumour is recorded. If doughnuts are not sectioned because it is deemed unnecessary locally, or if no doughnuts are submitted for examination by the surgeon, this item should be recorded as not applicable.

Margin (cut end)

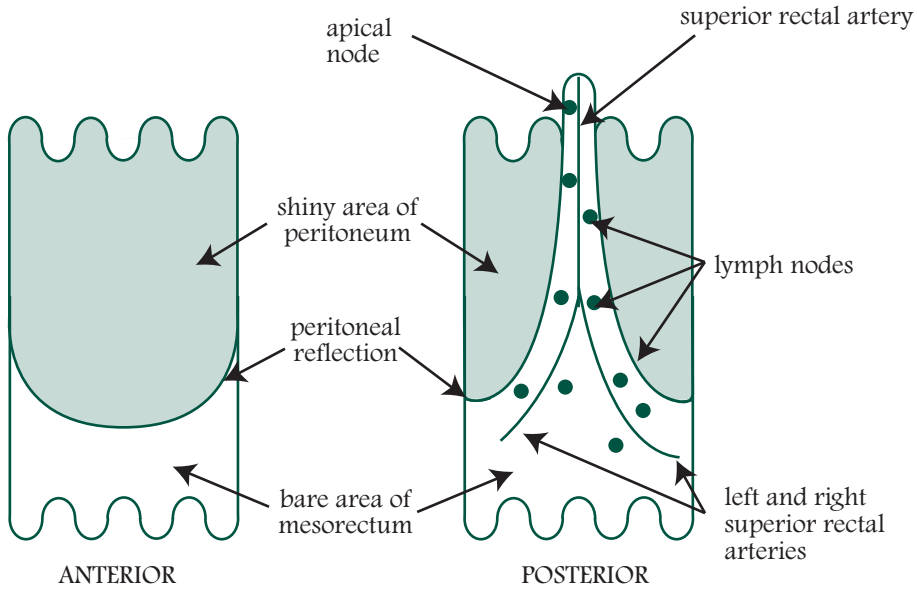
When cut ends are examined histologically (see criteria above) the presence or absence of tumour should be recorded. If margins are not examined histologically they should be recorded as not applicable.

Circumferential Margin (Rectal cancers only)

Accurate assessment of the circumferential (radial) margins of these rectal tumours is very important because it influences post-operative therapy.

Note that the circumferential margin is reported only for rectal cancers; for tumours at other sites the "not applicable" box is marked. It represents involvement of the surgical margins of the connective tissues around the rectum in an area where there is no peritoneal covering, i.e. the unshaded area in Fig. 2. Hence involvement of this margin is different from, and quite unrelated to, serosal involvement.

Fig. 2

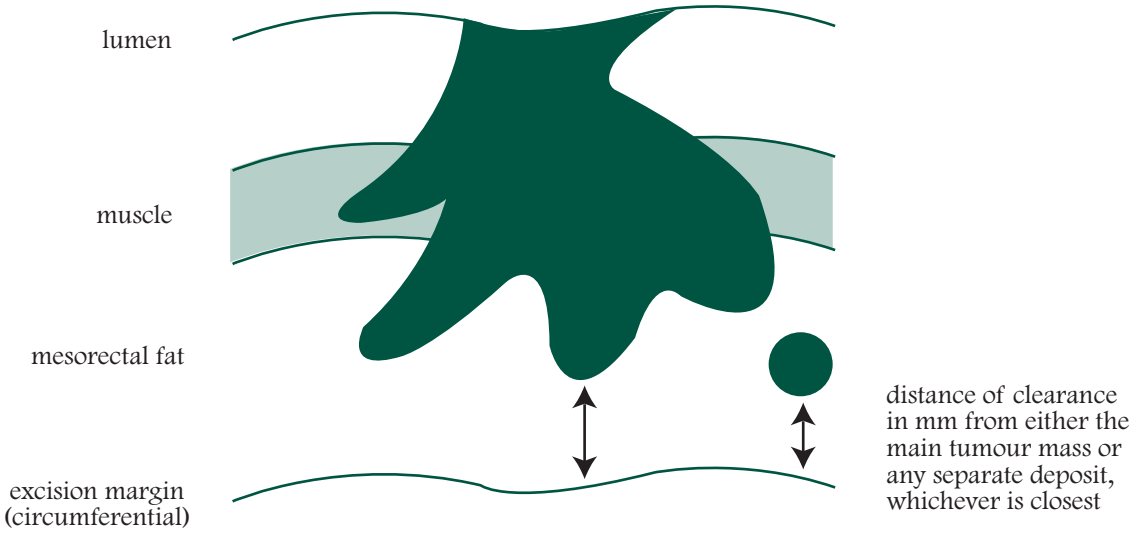


Anteriorly the rectum is covered by peritoneum and only the area below the peritoneal reflection (unshaded in Fig. 2) is at risk of circumferential margin involvement. Posteriorly this area, and the area above it, a triangular shaped bare area running up to the start of the sigmoid mesocolon, are at risk from not only direct tumour spread but also metastatic deposits in lymph nodes that lie against the circumferential margin.

It is recommended that the whole of this margin (i.e. the mesorectum) is painted with a marker such as silver nitrate or India ink before dissecting the specimen. The tumour is then best sliced serially at 3-4 mm intervals to select blocks from areas that are closest macroscopically to the circumferential margin. Slices should then be made of the area above and below the tumour to look for metastatic deposits. If lymph nodes lie against the circumferential margin then this margin should be included in the block.

The minimum distance between the tumour and the circumferential margin in millimetres is also recorded from the histological slides (see Fig. 3). If this is <1 mm then the circumferential margin is *regarded as involved* in the assessment on 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.

Fig. 3



Metastatic Spread

Number of lymph nodes examined
All lymph nodes found in the specimen should be sampled and counted, regardless of their site or size.

Number of positive lymph nodes
This must be equal to or less than the number of lymph nodes sampled.

Extramural tumour deposits measuring >3 mm are counted as involved lymph nodes even if no residual lymph node structure can be identified. Smaller deposits are regarded as apparent discontinuous extensions of the main tumour.

In the TNM staging system, pN1 corresponds to involvement of 1-3 nodes and pN2 to involvement of 4 or more nodes (A previously used pN3 category was dropped in the 1997 TNM revision).

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

Background Abnormalities

The presence or absence of the following in the background bowel is recorded:

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

PATHOLOGICAL STAGING

It is recommended that Dukes' and TNM staging is used. The proforma is designed for both systems. Complete resection at all margins

This includes the doughnuts, the ends of the specimen and, for rectal tumours, the mesorectal circumferential resection plane.

Where doughnuts and the ends of the specimen are not examined histologically because the tumour is >30 mm away these are assumed to be tumour-free. Circumferential margins of rectal tumours are regarded as involved if tumour extends histologically to <1 mm from this margin. Peritoneal (serosal) involvement alone is not reason to categorise the tumour as incompletely excised.

TNM

Here the T stage and the N stage are derived from the extent of local spread and lymph node metastases, the criteria for each stage being defined on the form. The appropriate figure is entered in each box. The pre-fix "p" is used to indicate pathological staging. If the patient has had preoperative chemotherapy or radiotherapy then the prefix "yp" should be used to indicate the stage found may not be the presenting stage of the tumour.

