Malignant colorectal carcinoma

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Epidemiology In the UK, colorectal cancer is the second most common cause of cancer death. Approximately 42 /uni00A0 000 patients are diagnosed with colorectal cancer every year in the UK. Approximately one-third of these tumours are in the rectum and two-thirds in the colon. The burden of disease is greater in men than - in women (56% versus 44%). Colorectal cancer occurs less frequently in resource-poor than in resource-rich countries. Aetiology Most colorectal cancers are thought to develop from adeno - matous polyps through a sequence of genetic mutations influenced by environmental factors. This adenoma–carci - noma sequence is based on strong observational evidence (Summary box 77.4). The adenoma–carcinoma sequence is not a simple step wise progression of mutations b ut a complicated array of multiple genetic alterations, ultimately resulting in an invasive tumour. Mutations of the APC gene occur in two-thirds of colonic adenomas and are thought to develop early in the carcinogenesis pathway . K-ras mutations result in activation of cell signalling pathways and are more common in larger lesions, suggesting that that they are later events in mutagenesis. The p53 gene is frequently mutated in carcinomas but not in adenomas and therefore thought to be a marker of invasion. A recent international consortium - has identified four consensus molecular subtypes (CMSs) of colorectal cancer based on bioinformatic analysis of gene expression in more than 4000 patients. MSI, a feature of Lynch syndrome, may occur sporadically , particularly in right- sided tumours (CMS1), while others show WNT and MYC signalling activation (CMS2), metabolic dysregulation (CMS3) and transforming growth factor beta activation (CMS4). The value of this classification in interpreting tumour aetiology , biology and targeted treatment remains to be determined. Summary box 77.4 Evidence for adenoma–carcinoma sequence /uni25CF /uni25CF /uni25CF - /uni25CF /uni25CF

The distribution of adenomas is similar to that of cancers (70% left sided) Larger adenomas are more likely to be dysplastic than small adenomas The majority of early cancers have adjacent adenomatous tissue Adenomas are found in one-third of specimens resected for colorectal cancer Incidence of colorectal cancer decreases within a screening programme that involves colonoscopy and polypectomy

associated with intake of red meat and particularly processed meat products (haem and N -nitroso compounds). A protective e ff ect of dietary fibre is also suggested by epidemiological stud ies. A long-held hypothesis is that increased roughage is asso ciated with reduced colonic transit times that in turn reduce exposure of the mucosa to dietary carcinogens. However, there is increasing evidence associating the colonic microbiota with inflammation, gene meth ylation and dysplastic changes. Increased risks for colorectal cancer have also been associated with smoking and alcohol. Conversely , high magnesium and calcium intake may be protective. A protective potential for

