COLORECTAL SURGERY

Clinical Care and Management

Edited by

Bruce George, Richard Guy,
Oliver Jones and Jon Vogel

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Foreword

Mastering the art and science of surgery is becoming increasingly difficult. The explosion of knowledge and technology is a threat to even a relatively new specialty like colorectal surgery. Our medical students have little exposure to the subject and need instant tutorials, our trainees struggle with the increasing complexity of operative surgery, and consultant staff are beginning to subspecialize. Everyone is finding it difficult to keep up. If you agree then this accessible, readable, and very enjoyable book will help.

Although not in quite the same league as the Case Records of the Massachusetts General Hospital, we have a weekly academic meeting in Oxford at which one of the residents or consultant staff presents a "case of the week." The diagnosis, management, and outcome of each are poked, prodded, and recorded so that we can address our ignorance, learn from our mistakes, and look at controversies from every point of view.

This book distils some of these cases into 52 clinical vignettes arranged into groups of colorectal cancer, inflammatory bowel disease, proctology, and emergency surgery. For each group, there is a background chapter, and then the cases are presented with a discussion point, a series of learning points, and an important paragraph, "Could we have done better?" A particularly nice touch is the Letter from America in which one of our former residents looks at how US guidelines and practice might have differed from ours.

The Editors have done a great job choosing and putting together a terrific range of cases, some of which I remember only too well. And on reflection, yes, we could have done better.

Neil Mortensen, Oxford

SECTION A

Colorectal cancer

Bruce George
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Incidence

Colorectal cancer (CRC) is the second most common cause of cancer-related mortality in the Western world. Approximately 6% of the population will develop CRC during their lifetime.

Pathogenesis

Colorectal cancer develops through a stepwise accumulation of genetic and epigenetic alterations. There are three major molecular mechanisms involved in colorectal carcinogenesis:

- chromosomal instability
- microsatellite instability
- CpG island methylation.

Chromosomal instability

In the late 1980s, Vogelstein *et al.* described a series of genetic alterations resulting in change from normal colonocytes through adenoma to carcinoma. Key genes in this process include adenomatous polyposis coli (APC), k-ras and p53, all of which code for proteins critically involved in regulation of cell turnover. APC is a tumor suppressor gene on chromosome 5q21 (long arm of chromosome 5). The APC protein controls degradation of beta-catenin which is involved in the control of epithelial cell turnover. Mutation of the APC gene results in accumulation of beta-catenin which, in turn, alters expression of several genes affecting cell proliferation, differentiation, and apoptosis. Germline mutation in the APC gene results in familial adenomatous polyposis (FAP).

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Microsatellite instability

Microsatellites are short repeat nucleotide sequences found throughout the genome and are prone to errors during replication. Mutations in mismatch repair genes result in an increased risk of CRC. Tumors associated with defects in DNA mismatch repair are characterized by increased microsatellite instability. Germline mutations in mismatch repair genes result in hereditary nonpolyposis colorectal cancer (HNPCC).

CpG island methylation

More recently, epigenetic influences such as DNA methylation have been found to be involved in tumorigenesis. Normally, only about 3–4% of all cytosines in DNA are methylated and methylation only occurs at cytosines at the 5′ end of guanine (CpGs). Clusters of CpGs tend to occur in the promoter region of many genes. Increased methylation of CpGs at the promoter end of tumor suppressor genes may result in reduced activation of the genes, resulting in increased tumor risk. Environmental factors may exert their influence on carcinogenesis through epigenetic mechanisms.

Awareness of the molecular changes in individual tumors is likely to become increasingly important in individualizing treatment. Sporadic tumors, for example, with features of high microsatellite instability, tend to respond poorly to 5-fluorouracil (5FU) chemotherapy.

Risk factors for colorectal cancer

Increasing age, a family history of CRC and long-term ulcerative colitis (UC) or Crohn's colitis are major risk factors for the development of CRC. Rare situations in which the risk is slightly increased include acromegaly, renal transplantation, and a history of abdominal irradiation.

Family history

Twin studies suggest that about 20% of CRC have an inherited predisposition. The mechanism of inherited risk is well characterized in patients with FAP (about 1% of all CRC) and HNPCC (about 3–5% of all CRC), but not in the remainder of those with a positive family history.

Familial adenomatous polyposis is an autosomal dominant condition resulting from mutation in the APC gene. The disease is characterized by the development of multiple polyps, usually over 100, in adolescence and, unless treated, inevitable progression to colon cancer. Extracolonic features include gastroduodenal polyps – with a lifetime risk of duodenal cancer of 12% – and desmoid

tumors. The precise site of the mutation in the APC gene correlates with the clinical phenotype, for example the risk of developing desmoid tumors.

Hereditary nonpolyposis colorectal cancer is an autosomal dominant condition caused by a germline mutation in DNA mismatch repair genes. Loss of mismatch repair genes results in replication errors, increased mutations, and an increased risk of malignancy. The hallmark of HNPCC is microsatellite instability. Individuals with HNPCC tend to develop tumors at a younger age than those with sporadic tumors and are also at increased risk of other tumors, especially endometrial, gastric, ovarian, and urinary tract.

It is impractical to genetically test all family members of patients with CRC for HNPCC, and various criteria have been developed to identify patients and families likely to have HNPCC, the most common being the Amsterdam Criteria (Box A.1).

Box A.1 Amsterdam criteria for the diagnosis of HNPCC.