The following should be noted:

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 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 Pre-operative radiotherapy (including short course) diminishes lymph node yield and downstages tumours. Identification of such tumours is essential in comparing outcomes. The pathological staging of these tumours can be identified by insertion of a y prefix (fro example a "pT3" tumour becomes a "ypT3" tumour to indicate that this tumour has received per-operative irradiation. (TNM classification of Malignant Tumours 5th edition III).

vi 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 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, 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 counted as distant metastases and hence pM1.

Dukes

Here one of the four boxes is marked, corresponding to the Dukes' stage. Criteria used for Dukes' staging are given on the form. Note that Dukes' so-called stage D is not used.

Histologically confirmed liver metastases

Here one of the two boxes is marked. If no liver biopsy is submitted with the resection specimen then the "No" box is marked.

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

Recommendation grading: 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 grading: 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 grading: 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 grading: B

REFERENCES

Abulafi AM, Williams NS. Local recurrence of colorectal cancer: the problem, mechanisms, management and adjuvant therapy. Br J Surg 1994; 81: 7-19

ACCMP (Advanced Colorectal Cancer Meta-analysis Project). Modulation of 5-fluorouracil in patients with advanced colorectal cancer: evidence in terms of response rates. J Clin Oncol 1991; 10: 896-903

Adam IJ, Mohamdee MO, Martin IG et al. Role of circumferential margin involvement in the local recurrence of rectal cancer. Lancet 1994; 344: 707-711

Allen-Mersh TG, Earlam S, Fordy C et al. Quality of life and survival with continuous hepatic-artery floxuridine infusion for colorectal liver metastases. Lancet 1994; 344: 1255-1260

Allum WH, Slaney G, McConkey CC et al. Cancer of the colon and rectum in the West Midlands, 1957-1981. Br J Surg 1994; 81: 1060-1063

Allum WH, Mack P, Priestman TJ, et al. Radiotherapy for pain relief in locally recurrent colorectal cancer. Ann R Coll Surg Engl 1987; 69: 220-221

Al-Shahi R & Warlow C. Using patient-identifiable data for observational research and audit. (Editorial) Br Med J 2000; 321:1031-1032.

Atkin WS, Morson BC, Cuzick J. Long term risk of colorectal cancer after removal of rectosigmoid adenomas. N Engl J Med. 1992; 326:658-662.

Atkin WS, Hart A, Edwards R et al. Single blind randomised trial of efficacy and acceptability of oral picolax versus self administered phosphate enema in bowel preparation for flexible sigmoidoscopy screening BMJ 2000; 320 (7248):1504-8.

Baig MK, Marks CG. Referral Guidelines for colorectal cancer, a threat or a challenge? Hospital Med 2000; 61(7):452-453.

Baigrie RJ, Berry AR. Management of advanced rectal cancer. Br J Surg 1994; 81: 343-352

Banerjee AK, Jehle EC, Shorthouse AJ et al. Local excision of rectal tumours. Br J Surg 1995; 82: 1165-1173

Barillari P, Ramacciato G, De Angelis R et al. Effect of preoperative colonoscopy on the incidence of synchronous and metachronous neoplasms, Acta Chir Scand 1990; 156: 163-166

Barlow AP, Thompson MH. Colonoscopic follow-up after resection for colorectal cancer : a selective policy. Brit J Surg 1993; 80: 781-784

Barr LC, Skene AI, Meirion Thomas J. Metastasectomy. Br J Surg 1992; 79: 1268-1274

Barratt PL, Seymour MT, Stenning S et al. Molecular markers to predict survival and benefit from adjuvant intraportal 5FU in colon cancer. Proc ASCO 1999; abs. 1030

Beart RW, Kelly KA. Randomised prospective evaluation of the EEA stapler for colorectal anastomoses. Am J Surg 1981; 141: 143-147

Beets-Tan RGH, Beets GL, Vliegen RFA et al. Accuracy of magnetic resonance imaging in prediction of tumour-free resection margin in rectal cancer. Lancet 2001; 357:497-504.

Bell GD, McCloy RF, Charlton JE et al. Recommendations for standards of sedation and patient monitoring during gastrointestinal endoscopy. Gut 1991; 32: 823-827.

Bentzen SM, Balsev I, Pedersen M et al. Blood transfusion and prognosis in Dukes' B and C colorectal cancer. Eur J Cancer 1990; 26: 457-63

Beretta G, Bollina R, Martignoni M et al. Fluorouracil + folates as standard treatment for advanced/metastatic gastrointestinal carcinomas. Annals Oncol 1994; 5: 239.

Berman JM, Cheung RJ, Weinberg DS. Surveillance after colorectal cancer resection Lancet 2000; 355:395-398.

Bowles CJA, Leicester R, Swarbrick E et al. Intercollegiate-BSG National Colonoscopy (IBNC) Audit: Methods used to identify the caecum and caecal intubation rate. Gut 2001; (Suppl 1) 48:A10/036.

Brady PG, Straker RJ, Goldschmid S. Surveillance Colonoscopy After Resection for Colon Carcinoma. Southern Medical J 1990; 83: 765-768

Brennan SS, Pickford IR, Evans M et al. Staples or sutures for colonic anastomoses - a controlled clinical trial. Br J Surg 1982; 69: 722-724

Brierley JD, Cummings BJ, Wong CS et al. Adenocarcinoma of the rectum treated by external beam radiation therapy. Int J Radiat Oncol Biol Phys 1995; 31: 255-259.

Brown G, Richards CJ, Newcombe RG et al. Rectal Carcinoma: Thin-Section MR Imaging for Staging in 28 Patients. Radiology 1999; 211:215-222.

Brown G, Richards CJ, Bourne MW et al. Rectal carcinoma: thin section MR imaging for staging in 28 patients. Radiology 1999; 357: 497-504.

Brown G, Richards CJ, Bourne MW et al, Discriminant analysis of thin slice MR imaging characteristics in detecting local lymph node involvement in patients with rectal carcinoma. Radiology 1999a; 213: 299

Bruinvels DJ, Stiggelbout AM, Kievit J et al. Follow-Up of Patients with Colorectal Cancer. A Meta-Analysis. Ann Surg 1994; 219: 174-182

Bull AD, Biffin AHB, Mella J et al. Colorectal cancer pathology reporting: a regional audit. J Clin Pathol 1997; 50:138-142.

Burke P, Mealy K, Gillen P et al. Requirement for bowel preparation in colorectal surgery. Br J Surg 1994; 81: 907-910

Burke W, Petersen G, Lynch P et al. Recommendations for follow up care of individuals with an inherited predisposition to cancer. JAMA 1997; 277: 915-919.

Burrows L, Tartter P. Effect of blood transfusions on colonic malignancy recurrence rate. Lancet 1982; ii: 662

Burt RW, Bishop T, Cannon LA et al. Dominant inheritance of adenomatous colonic polyps and colorectal cancer. New Engl J Med 1985; 312: 1540-4.

Busch ORC, Hop WCJ, Hoynck van Papendrecht MAW et al. Blood transfusions and prognosis in colorectal cancer New Engl J Med 1993; 328: 1372-1376

Buyse M. Reappraisal of hepatic arterial infusion in the treatment of nonresectable liver metastases from colorectal cancer. J Natl Cancer Inst. 1996; 88:252-258.