antioxidants such as vitamin E and selenium is as yet unproven. The epidemiological evidence supporting prostaglandin inhibitors, particularly aspirin, in preventing colorectal cancer is substantial. Given the potential hazards of taking long-term aspirin, the challenge is to identify individuals for whom the pro tective benefits outweigh the har m. Other factors that increase the risk of developing colorectal cancer include inflammatory bowel disease (IBD) (see Chapter 75). Cholecystectomy may marginally incr ease the risk of right-sided colon cancer. Pathology Macroscopically , the tumour may take one of several forms: annular cancers tend to give rise to obstructive symptoms whereas ulcerating cancers tend to present with bleeding. Most large bowel cancers (Figure 77.4) arise from the left colon, notably the rectum (38%), sigmoid (21%) and descending colon (4%). Cancer of the caecum (12%) and ascending colon (5%) is less common but may be gradually increasing in incidence. Cancer of the transverse colon (5.5%), flexures (2–3%) and appendix (0.5%) are relatively uncommon. Microscopically , the neoplasm is a columnar cell adenocarcinoma. Spread Colonic cancer can spread locally , via the lymphatics, bloodstream (haematogenous) or across the peritoneal cavity Friedrich Ernst Krukenberg , 1871–1946, Professor of Gynaecology , Bonn, Germany Cuthbert Esquire Dukes , 1890–1977, pathologist, St Mark’s Hospital, London, UK. The original Dukes’ classification in 1932 gave three stages, A–C. radial. Radial spread may be retroperitoneal into the ureter, duodenum and posterior abdominal wall muscles or intraper - - itoneal into adjacent organs or the anterior abdominal wall. - In general, involvement of the lymph nodes by tumour progresses from those closest to the bowel along the course of lymphatics to central nodes. However, this order ly process does not always occur. Haematogenous spread is most com - monly to the liver via the portal vein. One-third of patients will have liver metastases at the time of diagnosis and 50% will develop metastases at some point, accounting for the majority of deaths. The lung is the next most common site of metastatic disease wher eas spread to the ovaries, brain, kidney and bone is less common. Colorectal cancer can spread from the serosa of the bowel or via subperitoneal lymphatics to other structures within the peritoneal cavity , including peritoneum, ovary and - omentum. Staging colon cancer Preoperative staging is important to decide whether patients can be managed with curative intent and whether they should have neoadjuvant therapy , undergo palliative interventions including colonic stenting or have symptomatic treatment. Additional interventions include ureteric stenting, en bloc resec - tion for locally advanced disease, intraoperative chemotherapy (hyperthermic intraperitoneal chemotherapy [HIPEC]) for peritoneal disease or synchronous organ resection (e.g. liver, ov aries [Krukenberg tumour]). Information is collated, including patient characteristics (age, frailty , symptoms and comorbidities), endoscopic assessment, histological analysis of biopsies and imaging studies. These factors should be discussed in a dedicated preoperative multidisciplinary meeting. Postop - erative pathological staging should also be discussed in the same forum, allowing for decisions about adjuvant therapy . A variety of staging systems are described for colorectal cancer. Dukes’ classification was originally described for rectal tumours but has been adopted for histopa thological reporting of colon cancer. Although it is simple and widely recognised (Summary box 77.5) the more detailed TNM system is r egarded as the international standard (Summary box 77.6). Summary box 77.5 Dukes’ staging for colorectal cancer /uni25CF /uni25CF /uni25CF

Transverse Splenic colon 5.5% /f_l exure 3% Hepatic /f_l exure 2% Ascending colon 5% Descending colon 4% Caecum 12% Sigmoid Appendix 0.5% colon 21% Rectum 38% Anus 2% Figure 77.4 Distribution of colorectal cancer by site. A: Invasion of but not breaching the muscularis propria B: Breaching the muscularis propria but not involving lymph nodes C: Lymph nodes involved Dukes

himself never described a stage D, but this is often used to describe metastatic disease

TNM classification for colonic cancer /uni25CF /uni25CF /uni25CF Clinical features Carcinoma of the colon typically occurs in patients over 50 years of age and is most common in the eighth decade of life. Emergency presentation occurs in 20% of cases and is associated with a considerably worse prognosis, even when matched for disease stage. A careful family history should be taken. A first-degree relative who has developed colorectal cancer before the age of 50 years may indicate one of the colorectal cancer familial syndromes. Tumours of the left side of the colon usually present with a change in bowel habit or rectal bleeding, while proximal lesions typically present with iron deficiency anaemia or a mass (Figure 77.5). Patients may present with metastatic disease. Investigation of colon cancer Screening Colon cancer is suited to screening as the prognosis is better the earlier stage the disease is diagnosed and polypectomy allows the prevention of cancer development. In the UK screening is o ff ered every 2 years to men and women aged 60–74 years, followed by colonoscopy in those who test positive. Originally a guaiac-based test was used, which detects peroxidase-like activ ity of faecal haematin. Studies suggested a 15–20% reduction in colorectal cancer-specific mortality in the screened popu lation. More recently the faecal immunochemical test (FIT) has been introduced. This test is more accurate and easier to complete than the old faecal occult blood test. A one-o ff flexible sigmoidoscopy for people aged 55 was o ff er ed as a screening tool in the UK. It was shown to reduce colorectal screening. Endoscopy For symptomatic patients with rectal bleeding, direct referral from primary care for a flexible sigmoidoscopy is increasingly used. The patient is prepared with an enema and sedation is not usually necessary . The bowel can be assessed as far as the splenic flexure, allowing detection of up to 70% of cancers and almost all that cause fresh rectal bleeding. Finding left-sided colonic polyps or cancer mandates subsequent completion colonoscopy . Colonoscopy is the investigation of choice if colorectal can - cer is suspected (Figure 77.5). It has the advantage of not only securing histological diagnosis of a primary cancer but also detecting synchronous polyps or carcinomas, which occur in 3–5% of cases. There is a small risk of perforation (1:1000). Radiology Double-contrast barium enema has now been largely replaced by computed tomography (CT) colonography , which is extremely sensitive in picking up polyps to a size of 6 /uni00A0 mm (Figure 77.6). It has the advantage of being less invasive than colonoscopy but, if a biopsy is required, an endoscopy will still be needed. CT is used as a diagnostic tool in patients with a palpable abdominal mass. CT of the thorax, abdomen and pelvis now represents the standard means of staging colorectal cancer; patients with rectal cancer require magnetic resonance imaging (MRI) for local staging (see Chapter 79). Surgical treatment Preoperative preparation With the advent of perioperative enhanced recovery after surgery (ERAS) protocols, mechanical bowel preparation fell out of favour. However, there is evidence that preoperative mechanical bowel preparation in combination with pre - operative oral antibiotics not only reduces surgical site infection rates but also rates of anastomotic leak, postoperative ileus, reoperation and even mortality . Further research is required - -