Amsterdam I

- At least three relatives with CRC, one of which should be a first-degree relative of the other two
- At least two successive generations affected
- At least one CRC diagnosed before the age of 50 years
- FAP excluded
- Tumors verified histologically

Amsterdam II

- At least three relatives with an HNPCC-associated cancer, one of which should be a first-degree relative of the other two
- At least two successive generations affected
- At least one CRC diagnosed before age 50 years
- FAP excluded
- Tumors verified histologically

Diet and lifestyle

A high-fiber diet has been postulated for many years to be associated with a reduced risk of CRC, although results from several meta-analyses show conflicting results. The EPIC study suggests that a high-fiber diet is associated with a 40% risk reduction. On the other hand, red meat, smoking, alcohol, and obesity have been associated with an increased risk. Increased physical exercise has been shown to be independently associated with a reduced risk.

Long-term aspirin therapy has been shown in several studies with over 20-year follow-up to be associated with a reduced risk, although a recent

consensus group felt that further research was needed before aspirin could be recommended as chemoprevention for high-risk groups [1].

Pathology

Most CRCs are thought to arise from adenomatous polyps. A variety of polyps is found in the colon and rectum, varying in their premalignant potential (Box A.2).

Box A.2 Types of polyp in the colon and rectum.

- Adenoma
- Serrated lesions
- Hamartomatous
- Inflammatory
- Pseudo-polyps

The site, size, number, and shape of polyps are important in assessing risk. The majority of polyps are sessile or pedunculated, although the Paris classification is useful, particularly when assessing small flat lesions (Figure A.1).

When viewed colonoscopically using adjuncts such as chromoendoscopy ("dye spray") and high-definition imaging, different "pit patterns" may be observed on the surface of polyps, which may help to identify the type of polyp (Figure A.2).

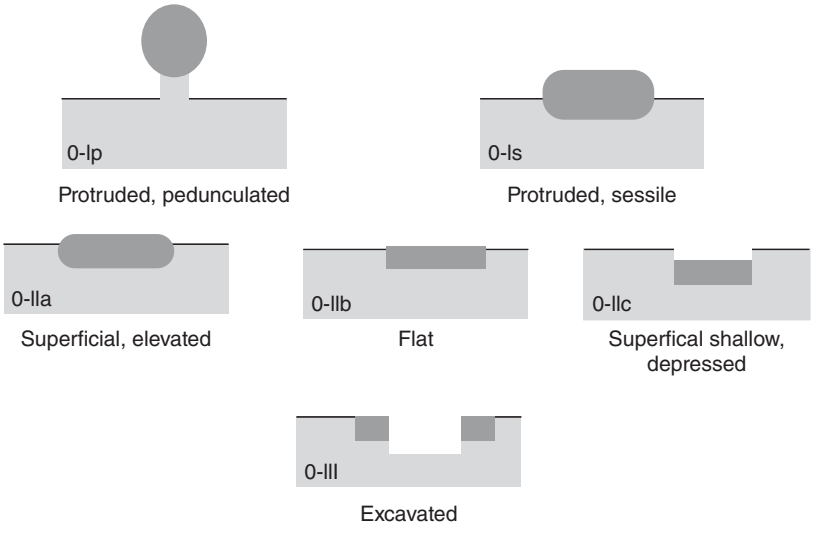

Figure A.1 Paris classification. *Source*: Participants in the Paris Workshop. 2003. Reproduced with permission of Elsevier.

Pit pattern type	Characteristics
I	roundish pils
II	stellaror papillary pits
III S	smallroundish or tubular pits (smaller than type I pits)
III L	large roundish or tubular pits (larger than type I pits)
IV	branch-like or gyrus-like pits
V	non-structured pits

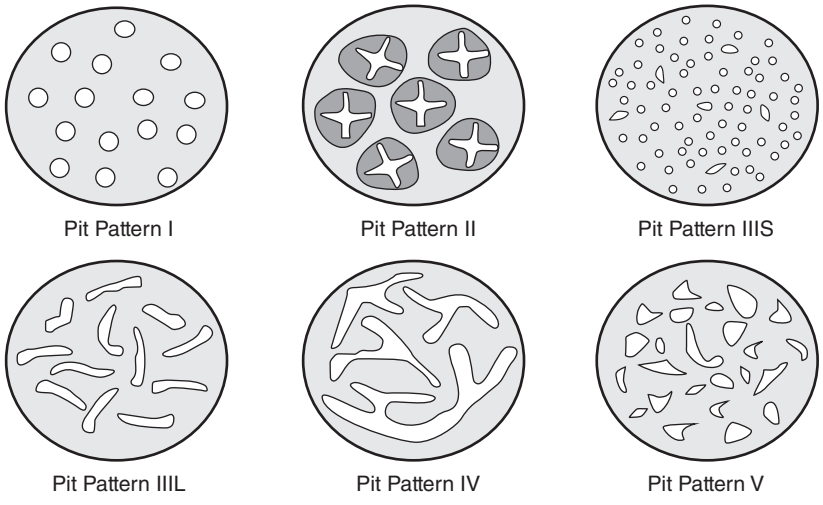

Figure A.2 Polyp pit patterns. *Source*: Williams [2]. Reproduced with permission of Wiley.

Broadly speaking, pit patterns 1 and 2 tend to be associated with normal or nonneoplastic lesions, types 3 and 4 with adenomas, and type 5 with invasive malignancy.

Adenomatous polyps show cellular dysplasia and are potentially premalignant. Architecturally, they may be classified as tubular, tubulovillous or villous. Thus, larger villous lesions with high-grade dysplasia have a higher risk of malignant transformation.

Serrated lesions are being increasingly recognized, particularly since the advent of screening programs, although their natural history remains unclear. There are three types of serrated lesions.