Byles JE, Redman S, Hennrikus D et al. Delay in consulting a medical practitioner about rectal bleeding. J Epidemiol Community Health 1992; 46:241-244.

Cali RL, Pitsch RM, Thorson AG et al. Cumulative incidence of metachronous colorectal cancer. Dis Colon Rectum 1993; 36:388-393.

Cannon-Albright LA, Skolnick MH, Bishop DT et al. Common inheritance of susceptibility to colonic adenomatous polyps and associated colorectal cancer. New Engl J Med 1988; 319: 533-537.

Cannon-Albright LA, Thomas TC, Bishop DT et al. Characteristics of familial colon cancer in a large population database. Cancer 1989; 64(9):1971-1975.

Carter DC. Lothian and Borders large bowel cancer project: immediate outcome after surgery. Br J Surg 1995; 82: 888-890

Carmichael J, Popiela T, Radstone D et al. Randomised comparative study of ORZEL(plus leucovorin versus parenteral 5FU plus LV in patients with metastatic colorectal cancer. Proc Am Soc Clin Oncol 1999; 18:1015.

Carty NJ, Keating J, Campbell J et al. Prospective audit of an extramucosal technique for intestinal anastomosis. Br J Surg 1991;78:1439-1441

Cocconi G, Cunningham D, van Cutsem E et al Open Randomised multicentre trial of raltitrexed versus fluorouracil plus high-dose leucovorin in patients with advanced colorectal cancer. J Clin Oncol 1998; 16:2943-52.

Collins R, Scrimgeour A, Yusuf S et al. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. N Engl J Med 1988; 318: 1162-1173

Colorectal Cancer Collaborative Group. Palliative Chemotherapy for Advanced Colorectal Cancer : Systematic Review and Meta-analysis. British Medical Journal 2000; 321,531-535.

Cotton PB, Williams CB. Practical Gastrointestinal Endoscopy 3rd Ed Blackwell Scientific Publications 1990

Cox JV, Pazdur R, Thibault A et al. A phase III trial of Xeloda (Capecitabine) in previously untreated advanced/metastatic colorectal cancer. Proc Am Soc Clin Oncol 1999; 18:1016.

CRC (Cancer Research Campaign). Facts on Cancer. Factsheets 18.1 - 18.4 1993.

CRC (Cancer Research Campaign). CancerStats: Large Bowel - UK. November 1999.

Cross SS, Feeley KM, Angel CA. The effect of four interventions on the informational content of histopathology reports of resected colorectal carcinomas. J Clin Pathol 1998; 51:481-482.

Cunningham D, Zalcberg JR, Rath U, et al. Final results of a randomised trial comparing "Tomudex" (raltitrexed) with 5-fluorouracil plus leucovorin in advanced colorectal cancer. Annals Oncol 1996; 7:961-965.

Cunningham D, Pyrhonen S, James RD et al Randomised trial of irinotecan plus supportive care versus supportive care alone after fluorouracil failure for patients with metastatic colorectal cancer. Lancet. 1998; 352(9138):1413-1418.

Curley SA, Izzo F, Delrio P et al. Radiofrequency ablation of unresectable primary and secondary hepatic malignancies. Ann Surg 1999; 230: 1-8

Dahlberg M, Glimelius B, Graf W et al. Preoperative irradiation affects functional results after surgery for rectal cancer: results from a randomised study. Dis Colon Rectum 1998; 41:543-549.

Deans GT, Krukowski ZH, Irwin ST. Malignant obstruction of the left colon. Br J Surg 1994; 81: 270-1276.

de Gramont A, Figer A, Seymour M et al. Leucovorin and fluorouracil with or without oxaliplatin as first-line treatment in advanced colorectal cancer. J Clin Oncol. 2000; 18(16):2938-2947.

Department of Health. A policy framework for commissioning Cancer Services. 1995; London

Desch CE, Benson AB, Thomas TJ et al: Recommended colorectal cancer surveillance guidelines by the American Society of Clinical Oncology 1999; J Clin Oncol 1999; 17:1312.

Devlin HB. Stoma Therapy Review. Coloproctology 1982.

Devlin HB, Plant JA, Griffin M. Aftermath of Surgery for Anorectal Cancer. Br Med J 1971; 3: 413-418

Dixon AR, Maxwell WA, Thornton Holmes J. Carcinoma of the rectum: a 10-year experience. Br J Surg 1991; 78: 308-311

Dixon AR, Thornton-Holmes J, Cheetham NM. General Practitioners' awareness of colorectal cancer; A 10 year review. BMJ 1990; 301:152-3.

Dodds S, Dodds A, Vakis S et al. The value of various factors associated with rectal bleeding in the diagnosis of colorectal cancer. Gut 1999; 44:A99.

Domjan J, Blacquiere R, Odurny A. Is minimal preparation computed tomography comparable with barium enema in elderly patients with colonic symptoms? Clinical Radiology 1998; 53:894-898.

Dorudi S, Wilson NM, Heddle RM.. Primary restorative colectomy in malignant left-sided large bowel obstruction. Ann Roy Coll Surg Eng 1990; 72: 393-395

Douillard JY, Cunningham D, Roth AD et al. Irinotecan combined with fluorouracil compared with fluorouracil alone as first-line treatment for metastatic colorectal cancer: a multicentre randomised trial. Lancet 2000; 355:1041-47.

Dube S, Heyen F, Jenicek M. Adjuvant chemotherapy in colorectal carcinoma: results of a meta-analysis. Diseases of the Colon & Rectum. 1997; 40(1):35-41.

Dworak O. Morphology of lymph nodes in the resected rectum of patients with rectal carcinoma. Path Res Pract 1991; 187:1020-1024.

Edelman MJ, Meyers FJ, Siegel D. The utility of follow up testing after curative cancer therapy. J Gen Intern Med 1997; 12: 318-331

Ellis BG, Baig KM, Senapati A et al. Common modes of presentation of colorectal cancer patients. Colorect Dis 1999; 1 (Supple 24).

European Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine: Convention on Human Rights and Biomedicine. Oviedo: European Treaty Series, 1997.

Everett WG, Friend PJ, Forty J. Comparison of stapling and hand suture for left-sided large bowel anastomosis. Br J Surg 1986; 73: 345-348

Feinstein AR. Symptoms as an index of biological behaviour and prognosis in human cancer. Nature 1966; 209: 41-245.

Fenlon HM, Nunes DP, Calrke PD et al, Colorectal neoplasm detection using virtual colonoscopy: a feasibility study. Gut 1998; 43: 806-811.

Fielding LP, Stewart-Brown S, Blesovsky L, et al. Anastomotic integrity after operations for large bowel cancer: a multi-centre study. Br Med J 1980; 281: 411-414

Finan PJ, Ritchie JK, Hawley PR. Synchronous and 'early' metachronous carcinomas of the colon and rectum. Br J Surg 1987; 74:945-94.

Florey CdV, Yule B, Fogg A et al. A randomised trial of immediate discharge of surgical patients to general practice. J Publ Health Med 1994; 16:455-464.

Fontzilas G, Gossios K, Zisiadis A et al. Prognostic variable in patients with advanced colorectal cancer treated with fluorouracil and leucovorin-based chemotherapy. Medical and Paediatric Oncol 1996; 26: 305-317.