(note the pre /f_i x y refers to neoadjuvant radio- or chemotherapy, p refers to pathological con /f_i rmation of stage; Union for International Cancer Control, 8th edn) T Tumour stage T1 Tumour invades into submucosa T2 Tumour invades into muscularis propria T3 Tumour invades into non-peritonealised pericolic tissues or subserosa T4a Tumour breaches visceral peritoneum T4b Tumour directly invades another organ/structure N Nodal stage N0 No nodes involved N1 1–3 nodes involved (N1a, 1 regional lymph node involved; N1b, 2 or 3 regional lymph nodes involved; N1c,

satellite extranodal tumour deposits) N2 4 or more nodes involved (N2a, 4–6 regional lymph nodes involved; N2b, 7 or more regional lymph nodes involved) M Metastases M0 No metastases M1 Metastases (M1a, metastasis con /f_i ned to 1 organ; M1b, metastasis to more than 1 organ; M1c, metastasis to the peritoneum) Figure 77.5 Colon cancer seen at colonoscopy (courtesy of Dr Adolfo Parra-Blanco, Nottingham University Hospitals, Nottingham, UK).

but mechanical bowel preparation with oral antibiotics appears safe and could reasonably be used in combination with a surgi cal site infection bundle. This bundle should contain common and variable components such as preoperative bathing, intra venous prophylactic antibiotics given bef ore surgical incision, maintenance of normoglycaemia and normothermia and use of wound protection devices. Antithrombotic stockings should be fitted, and the patient started on prophylactic subcutaneous lo w-molecular-weight heparin. Manual compression boots may be used perioperatively . In all cases where a stoma is anticipated, careful preoperative counselling and marking of an appropriate site by an enterostomal therapist is essential. ERAS programmes are widely used to reduce the physiological insult of surgery and improve postoperative outcomes (Summary box 77.7). Key elements of an ERAS programme /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF Operations The operations described are designed to remove the primary tumour and its draining locoregional lymph nodes. It is unusual to find unsuspected metastases at laparotomy (or laparoscopy) after CT staging, but the presence of peritoneal metastases may predicate a palliative strategy with a segmental resection and less aggressive lymphadenectomy . Similarly , a complete preoperative colonoscopy or CT colonography will have excluded synchronous bowel lesions. The use of stapling and hand-suturing techniques for colonic anastomoses have been compared, and there is probably little di ff erence in leak rate. It is more important that healthy bowel, free of tension or distal obstruction, is used to construct an anastomosis and that patients are adequately nourished and free from active infection if anastomotic leakage is to be avoided. Carcinoma of the caecum or ascend - ing colon (Figure 77.7) is treated by right hemicolectomy (Figure 77. 8) . At open surgery the peritoneum lateral to the ascending colon is incised, and the incision is continued - -

