Over 33,000 patients are diagnosed with colorectal cancer in the UK every year. This article outlines the epidemiology, clinical features and non-pharmacological treatment of the disease.

Colorectal cancer is the third most common cancer in the UK, after cancer of the lung and breast. In 2000, there were 33,173 new cases of colorectal cancer diagnosed, with slightly more cases in men (17,249) than women (15,924) (worldwide data presented in Table 1, p176). The prevalence rate per 100,000 (all ages) is 57.1 for men and 37.5 for women. The incidence increases with age, the average age at diagnosis being 60–65 years.

In 2002, colorectal cancer was responsible for 16,220 deaths (66 per cent colon cancer, 34 per cent rectal cancer). It is the second most common cause of cancer death after lung, and accounts for over 10 per cent of cancer deaths.

Survival rates for colorectal cancer have improved in recent years with current five-year survival at around 40 per cent. Between the early 1970s and the early 1990s, five-year survival rates for colon cancer in men improved from 22 to 42 per cent, while for rectal cancer equivalent rates improved from 25 to 39 per cent. For colon cancer in women over the same period, five-year survival increased from 23 to 40 per cent and for cancer of the rectum, 27 to 43 per cent.

Risk factors

The development of colorectal cancer is still poorly understood, although there is evidence for the influence of a range of environmental and genetic factors. These include:

- Age — incidence increases over the age of 50 years
- Nutrition
- Low physical activity
- Smoking
- Inflammatory bowel disease
- Family history of bowel cancer (particularly with relatives diagnosed under the age of 45 years)

It is thought that less than 10 per cent of all cases can be explained genetically — the rest are caused by diet and lifestyle. It is estimated that up to 80 per cent of cases of colorectal cancer are caused by diet alone. The disease is more common in westernised countries than in Asia or Africa — the higher intake of plant-based foods in Asia and Africa has been proposed as accounting for these differences. There is epidemiological evidence for a protective effect of vegetable intake and there is also evidence that a diet rich in red meat may increase risk.

Patients with long-standing ulcerative colitis or Crohn’s colitis are at higher risk of developing colorectal cancer than the rest of the population. In ulcerative colitis, the cumulative risk of developing colorectal cancer appears to be 2 per cent at 10 years, 8 per cent by 20 years and 18 per cent by 30 years. There is also evidence that the risk of developing several cancers, including colorectal cancer, is reduced in those taking aspirin. Use of hormone replacement therapy is also increasingly being linked with reduced risk of colorectal cancer.

Family history is important and there are two well-established inherited conditions predisposing to colorectal cancer. These are familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC). FAP accounts for approximately 1 per cent of all colorectal cancers and is due to a germline mutation on the APC gene [a tumour suppressor gene]. HNPCC represents around 5 per cent of cases, and the majority of people with this condition have a germline mutation in one of the DNA mismatch repair genes. However, subtle genetic polymorphisms, arising from genes yet to be identified, are likely to be responsible for the majority of inherited cases.

Clinical features

Most colorectal cancers develop as a result of a stepwise progression from normal mucosa to adenoma to invasive cancer. Development involves the lymphatics and blood vessels, with subsequent spread, most commonly to the liver.

Change in bowel habit, with or without abdominal pain, rectal bleeding and blood in the stool are common symptoms of colorectal cancer. Any of these symptoms, particularly in patients over the age of 35 years, should be investigated.

Anorexia and weight loss may also occur. However, cancers arising in the caecum are sometimes asymptomatic and may present as iron-deficiency anaemia. Older people often...
present with intestinal obstruction. If the cancer is in the rectum, the mass may be palpable.

### Diagnosis

Colonoscopy is the gold standard for investigation. This involves a telescopic examination of the colon by means of a fiberoptic endoscope. During the procedure, biopsies can be taken to allow histological examination of tissue.

Double-contrast barium enema is also widely used in the UK. This procedure can allow visualisation of the large bowel, but is less sensitive and specific than colonoscopy, and it can underdiagnose cancers in the sigmoid colon (connection between the descending colon and the rectum) and overdiagnose those in the cecum. Thus, unless lesions are unequivocal, barium enema should be confirmed by flexible sigmoidoscopy.

### Staging

Once the diagnosis of colorectal cancer has been made it is important to establish the extent of the disease. Ultrasound, computed tomography and magnetic resonance imaging may be used to help evaluate tumour size and local and secondary spread, including metastases in the liver and lung. Digital rectal examination is useful for evaluating cancer of the rectum.