Fuchs CS, Giovannucci EL, Colditz GA et al. A prospective study of family history and the risk of colorectal cancer. New Engl J Med 1994; 331: 1669-74.

Giacchetti S, Itzhaki M, Gruia G et al. Long-term survival of patients with unresectable colorectal cancer liver metastases following infusional chemotherapy with 5-fluorouracil, leucovorin, oxaliplatin and surgery. Annals of Oncology. 1999: 10(6): 663-9.

Giacchetti S, Perpoint B, Zidani R et al. Phase III multicentre randomised trial of oxaliplatin added to chronomodulated fluorouracil-leucovorin as first-line treatment of metastatic colorectal cancer. J Clin Oncol. 2000 18(1):136-147.

GIVO Investigators. Impact of follow-up testing on survival and health-related quality of life in breast cancer patients: a multicentre randomized controlled trial. JAMA 1994; 271: 1587-1592

Glimelius B. Expectancy or primary chemotherapy in patients with advanced asymptomatic colorectal cancer: a randomised trial. Eur J Cancer 1991; 27(Suppl 2): S82

Goligher J. Surgery of the Anus, Rectum and Colon. Baillière Tindall, London 1984

Gooszen AW, Geelkerken RH, Hermans J et al. Quality of life with a temporary stoma Diseases of the Colon and Rectum. 2000; 43:650-655.

Graham RA, Garnsey L, Jessup JM. Local excision of rectal carcinoma. Am J Surg 1990; 160: 306-312

Grunfield E, Mant D, Yudkin P et al. Routine follow up of breast cancer in primary care: randomised trial. Brit Med J 1996; 313: 665-9.

Hackett TP, Cassem NH, Raker JW. Patient delay in cancer. N Eng J Med 1973; 289:14-2.

Haller DJ, Catalano PJ, Macdonald RJ et al. Fluorouracil (FU) leucovorin (LV) and levamisole (LEV) adjuvant therapy for colon cancer: Five year final report of Int-0089. . Proc Am Soc Clin Oncol 17:256, 1998 (abstr).

Halvorsen TB, Seim E. Degree of differentiation in colorectal adenocarcinomas: a multivariate analysis of the influence on survival. J Clin Pathol 1988; 41: 532-537

Haward RA Improving outcomes in colorectal cancer: the manual. NHS Executive Guidance on commissioning cancer services. 1997.

Heald RJ. The "holy plane" of rectal surgery. J R Soc Med 1988; 81: 503-508

Heald RJ, Husband EM, Ryall RDH. The mesorectum in rectal cancer surgery - the clue to pelvic recurrence? Br J Surg 1982; 69: 613-616

Heald RJ, Lockhart-Mummery HE. The lesion of the second cancer of the large bowel. Br J Surg 1972; 59: 16-19

Heald RJ, Ryall RDH. Recurrence and survival after total mesorectal excision for rectal cancer. Lancet 1986; i: 1479-1482

Heriot AG, Grundy A, Kumar D. Pre-operative staging of rectal carcinoma. Br J Surg 1999; 86:17-28.

Hermanek P, Wiebelt H, Staimmer D et al. Prognostic factors of rectal cancer - experience of the German multicentre study SGCRC. Tumori 1995; 81:60-64.

Hockley JM, Dunlop R, Davis RJ. Survey of distressing symptoms in dying patients and their families in hospital and the response to a symptom control team. Br Med J 1988; 296: 1715-1717

Holm T, Rutqvist LE, Johansson H et al. Abdominoperineal resection and anterior resection in the treatment of rectal cancer: results in relation to adjuvant preoperative radiotherapy. Br J Surg 1995; 82: 1213-1216

Houghton A. Variation in outcome of surgical procedures. Br J Surg 1994; 81: 653-60

Houlston RS, Murday V, Harocopos C et al. Screening and genetic counselling for relatives of patients with colorectal cancer in a family cancer clinic. Br Med J 1990; 301: 366-368

Hughes KS for the Registry of Hepatic Metastases. Resection of the liver for colorectal cancer metastases: A multi-institutional study of indications for resection. Surgery 1988; 103: 278-288

Hurst PA, Proust WG, Kelly JM et al. Local recurrence after low anterior resection using the staple gun. Br J Surg 1982; 69: 275-276

IMPACT (International multicentre pooled analysis of colon cancer trials) investigators. Efficacy of adjuvant fluorouracil and folinic acid in colon cancer. Lancet 1995; 345: 939-944

IMPACT B2 (International multicentre pooled analysis of B2 colon cancer trials) investigators. Efficacy of adjuvant fluorouracil and folinic acid in B2 colon cancer. J Clin Oncol 17:1356-1363, 1999.

Irving AD, Scrimgeour D. Mechanical bowel preparation for colon resection and anastomosis. Br J Surg 1987; 74: 580-581

James RD et al AXIS Proc Am Soc Clin Oncol, 1999.

Jarvinen HJ, Mecklin JP, Sistonen P. Screening reduces colorectal cancer in families with hereditary nonpolyposis colorectal cancer. Gastroenterol 1995; 108(5):1405-11.

Jarvinen H.J, Aarnio M, Mustonen H et al. Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer. Gastroenterology 2000; 118 : 829-834.

Johnson WR, McDermott FT, Pihl E et al. Palliative operative management in rectal carcinoma. Dis Colon Rectum 1981; 24: 606-609

Juhl G, Larson GM, Mullins R et al. Six-Year Results of annual colonoscopy after resection of colorectal cancer. World J Surg 1990; 14: 255-261

Kapiteijn E, Marijnen CA, Nagtegaal ID et al. Preoperative radiotherapy combined with total mesorectal excision for respectable rectal cancer. N Engl J Med 2001; 345: 638-646

Kakkar VV, Cohen AT, Edmonson RA et al. Low molecular weight versus standard heparin for prevention of venous thromboembolism after major abdominal surgery. Lancet 1993; 341: 259-265

Karanjia ND, Corder AP, Bearn P et al. Leakage from stapled low anastomosis after total mesorectal excision for carcinoma of the rectum. Br J Surg 1994; 81: 1224-1226

Karanjia ND, Schache DJ, North WRS, et al. "Close shave" in anterior resection. Br J Surg 1990; 77: 510-512

Keddie N, Hargreaves A. Symptoms of carcinoma of the colon and rectum. Lancet 1968; ii: 749-750

Keighley MRB Infection prophylaxis. Br Med Bull 1988; 44: 374-402

Kiebert GM, Welvaart K, Kievit J. Psychological effects of routine follow-up on cancer patients after surgery. Eur J Surg 1993; 159: 601-607

Kikuchi R, Takano M, Takagi K et al. Management of early invasive colorectal cancer. Risk of recurrence and clinical guidelines. Dis Colon Rectum 1995; 38:1286-1295.

Kjeldsen BJ, Kronberg, Fenger C et al. A prospective randomised study of follow up after radical surgery for colorectal cancer. Brit J Surg 1997; 84: 666-9

Kjeldsen BJ, Thorsen H, Whalley D et al. Influence of follow up on health related quality of life aftyer radical surgery for colorectal cancer. Scand J Gastroenterol 1999; 34: 509-15.