(b) Figure 77.6 Virtual colonoscopy of the right colon. (a) Computed tomography scan of the abdomen showing a caecal tumour (arrow). (b) Formatted ‘virtual’ image of the same lesion as in (a) (courtesy of Dr A Slater, John Radcliffe Hospital, Oxford, UK). Preadmission counselling Preoperative carbohydrate loading Avoidance of preoperative dehydration Avoidance of nasogastric tubes Short, transverse incisions (or laparoscopic procedure) Short-acting anaesthetic drugs Avoidance of perioperative /f_l uid/salt overload Avoidance of opiate analgesia Maintenance of perioperative temperature Prevention of postoperative nausea and vomiting Early mobilisation Early introduction of oral /f_l uids/diets/supplements Early removal of urinary catheters Continual audit of outcomes Right hemicolectomy Figure 77.7 Right hemicolectomy specimen showing an ascending colon cancer (courtesy of Dr Philip Kaye, Nottingham University Hospitals, Nottingham, UK).

around the hepatic flexure. The right colon and mesentery are elevated, taking care not to injure the ureter, gonadal vessels or the duodenum. The ileocolic artery is ligated close to its origin from the superior mesenteric artery (‘high-tie’) and divided. Complete mesocolic excision with dissection

along embryological planes (see Chapter 65) and removal of the lymphovascular supply of the resected colon with flush ligation of the ileocolic and right colic vessels at their origin from the superior mesenteric artery may improve survival in node- positive disease (Hohenburger). The mesentery of the distal 10 cm of the ileum and the mesocolon as far as the proximal third of the transverse colon is divided. The greater omentum is divided up to the point of intended division of the transverse colon. When it is clear that there is an adequate blood supply at the resection margins, the right colon is resected and an anastomosis is fashioned between the ileum and the transverse colon. If the tumour is at the hepatic flexure the resection must be extended further along the transverse colon and will involve dividing the right branch of the middle colic artery . Carcinomas of the trans verse colon and splenic flexure are most commonly treated by an extended right hemicolectomy . The mobilisation is as for a right hemicolectomy but dissection continues to include the tumour, this may include taking down the splenic flexure and excising the w hole transverse mesocolon. Some surgeons prefer to perform a left hemicolectomy for a splenic flexure cancer. This is the operation of choice for descending colon and sigmoid cancers (Figure 77.9) Werner Hohenburger , contemporary , surgeon, Erlangen, Germany . left half of the colon is mobilised completely along the ‘white line’ that marks the lateral attachment of the mesocolon (see Chapter 65). As the sigmoid mesentery is mobilised, the left ureter and gonadal vessels must be identified and protected. The splenic flexure may be mobilised by extending the lateral dissection from below and completed by entering the lesser sac. The inferior mesenteric artery below its left colic branch, together with the related paracolic lymph nodes, is included in the resection by ligating the inferior mesenteric artery close to its origin (‘high-tie’). For full mobility the inferior mesenteric vein is also ligated and divided at the lower border of the pancreas. The bowel and mesentery can then be resected to allow a tension-free anastomosis. A temporary diverting stoma may be fashioned proximally , usually by formation of a loop ileostomy . This is usually undertaken if the anastomosis is below the peritoneal reflection of the rectum, because of the greater risk of anastomotic leakage. Laparoscopic surgery Laparoscopic surgery for colon cancer has been shown to - have equivalent overall and cancer-related outcomes to open surgery . Lymph node harvests are equivalent to open surgery and initial concerns about reports of port-site recurrence have been dispelled as world experience has grown. In the UK, the National Institute for Health and Care Excellence (NICE) has stated that laparoscopic colorectal surgery should be o ff ered to suitable patients. Operation times are longer but wound infection rates, blood loss and postoperative pain scores are lower than for open surgery . The costs of laparoscopic surgery are, however, generally higher and this may be particularly . The relevant where funds are limited.

