GASTROINTESTINAL CANCER
This working paper has been written by Mr J D Stamatakis, Consultant Surgeon at Bridgend and District NHS Trust and member of the Cancer Services Expert Group (CSEG). Proposals have been reviewed by a large number of health care professionals all of whom are in active clinical practice and are acknowledged at the end of this Report. Recommendations are made regarding the individual cancer sites and are, wherever possible, based on published evidence and referenced accordingly. The recommendations, regarding the general management of gastrointestinal cancer on pages 145 and 146 are also included in Volume 1 and have been agreed by CSEG.
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1. EXECUTIVE SUMMARY

1. The majority of gastrointestinal (GI) tumours present to Acute General Hospitals. In Wales, with many relatively small DGHs, individual units can avoid isolation and provide an expert service by close association with a Cancer Centre, working to joint protocols and sharing joint oncology appointments.

2. Designated specialist rapid access clinics (upper GI endoscopy, rectal) enable diagnoses at an early stage, crucial for a favourable outcome.

3. Multidisciplinary team care should be available to all patients with GI cancer. It enhances the possibility of a broader based decision making process compared with a non team approach. All aspects of management are given due weight and the "maverick" opinion is less likely to prevail in a group. The core team includes specialists in surgery and oncology (both with site specific expertise), pathology, radiology and stoma/colorectal nurses. To function as a team, clerical and IT support is essential, with adequate office and meeting facilities.

4. Accurate preoperative staging is imperative to avoid unnecessary or inappropriate major surgery, plan multimodal therapy, determine eligibility for clinical trials and compare the results of treatments between centres. Staging protocols should be agreed on an All Wales basis and monitored by audit.

5. Multimodal therapy characterises the modern management of malignant tumours of the GI tract. Various combinations of multimodal adjuvant therapy are under review and such treatments should be in association with the Cancer Centre by joint protocol, preferably within a clinical trial. For advanced tumours, evidence increasingly supports preoperative multimodal therapy with resection in responders.

6. Histopathological staging is fundamental in deciding the need for adjuvant or additional therapy, entry into clinical trials, comparison of outcome between units and determining prognosis for all forms of GI malignancy. A lead pathologist, with sufficient time to devote to GI cancer is an integral member of the team.

7. Implications for the NHS. Additional sessions from specialist staff (surgeons, oncologists, radiologists, pathologists) will be necessary to maintain a multidisciplinary team. Joint meetings will require more than reorganisation of working practices. Adequate facilities such as endoscopic ultrasound, endoscopy, clinic time and space, are required to support earlier diagnosis. An All-Wales clinically based cancer registry, with ease of access by Cancer Units and Centres, is urgently required. Improved communication between patients, their carers, primary care, cancer units and centres requires investment in secretarial, IT and clerical support. The potential for improvement should be based on accurate focused audit which requires a significant financial investment.
2. CURRENT PROVISION OF GASTROINTESTINAL SERVICES IN WALES

2.1 Gastrointestinal cancer is treated in all acute hospitals in Wales. Other than the Welsh Office funded, independent, Colorectal Cancer Audit, there are no current data of “who does what and where” in GI cancer in Wales. However, additional information will shortly be available from a similarly funded and organised Oesophagogastric Cancer Audit, of cases treated in Wales in 1995/96. The situation regarding outcome data is similarly lacking, the only all-Wales data available being from the studies above.

2.2 There is no information available on the management and outcome of other GI cancers (pancreas, primary and secondary hepatobiliary, anal and the small number of rare tumours).

- A full report, including 2 year follow-up data, of the Welsh Colorectal Cancer Audit will be published in November 1996.
- The initial report of the Welsh Oesophagogastric Cancer Audit will be available in May 1997.

2.3 The following general information is available as a result of the CSEG questionnaire and visits to acute hospitals in Wales.

Diagnostics

2.4 Contrast radiology, ultrasound and CT scanning are available in all acute hospitals. Increasing evidence supports the use of more specialised investigation using endoscopic, intraoperative and endoanal ultrasound, none of which is widely available in Wales. Many hospitals provide rapid access clinics for endoscopy and rectal bleeding.

Specialist Clinics

2.5 The majority of acute general hospitals have site specific specialists and a colorectal/stoma specialist nurse. Clinical oncologists from Singleton and Velindre NHS Trusts provide extensive outreach services (The Baseline, Appendix 1, Table 5). Recent clinical trials support the use of radiotherapy in the treatment of potentially curative rectal cancer, which has resulted in an increased requirement for this therapy. Palliative radiotherapy is also widely used. Ongoing national trials of chemo-radiotherapy in colorectal cancer have also increased the demand for GI oncology services. A similar growth in demand is anticipated for oesophagogastric cancer.

GI Cancer Specialist Interest Groups

2.6 In South Wales (SW and SE) two multidisciplinary groups have been established. Both are concerned with providing a uniformity high standard of care for all patients and have prepared draft guidelines for the management of upper GI (oesophagus and stomach) cancers. Protocols for hepatobiliary and colorectal carcinomas are being developed.

Clinical Trials

2.7 Clinical trials for gastrointestinal cancer, for example MRC colorectal and oesophagogastric trials, are supported in a number of hospitals in Wales.

Information

2.8 There is no centrally-held database of resources for the investigation and management of GI cancer in Wales. Clinicians rely on professional contact with colleagues in other trusts for awareness of, and access to, equipment essential for staging and treatment.

2.9 Increasing professional specialisation and the introduction of all-Wales specialist multidisciplinary groups for cancer care should result in optimal use of resources. An all-Wales clinical database for GI cancer would provide data on epidemiology, management and outcome. None of this is currently available other than from the Colorectal Cancer and Oesophagogastric Audits, both of which collected data for a single year only.
3. THE ORGANISATION OF AN INTEGRATED CLINICAL SERVICE FOR GASTROINTESTINAL CANCER

Introduction
3.01 In 1990, 3,320 residents in Wales were diagnosed with cancer of the gastrointestinal (GI) tract. Cancers at this site accounted for 23% of all malignancies and, in 1994, 30% of all cancer related deaths. Welsh data for GI cancers, as a group, are included in Volume 1 and are summarised as follows:

- Average yearly (1984-88) registrations: 3,707
- Registrations in 1990: 3,320
- Projected new registrations in the year 2000: 4,309
- 5 Year Survival: Colon cancer 39%; Rectal cancer 39%; Stomach Cancer 11%;
  Oesophageal cancer 8%; Pancreatic cancer 1.2%
- Deaths from 1985-94: 25,041
- Years of Life Lost for death under 70 years: 86,924

Survival data are from the West Midlands Cancer Registry. For other data Sources and ICD9 codes: see CSEG Report, Volume 1

3.02 Although there may be symptoms specific for the involved organ, this is not always so and considerable overlap occurs in clinical presentation, diagnosis, staging and the principles of management of tumours of the GI tract.

3.03 The aim of this section is to outline the care of patients with GI cancer, emphasising aspects of service provision and management which are common to all GI cancers. Section 4-8 deal with site-specific GI cancers.

3.04 Some recommendations, for example, the adoption of a multidisciplinary team approach in the management of gastrointestinal cancer, do not have a robust reference base and are not amenable to formal randomised study. In such instances, validity is based on expert committee reports or opinions and/or clinical experience of respected authorities (see Appendix IV).

3.05 A number of reviewers commented on the need for centralisation for the care of some cancers, low volume and technically demanding oesophageal and pancreatic surgery being the most quoted. This remains a difficult area. Data from the Welsh Oesophagogastric Cancer Audit may contribute to resolving this issue. However, many studies of rectal cancer have failed to show a relationship between volume and outcome, and even among specialists, there are wide variations in all outcome measures.

3.06 It is envisaged that specialist care and cross-Trust referral will evolve as a consequence of adopting proposals in the Calman-Hine and CSEG reports. These include specific recommendations:

- Cancer management should be by multidisciplinary groups.
- The development of all-Wales site specific cancer groups working to agreed protocols.
- An all-Wales clinical cancer registry, to include outcome data.

Standards of Service Provision in the Cancer Unit and Centre

3.07 Every person referred should have the benefit of an accurate and timely diagnosis.

3.08 Treatment of patients with gastrointestinal cancer should be carried out by specialist medical staff with a named lead clinician to co-ordinate services for each patient.

3.09 There should be collaborative management between primary care practitioners and the specialists involved in diagnosis, assessment and treatment; with evidence of clear communication pathways between primary and secondary care.