Koruth NM, Koruth A, Matheson NA. The place of contrast enema in the management of large bowel obstruction. J Roy Coll Surg Edin 1985; 30: 258-260

Koruth NM, Krukowski ZH, Youngson GG et al. Intraoperative colonic irrigation in the management of left-sided large bowel emergencies. Br J Surg 1985; 72:708-711.

Kronborg O, Hage E, Deichgraeber E. The remaining colon after radical surgery for colorectal cancer. The first three years of a prospective study. Dis Colon Rectum 1983; 26: 172-176

Krook JE, Moertel CG, Gunderson LL et al. Effective surgical adjuvant therapy for high risk rectal carcinoma. N Engl J Med 1991; 324: 709-715

Kumar A, Scholefield JH. Endosonography of the Anal Canal and Rectum. World J Surg 2000; 24:208-215.

Langevin JM, Nivatvongs S, The true incidence of synchronous cancer of the large bowel: A prospective study. Am J Surg 1984; 147: 330-333

Lauer JD, Carlson HC, Wollaeger EE. Accuracy of roentgenologic examination in detecting carcinoma of the colon. Dis Colon Rectum 1965; 8: 190

Laufer I. Tumours of the colon. In: Double Contrast Gastrointestinal Radiology with Endoscopic Correlation. Laufer I (ed) Philadelphia: Saunders 1979.

Lennon T, Houghton J, Northover J. Postoperative CEA monitoring and second look surgery in colorectal cancer. Brit J Cancer 1994; 70:16.

Lichtenstein P, Holm NV, Verkasalo PK et al. Environmental and heritable factors in the causation of cancer - analyses of cohorts of twins from Sweden, Denmark and Finland. New Engl J Med 2000; 343:78-85.

Lieberman DA, Weiss, DG, Bond JH et al. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. New Engl J Med 2000; 343:162-168

Liver Infusion Meta-analysis Group. Portal vein chemotherapy for colorectal cancer: a meta-analysis of 4000 patients in 10 studies. J Natl Cancer Inst 1997; 89:497-505.

Lockhart-Mummery HE, Ritchie JK, Hawley PR. The results of surgical treatment for carcinoma of the rectum at St Mark's Hospital from 1948 to 1972. Br J Surg 1976; 63: 673-677

Lovett E. Family studies in cancers of the colon and rectum. Br J Surg 1976; 63: 13-18

Lund JN, Buckley D, Bennett D, et al. A randomised trial of hospital versus home administered enemas for flexible sigmoidoscopy. BMJ 1998; 317(7167):1201.

MacArthur C, Smith A. Delay in diagnosis of colorectal cancer; J Roy Coll Gen Pract 1983; 33:159-161.

MacBride and Whyte F. Survivorship and the cancer follow up clinic. European J Cancer 1998; 7: 47-55.

Mäkelä JT, Laitinen SO and Kairaluoma MI. Five-year follow up after radical surgery for colorectal cancer: results of a prospective randomised trial Arch Surg 1995; 130: 1062-7

Mamounas E, Wieand S, Wolmark N et al. Comparative efficacy of adjuvant chemotherapy in patients with Dukes B versus Dukes C colon cancer: results from four national surgical Adjuvant Breast and Bowel Project adjuvant studies (C-01, C-02, C-03 and C-04). J Clin Oncol 1999; 17: 1349-1355.

Mandel JS, Bond JH, Church TR et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. N Engl J Med 1993; 328: 1365-1371

Marsh PJ, James RD, Schofield PF. Adjuvant preoperative radiotherapy for locally advanced rectal carcinoma: results of a prospective randomised trial. Dis Colon Rectum 1994; 37: 1205-1214.

Marson LP, Stevenson J, Gould A et al. Intersurgeon variation following colorectal cancer surgery appears to decrease with progressive audit. Br J Surg 1997;84 suppl 1: 24.

Martling Al, Holm T, Rutqvist LE et al. Effect of a surgical training programme on outcome of rectal cancer in the county of Stockholm. Lancet 2000; 356:93-96.

Matheson NA, McIntosh CA, Krukowski ZH. Continuing experience with single layer appositional anastomosis in the large bowel. Br J Surg 1985; 70: S104-106

Maughan TS, James RD, Kerr D et al. Preliminary results of a multicentre randomised trial comparing 3 chemotherapy regimens in metastatic colorectal cancer. Proc Am Soc Clin Oncol 1999; 18: 1007.

Maughan TS, James RD, Kerr D et al. Continuous versus intermittent chemotherapy for advanced colorectal cancer: preliminary results of MRC CR06b randomized trial. Proc Am Soc Clin Oncol 2001;20: 125a.

McArdle CS, Hole D. Impact of variability among surgeons on postoperative morbidity and mortality and ultimate survival. Br Med J 1991; 302: 1501-1505

McArdle CS, Hole D, Hansell D, et al. Prospective study of colorectal cancer in the west of Scotland: ten-year follow-up. Br J Surg 1990; 77: 280-282

McDermott F, Hughes E, Pihl E, Milne B, Price A. Symptom duration and survival prospects in carcinoma of the rectum. Surg Gynecol Obstet 1981; 153:321-326.

McGinn FP, Gartell PC, Clifford PC, Brunton FJ. Staples or sutures for low colorectal anastomoses: a prospective randomised trial. Br J Surg 1985; 72: 603-605

McSherry CK, Cornell GN, Glenn F. Carcinoma of the Colon and Rectum. Ann Surg 1969; 169:502-509.

Medical Research Council Rectal Cancer Working Party. Randomised trial of surgery alone versus surgery followed by radiotherapy for mobile cancer of the rectum. Lancet 1996; 348; 1610-14.

Mella J, Datta S, Biffin A et al. Surgeon's follow up practice after resection of colorectal cancer. Roy Coll Surg Engl.1997; 79: 206-209.

Meta-Analysis Group in Cancer. Reappraisal of hepatic arterial infusion in the treatment of nonresectable liver metastases from colorectal cancer. J Natl Cancer Inst 1996; 88: 252-258.

Meta-analysis Group In Cancer. Efficacy of intravenous continuous infusion of fluorouracil compared with bolus administration in advanced colorectal cancer. Journal of Clinical Oncology. 1998; 16(1):301-308.

Meta-Analysis Group In Cancer.Toxicity of fluorouracil in patients with advanced colorectal cancer: effect of administration schedule and prognostic factors Journal of Clinical Oncology. 1998; 16(11):3537-3541.

Michelassi F, Vannucci L, Ayala JJ et al. Local recurrence after curative resection of colorectal adenocarcinoma. Surgery 1990; 108: 787-793

Moertel CG, Fleming TR, Macdonald JS et al. Fluorouracil and levamisole as effective adjuvant therapy after resection of stage III colon carcinoma: a final report. Ann Intern Med 1995; 122:321-326.

Moertel CG, Fleming TR, Macdonald JS et al. An evaluation of the carcinoembryonic antigen (CEA) test for monitoring patients with resected colon cancer. JAMA 1993; 270:943-947

Moore HCF & Haller DG. Adjuvant therapy of colon cancer. Semin Oncol 1999; 26: 545-555.

