

COLORECTAL CANCER

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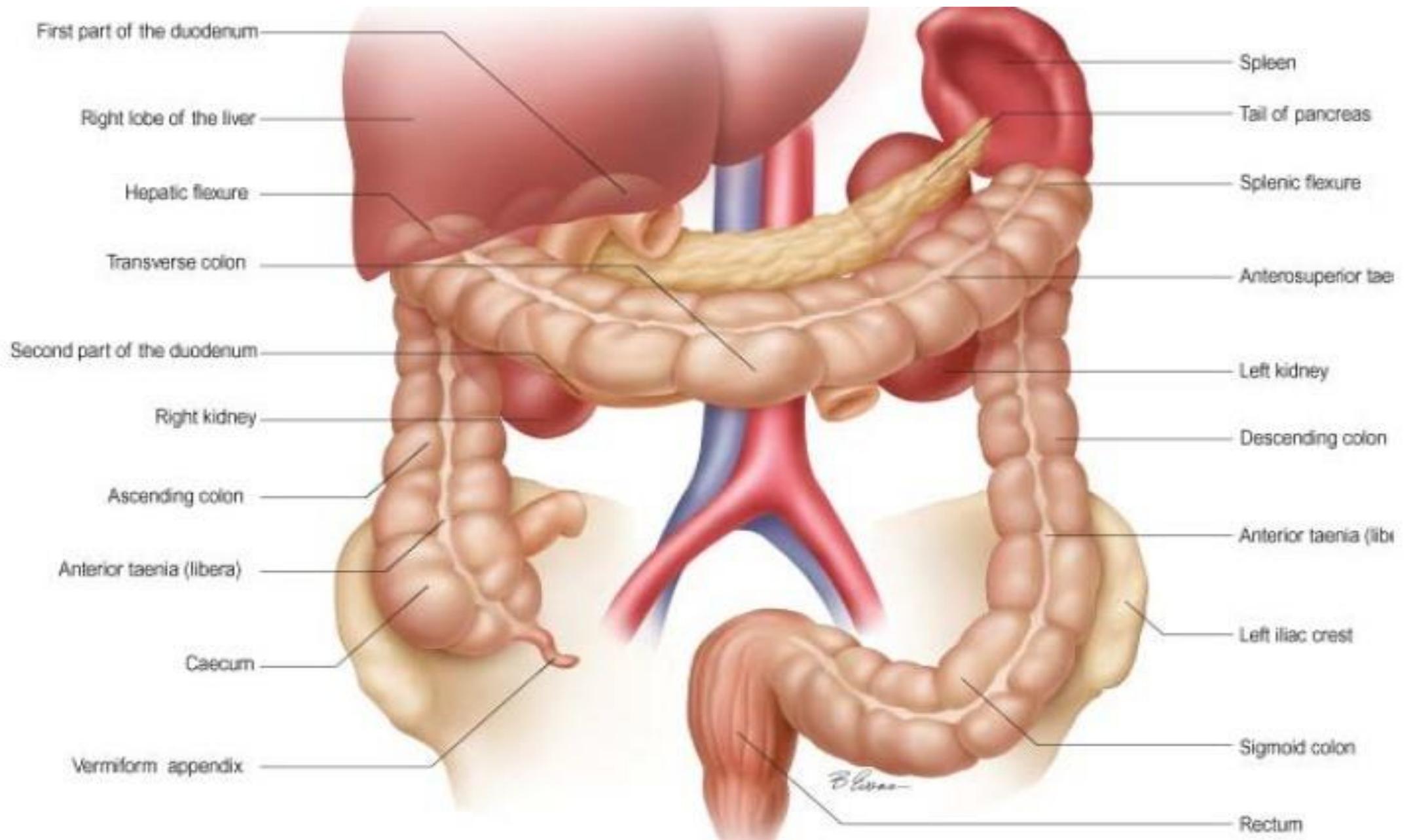


Outlines ...

