

Physician notes

Module 1 - Polyp development

The frequency of sporadic polyps correlates with age, and subjects aged >50 years have the largest number. Patients with hereditary polyposis syndromes may present at a much earlier age.

Most polyps are small (<0.5 cm) and entirely benign. Nevertheless, it is believed that the majority of bowel cancers arise from pre-existing adenomatous polyps, which may be tubular, tubulovillous or villous.

The 'polyp-to-cancer' sequence provides the rationale for bowel cancer screening, which is aimed at detecting pre-malignant polyps or small early cancers.

Polyps may be entirely asymptomatic but can release blood into the bowel. Although this might not be visible in the stool, it can be detected using a faecal occult blood test (FOBT). A national screening programme is currently underway in England to screen healthy individuals aged 60-69 years, offering colonoscopy for those with a positive FOBT result.

Colonoscopy is now established as a safe and effective means of both identifying and removing polyps.

Module 1 - Further reading

1. Lieberman DA, Weiss DG, Bond JH et al. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. *N Engl J Med* 2000;**343**:162-8.
2. Stryker SJ, Wolff BG, Culp CE et al. Natural history of untreated colonic polyps. *Gastroenterology* 1987;**93**:1009-13.
3. Villavicencio RT, Rex DK. Colonic adenomas: prevalence and incidence rates, growth rates, and miss rates at colonoscopy. *Semin Gastrointest Dis* 2000;**11**:185-93.
4. NHS Bowel Cancer Screening Programme: www.cancerscreening.nhs.uk/bowel. Accessed on: 09/10/06.

Module 2 - Malignant transformation

The majority of colorectal cancers appear to arise from polyps. The risk of progression from benign polyp to cancer varies, but approximately 10% of adenomatous polyps >1.5 cm contain an invasive carcinoma. The presence of high-grade dysplasia also correlates with a risk of malignancy. A study by Stryker et al. showed that the risk of developing cancer from sporadic 1 cm polyps was 8% at 10 years and 24% at 20 years.

Although the cellular and genetic events that lead to malignant transformation are still being elucidated, a number of critically important genetic alterations have been found to contribute to the development of bowel cancer. The earliest event appears to involve the adenomatous polyposis coli (*APC*) gene, which has been found to be mutated in individuals affected by familial adenomatous polyposis. The protein encoded by *APC* targets the degradation of β -catenin, which is involved in the activation of various growth-promoting oncogenes.

An imbalance in DNA methylation seems to be a relatively early event in the development of colorectal cancers and has been found at the polyp stage. Imbalances in DNA methylation can lead to activation of oncogenes and inactivation of tumour suppressor genes.

Chromosomal deletions at 18q, losses at 17p and mutations of the *p53* tumour suppressor gene appear to be late events in the development of bowel cancer.

At the macroscopic level, malignant change usually seems to occur at the tip of the polyp and, as the cancer cells divide, advances down to its base. A malignant polyp may be completely removed at colonoscopy, provided that disease has not progressed beyond the polyp stalk and into the bowel wall.

Module 2 - Further reading

1. Cho KR, Vogelstein B. Genetic alterations in the adenoma-carcinoma sequence. *Cancer* 1992;**70**(6 Suppl):1727-31.
2. Colucci PM, Yale SH, Rall CJ et al. Colorectal polyps. *Clin Med Res* 2003;**1**:261-2.
3. Kim EC, Lance P. Colorectal polyps and their relationship to cancer. *Gastroenterol Clin North Am* 1997;**26**:1-17.
4. Stryker SJ, Wolff BG, Culp CE et al. Natural history of untreated colonic polyps. *Gastroenterology* 1987;**93**:1009-13.
5. Winawer SJ. Natural history of colorectal cancer. *Am J Med* 1999;**106**:3S-6S.

Module 3 - Tumour invasion

The probability of distant tumour spread, and of cure, is closely correlated with the extent of local disease. A number of classification systems have been used to describe the extent of spread (including Tumour-Node-Metastasis [TNM], Modified Astler-Coller and Dukes' staging systems). The Dukes' and TNM classifications can be used to define the depth of involvement as follows:

Stage A - T1/T2, N0, M0

The cancer has spread through the mucosa into the submucosa and may have grown into the muscularis propria (muscular layer).