- *Hyperplastic polyp*. These tend to be small sessile lesions mainly in the rectum and have no malignant potential.
- *Sessile serrated adenoma (SSA)*. These tend to occur in the right colon, may be large in size but can be difficult to identify colonoscopically. They are associated with a risk of synchronous advanced neoplasms.
- *Traditional serrated adenoma (TSA)*. These are more likely to be situated in the left colon and are easier to identify colonoscopically.

It is thought that SSAs and TSAs may progress to invasive malignancy by a distinct molecular pathway, involving BRAF mutation and epigenetic silencing

of mismatch repair genes. The importance of thorough colonoscopic clearance and surveillance is being realized. Multiple hyperplastic polyposis syndromes are being increasingly recognized and have a 50% lifetime risk of CRC (see **Case 2**).

Appearance and distribution

Macroscopically, CRC may be polypoid, ulcerated or annular. The distribution of tumors is approximately as follows: 40% rectum or rectosigmoid junction, 25% sigmoid, 25% cecum or ascending colon, and the remainder (10%) in the transverse or descending colon.

Pathological features

Microscopically, tumors are adenocarcinomas with varying degrees of differentiation. Histological features associated with a poor prognosis include mucinous, signet ring, and neuroendocrine differentiation. Immunohistochemically, colorectal carcinomas tend to be CK20 positive and CK7 negative.

Colorectal cancer staging

The most common pathological staging systems in use are the Dukes and TNM (Tumor, Node, Metastases) systems (Table A.1). Dukes' original stages are as follows.

- A – tumor confined to the bowel wall without lymph node involvement
- B – tumor beyond the wall with no lymph node involvement
- C – any tumor with lymph node involvement

Later modifications included C1 (apical node not involved), C2 (apical node involved), and Dukes' D to indicate distant metastases.

The prognosis following CRC resection is largely dependent upon the pretreatment radiological staging [3, 4]. This can only be determined for TNM stages, in various permutations and combinations (Table A.2), as Dukes' staging relies on the histopathological examination of a resected specimen.

Clinical presentation

Colorectal malignancy may be detected in asymptomatic individuals, either through screening or incidentally during investigation of other problems. More commonly, tumors present due to symptoms related to the primary tumor or due to metastatic spread.

Symptoms of colorectal cancer

The classic symptoms of colorectal malignancy depend on the site of the tumor. Rectal tumors tend to present with overt rectal bleeding, passage of mucus or

Table A.1 TNM classification system for colorectal cancer.

T stage	N stage	M stage
T1 Tumor confined to the submucosa	**N0** No lymph nodes contain tumor cells	**M0** No metastases seen in distant organs
T2 Tumor has grown into (but not through) the muscularis propria	**N1** Tumor cells seen in up to 3 regional lymph nodes*	**M1** Metastases seen in distant organs
T3 Tumor has grown into (but not through) the serosa	**N2** Tumor cells seen in 4 or more regional lymph nodes**	
T4 Tumor has penetrated the serosa and peritoneal surface **T4a** Extension into adjacent structures or organs **T4b** Bowel perforation		

*A tumor nodule in the pericolic or perirectal adipose tissue without evidence of residual lymph node is regarded as a lymph node metastasis if it is >3 mm in diameter. If it is <3 mm in diameter, it is regarded as discontinuous tumor extension.
**If there are tumor cells in nonregional lymph nodes (i.e. in a region of the bowel with a different pattern of lymphatic drainage to that of the tumor), that is regarded as distant metastasis (pM1).
Source: American Joint Committee on Cancer [5].

Table A.2 Five-year survival rate based on TMN staging of colon and rectal cancers.

TMN	Colon 5-year survival rate	Rectal 5-year survival rate
T1, T2 N0	97.1%	94.4%
T3 N0	87.5%	78.7%
T4 N0	71.5%	61.4%
T1, T2 N1	87.1%	85.1%
T1, T2 N2	75.0%	63.9%
T3 N1	68.7%	63.3%
T3 N2	47.3%	43.7%
T4 N1	50.5%	47.1%
T4 N2	27.1%	29.5%

tenesmus. Sigmoid and descending colon lesions tend to present with darker blood mixed with stool or an alteration in bowel pattern. Cancers in the right colon are more likely to be "silent" and to present with anemia, weight loss or anorexia.

In clinical practice, many patients present with symptoms which may fit for CRC but could also be attributed to a variety of benign disorders. Identification

of significant ("red flag") symptoms (Box A.3) has been attempted in order to expedite appropriate investigations, and to exclude those who probably do not warrant urgent referral. In the UK, these have been used to facilitate rapid assessment, although the efficacy is questioned and there may still be a tendency for overreferral.

Box A.3 "Red flag" symptoms suggesting CRC.

- Rectal bleeding for more than 6 weeks without anal symptoms
- Change of bowel habit to looser, more frequent stools for more than 6 weeks in a person over 60 years of age
- Change of bowel habit to looser/frequent stools for >6 weeks and rectal bleeding in a person over 40 years
- Right iliac fossa mass
- Rectal mass
- Unexplained iron deficiency anemia (<11 g/dL in men, <10 g/dL in nonmenstruating women)

The majority of patients presenting with significant symptoms require luminal investigation, either by colonoscopy or CT colonography ("virtual colonoscopy"). A recent UK multicenter trial compared colonoscopy to CT colonography in patients referred with bowel symptoms [6]. Detection rates for cancers and large polyps were similar (11%), although significantly more patients required additional investigation after CT colonography than after colonoscopy.