Anatomy

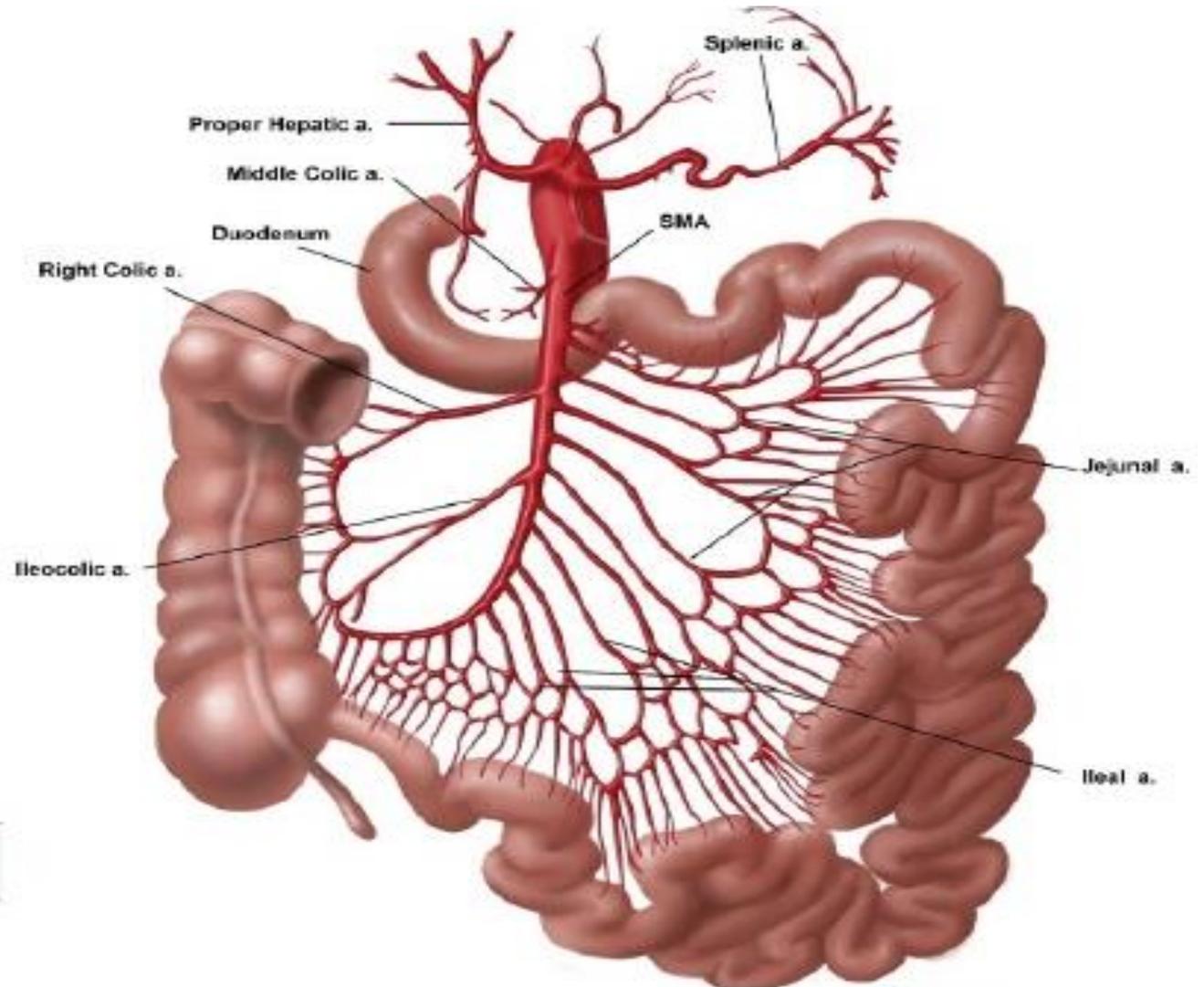
Colon
cancer

Rectal
Cancer

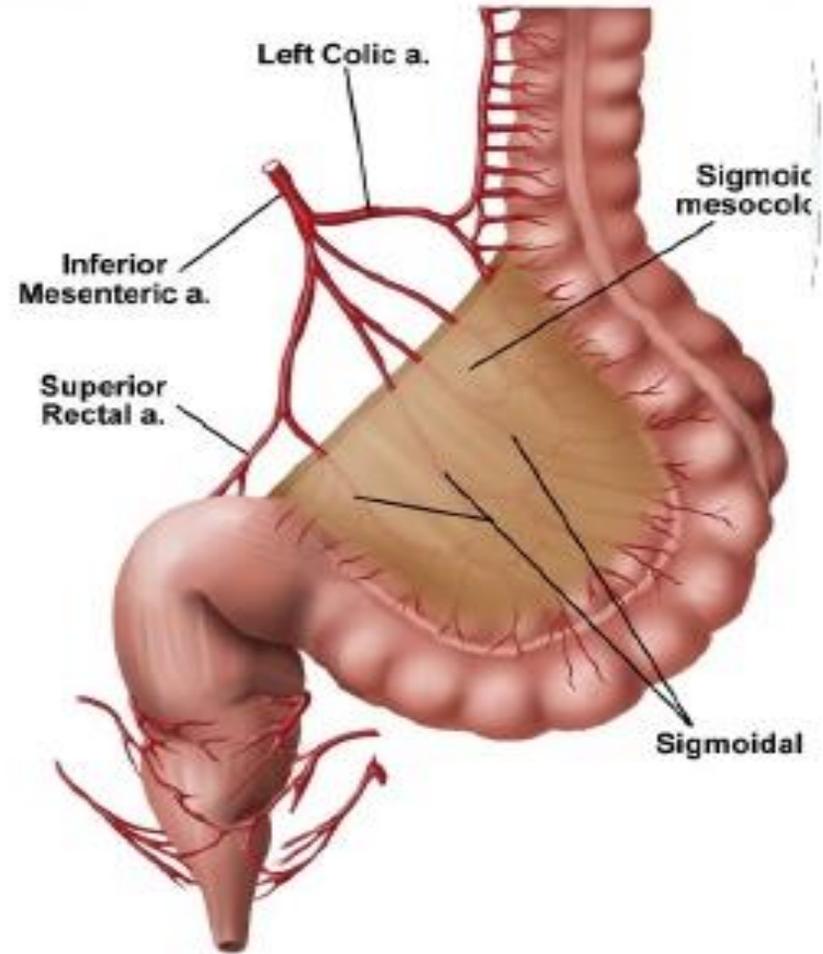


Blood Supply

- The **Superior Mesenteric Artery (SMA)**:
 - Supplies blood to the duodenum, pancreas, jejunum, ileum, and the right and transverse colon.
 - The **ileocolic artery** provides blood supply to the ileocolic region, cecum and appendix.
 - The **right colic artery** provides blood supply to the ascending colon and the hepatic flexure.
 - The **middle-colic (mid-colic) artery** provides blood supply to the transverse colon and the hepatic and splenic flexures.



- The **Inferior Mesenteric Artery (IMA)**
 - Supplies blood to the left colon, rectosigmoid and the superior 2/3 of the rectum.
 - The **left colic artery** supplies blood to the descending colon.
 - The **sigmoidal arteries** traverse the mesosigmoid and supply blood to the sigmoid colon.
- After supplying the sigmoidal arteries, the inferior mesenteric artery becomes the **superior rectal artery**.
- This artery divides to **left and right superior rectal arteries**, and supplies the upper rectum.



Adjacent branches of the superior and inferior mesenteric arteries anastomose so there is usually a complete vascular supply along the colon named the 'marginal artery of Drummond'

Venous and lymphatic drainage of the colon follows the arterial supply and as for the small intestine system, venous drainage is into the portal system.

The parasympathetic nerve supply to the right and transverse colon is through the vagus nerve.

While the distal colon and the rectum are supplied by the nervi erigentes (the pelvic splanchnic nerves) from S2,3,4.

The sympathetic system supplies the blood vessels through the greater and lesser splanchnic nerves.