Morris S, Corder AP, Taylor I. What are the benefits of routine breast cancer follow-up? Postgrad Med J 1992; 68: 904-907

Morson BC, Vaughan EG, Bussey HJR. Pelvic recurrence after excision of rectum for carcinoma. Br Med J 1963; ii: 13-18

Mortensen NJM, Ramirez JM, Takeuchi N, et al. Colonic J pouch-anal anastomosis after rectal excision for carcinoma: functional outcome. Br J Surg 1995; 82: 611-613

Morton DG, Macdonald F, Haydon J et al. Screening practice of familial adenomatous polyposis; the potential for regional registers. Br J Surg 1993; 80: 255-258.

National Institute for Clinical Excellence. Technology Appraisal Guidance no.17, London 2000

NHS Executive. Guidance on Commissioning Cancer Services. Improving outcomes in Colorectal Cancer, The Manual. 1997, Dept of Health, London (97CV0119).

NHS Executive. Guidance on Commissioning Cancer Services. Improving outcomes in Colorectal Cancer, The Research Evidence. 1997, Dept of Health, London (97CV0120).

NHS Executive. NHS Plan, A plan for investment, A plan for reform, London. July 2000 (Cm4818-I).

NHS Executive. NHS Cancer Plan, A plan for investment, A plan for reform, London. September 2000.

Nduka CC, Monson JRT, Menzies-Gow N et al. Abdominal wall metastases following laparoscopy. Br J Surg 1994; 81: 648-652

Neugut AI, Jacoson JS, Ahsan H et al. Incidence and recurrence rates of colorectal adenomas: A prospective study. Gastroenterology 1995; 108: 402-408.

Neville R, Feilding LP, Amendola C. Local tumour recurrence after curative resection of rectal cancer. A ten-hospital review. Dis Colon Rectum 1987; 30: 12-17

Ng IOL, Luk ISC, Yuen ST et al. Surgical lateral clearance in resected rectal carcinomas. A multivariate analysis of clinicopathological features. Cancer 1993; 71; 1972-76.

NGTATG (Nordic Gastrointestinal Tumour Adjuvant Therapy Group). Expectancy or primary chemotherapy in patients with advanced asymptomatic colorectal cancer: a randomized trial. J Clin Oncol 1992; 10: 904-911.

NHS Executive. Recurrent and advanced disease. In: Improving outcomes in colorectal cancer: The research evidence. 1997, CCO1200, p98-125.

Nicholls J. Large bowel cancer. In: Slevin ML, Staquet MJ, eds. Randomised Trials in Cancer: A Critical Review by Sites. New York: Raven Press, 1986: 241-271

NIH Consensus Conference. Adjuvant therapy for patients with colon and rectal cancer. JAMA 1990; 264: 1444-1450

Norum J. Adjuvant chemotherapy in Dukes' B and C colorectal cancer has only a minor influence on psychological distress. Supportive Care in Cancer. 1997; 5(4):318-321.

O'Connell MJ, Laurie JA, Kahn M et al. Prospectively randomised trial of adjuvant chemotherapy in patients with high risk colon cancer J Clin Oncol. 1998; 16:295-300.

O'Connell MJ, Martenson JA, Weiand HS et al. Improving adjuvant therapy for rectal cancer by combining protracted infusional fluorouracil with radiation therapy after curative surgery. N Engl J Med 1994; 331:502-507.

Ohlsson B, Breland U, Ekberg H et al. Follow up after curative surgery for colorectal carcinoma. Randomised comparison with no follow up. Dis Colon Rectum 1995; 38: 619-26.

Ooi BS, Tjandra JJ & Green MD. Morbidities of adjuvant chemotherapy and radiotherapy for respectable rectal cancer: an overview. Dis colon rectum. 1999; 42:403-418.

Padhani A R. Advances in imaging of colorectal cancer. Clinical Reviews in Oncology/Hematology 1999; 30:189-199.

Page CP, Bohnen JMA, Fletcher JR et al. Antimicrobial prophylaxis for surgical wounds. Guidelines for clinical care. Arch Surg 1993; 128: 79-88

Påhlman L, Glimelius B. Pre-operative and post-operative radiotherapy and rectal cancer. World J Surg 1992; 16: 858-865

Pappalardo G, Polettini E, Frattaroli F et al. Magnetic resonance colography versus conventional colonoscopy for the detection of colonic endoluminal lesions. Gastroenterology 200; 119: 300-304

Parry GJ, Gould CR, McCabe CJ et al. Annual league tables of mortality in neonatal lintensive care units, Longtitudinal study. BMJ 1998; 316:1931-1935.

Patel SC, Tovee EB, Langer B. Twenty-five years experience with radical surgical treatment of carcinoma of the extraperitoneal rectum. Surgery 1977; 82: 460-465

Pazdur R, Vincent M. Raltitrexed versus 5-fluorouracil and leucovorin in patients with advanced colorectal cancer: results of a randomized multicentre North American trial. Proc ASCO 1997; 1(16):801 (abstract), 1997.

Pazdur R, Douillard J-Y, Skilings JR et al. Multicentre phase III study of 5FU or UFT in combination with leucovorin in patients with metastatic colorectal cancer. Proc Am Soc Clin Oncol 1999; 18:1009.

Persson AV, Davis RJ, Villavicencio JL. Deep Venous Thrombosis and Pulmonary Embolism. Surg Clin N Amer 1991; 71: 1195-1199

Phillips RKS, Hittinger R, Blesovsky L et al. Local recurrence following "curative" surgery for large bowel cancer: I. The overall picture. Br J Surg 1984; 71: 12-16

Phillips RKS, Hittinger R, Blesovsky L et al. Local recurrence following "curative" surgery for large bowel cancer: II. The rectum and rectosigmoid. Br J Surg 1984; 71: 17-20

Pietra N, Sarli L, Costi R et al. Role of follow up in management of local recurrences of colorectal cancer: a prospective randomiswd study. Dis Colon Rectum 1998; 41:1127 - 1134

Pollard SG, Macfarlane R, Everett WG. Surgery for recurrent colorectal carcinoma - is it worthwhile? Ann R Coll Surg Engl 1989; 71: 293-298

Poloniecki J, Valencia O, Littlejohns P. Cumulative risk adjusted mortality chart for detecting changes in death rate; observational study of heart surgery. BMJ 1998;316:1697-1700.

Ponz de Leon M, Antonioli A, Ascari A et al. Incidence and familial occurrence of colorectal cancer and polyps in a health care district of Northern Italy. Cancer 1987; 60: 2848-59.

Puthwala AA, Syed AMN, Gates TC et al. Definitive treatment of extensive anorectal carcinoma by external and interstitial irradiation. Cancer 1982; 50: 1746-1750

QUASAR colorectal cancer study group. Adjuvant chemotherapy with 5-fluorouracil, l-folinic acid and levamisole for patients with colorectal cancer: comparison of weekly versus monthly schedules. Annals of Oncology 2000; 11: 947-955

QUASAR Collaborative Group. Comparison of 5 Fluorouracil with additional levamisole, higher dose folinic acid or both as adjuvant chemotherapy for colorectal cancer: a randomised trial. Lancet 2000; 355: 1588-1596.

Quirke P, Durdey P, Dixon MF et al. Local recurrence of rectal adenocarcinoma due to inadequate surgical resection: histopathological study of lateral tumour spread and surgical excision. Lancet 1986; ii: 996-999

Quirke P. Limitations of existing systems of staging for rectal cancer: The forgotten margin. Rectal Cancer Surgery. Ed. Soreide O & Norstein J. Springer-Verlag 1997, 63-81.