Emergency presentation

About 25% of patients with CRC present as an emergency, most commonly with colonic obstruction. Tumor perforation, major bleeding or anemia may also prompt emergency admission.

Symptoms due to metastatic disease

Approximately 25% of patients with CRC have metastatic disease at the time of presentation, often with nonspecific symptoms such as weight loss, anorexia, lethargy or anemia. Less commonly, patients present with focal symptoms due to metastases in the liver (such as capsular pain), lung or brain.

Incidental detection following other investigations

Potentially important colorectal lesions may be detected on radiological imaging during investigations for unrelated pathology. Focal colonic uptake on PET scans, for example, is quite often an indicator of significant pathology. In a recent study [7], CRC was diagnosed in 12 of 28 patients undergoing colonoscopy for PET scan abnormalities.

Screening (see Cases 1, 2 and 8)

Colorectal cancer may be "the most screenable but least screened" of the major cancers. Screening methods include stool tests for occult blood, flexible sigmoidoscopy, colonoscopy or CT colonography.

Guaiac fecal occult blood testing (FOBT) is the most widely used screening method. Blood in the stool is detected by peroxidase activity of the heme part of the hemoglobin molecule, which is not specific to human blood. A positive test usually triggers further assessment by colonoscopy, and this forms the basis of the UK's NHS Bowel Cancer Screening Programme (BCSP) for individuals aged 60–75 years. A Cochrane review of major screening trials worldwide concluded that screening by FOBT decreases mortality from colorectal cancer by about 16%, although there may not be a difference in all-cause mortality between screened and unscreened groups [8].

Newer occult blood tests which are specific to human hemoglobin, such as detection of globin, may yield better results than guaiac-based FOBT.

Colonoscopy as a primary screening modality is attractive in being both diagnostic and potentially therapeutic and is generally considered to be the gold standard investigation for colorectal neoplasia. Whilst not perfect, with a measurable "miss rate" for adenomas, and the requirement for oral bowel preparation carrying some risk, application to large populations has been proven in the NHS BCSP, and endoscopist expertise continues to improve.

Flexible sigmoidoscopy (FS) as a screening tool has been subject to a major UK-based trial [9], involving 55–64 year olds. Polyps detected at flexible sigmoidoscopy were removed and high-risk patients underwent colonoscopy. At median follow-up of 11 years, screening was associated with a 31% reduction in mortality from colorectal cancer and a 23% reduction in CRC incidence. FS has now been incorporated into the NHS BCSP for those aged 55 years and over. The American College of Gastroenterology recommends screening by colonoscopy from the age of 50 years at 10-yearly intervals [10].

Radiological imaging of the colon by CT colonography (virtual colonoscopy) may be used as a screening investigation, and is incorporated into the NHS BCSP for less fit patients and for those in whom colonoscopy was incomplete. There are few procedural risks but exposure to ionizing radiation is of slight concern (see **Case 14**). A head-to-head comparison of colonoscopy and CT colonography [11] showed broadly similar detection rates, with CT colonography slightly outperforming colonoscopy for larger lesions.

Investigation of colorectal cancer

Ideally, all patients with CRC should be assessed by full colonoscopy with biopsy of the primary tumor. Synchronous tumors may be detected in around 4% of cases. Convincing CT colonography may negate the requirement for

colonoscopic biopsy, particularly for proximal colonic tumors. All rectal cancers should have histological confirmation.

Staging should be undertaken with CT scanning of the abdomen and chest in order to exclude metastatic disease. Rectal tumors usually require MRI for local staging, allowing assessment of T stage, N stage, vascular invasion, and the mesorectal margin. Endoanal ultrasound may be useful for assessing the T stage of small or early tumors. Liver MRI or PET-CT may be indicated for further clarification of disease stage.

Measurement of serum carcinoembryonic antigen (CEA) at the time of diagnosis is controversial and not universal, but may be useful for assessing response to treatment and during follow-up, particularly in the presence of liver metastases [12].

Decision making: the multidisciplinary team (MDT)

There is some evidence that outcomes may be improved by formal discussion in multidisciplinary meetings at which surgeons, radiologists, oncologists, and pathologists, amongst others, review individual cases. Burton *et al.* [13] showed that this process was associated with a lower R1 resection rate and Morris *et al.* [14] demonstrated better surgical and oncological outcomes.

Colonic cancer

Most patients without metastatic disease proceed to surgical resection. A small proportion of locally advanced colonic tumors may benefit from preoperative neoadjuvant chemotherapy, although good evidence and indications are lacking.

Malignant colonic obstruction (see Cases 4 and 10)

Surgical options for the management of malignant colonic obstruction have traditionally included defunctioning stoma, Hartmann's procedure or resection with on-table colonic lavage and primary anastomosis. Self-expanding metallic stents, usually inserted under endoscopic and radiological guidance, may rapidly relieve obstruction. In the elderly, unfit patient or those with advanced or metastatic disease, stenting is an attractive palliative option but stenting as a "bridge to surgery" with curative intent is more controversial. The aim is to relieve obstruction, allow correction of physiological abnormalities and then proceed to semi-elective surgery, potentially after bowel preparation. Such surgery is more likely to be undertaken laparoscopically and to be restorative. A recent metaanalysis of randomized trials describes technical and clinical success rates for stenting of 71% and 69%, respectively [15]. Potential complications include stent migration, blockage, and, more seriously, perforation, a clinical perforation rate of 7% and a silent perforation rate of 14% being reported

in the metaanalysis. Stenting may cause tumor fracturing [16] and perhaps hematological and lymphatic dissemination.