T1: Invasion into mucosa and submucosa.

T2: Invasion into muscularis propria.

The 5-year survival rate at this stage is 90%.

Stage B - T3/T4, N0, M0

The cancer has grown through the bowel wall to the outermost layers or other tissues, but there is no involvement of local lymph nodes.

T3: The tumour extends through the muscularis propria.

T4: The tumour spreads through the bowel wall into nearby tissues.

The 5-year survival rate at this stage is 77%.

Stage C - T1/T2/T3/T4, N1/N2, M0

Cancer has spread to involve local lymph nodes but not distant sites.

N1: Cancer cells found in 1-3 lymph nodes.

N2: Cancer cells found in ≥ 4 lymph nodes.

The 5-year survival rate at this stage is 35-60%.

Stage D - T1/T2/T3/T4, N1/N2, M1

Metastatic spread (common sites include liver, lung and bone).

M1: Distant spread is present.

The 5-year survival rate at this stage is <5%, although surgical resection of liver metastases with curative intent is increasingly being used.

Metastatic spread to distant sites within the body occurs through the bloodstream and lymphatic system. The liver is the most common site for secondary tumours in bowel cancer.

Module 3 - Further reading

1. Compton CC, Greene FL. The staging of colorectal cancer: 2004 and beyond. *CA Cancer J Clin* 2004;**54**:295-308.
2. Curley SA. Outcomes after surgical treatment of colorectal cancer liver metastases. *Semin Oncol* 2005;**32**(6 Suppl 9):S109-11.
3. Deans GT, Parks TG, Rowlands BJ et al. Prognostic factors in colorectal cancer. *Br J Surg* 1992;**79**:608-13.
4. Dukes CE, Bussey HJ. The spread of rectal cancer and its effect on prognosis. *Br J Cancer* 1958;**12**:309-20.
5. Wong SY, Hynes RO. Lymphatic or hematogenous dissemination: how does a metastatic tumor cell decide? *Cell Cycle* 2006;**5**:812-17.
6. Colorectal cancer staging: www.oncologychannel.com/coloncancer/staging.shtml. Accessed on: 10/04/06.

Module 4 - Polyp resection and removal

One of the advantages of colonoscopy, whether performed in symptomatic patients or as part of a screening programme, is that it allows both the identification and removal of polyps.

Small polyps

Small polyps (<5 mm) should be biopsied to determine whether they are hyperplastic or adenomas. They can then be removed with biopsy forceps or snare resection, with or without electrocautery.

Pedunculated polyps

Pedunculated polyps can be easily removed by closing a snare around the stalk of the polyp and applying electrocautery.

Flat sessile polyps

Flat polyps may exhibit severe dysplasia and have a tendency to invade the bowel wall and metastasize early compared with pedunculated polyps. Flat polyps can be hard to detect because they lie close to the bowel wall and sometimes occur below the level of the normal mucosa.

To remove flat polyps, saline can be injected into the submucosa to elevate the polyp before removal by snare. This is also known as endoscopic mucosal resection (EMR). Particular care is needed to remove flat lesions from the caecum and right-hand-side of the colon where the bowel wall is thinner.

Large polyps

Large sessile polyps can be resected in sections using a snare and electrocautery. It is sometimes useful to mark the polypectomy site with an ink injection for subsequent colonoscopies.

Lateral spreading tumours and depressed lesions

Lateral spreading tumours and depressed lesions display a significantly higher rate of malignancy than other lesion types. These may be removed by EMR.

Module 4 - Further reading

1. George SMC, Mäkinen MJ, Jernvall P et al. Classification of advanced colorectal carcinomas by tumor edge morphology. *Cancer* 2000;**89**:1901-9.
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3. Lieberman DA, Weiss DG, for the Veterans Affairs Cooperative Study Group 380. One-time screening for colorectal cancer with combined fecal occult-blood test and examination of the distal colon. *N Engl J Med* 2001;**345**:555-60.
4. Su MY, Ho YP, Hsu CM et al. How can colorectal neoplasms be treated during colonoscopy? *World J Gastroenterol* 2005;**11**:2806-10.
5. Waye JD. Advanced polypectomy. *Gastrointest Endosc Clin N Am* 2005;**15**:733-56.