SMA MCA RCA Carcinoma ICA Figure 77.8 Schematic showing right hemicolectomy. This shows the basic plane of dissection for a

complete mesocolic excision. ICA, ileocolic artery; MCA, middle colic artery; RCA, right colic artery; SMA, superior mesenteric artery. Extended right hemicolectomy Left hemicolectomy Marginal artery SMA IMA LCA Carcinoma Figure 77.9 Schematic showing left hemicolectomy. This shows the basic plane of dissection for a complete mesocolic excision. IMA, inferior mesenteric artery; LCA, left colic artery; SMA, superior mes

enteric artery.

If laparoscopic surgery is planned it is useful to tattoo the lesion at prior colonoscopy as it not possible to locate lesions by palpation. The laparoscopic operation has particular advan tages if performed in a medial to lateral manner, i.e. starting the dissection by controlling and dividing the major vascular pedicles and only taking the lateral peritoneal reflection once the mesocolon is completely free. Specimen retrieval and bowel anastomosis can then be perfor med via a small incision. Ded icated training in laparoscopic colorectal surgery is important as there is a relatively

long learning curve. Emergency surgery In the UK, 20% of patients with colonic cancer will present as an emergency , the majority with obstruction, but occasionally with haemorrhage or perforation. If the lesion is right sided, it is usually possible to perform a right hemicolectomy and anastomosis in the usual manner. If there has been perforation with substantial contamination or if the patient is unstable, it may be advisable to bring out an ileocolostomy following resection of the lesion rather than forming an anastomosis. For a left-sided lesion the decision lies between a Hartmann's procedure and a resection and anastomosis. An on-table washout may be necessary to remove residual faecal content in the proximally obstructed bowel. Alternatively , removal of the whole proximal bowel may be required if the colon is markedly distended or if there is concern regarding its viability . Where endoscopic and radiological facilities are present an obstructing left-sided lesion can often be treated initially with an expanding Henri Albert Antoine Hartmann , 1860–1952, Professor of Clinical Surgery in the Faculty of Medicine, University of Paris, Paris, France. obstructed bowel and may allow conversion of an emergency operation with a high chance of a stoma to a situation that can be managed semielectively b y resection and anastomosis. Although early studies cast doubt on the benefits of colorectal stenting, more recently evidence has emerged that stenting leads to a reduction in stoma rates. Postoperative care Patients should be closely monitored after colonic resection as there is a small incidence of postoperative bleeding. Anti - thrombosis measures should be continued and as currently recommended for 28 days postoperatively . There is no advan - tage to placing intra-abdominal drains after colonic surgery . Wound infections are relatively common after colonic surgery and may well be more frequent than the 10% usually quoted. Anastomotic leaks occur in 4–8% of ileocolic or colocolic anastomoses. The possibility should be borne in mind in any patient not progressing as expected or with unexplained cardiac abnormalities, fever or worsening abdominal pain. Early investigation with contrast-enhanced CT scan is appropriate. In the presence of sepsis or peritonitis, early return to theatre and taking down the leaking anastomosis with the formation of stomas is usually advised. Prolonged nasogastric drainage, intravenous fluid therapy and cautious introduction of oral fluid and diet represented traditional postoperative practice. ERAS programmes tha t include preoperative, intraoperative and postoperative com - ponents have been shown to reduce length of hospital stay from 10–14 days to as little as 3–5 days by modulating the surgical stress response and reducing postoperative ileus - (Summary box 77.7). It is important to appreciate that these pr ogrammes require multiple interventions and considerable time, e ff ort and education from the surgical, anaesthetic and ward teams. Adjuvant therapy - In most patients with colon cancer preoperative chemotherapy is not required; however, a recent research study (FOxTROT) has shown that it is safe and further work on case selection has been recommended. Adjuvant chemotherapy improves survival after surgery in patients with node-positive colon cancer (stage III/Dukes' C). Fluoropyrimidine regimes are often used, with the addition of oxaliplatin in patients who are otherwise fit and have high-risk stage III disease. Patients with stage II disease show less benefit in overall survival with adjuvant chemother - apy , thus it is reserved for those with high-risk stage II disease. Presence of MSI (in the tumour histology) also a ff ects tumour recurrence and is taken into account when making decisions with patients about chemotherap y (see Chapter 12). Metastatic disease Hepatic and pulmonary metastases can be resected and series have demonstrated 5-year survival of around 40% in resectable disease. CT , MRI and positron emission tomography (PET) scanning are all used to identify colorectal metastases and assess patients' suitability for further resection (Figure 77.11).