3.10 Methods of diagnosis, staging and treatment should be in accordance with guidelines agreed with the Cancer Centre and based on advice from National Specialist Groups, the Cochrane Centre, the Clinical Outcomes Group (Cancer Subgroup) etc.

3.11 Guidelines, shared by primary and secondary care, for referral, follow up and the treatment of patients with gastrointestinal cancer should be the subject of continuous local audit and reappraisal, including methods for monitoring quality and outcome.
3.12 There should be co-ordinated multiprofessional services, including clinical nurse specialists, for the range of treatments and for dealing with the physical and psychological effects of the disease. Explicit routes of communication should exist between the patient, primary care, the cancer unit and cancer centre.

3.13 Definitive arrangements should be established for:
- continuity of care with the primary team
- counselling of patients pre-treatment
- psychosocial support for patients and their families
- palliative care.

Requirements
3.14 In order to achieve a timely diagnosis, a properly equipped and resourced diagnostic/staging service must be accessible to GPs for rapid referral of patients with symptoms suggestive of GI cancer. In confirmed cancer patients, facilities must be available to stage the disease, according to clearly defined protocols. This will involve considerable input from radiology and pathology.

3.15 The core team includes specialists in surgery (who will usually be the team leader), oncology, pathology, radiology, and stoma/colorectal nurses. Associates, who would be involved with selective patients, include: consultants and nurse specialists in palliative care, endoscopy, gastroenterology, care of the elderly and clinical genetics, a clinical trials nurse or data manager, oncology pharmacist, oncology nurse, and a clinical psychologist. Clerical and IT support are an integral part of the team.

3.16 The multiprofessional team within the Cancer Unit and Cancer Centre should have a specific base with clerical and data management support.

3.17 The team will need facilities to meet regularly to agree guidelines, audit outcome and for training and education. Regional collaboration between teams on an "all Wales" basis, to plan clinical trials and associated research strategies should be encouraged.

3.18 The specialist oncology service will be provided by a Cancer Centre, equipped and resourced to provide pre/post-operative chemotherapy and radical/palliative radiotherapy.

3.19 Integrated support services should be available, including the resources for counselling at diagnosis, palliative care, nutritional support and psychological care for patients and families.

3.20 Data should be recorded on a shared data base, such as ISCO, which could be networked to provide a contemporary All Wales Cancer Database. This will require investment in manpower and information technology.

4. OESOPHAGEAL CANCER (OC)

Epidemiology and Incidence
4.01 Increased alcohol ingestion and smoking, especially in association predispose to OC (Mooler et al 1990)
4.02 Recent increased incidence in young non-smoking males may be related to Barrett's oesophagus (vide infra).

The Clinical Problem
4.03 Presentation is usually with progressive dysphagia and weight loss.
4.04 At presentation many patients are elderly, infirmed or wasted as a result of the disease and therapeutic options are thus limited.
4.05 At diagnosis, OC is disseminated in up to 80% of cases (Andersen et al 1982, Bosch et al 1979)

Referral
4.06 The symptom of dysphagia should always prompt urgent referral from primary care for rapid (open) access endoscopy (see cancer of the stomach), barium meal or outpatient appointment (GI surgeon or medical gastroenterologist) depending on local circumstances.
4.07 The diagnosis of Barrett's oesophagus is usually made at endoscopy carried out for symptoms of reflux. Barrett's oesophagus is known to have a malignant potential for adenocarcinoma with a 44-fold increased risk (Spechler et al 1984). There is considerable controversy over the value of endoscopic screening in this group of patients.
4.08 The case for long-term screening is based on the following observations:

- In the 1960s adenocarcinoma of the oesophagus accounted for less than 8% of all oesophageal cancers in the USA. In the last two decades this has increased at a rate exceeding that of any other cancer and today 50% of all OC in caucasian males are adeno-carcinomas. (Spechler et al 1992)
- Endoscopic surveillance to look for dysplasia relies on pathological interpretation which is largely subjective (Reid et al 1988)
- There is evidence that brush cytology is superior to biopsy for the diagnosis of cancer but not dysplasia (Geisinger et al 1992, Altorki et al 1990), it is suggested that the use of both techniques will keep false negatives to a minimum.
- There is little benefit in screening elderly or infirm patients who would not be fit for oesophageal resection.
- Recommendations for screening have been published by the Barrett's Esophagus Working Party of The World Congress of Gastroenterology (Dent et al 1991). Sufficient information is available about the value of biopsy surveillance as a component of good clinical practice (Dent et al 1991), but there is, as yet, no proof that screening programs reduce the mortality from cancer in Barrett's oesophagus.

**Recommendations for Referral and Screening**

1. Open (rapid) access endoscopy with referral guidelines for Primary Care. The value of a surveillance programme for cancer in Barrett’s Oesophagus is uncertain. If carried out, screening should be based on the World Congress of Gastroenterology recommendations.

**Staging**

4.09 Accurate staging is essential for all gastrointestinal cancers in order to:

- Avoid unnecessary / inappropriate major surgery
- Enable treatment to be given with proper informed consent
- Plan multimodal therapy
- Permit comparison of treatments between and within centres
- Determine eligibility for entry into clinical trials

and includes some or all of the following:

- Clinical examination, routine bloods and chest X-ray
- Upper gastrointestinal biopsy / cytology to confirm a diagnosis of cancer, identify its site and extent and demonstrate the histological type.
- Barium meal, though not essential in all cases, may be diagnostic as the first investigation, and will show the tumour length which is related to operability and disease stage.

4.10 Computed tomography (CT) is inferior to endoscopic ultrasound (EUS) in staging the depth of tumour invasion (T stage). EUS is also the best available method for detecting mediastinal and coeliac lymph node involvement. However contrast enhanced CT is of value in detecting distant metastases and some stage IV disease and the two examinations are complimentary (Botet et al 1991). In some patients EUS gives only limited information as the transducer will not pass through the tumour, however the majority of these patients have stage IV disease. MRI has not yet shown any additional benefit in staging.

4.11 Laparoscopy and laparoscopic ultrasound are superior to any imaging technique for the detection of peritoneal and small metastatic liver deposits (see stomach cancer).

**Recommendation for Staging**

1. Staging, by a combination of careful clinical assessment, chest X-ray, barium study/ endoscopy, EUS, CT and laparoscopy, should identify “operable tumours”. These may be defined as <5 cm in length, T1-3 and N0-1.
Treatment

4.12 The results of surgical resection of OC depend on the stage of the disease, presence of co-morbidity and the skill of the operating team (surgeon, anaesthetist, theatre staff, ITU). These three factors make comparison of surgical results between centres difficult. Extensive literature review of publications on surgical treatment of OC between 1980 and 1988, found an increase in resectability and 50% fall in operative mortality. However there was no increase in long term survival (Muller et al 1990). This study concluded that of every 100 patients with OC, presenting to a surgeon, 56 will have resectable disease. Of these, 7 will die from postoperative complications and 47 will be discharged from hospital after an average stay of 3 weeks. Of these patients, 27 will survive the first, 12 the second and 10 the fifth year. Individual surgeons report a lower operative mortality and better survival figures (Watson 1994). There has never been a comprehensive population audit of oesophageal cancer, the Welsh Office is currently funding such a study which is based on the methodology used in the Welsh Colorectal Cancer Audit. Results will be available in early 1997.

4.13 Surgery gives the best restoration of swallowing and offers the potential for cure. However many patients will be medically unfit for major surgical procedures and many fit patients will have metastatic disease. For these patients, palliative therapy to relieve dysphagia is the main aim of treatment and there are a number of methods for achieving this (vide infra).

4.14 The ability to withstand the physiological trauma of oesophagectomy is an important aspect of assessment. Clinical judgement of fitness for oesophagectomy may be supplemented by measuring:

- Cardiac function, the systolic ejection fraction should be greater than 40%, and there should be no history of cardiac failure or of myocardial infarction in the preceding 12 months.
- Respiratory function, the FEV1 should be greater than 1.25L and there should be no chronic lung disease.

4.15 A number of technical approaches are described for resecting OC. There are very few trials to evaluate these techniques, and comparisons have failed to favour a particular method. The surgeon should be familiar with, and able to carry out a variety of procedures (Launois et al 1983, Putnam 1994).

4.16 There is minimal published data to support a volume - outcome effect in oesophageal surgery. However, because of the magnitude of the procedure, oesophagectomy should only be carried out in hospitals where there are surgeons with an interest in the disease who take part in National studies and are prepared to audit their results. The anaesthetist should have expertise in the care of patients undergoing thoracic surgery. There is evidence that thoracic epidural anaesthesia is associated with fewer respiratory complications (Watson and Allen 1994) and there should be access to an Intensive Care Unit for early postoperative management. Physiotherapy and nutritional support are essential aspects of care.