Effects on local or distant recurrence have not been fully evaluated, although a Dutch study did not identify a major increased risk of recurrence [17], despite a high perforation rate. A study from Oxford, however, did identify a higher rate of local recurrence in patients treated by stenting before surgery compared to resection alone [18].

The randomized CReST trial (www.crest.bham.ac.uk) is evaluating short- and long-term outcomes from stenting as a bridge to surgery and may shed more light on these important questions.

Rectal cancer

The challenge of rectal cancer management in the absence of advanced metastatic disease is to achieve curative treatment with minimal morbidity. Total mesorectal excision, popularized by Heald [19], and preoperative radiotherapy [20, 21] have been associated with dramatic improvements in oncological outcome. Furthermore, improvements in preoperative imaging have permitted a more tailored approach to patient management.

Anterior resection remains the default treatment for rectal cancer. The MDT must identify:

- patients with early tumors amenable to local resection
- patients with tumors at risk of local recurrence who may require preoperative radiotherapy or chemoradiotherapy
- cases of complete clinical response after chemoradiotherapy
- patients who require abdominoperineal excision of the rectum (APER) or are "on the cusp" of ultra-low anterior resection or APER
- patients with potentially curative synchronous liver and rectal tumors
- patients with locally advanced or recurrent disease (see case 11).

Local excision

Local excision may be reasonably considered for early rectal tumors. Whilst the avoidance of major abdominal and pelvic surgery may be attractive and less morbid, the reduced radicality of the resection, and the lack of lymph node retrieval, may have consequences which must be discussed with the patient.

The risk of lymph node involvement in T1 tumors may be difficult to estimate but depends on tumor size, extent of penetration into the submucosa, and degree of differentiation.

Invasive tumor within a pedunculated polyp is assessed by the Haggitt system [22] (Figure A.3) (see **Case 1**). Invasion in a sessile polyp is assessed by the Kikuchi *et al.* [23] system (Figure A.4). This simply describes invasion into the upper third (sm1), the middle third (sm2) or the lower third (sm3) of the submucosa.

Disruption of a locally excised specimen or piecemeal removal of a sessile polyp by endoscopic mucosal resection (EMR) may prevent accurate Kikuchi

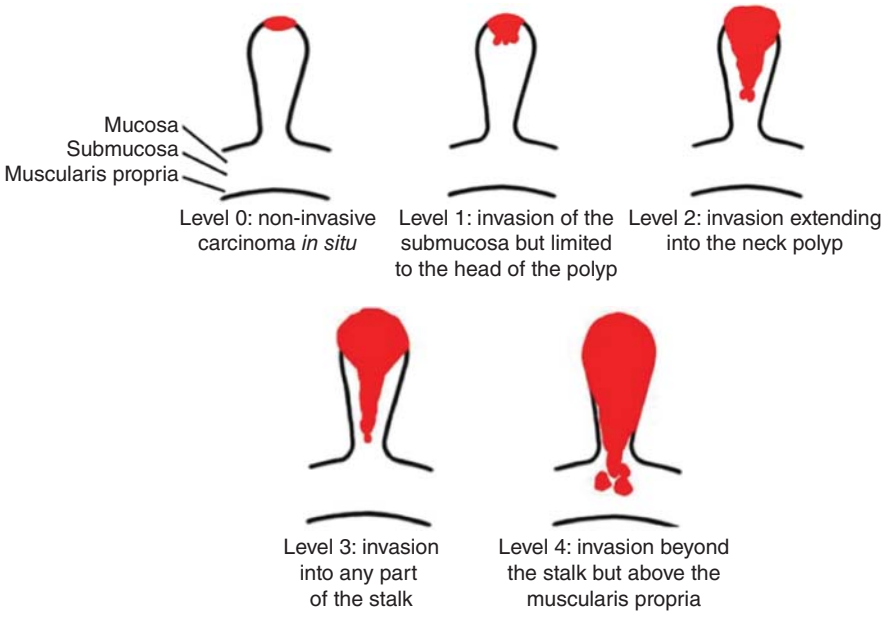

Figure A.3 Haggitt system for cancer invasion in a pedunculated polyp. *Source*: Haggitt *et al*. [22]. Reproduced with permission of Elsevier.

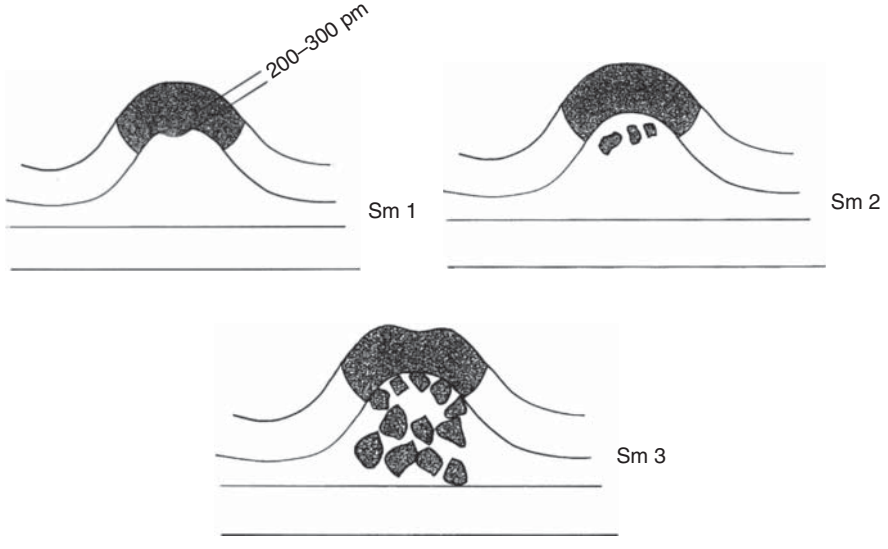

Figure A.4 The Kikuchi classification for sessile malignant polyps. *Source*: Kikuchi *et al*. [23]. Reproduced with permission of Springer publications.

assessment. An alternative approach focuses on the depth and width of invasion beyond the muscularis mucosa.