Colorectal cancers are classified according to the Dukes’ or TNM staging systems, and in recent years there has been a gradual move towards the TNM system (Table 2). The T refers to the depth that the tumour has grown through the bowel wall, the N to the number of lymph nodes affected and the M to the presence of metastases. Earlier detection increases the success of treatment. If patients can be treated while the disease is still localised, the cure rate is much more promising.

### Treatment

Treatment options largely depend on the site and extent of the tumour and the patient’s general condition. The treatment of choice for most types of colorectal cancer is surgical excision of the tumour, although radiotherapy and chemotherapy have important roles to play. (Chemotherapy is covered in a further article on p179 and will not be mentioned again here.)

Nutritional support should also be part of the patient’s care plan. Some patients will have lost weight even before diagnosis, depending on the stage at presentation. Surgery, for example, is associated with weight loss due to periods of “nil by mouth”. Malnutrition in cancer patients is associated with a poorer prognosis and reduced response to treatment. Routine nutritional assessment and early initiation of nutritional support in at-risk patients is therefore vital. Patients should be encouraged to maximise their oral intake, but a period of enteral nutrition may also be required. Dietetic intervention may be required, particularly in those who have surgery leading to a colostomy as well as in those who have radiotherapy and chemotherapy.

### Surgery

Surgery is the definitive treatment for localised colorectal cancer and the patient should undergo appropriate pre-operative preparation. Bowel preparation is usually employed, although if there is intestinal obstruction or bowel perforation it is unsafe. Prophylactic antibiotics are given — usually intravenously as a single dose within 30 minutes of induction of anaesthesia — to reduce the incidence of wound infection. Cefuroxime and metronidazole or co-amoxiclav are commonly used.

Prophylaxis against deep vein thrombosis is also important, and the most commonly used method is low-dose heparin. Patients should also be given graduated compression hosiery until they are fully mobile, unless they have peripheral vascular disease.

The type of surgery performed depends on whether the cancer is in the colon or rectum. In colon cancer, right-sided cancers are treated by right hemicolectomy and left-sided cancers by left hemicolectomy or sigmoid colectomy as appropriate. Other techniques, including transverse hemicolec- tomy, may be used depending on the region of the tumour and the opinion and experience of the surgeon.

In an emergency situation where there is an obstructing colonic cancer on the right side, a right hemicolectomy is performed with primary anastomosis. For left sided lesions, a Hartmann’s procedure is usually carried out.

In rectal cancer, total mesorectal excision (TME), is an increasingly commonly used approach. There is some evidence that TME may reduce recurrence rates and improve survival.

Surgery also has a role in the management of advanced disease. In locally advanced disease, either primary or recurrent, surgical excision provides the only hope of cure. If the primary tumour invades adjacent structures such as the kidney, bladder, duodenum or stomach, an adequate portion of these organs may be removed along with the tumour.

In patients with operable metastases of the liver, liver resection may be attempted if the patient is fit enough to withstand the surgery and sufficient functioning liver can be retained. There is some evidence that survival may be prolonged.

If it is not possible to operate on the liver, it may be possible to destroy metastases using in situ techniques such as cryoaftlation (freezing) and radiofrequency ablation. Again, there is some evidence for prolonged survival with these techniques, although it is weaker than for liver resection.

### Radiotherapy

Radiotherapy is used (in addition to surgery) for rectal cancer only. It is not used for cancer in the colon because the

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**Table 1: Incidence of colorectal cancer 2000***

<table>
<thead>
<tr>
<th></th>
<th>Incidence</th>
<th>Incidence ASR</th>
<th>Deaths</th>
<th>Deaths ASR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>World</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>498,754</td>
<td>19.11</td>
<td>254,816</td>
<td>9.78</td>
</tr>
<tr>
<td>Women</td>
<td>445,963</td>
<td>14.44</td>
<td>237,595</td>
<td>7.58</td>
</tr>
<tr>
<td><strong>UK</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>17,249</td>
<td>35.37</td>
<td>9,341</td>
<td>18.73</td>
</tr>
<tr>
<td>Women</td>
<td>15,924</td>
<td>25.28</td>
<td>9,047</td>
<td>13.76</td>
</tr>
</tbody>
</table>

Incidence is the number of new cases arising in a given period in a specified population. Age standardised ratio (ASR) is a measure of a rate that a population would have had the disease if it had had a standard age structure. Standardisation is necessary when comparing several populations that differ with respect to age because age has such a powerful influence on cancer. ASR is expressed per 100,000 people.