Raymond E, Chaney SG, Taamma A et al. Oxaliplatin: a review of preclinical and clinical studies. Annals of Oncology. 1998; 9(10):1053-1971.

RCP (Royal College of Physicians). Palliative Care. Guidelines for good practice and audit measures. 1991

RCS (Royal College of Surgeons). Guidelines for Clinicians on Medical Records and Notes. 1990.

Rees M, Plant G, Bygrave S. Late results justify resection for multiple hepatic metastases from colorectal cancer. Br J Surg 1997; 84: 1136-1140.

Richards CS, McLeod RS. Follow up of patients after resection for colorectal cancer: a position paper of the Canadian Society of Surgical Oncology and the Canadian Society of Colon and Rectal Surgeons. JCC 1997; 40: 90-100.

Rodel C, Grabenhauer GG, Matzel KE et al. Extensive surgery after high-dose pre-operative chemoradiotherapy for locally advanced recurrent rectal cancer. Dis Colon Rectum 2000; 43, 312-319.

Rosen M, Chan L, Beart RW et al. Follow up of colorectal cancer: a meta-analysis. Dis Colon Rectum 1998; 41:1116-1126

Ross P,. Norman A, Cunningham D. et al A prospective randomised trial of protracted venous infusion 5-fluorouracil with or without mitomycin C in advanced colorectal cancer Annals of Oncology. 1997; 8(10):995-1001.

Rossi S, Di Stasi M, Buscarini E et al. Percutaneous RF interstitial thermal ablation in the treatment of hepatic cancer. Am J Roentgenology 1996;

Rougier P, Van Cutsem E, Bajetta E et al. Randomised trial of irinotecan versus fluorouracil by continuous infusion after fluorouracil failure in patients with metastatic colorectal Lancet. 1998; 352(9138):1407-1412.

Rougier P, Sahmoud T, Nitti D et al. Adjuvant portal vein infusion of fluorouracil and heparin in colorectal cancer: a randomised trial. Lancet 1998; 351:1677-1681.

Rowe-Jones DC, Peel ALG, Kingston RD et al. Single dose cefotaxime plus metronidazole versus three dose cefotaxime plus metronidazole as prophylaxis against wound infection in colorectal surgery: multicentre prospective randomised study. BMJ 1990; 300:18-22

Saltz LB, Cox JV, Blanke C et al. Irinotecan plus fluorouracil and leucovorin for metastatic colorectal cancer. Irinotecan Study Group. New Engl J Med 2000; 343: 905-914.

Salzman EW, Davies GC. Prophylaxis of Venous Thomboembolism. Ann Surg 1980; 191: 207-218

Saunders B. The nurse's role in the care of patients with stoma. Br J Clin Pract 1976; 30: 81-82

Scheele J, Stangl R, Altendorf-Hofmann A. Hepatic metastases from colorectal carcinoma: impact of surgical resection on the natural history. Br J Surg 1990; 77: 1241-1246

Scheithauer W, Rosen H, Kornek GV et al. Randomised comparison of combination chemotherapy plus supportive care alone in patients with metastatic colorectal cancer. BMJ 1993; 306: 752-755

Schiessel R, Wunderlich M, Herbst F. Local recurrence of colorectal cancer: effect of early detection and aggressive surgery. Br J Surg 1986; 73: 342-344

Schoemaker D, Black R, Giles L et al Yearly colonoscopy, liver CT and chest radiography do not influence 5-year survival of colorectal cancer patients. Gastroenterology 1998; 114:1 - 14.

SCOTIA Study Group. Sub-total or segmental resection for malignant left-sided colonic obstruction: a randomised clinical trial. Gut 1994; 35(Suppl 2): S16

Scott N, Jackson P, Al-Jaberi T et al. Total mesorectal excision and local recurrence: a study of tumour spread in the mesorectum distal to rectal cancer. Br J Surg 1995; 82: 1031-1033

Seifert JK Morris DL. Prognostic factors after cryotherapy for hepatic metastases from colorectal cancer. Ann Surg 1998; 228: 201-8

Seow-Choen F, Goh HS. Prospective randomised trial comparing J colonic pouch-anal anastomosis and straight coloanal reconstruction. Br J Surg 1995; 82: 608-610

Shallow TA, Wagner FB, Colcher RE. Clinical Evaluation of 750 patients with Colon Cancer. Diagnostic Survey and Follow-Up Covering a 15 Year Period. Ann Surg 1955; 142:164-175.

SHPIC (Scottish Health Purchasing Information Centre). Follow up in colorectal tumours www.nhsconfed.net/shpic/ 1999.

Sischy B. The place of radiotherapy in the management of rectal adenocarcinoma. Cancer 1982; 50: 2631-1637

Slaney G et al (eds) Cancer of the large bowel. Clincal Cancer Monograph Vol 4. MacMillan Press 1991.

Sprangers MAG, Te Velde A, Aaronson NK et al. Quality of life following surgery for colorectal cancer: A literature review. Psycho-oncology 1993; 2: 247-259

Stamatakis JD, Thompson M, Chave H et al. A National Audit of Malignant Bowel Obstruction. June 2000. Monograph published by the Association of Coloproctology of Great Britian and Ireland.

Stamatakis JD, Aitken J, Smith J et al. What can we learn from colorectal cancer audits? In: Recent Advances in Surgery, Vol 24:103-113 Churchill Livingstone, Edinburgh 2001.

Steele RJC, Hirshman MJ, Mortensen NJMcC, et al. Trans Anal Endoscopic Micro-Surgery - initial experience from three centres in the UK. Br J Surg 1996; 83:207-210.

Stiggelbout AM, de Haes JC, Vree R et al. Follow up of colorectal cancer patients: quality of life and attitudes towards follow up. Brit J Cancer 1997; 75(6): 914-20.

St John DJB, McDermott FT, Hopper JL et al. Cancer risk in relatives of patients with common colorectal cancer. Annals Int Med 1993; 118:785-790.

Sugarbaker PH, Gianola FJ, Dwyer A et al. A simplified plan for follow-up of patients with colon and rectal cancer supported by prospective studies of laboratory and radiological results. Surg 1987; 102:79-87.

Tepper JE, O'Connell MJ, Petroni GR et al Adjuvant post-operative fluorouracil modulated chemotherapy combined with pelvic radiation therapy for rectal cancer: initial results of INT 0114. J Clin Oncol. 1997; 15:2030-2039.

Thirion P, Wolmark N, Haddad E et al. Survival Impact of Chemotherapy in Patients with Colorectal Metastases Confined to the Liver: A re-analysis of 1,458 Non-Operable Patients Randomized in 22 Trials and 4 Meta Analyses. Proc Am Soc Clin Oncol 1999;10(11): 1317-1320.

Thomas PR, Linbald AS. Adjuvant postoperative radiotherapy and chemotherapy in rectal carcinoma: A review of the Gastrointestinal Tumor Study Group Experience. Radiother Oncol 1988; 13: 245-52.

Thomas RD, Fairhurst JJ, Frost RA. Wessex Regional Radiology Audit: Barium enema in colorectal carcinoma. Clinical Radiology 1995; 50:647-650.

Tornqvist A, Eklund G, Leandoer L. Early diagnosis of metachronous colorectal carcinoma Aust N Z J Surg. 1981; 51:442-445.