Current opinion is that tumors suitable for local excision with curative intent should:

- be less than 3 cm diameter
- not be poorly differentiated
- have early T1 invasion only (sm1 or 2)
- have no evidence of nodal involvement on MRI.

Tumors which do not meet these criteria have a greater risk of tumor in lymph nodes and should generally be treated by conventional resection. A recent trial comparing local excision by transanal endoscopic microsurgery (TEM) with laparoscopic anterior resection for T1/T2 rectal tumors showed less morbidity following TEM. There were two local recurrences after TEM (2/28, 7%) compared to none after anterior resection, although this difference was not statistically significant [24].

Local excision may be employed as a compromise for patients who are medically unfit for major resection.

Preoperative radiotherapy (see Cases 5–7)

Preoperative radiotherapy (RT) may be delivered in short or long courses. Short-course RT is typically 5×5 Gy over 5 days followed by surgery the next week. Long-course RT is usually 45–50 Gy given over about 5 weeks with 5FU given during weeks 1 and 5. Surgery is undertaken about 6–8 weeks after completion of chemoradiotherapy. There is increasing evidence that a longer interval to surgery, perhaps out to 12 weeks, may be associated with more tumor shrinkage [25].

Several large trials have shown a significant reduction in local recurrence following surgery after short-course RT compared to surgery alone [20, 21, 26–28]. Only one of these trials – the Swedish rectal cancer trial – showed an improvement in overall survival.

Long-course chemoradiotherapy (CRT) has the advantage over short-course RT (with early surgery) of achieving tumor shrinkage ("downstaging"). This may permit surgical resection with negative margins – which might not have been achieved without CRT – with a significantly reduced risk of local recurrence. Downstaging by CRT may also increase the chance of sphincter-preserving surgery.

Complete clinical response

Around 10–15% of patients will achieve a complete pathological response to long-course CRT, with the result that no viable tumor cells are found in the surgical resection specimen. Such patients have a better prognosis [29]. The idea of avoiding major resectional surgery in patients with a complete clinical response has been popularized by Habr-Gama *et al.* from Brazil [30] although other groups

have not been able to obtain such good results [31]. It is recommended that a "watch and wait" approach after an apparently complete clinical response should only be considered within a rigorous follow-up regime or, ideally, a clinical trial (see **Case 5**).

Need for APER

Patients with very low rectal tumors are at the highest risk of positive margins, and either a poor functional outcome following restorative surgery or the need for a permanent stoma. The vast majority of such patients will receive preoperative chemoradiotherapy.

A decision regarding feasibility of sphincter preservation versus APER requires detailed clinical assessment, review of MR scans, and discussion with the patient. If a decision is made to undertake an APER, the plane of dissection, position of threatened margins, and the method of perineal reconstruction should be planned in advance.

Metastatic disease

In patients with metastatic disease, the dominant treatment is usually chemotherapy. Surgery may only be indicated to alleviate symptoms from the primary tumor not controllable by conservative means. For patients with potentially curative synchronous liver and colonic tumors, 60–70% undergo resection of the primary as initial treatment. This may be associated with significant postoperative morbidity preventing subsequent chemotherapy or liver surgery. Furthermore, R1/R2 rates are higher when the surgeon is aware of metastatic disease [32]. Over the last decade, there has been a move towards a "liver first" approach [33] or, in selected cases, simultaneous liver resections if both are relatively straightforward (see **Case 9**). A similar approach has been adopted for metastatic rectal disease [34]. Clearly, the liver first approach is not appropriate if the primary tumor is causing obstructive symptoms due to the risk of complete obstruction occurring during chemotherapy or liver surgery.

Surgical treatment

Colonic resections

Oral bowel preparation is not required for cancers proximal to the splenic flexure, but many surgeons still prefer to prepare the bowel prior to surgery for left-sided tumors. Venous thromboembolism (VTE) prophylaxis (usually with compression hosiery and subcutaneous fractionated heparin injections) should be administered, and prophylactic antibiotics given just prior to surgery.

The majority of colonic resections can be undertaken laparoscopically, although obstructing, perforated or locally advanced tumors may be better undertaken by open techniques. For right-sided and transverse colonic tumors,

resection is by right or extended right hemicolectomy. Distal transverse and descending colonic tumors may be resected by left hemicolectomy or extended right/subtotal colectomy. Subtotal colectomy may also be indicated for synchronous right and left-sided tumors, for obstructing cancers, and should be considered in patients with HNPCC. Sigmoid tumors are usually treated by high anterior resection with anastomosis of descending colon to upper rectum. Whatever resection is chosen, *en bloc* lymph node removal by high ligation of the relevant vessels should be ensured and a "harvest" of at least 12 lymph nodes is recommended for adequate nodal staging.

Rectal resections

Bowel preparation is more universally accepted for rectal resections, and antibiotic and VTE prophlaxis should be given.

Rectal cancer surgery may present considerable surgical challenges. The principles of surgery for patients with potentially curative disease include:

- high-quality surgical excision with clear margins
- safe restoration of gastrointestinal continuity where appropriate
- preservation of bladder and sexual function.