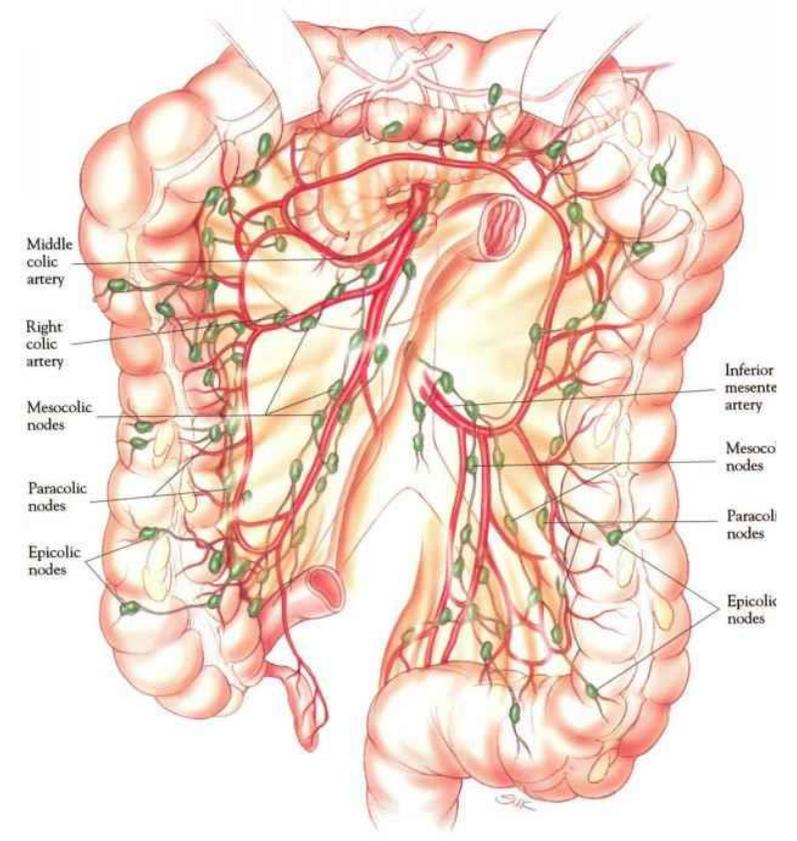
- **Lymphatic Drainage**

- 1-Epicolic nodes on the bowel wall

- 2-paracolic nodes between the marginal artery and the bowel