Twelves C, Harper P, Van Cutsem E et al. A phase III trial of Xeloda (Capecitabine) in previously untreated advanced/metastatic colorectal cancer. Proc Am Soc Clin Oncol 1999; 18:1010.

UKCCCR. Handbook for the clinicopathological assessment and staging of colorectal cancer. UKCCCR 1989.

Umpleby HC, Bristol JB, Rainey JB et al. Survival of 727 patients with single carcinomas of the large bowel. Dis Colon Rectum 1984; 27: 803-810

Umpleby HC, Fermor B, Symes MO et al. Viability of exfoliated colorectal carcinoma cells. Br J Surg 1984; 71: 659-663

Vasen HFA. High incidence of interval cancers in HNPCC. An update of the Dutch HNPCC registry. Presentation at the 10th Annual ICG-HNPCC Meeting. 1998

Virgo KS, Wade TP, Longo WE et al. Surveillance after curative colon cancer resection: Practice patterns of surgical subspecialists. Ann Surg Oncol. 1995; Nov 2(6):472-482.

Wade TP, Virgo KS, Li MJ et al Outcomes after detection of metastatic carcinoma of the colon and rectum in a national hospital system. J Am Coll Surgeons, 1996; 182, 353-361.

Wallis YL, Morton DG, McKeown CM, et al. Molecular analysis of the APC gene in 205 families: extended genotype-phenotype correlations in FAP and evidence for the role APC amino acid changes in colorectal cancer pre-disposition. J Med Genet 1999; 36: 14-20.

West of Scotland and Highland Anastomosis Study Group. Stapling or suturing in gastrointestinal surgery: a prospective randomised study. Br J Surg 1991; 78: 337-341

Wexner SD, Cohen SM. Port site metastases after laparoscopic surgery for cure of malignancy. Br J Surg 1995; 82: 295-298

Wexner SD, Cohen SM, Johansen OB, et al. Laparoscopic colorectal surgery: a prospective assessment and current perspective. Br J Surg 1993; 80: 1602-1605

Whiteway J, Nicholls RJ, Morson BC. The role of surgical local excision in the treatment of rectal cancer. Br J Surg 1985; 72: 694-697

Whittaker M, Goligher JC. The prognosis after surgical treatment for carcinoma of the rectum. Br J Surg 1976; 63: 384-388

Wiggers T, Arends JW, Volovics A. Regression analysis of prognostic factors in colorectal cancer after curative resections/ Dis Colon Rectum 1988; 31: 33-41

Wiggers T, Jeekel J, Arends JW et al. No-touch isolation technique in colon cancer: a controlled prospective trial. Br J Surg 1988; 75: 409-415

Williams NS, Dixon MF, Johnston D. Reappraisal of the 5 cm rule of distal excision for carcinoma of the rectum: a study of distal intramural spread and of patient survival. Br J Surg 1983; 70: 150-154

Williams NS, Durdey P, Johnston D. The outcome following sphinter-saving resection and abdomino-perineal resection for low rectal cancer Br J Surg 1985; 72: 595-598

Williams NS, Johnston D. Survival and recurrence after sphincter saving resection and abdominoperineal resection for carcinoma of the middle third of the rectum. Br J Surg 1984; 71: 278-282

Williams NS, Johnston D. The quality of life after rectal excision for low rectal cancer. Br J Surg 1983; 70: 460-462

Williams NS, Nasmyth DG, Jones D et al. Defunctioning stomas: a prospective controlled trial comparing loop ileostomy with transverse loop colostomy. Br J Surg 1996; 73:566-70

Williams PL, Warwick R. Gray's Anatomy. Churchill Livingstone 1980. p 1356

Winawar SJ, Zauber AG, O'Brien MJ et al. Randomised comparison of surveillance intervals after colonoscopic removal of newly diagnosed adenomatous polyps. New Engl J Med 1993; 328: 901-906.

Winawer SJ, Fletcher RH, Miller L et al. Colorectal cancer screening: Clinical guidelines and rationale. Gastroenterol. 1997; 112:594-642

Winawer SJ, Stewart ET, Zauber AG et al for the National Polyp Study Work Group. A Comparison of colonoscopy and double-contrast barium enema for surveillance after polypectomy. N Eng J Med 2000; 342(24):1766.

Wolmark N, Bryant J, Smith R et al. Adjuvant 5-fluorouracil and leucovorin with or without interferon alfa-2a in colon carcinoma: National Surgical Adjuvant Breast and Bowel Project protocol C-05. J Nat Cancer Inst 1998; 90(23):1810-1816.

Wolmark N, Wieand HS, Hyams DM et al. Randomized trial of postoperative adjuvant chemotherapy with or without radiotherapy for carcinoma of the rectum: National Surgical Adjuvant Breast and Bowel Project Protocol R-02. J Nat Cancer Inst. 2000; 92(5):388-396.

Wong R, Thomas G, Cummings B et al. In search of a dose-response relationship with radiotherapy in the management of recurrent rectal carcinoma in the pelvis: a systematic review. Int J Radiat Oncol Biol Phys 1998; 40(2):437-446.

Woolf CM. A genetic study of circinoma of the largfe intestine. Am J Hum Genet 1958; 10: 42-47

Zaniboni A, Labianca R, Marsoni S et al. GIVIO-SITAC 01: A randomized trial of adjuvant 5-fluorouracil and folinic acid administered to patients with colon carcinoma-long term results and evaluation of the indicators of health-related quality of life. Cancer. 1998; 82(11):2135-2144.

Zirngibl H, Husemann B, Hermanek P. Intraoperative spillage of tumours cells in surgery for rectal cancer. Dis Colon Rectum 1990; 33:610-614.

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 (JM), 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.

Definitions

For the purposes of both 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. It is therefore suggested that an operation note for a patient with colorectal cancer should contain the following:

1. Names of operators, assistants and anaesthetists

2. The ASA status of the patient

3. The findings at operation, specifically:

   i) Site of primary tumour together with size, fixity and involvement of other structures. With a rectal tumour, its relationship to the pelvic brim and peritoneal reflection should be clearly stated.

   ii) Presence or absence of liver metastases, peritoneal metastases and lymphadenopathy

   iii) The state of the remaining colon, with specific mention of the presence of absence of synchronous tumours.

4. The operative procedure, specifically:

   i) Site of the vascular ligation

   ii) The extent of resection. With rectal tumours, specific mention of the degree of mesorectal excision should be made.

   iii) The level and method of anastomosis

   iv) The use and content of any peritoneal lavage

   v) The use and content of any rectal washout

   vi) A statement as to whether or not the surgeon regards the resection as curative (ie no residual macroscopic tumour)

   vii) Sites and reasons for stomas

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	Def: Lower margin of tumour 15cm or less from anal verge.

Synchronous tumour ?

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
- 5 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 re-enter 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

• 7 Subtotal colectomy	H11.8	To include ileo-rectal or ileo-sigmoid
• 8 Transverse colectomy	H08.8	Excision of transverse colon
• 9 Left hemicolectomy	H09.8	Excision of the descending and/or sigmoid colon with colorectal anastomosis
• 10 Sigmoid colectomy	H10.8	Excision of the sigmoid colon with colorectal anastomosis
• 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
pT4	Tumour 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