Figure 77.10 Abdominal radiograph demonstrating a colonic stent in position (arrow) (courtesy of Dr D Kasir, Hope Hospital, Salford, UK).

The role of chemotherapy and the timing of colonic and hepatic surgery in synchronous metastases is still a matter of debate and such cases should be carefully discussed by a multi disciplinary team. Many centres o ff er adjuvant chemotherapy as standard and neoadjuvant therapy also in those with high- risk disease. Isolated lung metastases may be suitable for resection or stereotactic radiofrequency ab lation, but they are more com monly accompanied by metastases elsewhere. In patients with widespread disease, palliative c hemotherapy is o ff ered along side symptomatic treatment and support by a palliative care team. Prognosis Overall 5-year survival for colorectal cancer is approximately 58%. While there are numerous factors that may predict prog nosis (Summary box 77.8) the most important determinant is tumour stage and, in particular, lymph node status. Patients with disease confined to the bowel wall (TNM stage 1, Dukes' stage A) will usually have cure by surgical resection alone and around 95% will have disease-free survival a t 5 years. Spread beyond the bowel wall (TNM stage 2, Dukes' B) reduces 5-year disease-free survival to approximately 85% with surgery alone. Patients with lymph node metastases (TNM stage 3, Dukes' C) have a 5-year disease-free survival of around 45–50% with surgery alone. Adjuvant chemotherapy based on 5-fluorouracil (5-FU) and folinic acid (leucovorin) usually in combination with oxaliplatin (FolFox) is used on an individual basis for those with stage II disease (Dukes' stage B), although the benefit is uncertain. In those with stage III disease adjuv ant chemotherapy incr the chance of 5-year disease-free survival by approximately 20% to 67–70%. Those presenting with unresectable meta static disease at diagnosis have a 5-year survival of approxi mately 10%. In metastatic disease chemotherapy based on 5-FU and folinic acid in combination with irinotecan (FolFiri) is often used as first-line treatment. Second-line therapy may include introduction of a monoclonal antibody such as a vascular endothelial growth factor (VEGF) inhibitor (be vacizumab) or an epidermal growth factor receptor (EGFR) inhibitor in immunotherapy (pembrolizumab) has been shown to have a role in MSI tumours. Tumours exhibiting the BRAF V660E mutation (approximately 10%) have a poor prognosis but may respond to treatment with combined BRAF (encorafenib) and MAP kinase (binimetinib) inhibitors. Summary box 77.8 Histopathological factors that influence prognosis /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF /uni25CF - Colorectal cancer follow-up Since the advent of safe liver resection for metastases the outcome benefit of follow-up has been clearly demonstrated. - Follow-up aims to identify synchronous bowel tumours (present in 3%) that were not identified at the time of original diagnosis. - Similarly , 3% of patients will develop a metachronous (at a di ff erent time) colonic cancer. Up to a half of all patients with colorectal cancer will develop liver metastases at some point. Regular imaging of the liver (CT scan) and measurement of carcinoembryonic antigen (CEA) is designed to diagnose this early , in order to allow curative metastectomy . Optimum - follow-up pathways continue to be developed. NICE guide - lines recommend CT scans of the abdomen, pelvis and thorax as well as CEA measurements during the first 3 years after treatment of colon cancer with curative intent but identified no clinically important di ff erence in colorectal cancer-specific survival with a more intensive follow-up schedule compared with a less intensive follow-up. Palliative care About 20% of patients present with metastatic disease and about one-fifth of these patients are suitable for potentially curative management. For the rest, quality of residual life is the main outcome but it should be borne in mind that with the combination of interventions including chemotherapy , metastectomy , cytoreductive surgery and intraperitoneal eases chemotherapy

some colonic disease may ‘convert to resectable’. For those whose disease remains incurable colonic surgery - may still be o ff ered, particularly if symptomatic. This may - be non-resectional (defunctioning stoma or internal bypass) or resectional (procedures detailed earlier but with a smaller segmental resection and less aggressive lymphadenectomy). Non-surgical techniques include palliative chemotherapy , stenting for obstruction, intraluminal laser, argon plasma coagulation and radiotherapy for bleeding and pain (especially in rectal cancers).