4.17 A single study of RT as primary monotherapy for OC showed survival at one year of 44% and five years of 22% (Pearson 1966). These results have never been repeated and there have been no trials comparing RT with surgery in this disease. There is no evidence that pre or post operative radiotherapy (RT) prolongs survival in OC, however RT reduces locoregional failure in some patients, and postoperative RT should be considered in patients with lymph node involvement or residual disease (Teniere et al 1991).

4.18 Cisplatin and 5-FU are both thought to have a radiosensitizing effect and used with radiotherapy show a survival advantage over radiotherapy alone (Herskovic et al 1992). This approach may be considered for patients who are not suitable for, or do not wish to undergo surgery. The addition of chemotherapy with 5 FU and Cisplatinum improved local control (35% to 56%), decreased distant failure (26% to 12%) and improved 2 year survival rate (10% to 40%) (Burmeister et al 1995).

4.19 Some workers have shown that neoadjuvant combined chemoradiation therapy improves survival. For example, one study of surgery following chemoradiotherapy showed a median survival of 26 months with 32% alive at 5 years (Forastiere et al 1993). However the German Oesophageal Cancer Study Group found side effects but no survival advantage in patients receiving chemoradiotherapy and surgery compared with surgery alone. Surgery alone remains the standard treatment and other regimes should be explored, but only within the context of a clinical trial.

4.20 Neoadjuvant chemotherapy alone may be of value in squamous OC (Smalley 1994). The MRC trial, OE 02, uses the combination of Cisplatin and Fluorouracil followed by surgery for both squamous and adenocarcinomas.
4.21 Surgical by-pass can be carried out as a palliative procedure to restore swallowing. However the mortality rate for this is greater than 20% and survival may be only months (Robinson et al 1982). By contrast, palliative intubation procedures will relieve malignant obstruction in up to 90% of patients with a 5% mortality (Wilton A & Smith PM 1995).

4.22 Non-surgical methods for palliation of dysphagia include a variety of endoluminal therapies for which, at present, no clear preference can be stated. Options available include laser therapy, intubation with an Atkinson-type tube or expanding metal stents, brachytherapy and alcohol injection. Each have their disadvantages and preference depends on the length and consistency of the tumour and locally available expertise. Laser therapy and alcohol injections can remove exophytic obstructing tumour, but both require repeated hospital treatments and the tumours may regrow rapidly. There are risks (perforation, swallowing problems, death) associated with the use of Atkinson and Celestin tubes which may be reduced with the use of more expensive expanding metal mesh stents. Endoluminal high dose rate brachytherapy can deliver a high dose of radiotherapy locally to the tumour with palliative benefit and its use can be combined with other modalities.

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<th>Recommendations for Treatment</th>
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<tr>
<td>1. In each hospital that carries out oesophageal resection there should be a designated surgeon(s) who manages all cases of OC. The anaesthetist should be familiar with anaesthesia for thoracotomy and there must be full ITU facilities.</td>
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<tr>
<td>2. Treatment depends on stage at presentation and the patient's fitness.</td>
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<tr>
<td>3. Fitness for surgery should be assessed on clinical grounds supplemented by measurement of cardiac and respiratory function.</td>
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<td>4. Surgery is recommended for fit patients with Stages I and IIA, disease. Stage I and IIA patients who do not wish to undergo surgery and stages IIB and III should be considered for neoadjuvant chemoradiation therapy, within the confines of a clinical trial whenever possible. Stage IIB and III may be suitable for resection after therapy.</td>
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<tr>
<td>5. The elderly, infirm and those with advanced disease and poor prognosis should receive endoscopic palliation for dysphagia.</td>
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Audit and Quality Issues  (see page 154)

Pathology Reporting

Pre-operative Biopsy

4.23 A pre-operative biopsy diagnosis of carcinoma should be obtained whenever feasible, and the histological type of the tumour (squamous carcinoma, adenocarcinoma and undifferentiated carcinoma etc), should be stated in the biopsy report. If the biopsy fails to demonstrate invasive malignancy in a lesion which histologically is unequivocally neoplastic, then clinical endoscopic and radiological features should be used to judge whether the lesion might be a pre-invasive neoplasm (i.e. an adenoma) and tailor the treatment accordingly.

4.24 Pre-operative biopsy of a flat adenocarcinomas in a Barrett's oesophagus, may only show severe (high grade) dysplasia. It is now widely accepted that, unless the lesion is polypoid, a biopsy diagnosis of high grade dysplasia, when agreed by two pathologists in consultation (one of whom should have a special interest in gastrointestinal pathology), is sufficient grounds to proceed with radical surgical treatment.

Intra-operative Frozen Section

4.25 Intra-operative frozen section may be used to evaluate proximal resection lines in cases where macroscopic assessment of clearance is difficult. Ideally the full circumference of submucosa should be seen in the plane of the resection line.
Resection Specimens

4.26 The pathological report should contain the following information:

**Macroscopic Description**
- Length of specimen, presence or absence of proximal stomach
- Size of the tumour (largest dimension)
- Site of the tumour in relation to the nearest resection margin
- Gross appearance of the tumour
- Gross evidence of involvement of the deep (radial) excision plane
- Any abnormalities of the background oesophagus (and stomach if present)

**Microscopic Description**
- Histological type and differentiation of tumour
- Maximum depth of invasion into/through oesophageal wall
- A statement on completeness of excision at the cut ends and at the deep (radial) resection plane
- The number of lymph nodes examined, and the number containing metastases
- Any abnormalities of the background oesophagus and/or stomach
- The stage may, if agreed with clinicians, be expressed according to the TNM system

**NB** In view of the prognostic importance of assessing completeness of excision at the deep (radial) resection plane, this should be painted with a suitable marker before gross dissection of the specimen, to allow its accurate histological identification.

**References**


5. GASTRIC CANCER (GC)

Epidemiology and Incidence

5.01 Cancer of the stomach accounts for approximately 25% of GI cancers in Wales. It is uncommon under the age of 45 years.

5.02 The incidence is falling although there has been a large increase in adenocarcinoma of the proximal stomach and gastro-oesophageal junction.

5.03 More common in people of low socio-economic status, smokers and drinkers, its incidence is also related to diet, especially increased salt, low quantities of fresh fruit and vegetables and preserved foods in which nitrosamines may be detected. Chronic gastritis is associated with a markedly increased risk and recent reports suggest this may be related to Helicobacter pylori infection. Seropositivity to \textit{H pylori} may be associated with an up to six times increased risk for GC. There is also a genetic predisposition in some individuals with a 2-4 fold increased risk in first degree relatives of affected patients. GC is also increased in patients who have undergone partial gastrectomy and those with gastric polyps and pernicious anaemia.

The Clinical Problem

5.04 Symptoms are often non-specific and include anorexia, upper abdominal discomfort after eating, a feeling of fullness, epigastric pain and weight loss.

5.05 Presentation is frequently with advanced disease. Although GC can be cured by surgery, up to 80% of cases are too extensive at the time of diagnosis. Earlier diagnosis is the key to improving outcome.

5.06 Five year survival, in a population study, was less than 5% and even after apparent curative resection, less than 20% (Allum et al 1989). However better results are reported from single centres (Sue-Ling et al 1993).

Referral

5.07 Prompt diagnosis increases the percentage of cases with early stage gastric cancer from 1% to 15% with an associated increase in operability from 31% to 53%. The effect of early diagnosis and radical surgical resection is to improve 5 year survival (Sue-Ling et al 1993). Population screening, undertaken in Japan, where the disease is common, is associated with an early GC detection rate of 30-40% (Kaneco et al 1977). Mass screening would probably not be cost effective in the UK, where the incidence of GC is much lower. However, in the UK, early referral of symptomatic patients to open access endoscopy, was associated with an increased detection rate of early CG. By examining dyspeptic patients over 40 years of age via open access endoscopy, the proportion of early gastric cancers was 26% and operable cases 63% (Hallissey et al 1990). Referral guidelines for upper gastrointestinal endoscopy have recently been produced by a joint UK working party (Axon, 1995).

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<th>Recommendation</th>
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<tr>
<td>1. A vigorous approach to diagnosis by open (rapid) access endoscopy is essential. Referral should be based on the recommendations produced by a multidisciplinary UK Working Party (Axon et al 1995).</td>
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Staging

5.08 Following the histological diagnosis of GC, patients should be assessed for therapy according to their clinical performance status (see oesophageal cancer) and the stage of disease.