The main rectal operations undertaken are:

- local peranal excision
- anterior resection
- Hartmann's procedure
- abdominoperineal excision (APER).

Local excision of early rectal cancer is most commonly undertaken by TEM. Posterior approaches to the rectum, e.g. transsphincteric (York–Mason) or transsacral (Kraske), are now very rarely undertaken for cancer, although these approaches remain useful in excision of presacral and retrorectal tumors and tail-gut cysts.

Anterior resection is the standard surgical procedure for most rectal tumors. The procedure may be undertaken by open techniques or a variety of minimally invasive methods, including totally laparoscopic, laparoscopically assisted, robotic or hybrid combinations.

For most anterior resections, the splenic flexure should be fully mobilized in order to achieve maximal length for a tension-free anastomosis. Rectal mobilization should be in the mesorectal plane with visualization and preservation of ureters and presacral hypogastric sympathetic nerves. Parasympathetic nervi erigentes may be seen anterolateraly at the level of the prostate but may be more difficult to see in an obese man with a narrow pelvis.

Dissection in the mesorectal plane is attractive as it is relatively bloodless and allows preservation of the mesorectal fascia. Oncologically, a total mesorectal excision (TME) is considered optimal treatment as viable tumor cells may be found within the mesorectum as far as 4 cm below the lower border of the tumor [35].

The level of distal rectal transaction depends on the precise site of the tumor. Patients with upper and mid rectal tumors should undergo TME with rectal transection at, or just above, the pelvic floor and it is important to ensure a clear margin of rectal wall below the tumor.

Tumors of the distal sigmoid and rectosigmoid can reasonably be resected with a 5 cm distal clearance.

For low rectal tumors, a 2 cm distal margin is considered standard [36], although a 1 cm margin is considered reasonable for very low tumors to permit sphincter preservation. Ueno demonstrated distal intramural spread beyond 1 cm in just 2.3% of cases, most of which were poorly differentiated [37]. Furthermore, a recent metaanalysis showed no difference in local recurrence or survival in patients with a distal margin less than 1 cm compared to more than 1 cm [38].

Tumors in the lower rectum may be treated by ultralow anterior resection with coloanal anastomosis or by APER, and deciding between these options may be very difficult. Factors involved in the decision making include certainty of distal tumor clearance, bowel function with an ultra-low join, especially after radiotherapy, and the need for a permanent colostomy. It may be appropriate to seek a second surgical opinion on the appropriate operation. Recently, transanal ("bottom-up") TME has become popular in a few centers, allowing a safe distal clearance under direct vision and a low coloanal anastomosis.

Abdominoperineal excision (APER) is indicated for tumors that are considered too low to resect with restoration of continuity with clear margins and reasonable bowel function. APER may be a difficult operation and, historically, resection margin involvement, tumor perforation, and long-term survival are all worse after APER compared to anterior resection [39]. Over recent years, however, the concept of extralevator excision (ELAPE), with avoidance of "waisting" of the specimen at the level of the pelvic floor, has gained popularity either in the conventional Lloyd-Davies position or, most elegantly, in the prone position. For ELAPE, compared with standard APER, lower margin positivity and low local recurrence rates have been reported [40].

Hartmann's procedure is occasionally indicated in frail elderly patients who would be technically appropriate for an anterior resection but who are not considered suitable for restoration of continuity, either in terms of their perceived inability to withstand the morbidity of an anastomotic leak, or to tolerate the likely poor function of a low anastomosis.

Postoperative management

Following elective colorectal surgery, most patients should be part of an enhanced recovery after surgery (ERAS) program. The process should start preoperatively with patient education, stoma teaching if necessary, and

carbohydrate drink loading. Operative factors to facilitate ERAS include minimally invasive techniques, local or regional analgesia, and avoidance of drains and nasogastric tubes. Early mobilization, early return to diet, and avoidance of excess intravenous fluids and opiate analgesia are some of the important postoperative ERAS measures.

Follow-up after resection

Pathological findings should be discussed at an MDT meeting in order to decide on the need for adjuvant therapy and to plan appropriate follow-up [41].

Several studies have compared intensive versus less intensive follow-up regimes. Although most have shown no major differences, a Cochrane meta-analysis suggested a reduction in all-cause mortality with intensive follow-up. Generally, regular clinical follow-up and CEA measurements with CT at 1, 2, 3, and 5 years, and colonoscopy at 1 year and subsequently 3–5 yearly are recommended for Dukes' B and C (stage 2/3) disease up to 5 years. Early tumors (Dukes' A) probably just need colonoscopic follow-up. There are no specific guidelines beyond 5 years.

Other tumors

Tumors of the appendix

Tumors of the appendix are rare but biologically diverse, and are traditionally subdivided into those of epithelial and nonepithelial origin. Nonepithelial tumors are extremely rare and include GISTs, sarcomas, and lymphomas. Epithelial tumors may be usefully considered in three groups – adenomas, carcinomas and carcinoids – although distinction between the groups is not absolute.

Appendiceal tumors are most commonly identified incidentally following appendicectomy. Some are detected on radiological scanning or at surgery for unrelated reasons and a small number of patients present with abdominal distension due to the "jelly belly" of pseudomyxoma peritonei.

Adenomas

Appendiceal adenomas are most commonly identified incidentally following appendicectomy, but increasing numbers of adenomas and serrated polyps are seen in association with the appendix orifice on accurate colonoscopy. Endoscopic removal of these polyps may be challenging and hazardous, and laparoscopic cecectomy may sometimes be necessary.