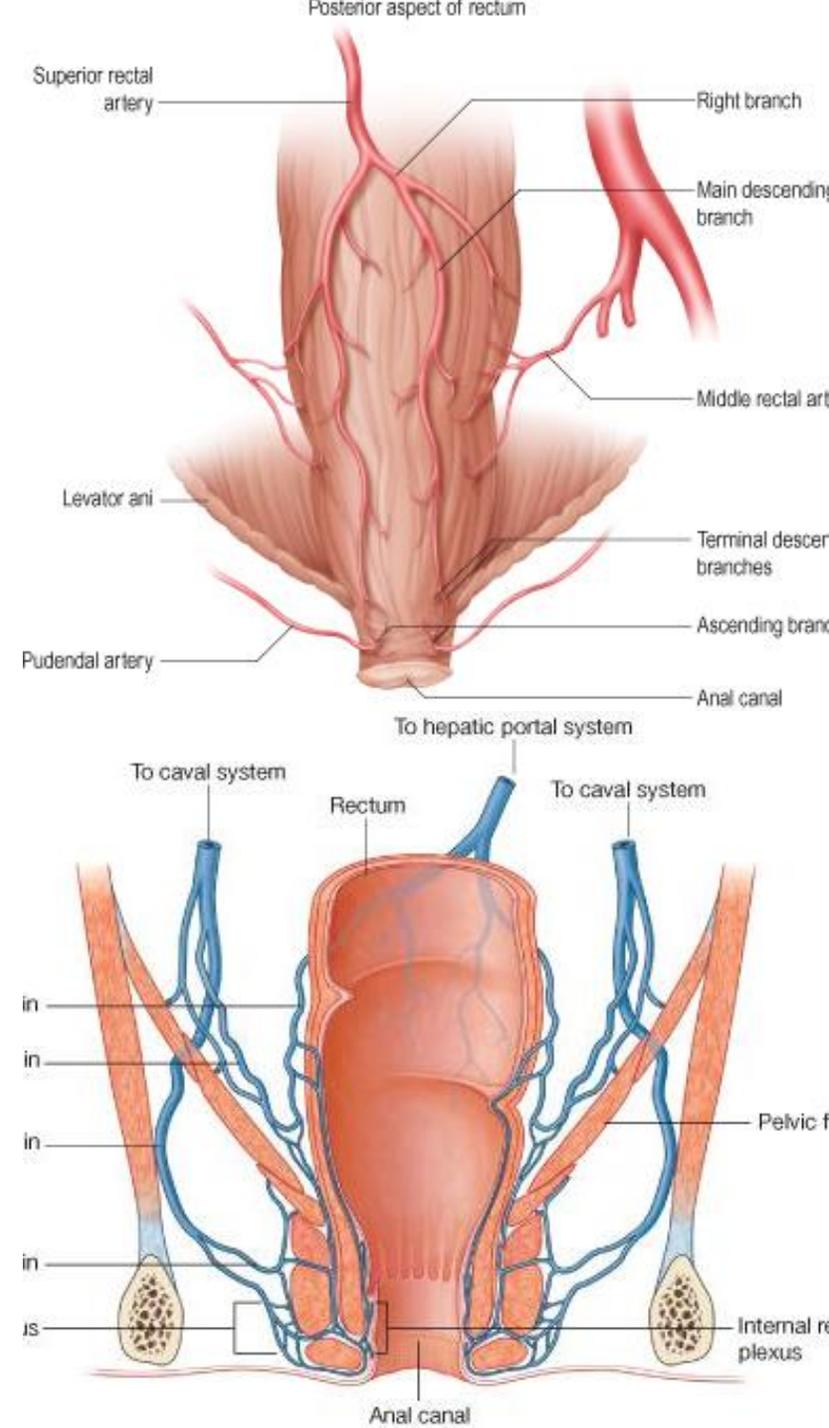
- 3-Intermediate nodes on the main vessels

- 4-Principal nodes alongside the superior and inferior mesenteric vessels.