5.09 Liver metastases and large coeliac nodal masses may be detectable by contrast enhanced CT and ultrasound scan.

5.10 Depth of invasion and nodal disease in proximity to the tumour are best detected by endoluminal ultrasound, which is superior to CT (Botet et al 1991). The concordance of EUS and CT with surgical pathology is 90% and 40% respectively (Lightdale 1992). EUS probably has little impact on survival and benefit appears to be that of sparing patients, with advanced disease, unnecessary surgery. In addition, accurate staging is necessary for trials of neoadjuvant therapy.
Laparoscopy enhances staging by detecting peritoneal metastases, thus avoiding unnecessary laparotomy (Possik et al 1986). This can be combined with laparoscopic ultrasound, the best imaging method available for detecting small liver metastases (Senaler et al 1995).

Despite the above, it may still be impossible to determine the operability of GC, in a small number of patients, without a laparotomy.

**Recommendation**

1. In addition to clinical examination, chest X-ray and diagnostic endoscopy, staging involves conventional ultrasound, EUS, contrast enhanced CT, laparoscopy and, if available, laparoscopic ultrasound.

**Treatment**

Surgical resection offers the only hope of cure for patients with GC. Prognosis following radical resection is dependant on the pathological stage with only 15-20% 5-year survival for stage I and II patients, 2% for stage III and IV (Appendix II). Following palliative or no resection, the majority of patients will die within one year.

The role of surgical specialization has been addressed in a 5 year review of 206 patients treated by 17 different surgeons in a single UK hospital. There was a wide variation between surgeons in all outcome measures, but the number of cases per surgeon was too small for statistical analysis (McCulloch 1994). This study concluded that concentration of management among fewer surgeons might represent one way in which results could be improved, citing the Japanese experience with specialisation as evidence. The increasing importance of multimodal therapy and multidisciplinary care in the modern management of GC also argues for cases to be treated by "designated surgeons" in each hospital.

The extent of gastric resection for antral tumours has been examined in a comprehensive review. Subtotal gastrectomy compared with total gastrectomy for distal tumours gave the same survival results, but the former procedure was associated with the least discomfort and better quality of life (Bozzetti 1992). There is a general consensus that total gastrectomy is indicated for cancers in the mid stomach and fundus. Cancers at the cardia require total gastrectomy with excision of at least 5 cms of the oesophagus proximal to the tumour.

One aspect of surgical technique which is a cause of considerable controversy is the extent of lymphadenectomy. Japanese surgeons are the champions of radical lymphadenectomy, citing their high cure rates as supporting evidence for this practice (Soga et al 1988). The superior Japanese results may be due to the younger age at which the disease presents in Japan and the greater ease of dissection in thin Japanese patients compared to Western European. However, detailed study has suggested that the superior results obtained in Japan, compared with those from two European countries, are not due to differences in prognostic factors and staging systems, focusing attention on surgical technique.

Two mature randomised trials from South Africa and Hong Kong have demonstrated that extended lymphadenectomy is associated with significant morbidity and mortality compared with a more modest resection (Dent et al 1988, Robertson et al 1994). In addition, a recent large prospective randomised trial from Holland, involving careful oversight by Japanese surgeons, showed an increased morbidity for patients undergoing more radical surgery. Details on long term survival are due in 1996 (Bonenkamp et al 1995). This issue is also the subject of an MRC study in the UK and the results are due in 1996. It cannot as yet be stated that radical (R2) resections should be the standard of surgical care for GC in the UK. A recent comprehensive review details the case for and against extensive lymph node resection (Roder et al 1995).

Locally advanced tumours should be considered for pre-operative chemotherapy followed by resection if possible. In a phase II study of epirubicin and cisplatin with continuous infusion fluorouracil, tumour regression occurred in 71% with complete remission, confirmed histologically in 12% (Findlay et al 1995). The role of perioperative chemotherapy, using a regimen based on this study is being evaluated by an MRC trial (ST 02). Ethical committee approval has been confirmed at Velindre for this, although the practicalities of increased hospitalisation, Hickman line placement, and the use of an infusion pump, coupled with the geography of Wales, may present problems.
5.19 A recent meta-analysis of post operative adjuvant chemotherapy for gastric cancer showed no survival advantage with chemotherapy (Hermans et al 1993). The British Stomach Cancer Group, in trials of adjuvant therapies after resection, found no survival advantage compared with surgery alone. Their report concluded that the use of adjuvant therapy after curative resection should be restricted to clinical trials.

5.20 Patients with advanced gastric cancer have a poor prognosis with a median survival of about 3 months with best supportive care. Two randomised studies have shown a survival advantage of about 7 months median with palliative chemotherapy (Pyrhonen, 1992, Murad, 1993). In the USA combined chemotherapy and radiotherapy is probably the treatment of choice but in the UK, oncologists have not felt so optimistic about radiotherapy.

5.21 Endoluminal intubations are much less effective in the stomach than the oesophagus. Palliative bypass operations may be necessary for patients with gastric outlet obstruction.

**Recommendations**

1. A team of GI surgeons should be identified to work as part of the integrated service for GC in each Cancer Unit.
2. A designated surgical team should be supported by experienced anaesthetic staff and ITU/HDU facilities. Adequate access to theatre time is necessary to be able to maintain a short waiting time for resections.
3. Suitable patients, whose disease has been adequately staged, may be offered perioperative chemotherapy carried out within a clinical trial (MRC Trial ST 02).
4. An oncology team should be identified to work within the integrated service. This team should be equipped to provide chemotherapy and radiotherapy according to most recent protocols, including facilities for continuous infusional ambulatory chemotherapy.

**Supportive Care**

5.22 Most patients with gastric and oesophageal cancers die of the disease. Symptoms can be most distressing with dysphagia, persistent vomiting and severe debility being very common. The close involvement of the palliative medicine team is most important to ensure improvements in quality of life for patients with these distressing symptoms. Dysphagia should always be dealt with by a suitably trained gastrointestinal endoscopist.

**Recommendations**

1. The palliative care members of the multidisciplinary team will be readily available for referral of patients to provide symptomatic, social, family and emotional support at all stages of disease.
2. The integrated gastro-oesophageal cancer team should be supported by appropriate paramedical specialists in counselling, nutrition and palliative care.
Audit and Quality Issues

Recommendations

1. All patients with a confirmed diagnosis of cancer will be registered with a local cancer registry and entered onto the joint cancer database with the Cancer centre.

2. Pathological examination of biopsy samples, aspiration or brush cytology and subsequent surgical resections should be carried out in accredited pathology departments according to attached criteria (see below).

3. Criteria for audit will include aspects of quality of care; time between presentation, diagnosis and treatment: accuracy of staging compared to pathological / operative findings, for radically treated patients; resectability rates, operative mortality, extent of nodal dissection, response to chemotherapy, survival from diagnosis, quality of life post resection. For palliatively treated patients; quality of swallowing after intervention, duration of freedom from dysphagia, quality of life, weight gain or loss, survival. Oncology issues will include; quality assurance in radiotherapy and chemotherapy administration; complications of chemotherapy and radiotherapy, response rates to CT and RT. Pathology issues will include audit against agreed guidelines for examination and reporting.

Pathology Reporting

Pre-operative Biopsy

5.23 A pre-operative biopsy diagnosis of carcinoma should be obtained whenever feasible. If a biopsy fails to demonstrate invasive malignancy in a lesion, which histologically is unequivocally neoplastic, then clinical, endoscopic or radiological features should be used to judge whether the lesion might be a pre-invasive neoplasm (i.e. adenoma) and to tailor the treatment accordingly. Pre-operative biopsies of flat carcinomas may only show severe (high grade) dysplasia. It is now widely accepted that, unless the lesion is polypoid, a biopsy diagnosis of high grade dysplasia, if agreed by two pathologists on consultation (one of whom should have a special interest in gastro-intestinal pathology), is sufficient grounds to proceed with radical surgical treatment.

Intra-operative Frozen Section

5.24 Although not required routinely, intra-operative frozen section may be used to evaluate resection lines in cases where macroscopic assessment of clearance is difficult, particularly for some carcinomas of the proximal stomach.

Resection Specimens

5.25 A pathological report should contain the following information:

Macrosopic Description
- Length of the specimen along the greater and lesser curvatures.
- Size of the tumour (largest dimension).
- Site of the tumour in relation to the nearest resection margin.
- Gross appearance of the tumour.
- Gross evidence of serosal involvement.
- Any abnormalities of the background stomach.