**Table 2: Staging classification of colorectal cancer***

<table>
<thead>
<tr>
<th>TNM classification</th>
<th>Dukes’ classification</th>
<th>Extent of disease</th>
<th>Five-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1–T3</td>
<td>A</td>
<td>Confined to bowel wall</td>
<td>&gt;80%</td>
</tr>
<tr>
<td>T4, N0</td>
<td>B</td>
<td>Involving the thickness of the bowel</td>
<td>45%</td>
</tr>
<tr>
<td>N1,N2,M0</td>
<td>C</td>
<td>Involvement of mesenteric lymph nodes</td>
<td>30%</td>
</tr>
<tr>
<td>M1</td>
<td>D</td>
<td>Distant metastatic spread</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>
Radiotherapy can also be used palliatively in patients with locally advanced rectal cancer. It can improve pain, stop haemorrhage and lessen straining. Pain from isolated bone metastases can also be alleviated with short courses of radiation.

### Screening

Screening can be divided into two categories — screening of people with a high-risk (eg, family history) and population screening.

Colonoscopy is the investigation of choice for high-risk patients. Patients with a family history of colorectal cancer or adenomas, particularly before the age of 60, should be considered for colonoscopy.

A previous study of individuals with FAP or HNPCC can be offered genetic screening and counselling, although there are currently only a few specialist centres in the UK offering this service. Carriers of these genetic traits should be offered early sigmoidoscopy and colonoscopy every two to three years.

Other high-risk patients include those who have had a history of adenomatous polyps, and it is generally agreed that patients should be offered colonoscopy at three to five yearly intervals after removal of polyps (polypectomy). Patients with ulcerative colitis of longstanding duration (ie, 10 years) should also be offered colonoscopy plus mucosal biopsy.

The value of population wide screening for colorectal cancer is widely debated. Screening tests available include colonoscopy, flexible sigmoidoscopy and faecal occult blood testing (FOBT), eg, guaiac based stool blood tests.

Although colonoscopy is the gold-standard technique for the examination of the rectum and colon, its expense, the need for full bowel preparation and sedation and the small risk of perforation obviate its use as a population screening tool at present. In the future, virtual colonoscopy (computed tomography colonography) and genetic testing may contribute to screening programmes.

In population based randomised trials to date, only FOBT has been shown to be effective in reducing colorectal cancer mortality. Trials carried out in Nottingham, the US and Denmark have all shown reductions in specific disease mortality, and nationally, it has been predicted that deaths from bowel cancer could fall by 15 per cent as a result of screening, saving approximately 1,200 lives each year.

Universal screening strategies have been recommended in the US, but not as yet in the UK. However, following a recent UK pilot, involving FOBT in men and women aged between 50 and 69 years, the National Screening Committee is working with the government to develop a national bowel cancer screening programme.

### References


### Panel 1: Surgical procedures

#### Right hemicolectomy

Is used to treat unobstructed carcinomas of the caecum, ascending colon and hepatic flexure (corner of the ascending and transverse colon). The growth is removed and an anastomosis is made between the ileum and transverse colon.

#### Left hemicolectomy

Is used to treat unobstructed carcinoma of the descending colon and splenic flexure (corner of the transverse and descending colon). The growth is resected and an anastomosis of the transverse colon to the rectosigmoid colon is performed.

#### Sigmoid colectomy

Is used to treat carcinoma of the sigmoid colon. The sigmoid colon is removed and an anastomosis of the rectum to the descending colon is performed.

#### Transverse hemicolectomy

Is used to treat unobstructed carcinoma of the transverse colon. The transverse colon is excised and an end anastomosis is made between the right and left colon.

#### Hartmann’s procedure

Is performed when a carcinoma of the rectum is found to be unresectable. The lower end of the rectum is closed and the upper end of the bowel is brought out as a descending colostomy.

#### Total mesorectal excision

Involves careful dissection in the plane outside the mesorectum (fatty tissue surrounding the rectum in the pelvis) so that the rectum and tumour can be removed as an entity and damage to the pelvic nerves minimised.12

Morbidly associated with its use on the abdomen is prohibitive. In Europe, including the UK, the emphasis is on pre-operative radiotherapy, while in the US, the emphasis is on post-operative radiotherapy.

Pre-operative radiotherapy can be used in two ways. First, it can be used to render rectal cancer operable by shrinking the tumour and it may be given on five days a week over a five-week period followed by an interval of six weeks before surgery is attempted.

The second approach is to use radiotherapy on clearly operable rectal cancer to reduce the risk of local recurrence. However, this approach is associated with significant morbidity and the role of radiotherapy in operable rectal cancer is currently unclear.

The aim of post-operative radiotherapy is to remove any remaining tumour cells, and reduce the chance of recurrence.