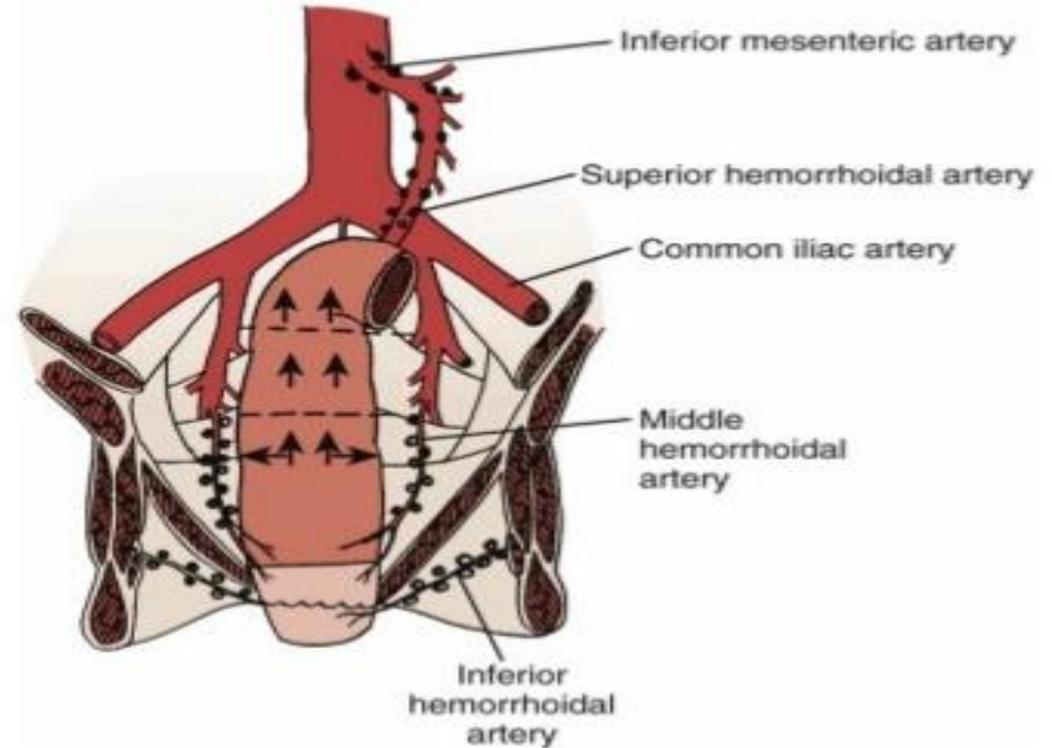
Rectum

- **Arterial supply**
 - Superior rectal A – fr. IMA; supplies upper and middle rectum
 - Middle rectal A- fr. Internal iliac A. (supplies lower rectum)
 - Inferior rectal A- fr. Internal pudendal A.
-
- **Venous drainage**
 - Superior rectal V- upper & middle third rectum
 - Middle rectal V- lower rectum and upper anal canal
 - Inferior rectal vein- lower anal canal
-
- **Innervations**
 - Sympathetic: L1-L3, Hypogastric nerve
 - ParaSympathetic: S2-S4



Lymphatic drainage

- **Upper and middle rectum**
 - **Pararectal** lymph nodes, located directly on the muscle layer of the rectum
 - **Inferior mesenteric** lymph nodes, via the nodes along the superior rectal vessels
- **Lower rectum**
 - **Sacral group** of lymph nodes or **Internal iliac** lymph nodes
- **Below the dentate line**
 - Inguinal nodes and external iliac chain



Function of The Colon



Absorption of water; 1000 mL of ileal contents enter the caecum every 24 hours of which only about 150–250 mL is excreted as faeces.



Sodium absorption is efficiently accomplished by an active transport system, while chloride and water are absorbed passively following gradients established by the sodium pump



Fermentation of dietary fiber in the colon by the normal colonic microflora leads to the generation of short chain fatty acids.



Some absorption of nutrients including glucose, fatty acids, amino acids and vitamins can also take place in the colon.



In general, faecal residue reaches the caecum 4 hours after a meal and the rectum after 24 hours.



Passage of stool is not orderly, however, because of mixing within the colon. It is thus common for residue from a single meal to still be passed 4 days later.

Classification of intestinal polyps

Inflammatory	Inflammatory polyps (pseudopolyps in ulcerative colitis)	
Metaplastic	Metaplastic or hyperplastic polyps	
Harmartomatous	Peutz–Jeghers polyp Juvenile polyp	
Neoplastic	Adenoma	Tubular Tubulovillous Villous
	Adenocarcinoma Carcinoid tumour	

Risk of Malignancy



A 10 % risk of cancer in a 1-cm diameter tubular adenoma, whereas with villous adenomas over 2 cm in diameter, there may be a 15 % chance of carcinoma.



Almost one-third of large (>3 cm) colonic adenomas will have an area of invasive malignancy within them at the time of resection.



Adenomas larger than 5 mm in diameter are usually excised because of their malignant potential.



Colonoscopic snare polypectomy is usually possible for colonic polyps, but larger sessile polyps can require endoscopic mucosal resection (EMR)



Larger rectal adenomas may require transanal resection or, where the adenoma is too high for safe conventional access, transanal endoscopic microsurgery (TEMS)

Colorectal Cancer

Is the second most common cause of cancer death.

Globally 800,000 new CRCs occur each year, accounting for 10% of all incident cancers with 450,000 deaths/year

Incidence :
35.8/100,000 (USA)

Aetiology

Environmental & dietary factors

Male sex

Family history of colorectal cancer

Personal history of colorectal cancer, ovary, endometrial, breast

Excessive BMI

Red meat ,animal fat, smoking and alcohol

Protective effect of dietary fibre

Low folate consumption

Neoplastic polyps.