Microscopic Description
- Histological type and differentiation of tumour
- Maximum depth of invasion into / through gastric wall
- Presence or absence of serosal ulceration by tumour
- A statement on completeness of excision
- The number of lymph nodes examined and number containing metastases in two groups, those less than 3 cmm and those more than 3 cmm from the primary tumour mass
- Any abnormalities in the background stomach
- Stage may be expressed in terms of the TNM system
References
Lightdale CJ. Endoscopic Ultrasonography and Staging and Follow up of Oesophageal and Gastric Cancer. Endoscopy 125 (supplement 1) 1992;297.
6. PANCREATIC AND PERIAMPULLARY CANCER

Epidemiology and Incidence
6.01 The incidence of pancreatic cancer in England and Wales is 12 per 100,000 population. It is the fifth commonest cause of cancer death and is characterised by an extremely poor prognosis.
6.02 Risk factors are smoking, alcohol consumption and possibly diabetes mellitus and chronic long standing pancreatitis.
6.03 More than 90% of pancreatic cancers are epithelial tumours, in particular adenocarcinoma. Recognition of the remaining 10%, which include cystic tumours, lymphomas and islet cell tumours, is important as prognosis is more favourable.
6.04 Periampullary cancer is far less common but has a better prognosis as resection rates are higher as the tumour may present at an earlier stage.

Presentation and Referral
6.05 Presentation is frequently with non-specific gastrointestinal symptoms which include weight loss, anorexia and back pain. Jaundice is usually the symptom which prompts urgent referral to hospital. Vomiting may occur due to duodenal obstruction.

Diagnosis
6.06 The aim of diagnostic investigations is to identify the type of tumour and, in fit patients, stage the tumour for resectability.
6.07 Trans-abdominal ultrasound scan (USS) will distinguish between "medical" and "surgical" jaundice. When the biliary tract is dilated, endoscopic retrograde cholangio pancreatography (ERCP) is the investigation of choice and will provide a reliable diagnosis in the majority of cases of cancer of the pancreas. Tissue diagnosis may also be made at ERCP by brush cytology or bile/pancreatic juice cytology, although negative results do not exclude the diagnosis of cancer.
6.08 Computed Tomography (CT) can be helpful in both diagnosis and staging. Dynamic contrast enhanced CT has a reported diagnostic accuracy rate of greater than 97% in specialist centres (Freeny et al 1993). Large volume dynamic contrast enhancement is essential for adequate imaging (Lees 1994). Helical CT scanning may offer considerable advantages but is not widely available (Dupuy et al 1992).
6.09 There is no convincing evidence that MRI is superior to CT in the diagnosis or staging of pancreatic cancer (Sterna et al 1989, Warshaw & Fernandez-del-Castillo 1992). However, MRI is an evolving modality and its use may be of greater importance in the future.

Staging
6.10 Accurate staging is important to identify patients who might benefit from resection. Staging is only necessary when operation is an option, many patients will be elderly or infirm and not candidates for major surgery.
6.11 Staging is carried out to assess resectability of the tumour, in particular to look for the presence of extrapancreatic disease and invasion of major, adjacent, vascular structures.
6.12 Transabdominal USS and contrast enhanced CT may show metastatic disease (vide supra). Laparoscopy (Warshaw 1994) and more recently laparoscopic ultrasound (John et al 1995) may alter management in up to a third of cases. Vascular invasion can be demonstrated by contrast enhanced CT or spiral CT. However a recent report has shown intra-operative ultrasound to be more specific and more accurate than a combination of pre-operative trans-abdominal ultrasound, dynamic CT scanning and angiography in assessing portal vein invasion by pancreatic cancer (Machi et al 1993).
6.13 Endoscopic ultrasound (EUS) also appears to be of value. One study prospectively compared EUS with transabdominal USS, CT scanning and angiography. EUS was superior for local pancreatic tumour staging (Rösch et al 1992). However, EUS cannot be expected to detect distant metastases and cannot be considered as a complete staging investigation.
6.14 Selective angiography was previously the investigation of choice to assess local tumour extent by encasement or occlusion of arteries and veins around the pancreas. However, angiography can be misleading, is invasive, and frequently adds little to high quality dynamic CT scanning (Freeny et al 1993, Murugiah et al 1993). Angiography can also be used to provide "a vascular map" that might be of help in the 30-35% of patients with peri-pancreatic vascular anomalies (Biehl et al 1993). Others believe that the provision of such a "map" is not in itself sufficient justification for routine selective arteriography (Carter 1996).

Tissue Diagnosis

6.15 This can be made at ERCP by biopsy of a visible ampullary tumour or cytological examination of pancreatic fluid or brushings. However, a negative result does not exclude the diagnosis. Percutaneous fine needle aspiration cytology has been practised for over 25 years but the sensitivity of this procedure rarely exceeds 80% and is often less (Parson et al 1989). There is some anxiety that the pancreatic tumour may seed along the needle track and a potentially curable tumour would be rendered incurable (Warshaw 1991). However, a recent controlled study has shown biopsy did not influence longevity (Balen et al 1995). There is general agreement that every reasonable effort should be made to make a tissue diagnosis by methods such as percutaneous Trucut or fine needle biopsy, particularly in the young patient with an unresectable tumour.

Recommendations

1. Urgent referral for obstructive jaundice.
2. Trans-abdominal USS will confirm bile duct obstruction, ERCP may provide both the diagnosis and means of initial treatment/palliation by biliary stenting.
3. If the diagnosis remains uncertain or tumour resection is considered, a high quality contrast enhanced CT scan should be obtained.
4. When the scan confirms localised disease, laparoscopy, combined if possible with laparoscopic ultrasound, should be carried out. Endoscopic ultrasound may also be used for local staging of the disease, if available.
5. Where possible, a tissue diagnosis should be obtained.

Treatment

6.16 Surgical resection provides the only hope of cure from pancreatic cancer. In many cases it is clear that, because of advanced disease, age or debility, a particular patient is not a candidate for such major surgery. However, if doubt exists then an appropriate surgical opinion should be obtained.

6.17 In the decade 1977-86, the resection rate for pancreatic cancer in the West Midlands was only 2.6%, the 30 day mortality rate for resection was 27.6% and the 5 year survival following resection 9.7% (Bramhall et al 1995). Data such as these encourage many clinicians to adopt a nihilistic attitude to any attempt at pancreatic resection for cancer. However more encouraging results are reported from specialist centres with resection rates of 10 - 20%, postoperative mortality rates of less than 10% and 5 year survival rates of up to 25% (Bramhall and Neoptolemos 1994). Two centres have reported series of 145 and 118 pancreatic resections without a postoperative death (Cameron et al 1993, Trede et al 1990). These results argue for the recognition of specialist referral for pancreatic resection. However it is difficult to base the definition of a specialist centre on selected referral and case volume alone. Recent data on 80 cases of Whipple resections from 7 University and 23 Community/District Hospitals in Norway, found no difference in operative mortality between the different types of hospital (overall 9%). There was a trend for University Hospitals to have a lower complication rate (Bakkevold and Kambestadt 1993).

6.18 In the otherwise fit patient who gives informed consent, Stage I tumours should always be resected and stage III tumours never, as survival is so short. Stage II tumours may be resectable and if technically feasible this option should be discussed with the patient.

6.19 The type of surgical procedure (pylorus preserving, Kausch-Whipple resection, total pancreatectomy) depends on the site and extent of the tumour and the surgeon's preferred technique. There are a number of options, particularly for the pancreatic anastomosis and surgeons use methods that work best in their hands.
6.20 **Adjuvant Treatment.** The Gastrointestinal Tumour Study Group (1987) used adjuvant radiochemotherapy following resection and found a doubling of mean survival time. These encouraging results should stimulate entry of suitable cases into clinical studies such as the ESPAC-1 trial (Neoptololemos and Kerr 1995). Therapy outside of such trials cannot be recommended.

6.21 **Palliative Care.** The majority of patients with pancreatic cancer, whether they undergo resection or not, will die from their disease, frequently in a debilitated state. Mean survival after the first symptom is 6 months, and in one series 30% of patients died within one month of diagnosis (Gudjonson et al 1978). Involvement of palliative care physicians and counselling services from the time of diagnosis is preferable for the majority of patients. Malabsorption and digestive problems may respond to pancreatic enzyme supplements. Methods of pain relief include opiates, epidural infusion, radiotherapy and coeliac plexus block.