Figure 77.11 Computed tomography scan of the liver showing mul tiple metastases from carcinoma of the colon (courtesy of Dr Rajpal Dhingsa, Nottingham University Hospitals, Nottingham, UK). Tumour stage Histological grade

Degree of mucin secretin Presence of signet cells Venous invasion Perineural invasion Pushing versus in /f_i ltrative margin Tumour in /f_i ltrating lymphocytes Presence of MSI

Gastrointestinal stromal tumours Gastrointestinal stromal tumours (GISTs) are extremely rare, constituting less than 0.1% of all colorectal tumours. They appear to arise from the interstitial cells of Cajal and are mainly due to a mutation in a specific gene called c-kit allows a specific marker to be used to diagnose most tumours as well as targeted chemotherapy with imatinib. Thirty per cent are malignant with mitotic rate, Ki-67 (>10%), size (>5 local invasion and cellularity the best indicators of malignant potential. Diagnosis is by CT or MRI and endoscopic biopsy . Surgical resection is the mainstay of treatment with imatinib for those tumours that are unresectable, have metastasised or recurred. Adjuvant imatinib may be used for tumours felt to be at high risk of recurrence. Carcinoid ‘Carcinoids’ are well-di ff erentiated neuroendocrine tumours of the colon and are part of a spectrum of disease with poorly di ff erentiated neuroendocrine carcinomas at the most aggres sive end of this spectrum. They constitute around 50% of all neuroendocrine tumours of the gut and about 5% of all colonic tumours. Fewer than 10% of colonic carcinoid tumours present with carcinoid syndrome (skin erythema, diarrhoea, cardiorespira tory symp toms) owing to

release of hormones. Surgery remains the only potentially curative treatment and, since the possibility of metastatic disease is directly related to the size of the primary tumour, the extent of resection should be determined accord /uni00A0 ingly . Tumours greater than 2 cm require en bloc resection of adjacent mesenteric lymph nodes. In the midgut (the area receiving its blood supply from the superior mesenteric artery) /uni00A0 even lesions less than 1 cm have been shown to metastasise /uni00A0 and radical resection is also indicated. Small (<1 cm) hindgut tumours (the area receiving its blood supply from the inferior mesenteric artery) can be safely locally excised (see Chapters 74 and 76). Lymphoma Primary lymphoma of the colon is rare, accounting for less than 1% of all colonic malignancies. The caecum is the most common site of occurrence, usually with non-Hodgkin's type lymphoma (NHL). Patients present with abdominal pain, a mass, change in bowel habit, per rectal bleeding, obstruction or intussusception. These tumours may occasionally perfo rate. The lack of specific complaints and rarity of intestinal obstruction probably accounts for the often delayed diagnosis. CT and colonoscopy with submucosal biopsy are required for diagnosis. Treatment is combination sur gery with systemic chemotherapy , although surgery alone may be considered adequate treatment for low-grade NHL disease that does not infiltrate beyond the submucosa. Santiago Ramon y Cajal , 1852–1934, Spanish neuroscientist, pathologist and Nobel prize winner (1906) for studies of cellular anatomy of the nervous system. Thomas Hodgkin , 1798–1866, pathologist, Guy's Hospital, London, UK, described 'Morbid appearances of the absorbent glands and spleen' in 1832. Metastatic disease to the colon from other primary sites constitutes about 1% of all colorectal cancers. There is often a known primary , usually lung, ovary , breast, kidney , skin, stomach or hepatobiliary system tumours. In most cases multiple lesions are seen and one-third may be asymptomatic. . This The most common pathway of spread is through peritoneal seeding (typical of ovarian cancer), although haematological and lymphatic dissemination is described in breast and lung /uni00A0 cm), cancer and melanoma. Patients may present with obstruction, per rectal bleeding (especially melanoma), anaemia and weight loss. CT and colonoscopic biopsy are required for diagnosis and treatment should be individualised to patient symptoms and prognosis.

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