IBD

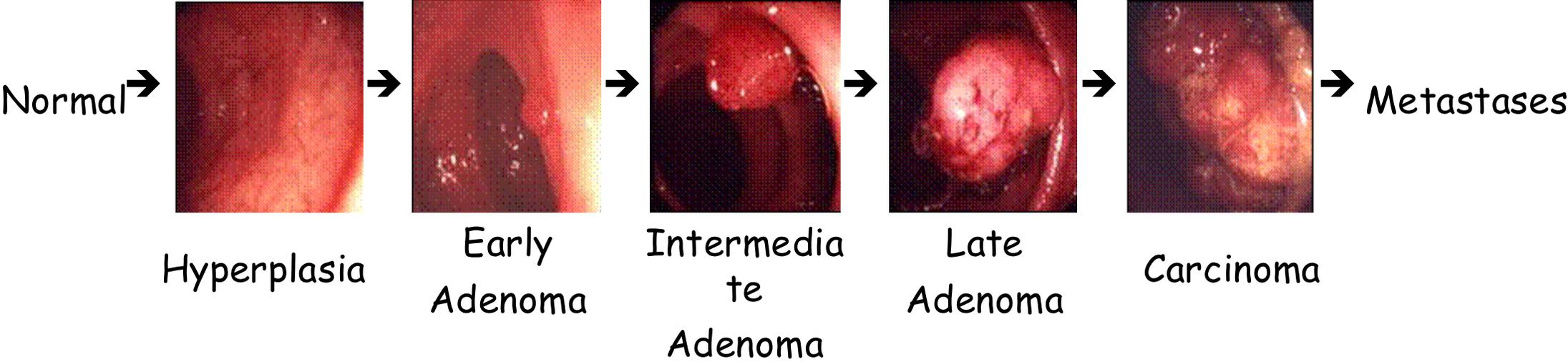
Cholecystectomy

Ureterosigmoidostomy.