6.22 **Malignant jaundice** can be relieved by biliary stenting or surgical by-pass. These two methods have been the subject of three prospective randomised trials (Shepherd et al 1988, Anderson et al 1989, Smith et al 1989). Both techniques are equally effective in relieving jaundice with no difference in long term survival. Endoscopic stenting is associated with a lower complication rate, lower procedure related mortality and shorter hospitalisation. In modern practice, a combination of endoscopic and radiological techniques should provide effective palliation of jaundice in a vast majority of cases. Problems with blockage of stents may be minimised by using the self-expandable metal type (Knyrin et al 1993), perhaps most appropriate in patients in whom a survival of more than 6 months is anticipated.

6.23 **Chemotherapy and radiotherapy** has recently been reviewed (Coulter & Mallison 1995, Bramhall and Neoptololemos 1994). There is no convincing evidence that chemotherapy or radiotherapy has a significant effect in the survival of unresectable pancreatic cancer, although radiotherapy may help in the control of local pain. The use of these treatments should preferably be only by entry into local or National trials.

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**Recommendations**

1. Pancreatic resection should be offered to patients in whom staging suggests operability.
2. Adjuvant therapy should only be given within a clinical trial.
3. Jaundice can almost always be relieved by palliative endoscopic or radiological biliary drainage. Surgical by-pass will rarely be required.
4. Patients with unresectable disease may be offered radiotherapy or chemotherapy on a selective basis and entry into national trials should be considered.
5. Palliative care specialists should be involved from the time of diagnosis.

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**Pathology Reporting**

6.24 See tissue diagnosis page 14 for biopsy details. At laparotomy tissue can be taken for histological diagnosis using Trucut or biopsy needles by the transduodenal route.

**Resection Specimen**

**Macroscopic Description**

- Type of operation (Whipple procedure, total or distal pancreatectomy)
- Organs present in specimen and their dimensions; weight of spleen
- Tumour characteristics; involvement of ampulla, duodenal mucosa, stomach, common bile duct, pancreatic duct, and pancreas: size, shape (papillary, flat, ulcerated)
- Common bile duct, main pancreatic duct and accessory pancreatic duct: location and relationship with each other: dilated? stones? tumour?
- Pancreas: tumour invasion? atrophy? fibrosis?
- Spleen: tumour invasion? other features
- Location, number and appearance of regional nodes
Microscopic Description

- Histological type and differentiation of tumour
- Invasion of tumour beyond pancreas and into which organs
- Completeness of excision with reference to planes of resection
- Involvement of lymph nodes by group
- Stage may be expressed as TNM

References


7. COLORECTAL CANCER

7.01 In 1987 there were over 28,000 new cases of colorectal cancer diagnosed in the United Kingdom, and in 1991 there were some 19,000 deaths. It is the second most common cause of cancer death after lung cancer, and the overall 5 year survival is less than 40% (CRC 1993). Advanced disease at first presentation is still common, and the recent Wales, Trent and Wessex audits have shown that only 60% of patients undergo potentially curative surgery. Even in this select group it is anticipated that approximately 30% will die from their cancer. The high incidence of this disease, together with the fact that improvement in mortality in recent years has been modest, highlights the urgency for research into better treatment, earlier diagnosis and prevention.

7.02 The Royal College of Surgeons of England and the Association of Coloproctology of Great Britain and Ireland have published guidelines for the management of colorectal cancer, (hereafter referred to as "The Guidelines") and this section is based on these. Detailed discussion and references will be found in the full document.

7.03 In 1992, the Department of Health commissioned the Royal College of Surgeons of England to produce guidelines for the management of Colorectal Cancer. These have been drawn up by a Drafting Committee, revised by an Expert Advisory Group, composed of distinguished representatives of the main groups involved with the management of colorectal cancer, and have been sanctioned by the Cancer Services Committee of the Royal College of Surgeons of England.

7.04 Three sources of information were used to produce The Guidelines: i) literature review in areas where unequivocal scientific bases for recommendations exist, ii) the results of contemporary population audits of the management of all patients presenting with colorectal cancer in Wales, Trent and Wessex, in order to define reasonable practice (benchmarks) where appropriate and iii) consensus where no other approach is feasible or currently available. These have been complemented with the best results from the literature to provide "gold standards" at which to aim.

7.05 Evidence for each guideline has been assessed using a system designed by the Health Services Research Unit, University of Aberdeen, and is summarised in Appendix IV. Each recommendation below, carries a grading according to this system. However the grade cannot be regarded as a 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. Furthermore, some recommendations cover topics which are not amenable to formal studies, and may be graded C despite being self-evident. The reader must therefore exert a degree of independent critical appraisal.

7.06 A number of target figures in the recommendations are based on the findings of the population audits, these are indicated by an asterisk (*) in the text and may not reflect the case-mix of an individual hospital or clinician.

7.07 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 will be charged with producing yearly "add on" monographs. The guidelines will be radically revised every 3-5 years.

**Summary of Guidelines**

**Investigation**

7.08 Patients with suspicious symptoms or a proven colorectal cancer should be investigated with either endoscopic visualisation of the whole rectum plus a high quality double contrast barium enema or a total colonoscopy. B

7.09 Doctors carrying out colonoscopy should audit their results, and expect to achieve a 90% total colonoscopy rate with a minimal perforation rate. B

7.10 All patients should have preoperative chest X-ray, full blood count and urea and electrolyte estimations, and, if the management will be influenced by the presence of liver metastases, screening by USS or contrast enhanced CT should be considered. C

7.11 Fixity of rectal tumours should be assessed preoperatively in all cases. C

7.12 Preoperative histology should be obtained from all rectal tumours. C

7.13 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 who can evaluate their risk of developing the disease, and advise on appropriate investigations and surveillance. B
Access to Treatment

7.14 Surgeons should expect to achieve maximum waiting times of 4 weeks between the diagnosis of colorectal cancer and operation. B

7.15 Colorectal cancer should be treated by surgeons with appropriate training and experience. B

7.16 All patients should have the benefit of a suitably informed surgical opinion. B

Preparation for surgery

7.17 All patients undergoing surgery for colorectal cancer should give informed consent. This implies being given information about the likely benefits and risks of the proposed treatment and details of any alternatives. C

7.18 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. C

7.19 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. A

7.20 Mechanical bowel preparation prior to surgery is generally recommended. C

7.21 Subcutaneous heparin or intermittent compression should be employed as thromboembolism prophylaxis in surgery for colorectal cancer unless there is a specific contraindication. A

7.22 All patients undergoing surgery for colorectal cancer should have antibiotic prophylaxis. It is impossible to be dogmatic regarding the precise regime, but a single dose of appropriate intravenous antibiotics appears to be effective. A

Elective Surgical Treatment

7.23 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. B

7.24 Any tumour with a distal margin 15 cm or less from the anal verge, using a rigid sigmoidoscope, should be classified as rectal. C

7.25 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 visualise and preserve the pelvic autonomic nerves and plexuses, and perforation of the tumour during operation should be avoided. B

7.26 Although no definite recommendations can be made regarding anastomotic technique, the interrupted serosubmucosal method has the lowest reported leak rate for rectal anastomoses, 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. Cytocidal washout prior to anastomosis should be used. B

7.27 The proportion of rectal tumours treated by 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. B

7.28 Local excision for cure in rectal cancer should be restricted to pT1 tumours. It must be accepted, therefore, that subsequent histopathological examination of tumours, thought to be suitable for local excision, will identify a small proportion which require more radical surgery. B

7.29 Laparoscopic surgery for colorectal cancer should only be performed by experienced laparoscopic surgeons who have been properly trained in colorectal surgery, and who are prepared to audit their results very carefully. B

Record Keeping

7.30 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. C

7.31 A check list should be used to construct an operation note for patients undergoing surgery for colorectal cancer (appendix V). C
Emergency Treatment

7.32 Emergency surgery should be carried out during daytime hours as far as possible, by experienced surgeons and anaesthetists. C

7.33 In obstruction, measures (sigmoidoscopy and water-soluble contrast enema) should be taken to exclude pseudo-obstruction before operation. B

7.34 Stoma formation should be carried out in the patient's interests only, and not because of inexperienced surgical staff. B

7.35 The overall mortality for emergency/urgent surgery should be 20%* or less. B

Adjuvant Therapy

7.36 Patients with Dukes' stage B/C cancer of the colon and rectum should be considered for the QUASAR Study. A

7.37 Patients with mobile Dukes' B and C tumours of the rectum should be considered for pre-operative radiotherapy to the posterior pelvis, using a three or four field technique, giving 25Gy in 5 fractions in one week, immediately prior to surgery. A

7.38 Patients with involved circumferential margins after surgery for rectal cancer, without preoperative radiotherapy, should be considered for post-operative radiotherapy to the pelvis using a three or four field plan, with the patient prone, giving 4500Gy in 25 fractions over 5 weeks.