Adenomas may undergo cystic degeneration with mucous filling of cysts leading to the clinical entity of mucocele. Rupture of mucoceles due to a cystadenoma is thought to be a potential cause of pseudomyxoma peritonei (PMP). Appendiceal mucoceles may be due to:

- mucosal hyperplasia (no risk of PMP)
- a fecolith with obstruction and accumulation of mucus (no risk of PMP)
- mucinous cystadenoma
- mucinous cystadenocarcinoma.

Care should always be taken to avoid rupture during removal of a mucocele of the appendix due to the risk of PMP if the mucocele turns out to be due to an underlying mucinous cystadenoma. Following appendicetomy for a mucinous neoplasm, recommended follow-up would be by abdominal CT or MR at 1 year if there was intraoperative spillage of mucin or if high-grade dysplasia was seen pathologically.

Carcinomas

Adenocarcinoma of the appendix is similar clinicopathologically to colonic adenocarcinoma and should be managed along the same lines. Well-differentiated mucinous adenocarcinoma is associated with mucin production and may progress to PMP. Poorly differentiated mucinous tumors have a poor prognosis.

Carcinoid tumors

Most classic carcinoid (neuroendocrine) tumors are small, located at the tip of the appendix, and are found incidentally in an appendicectomy specimen. Indeed, the vast majority are adequately treated by appendicectomy. Risk factors for carcinoid tumors with the potential to behave in a malignant fashion are:

- size over 2 cm
- invasion into the mesoappendix
- a positive resection margin
- vascular invasion.

If any of these adverse features are present, management should be discussed at a dedicated neuroendocrine tumor MDT. Right hemicolectomy, mainly for adequate lymph node removal and assessment, may be recommended.

Carcinoid tumors with a more aggressive biology include mucinous carcinoid (also called goblet cell carcinoid) and mixed carcinoid-adenocarcinoma. Such tumors tend to be managed along the lines of a standard adenocarcinoma.

Anal tumors

Tumors of the anal canal are defined according to their precise location. Tumors involving the anorectal junction are considered rectal tumors if the epicenter of the tumor is at least 2 cm above the dentate line, and anal cancers if the tumor is within 2 cm of the dentate line. Anal canal tumors are defined as such down to the anal verge. Anal margin tumors are defined as cancers within 5 cm of the anal margin.

The majority of anal tumors are squamous cell carcinomas. Anal margin (perianal) squamous cell carcinomas are keratinizing whilst the anal canal tumors from the distal end of the anal canal are nonkeratinizing. Tumors arising in the

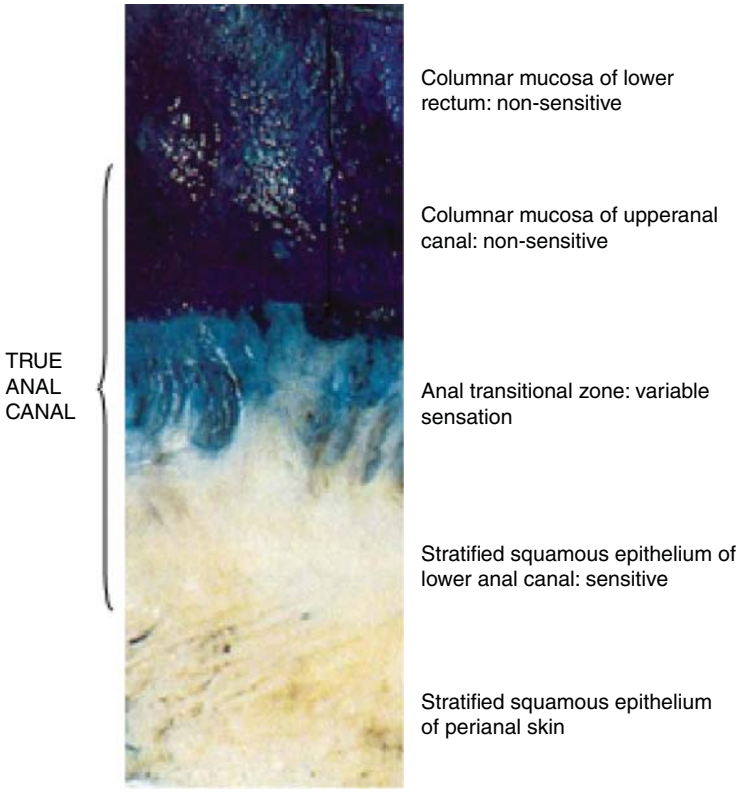

Figure A.5 Histological representation of the anal canal including the anal transition zone. *Source*: George [42]. Reproduced with permission of Elsevier.

transitional zone are defined as transitional tumors (also known previously as cloacogenic or basaloid tumors) (Figure A.5). Adenocarcinomas may arise from the upper columnar-lined part of the anal canal or from adjacent anal glands. The lymphatic drainage of the anal canal above the dentate line is to the perirectal, internal iliac or inferior mesenteric nodes, whilst below the dentate line the drainage is to the superficial inguinal lymph nodes.

Anal tumors are rare although the incidence appears to be rising. A higher incidence of anal squamous cell carcinoma (ASCC) is associated with human papillomavirus infection (HPV), genital warts, high numbers of sexual partners, anoreceptive intercourse, cigarette smoking, female gender, and infection with human immunodeficiency virus (HIV).

Clinical presentation

Anal intraepithelial neoplasia (AIN)

A high index of suspicion is needed for the diagnosis of AIN because patients may simply present with perianal irritation. Any unusual anal lesions should be