7.39 Patients with fixed rectal cancers should be considered for preoperative radiotherapy: 4000cGy in 20 fractions over 4 weeks using a 3/4 field plan, followed by further assessment of operability and attempted resection if appropriate. B

Treatment of Advanced Disease

7.40 It is recommended that effective palliation with optimal quality of remaining life should be the main aim of therapy in advanced disease. C

7.41 Consideration should be given to palliative radiotherapy and palliative chemotherapy in patients with local-advanced and metastatic disease. Thus, patients with advanced disease, who remain in good general condition, should have the opportunity to discuss the possible benefits of palliative therapy with an oncologist. Entry into MRC studies CR05 and CR06 should be considered. A

7.42 Consideration should also be given to surgical treatment in selected patients with local advanced or metastatic disease. In particular, for some patients with hepatic involvement liver resection might be possible and suitable cases should be referred to an experienced liver surgeon. B

7.43 Surgeons and oncologists who deal with colorectal cancer must build close links with palliative care specialists and units. B

Outcomes

7.44 Surgeons should carefully audit the outcome of their colorectal cancer surgery and:

7.45 They should expect to achieve an operative mortality of less than 20%* for emergency surgery and 5%* for elective surgery for colorectal cancer. B

7.46 Wound infection rates after surgery for colorectal cancer should be less than 10%*. A

7.47 Surgeons 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. B

7.48 Local recurrence rates after curative resection should be 10%* or less. A

7.49 Surgeons should carefully examine their practice with a view to meeting or improving on targets set by national long-term mortality statistics. B

Follow-up

7.50 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 at some time during the first two post-operative years, for the purpose of detecting operable liver metastases. B
Although there is no evidence that colonoscopic follow-up improves survival, it has been shown to produce a high yield of treatable tumours. If such a policy is pursued, it is recommended that a "clean" colon should be examined by colonoscopy at 3-5 year intervals. Even if restricted to younger patients, such a policy may have local resource implications.  

Some form of follow up is necessary for audit, which should be structured with particular reference to outcome measures, and should be regarded as a routine part of a consultant's work.

After discharge from hospital, all patients with a stoma should have ready access to specialist nursing staff.

Pathology

All resected colorectal tumours should be submitted for histological examination. For this to be useful, the report should reach an acceptable standard, providing information which will be useful in assessing prognosis, planning treatment, and carrying out audit.  

Pathology Reporting

Accurate, detailed and consistent pathology reporting is important for 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, study of the quality of pathology reporting has shown great variability among hospitals participating in the Wales/Trent Audit, and this has important implications for the interpretation of differences in outcomes in different units and between surgeons. This needs to be addressed with some urgency.

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.

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)

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

There is some 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), but this has not been confirmed in other studies (Geraghty et al 1991).

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 opened specimen and careful pathological dissection, prior to selecting tissue blocks for histology. In order to assess the circumferential resection margin, in rectal cancers below the peritoneal reflection, it is strongly recommended that this margin is painted with ink before sectioning. Dukes staging requires the separate identification of the “apical” lymph nodes, i.e. the node closest to the main vascular ligature.
Both macroscopic and histological appearances must be described in some detail, and the following should be included in the report:

**Macroscopic Description**
- size of the tumour (greatest dimension)
- site of the tumour in relation to the resection margins (or, for APER specimens, the dentate line) and the peritoneal reflection
- any abnormalities of the background bowel

**Microscopic Description**
- histological type (WHO classification, see Appendix III)
- differentiation of the tumour (Halvorsen et al 1988 IIb), based on the predominant grade within the tumour
- maximum extent of invasion into/through the bowel wall (submucosa, muscularis propria, extramural)
- serosal involvement by tumour (Shepherd et al 1995), if present
- a statement in the completeness of excision at the cut ends (including the "doughnuts" from stapling devices) and, for rectal cancers below the peritoneal reflection, the circumferential (lateral, radial) resection plane. In the latter assessment, tumours within 1mm of the circumferential margin are regarded as incompletely excised (Quirke et al 1986, Adam et al 1994)
- the number of lymph nodes examined, the number containing metastases, and whether or not the apical node is involved. It is also recommended that extramural tumour "deposits" measuring >3mm in diameter are also regarded as lymph node metastases, irrespective of whether they are accompanied by identifiable lymph node tissue (Hermanek et al 1993)
- extramural vascular invasion (Talbot et al 1981) if present
- pathological staging of the tumour according to the Dukes’ classification (Dukes 1958)

Dukes’ staging is recommended as it is simple, reproducible and widely recognised in the UK. TNM staging may also be employed, and the two systems are described in Appendix VI. Some pathologists may wish to use the Jass classification (Jass et al 1987 IIb) although its usefulness may be limited by observer variation in the degree of lymphocytic infiltration at the advancing margin of the tumour (one of the four parameters that contribute to the classification) and the fact that its prognostic value appears to be confined to rectal tumours.

In order to ensure that pathology reports contain all of the items of information required for optimal patient management, pathologists are encouraged to use template proformas for reporting, an example of which is given in Appendix III.

In addition, there are three other recommendations:
- pathological examination of colorectal cancer specimens should be carried out in laboratories that perform to a high technical standard, such as that required for CPA accreditation, and which also participate in external quality assessment schemes and regular audit of technical procedures and diagnosis.
- multidisciplinary clinicopathological meetings involving physicians, surgeons, radiologist and pathologists are recommended for the planning of patient treatment.
- 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.

<table>
<thead>
<tr>
<th>Recommendation</th>
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<tbody>
<tr>
<td>1. All resected colorectal tumours should be submitted for histopathological examination, which should reach acceptable quality standards as outlined above.</td>
</tr>
</tbody>
</table>

Recommendation grading : B
References

Adam IJ, Mohamdee MO, Martin IG, Scott N, Finan PJ, Johnston D, Dixon MF, Quirke P. Role of Circumferential Margin Involvement in the Local Recurrence of Rectal Cancer. Lancet 1994; 344: 707-711


Geraghty JM, Williams CB, Talbot IC. Malignant Colorectal Polyps, Venous Invasion and Successful Treatment by Endoscopic Polypectomy. Gut 1991; 32: 774-778


8. ANAL CANCER

Epidemiology and Incidence
8.01 This is a rare tumour, 20-30 times less common than colorectal cancer.
8.02 Many tumours contain DNA from the human papilloma virus. This may explain the association between anal cancer and sexually transmitted disease, particularly infection with the human immunodeficiency virus (Scholefield et al 1990).

The Clinical Problem
8.03 Presentation is with symptoms which are not specific, such as bleeding, pain, pruritus and tenesmus. Inguinal lymph node enlargement may be present in up to 10% of cases.

Diagnosis and Staging
8.04 Diagnosis is by biopsy. More than 90% of anal cancers are squamous cell tumours.
8.05 Staging depends on tumour site, either anal canal or anal margin. Canal tumours are staged by circumferential and extent of local spread and sphincter involvement. Margin tumours are staged by size, infiltration and inguinal node status (UICC staging, see Appendix VII).

Treatment
8.06 Because of its rarity and the relatively small published studies, guidelines for treatment have been difficult to establish (Greenhall 1988). Because of its rarity anal cancer should be treated by colorectal surgeons who enter patients into, and are aware of the results of national trials.
8.07 Smaller anal margin tumours can be treated by wide local excision, provided an adequate margin of clearance is obtained and inguinal nodes are not involved. Local excision is not satisfactory for anal canal tumours (Greenhall 1988).
8.08 Surgery was the mainstay of treatment for anal cancers, but several studies, within the last 20 years, show that comparable results could be achieved by radiotherapy, with or without chemotherapy (Nigro et al 1974, Cummings 1982). Such non-surgical treatment avoids the use of a colostomy.
8.09 The UKCCCR set up a National Trial in 1989, to compare radiotherapy with combined modality treatment (radiotherapy plus 5-FU and mitomycin C), with surgery reserved for treatment failures. At its close, 577 eligible patients, with tumours of the anal canal and margin had been randomised into the trial. This figure represents 30% of the national incidence during the study period. Analysis of the results (median follow-up of 42 months) confirms a large difference in local control rates between treatments and a cause-specific survival advantage for patients receiving 5-FU and Mitomycin C (data in: UKCCCR Anal Cancer Trials Winter Newsletter - February 1996).
8.10 The UKCCCR are currently finalising details of a further study which will include a Cisplatin based regimen. Patient entry into this new trial should be considered by Welsh surgeons and oncologists.

Follow-up
8.11 Regular clinic review, preferably by a surgeon and a radiotherapist, is recommended to look for evidence of residual or recurrent disease. Review is also essential for patients entered into clinical trials and to assess any late toxicity from treatment.

Recommendations
1. Anal canal and margin tumours should be managed by the colorectal multidisciplinary team in the cancer unit. Following biopsy and staging cases should be referred to the cancer centre according to joint protocol.
2. Local excision may be suitable for small margin tumours.
3. Larger margin and all anal canal tumours should be considered for chemoradiation therapy. Radical excision should not be carried out before chemo-radiotherapy has been tried.
4. Entry into the new UKCCCR study should be considered when final details are announced.
References

9. ACKNOWLEDGEMENTS
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Dr TS Maughan, Consultant Clinical Oncologist, Velindre NHS Trust
Professor G Williams, Department of Histopathology, University Hospital of Wales Healthcare NHS Trust

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Mr J Beynon, Consultant Colorectal Surgeon, Swansea NHS Trust
Mr P Billings, Consultant Colorectal Surgeon, Wrexham Maelor Hospital NHS Trust
Mr D Carey, Consultant Surgeon, University Hospital of Wales Healthcare NHS Trust
Mr M Crumplin, Consultant Surgeon, Wrexham Maelor Hospital NHS Trust
Mr M Jamieson, Consultant Surgeon, Gwynedd Hospitals NHS Trust
Dr B Hawthorn, Department of Gastroenterology, University Hospital of Wales Healthcare NHS Trust
Dr D Mort, Consultant Clinical Oncologist, Velindre NHS Trust
Mr J Pye, Consultant Surgeon, Wrexham Maelor Hospital NHS Trust
Mr A Radcliffe, Consultant Colorectal Surgeon, Llandough Hospital and Community NHS Trust
Dr P Smith, Consultant Gastroenterologist, Llandough Hospital and Community NHS Trust
Mr K Vellacot, Consultant Surgeon, Glan Hafren NHS Trust
Mr H Young, Consultant Surgeon, University Hospital of Wales Healthcare NHS Trust

The final draft was circulated to Consultant Surgeons in Wales for comments on the content or any omissions. Helpful comments was received from Professor R Mansel (University of Wales College of Medicine) and Professor J Baxter (Morriston Hospital NHS Trust) and have been incorporated in the final version.
APPENDIX I - STAGING OF OESOPHAGEAL CANCER

TNM

T- Primary Tumour
  T1  Tumour limited to lamina propra or submucosa
  T2  Tumour involving muscularis propria
  T3  Involvement of adventitia but no extraoesophageal structures
  T4  Extension to extraoesophageal structures

N- Regional Lymph Nodes
  N0  No nodal involvement
  N1  Any regional nodal involvement

M- Distant Metastases
  M0  No distant metastases
  M1  Distant metastases

Stage Grouping
Stage 1  T1N0M0
Stage 2A  T2-3N0M0
Stage 2B  T1-2N1M0
Stage 3  T3N1M0
       T4NxM0
Stage 4  TxNxM1
APPENDIX II - STAGING OF GASTRIC CANCER

TMN Staging

T - Primary Tumour
- **Tis** Tumour limited to mucosa, does not penetrate basement membrane
- **T1** Tumour limited to mucosa and submucosa
- **T2** Tumour to or into but not through serosa
- **T3** Through serosa but without invasion of adjacent structures
- **T4a** Involves immediately adjacent structures
- **T4b** Direct extension to unresectable adjacent organs

N - Regional Lymph Nodes
- **N0** No nodal involvement
- **N1** Perigastric nodea within 3cm of tumour
- **N2** Other regional nodes resectable
- **N3** Other intra-abdominal nodes

M - Distant Metastases
- **M0** No distant metastases
- **M1** Distant metastases

Stage Grouping

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>II</td>
<td>T2-3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>III</td>
<td>T1-3</td>
<td>N1-2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>N0-2</td>
<td>M0</td>
</tr>
<tr>
<td>IV</td>
<td>T4b or N3 or M1</td>
<td></td>
<td></td>
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</tbody>
</table>
APPENDIX III - STAGING OF PANCREATIC AND PERIAMPULLARY CANCER

Pancreatic Cancer
TNM
T - Primary Tumour
   Tx Histological examination of tumour not possible
   T0 Primary Tumour Not Found
   T1 Tumour limited to pancreas
   T1a Largest diameter of tumour < 2 cms
   T1b Largest diameter of tumour ≤ 2 cms
   T2 Tumour growth directly into duodenum, bile duct and/or peripancreatic tissues
   T3 Tumour directly into stomach, spleen, colon and/or large blood vessels

Stage Grouping for Pancreatic Cancer
Stage I T1,2 N0 M0
Stage II T3 N0 M0
Stage III any T N1 M0
Stage IV any T any N M1

Periampullary Cancer
TNM
   Tx Histological examination of primary tumour not possible
   T0 Primary tumour not found
   T1is Carcinoma in situ
   T1 Tumour limited to ampulla
   T2 Tumour infiltrating abdominal wall
   T3 Tumour infiltrating 2cm into the pancreas
   T4 Tumour infiltrating 2cm into the pancreas or other adjacent organs

Stage Grouping for Periampullary Cancer
Stage 0 Tis N0 M0
Stage 1 T1 N0 M0
Stage 2 T2,3 N0 M0
Stage 3 T1,2,3 N1 M0
Stage 4 T4 any N M0
or any T any N M1
APPENDIX IV - (SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK CRITERIA FOR GRADING OF EVIDENCE AND RECOMMENDATIONS)

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

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)

Some recommendations cover topics which are not amenable to formal studies, and are therefore graded C despite being self-evident.
APPENDIX V - 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 or 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 (i.e. no residual macroscopic tumour)
   vii) Sites and reasons for stomas
APPENDIX VI - 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
   Tis Carcinoma in situ
   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:** Direct invasion in T4 includes invasion of other segments of the colorectum by way of the serosa, e.g. invasion of the sigmoid colon by a carcinoma of the caecum

   **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
   N3 Metastasis in any lymph node along the course of a named vascular trunk

   **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
APPENDIX VII - STAGING OF ANAL CANCER

UICC Clinical Staging System

Anatomic Region:
1. Anal Canal with haemorrhoidal zone, crypts of Morgagni and Pecten
2. Anal Margin

Regional Nodes:
Anal Canal: perirectal and nodes to the origin of the inferior mesenteric margin.
Anal Margin: inguinal nodes.

1. Anal Canal

T - Primary Tumour
Tis  Pre-invasive carcinoma
T0  No evidence of Primary tumour
T1  Tumour occupying less than 1/3 of the circumference or length of the anal canal or tumour infiltrating the external sphincter muscle.
T2  Tumour occupying more than one third of the circumference or length of the anal canal or tumour infiltrating the anal sphincter muscle.
T3  Tumour with extension to rectum or skin but not to other neighbouring structures.
T4  Tumour with extension to other neighbouring structures.
TX  The minimum requirements to assess the primary tumour cannot be met.

N - Nodes
N0  No evidence of regional node involvement
N1  Evidence of involvement of regional nodes
NX  Minimum requirements to assess the regional nodes cannot be met.

2. Anal Margin:

T - Primary Tumour
Tis  Pre invasive carcinoma
T0  No evidence of primary tumour
T1  Tumour 2cm or less in its greatest dimension strictly superficial or exophytic.
T2  Tumour more than 2cm but not more than 5cm in its greatest dimension or tumour with minimal infiltration of the dermis.
T3  Tumour more than 5cm in its greatest dimension or tumour with deep infiltration of the dermis.
T4  Tumour with extension to muscle, bone etc.
TX  The minimum requirements to assess the primary tumour cannot be met.

N - Regional Lymph Node Involvement
N0  No evidence of regional lymph node involvement
N1  Evidence of involvement of movable unilateral regional nodes.
N2  Evidence of involvement of movable bilateral lymph nodes
N3  Evidence of involvement of fixed regional nodes
NX  Minimum requirements to assess the regional lymph nodes cannot be met.