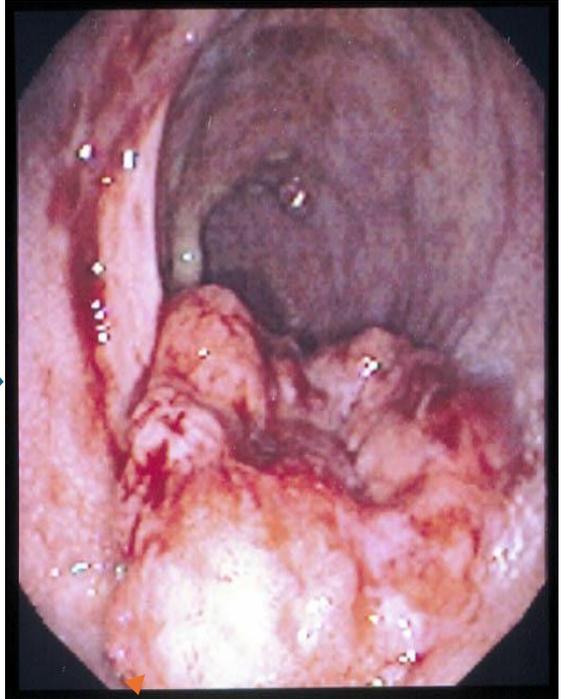
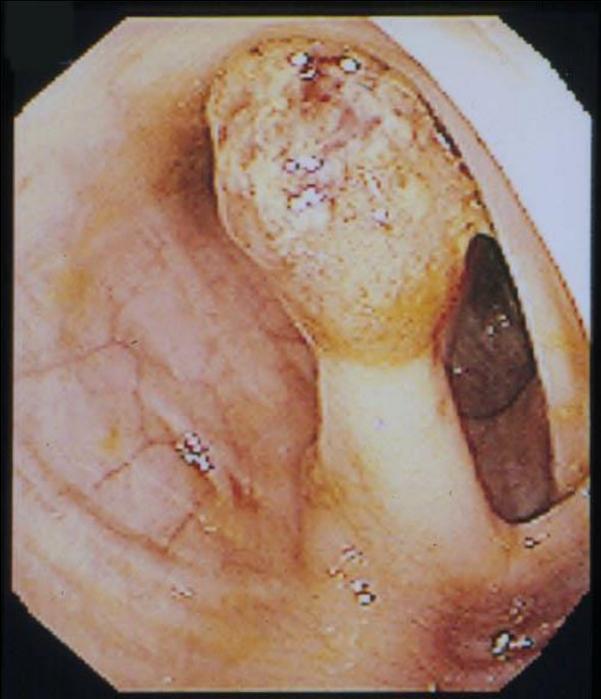
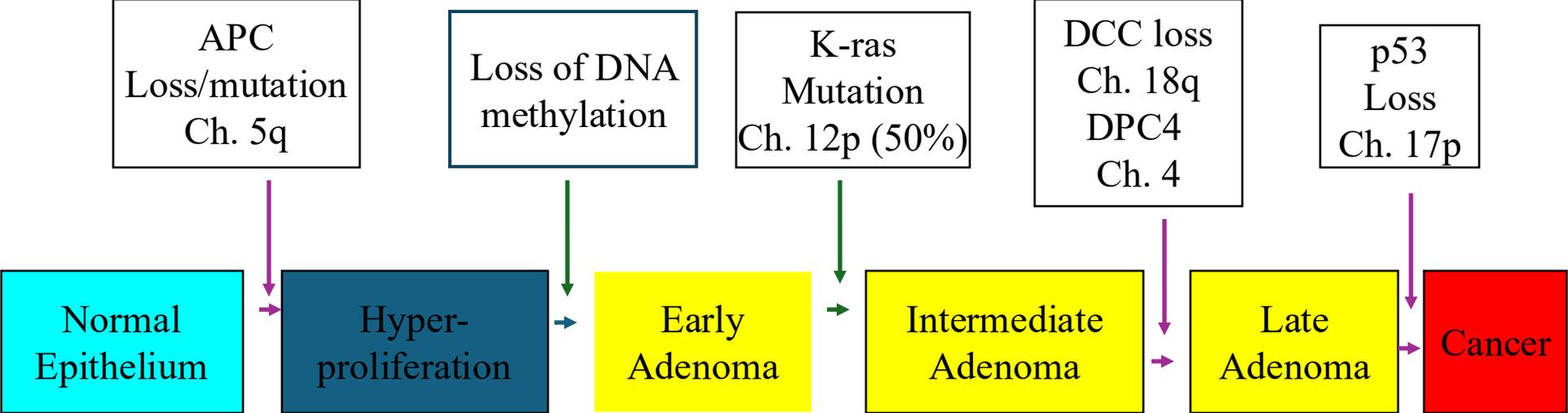
Adenoma– carcinoma sequence

Hereditary Conditions (FAP, HNPCC)

Adenoma– Carcinoma Sequence



Adenoma-Carcinoma Sequence





Familial Adenomatous Polyposis (FAP)

Inherited as an autosomal dominant

Mutations in the adenomatous polyposis coli (*APC*) gene

Presence of more than 100 colorectal adenomas

Characterised by duodenal adenomas and multiple extraintestinal manifestations.

Accounts for 1 % or less of all colon cancer

The risk of colorectal cancer is 100 %

Associated with benign mesodermal tumours such as desmoid tumours and osteomas

50 % of patients have congenital hypertrophy of the retinal pigment epithelium (CHRPE), which can be used to screen affected families if genetic testing is unavailable.

Extracolonic manifestations of familial adenomatous polyposis

- Endodermal derivatives
 - Adenomas and carcinomas of the duodenum, stomach, small intestine, thyroid and biliary tree
 - Fundic gland polyps
 - Hepatoblastoma
- Ectodermal derivatives
 - Epidermoid cysts
 - Pilomatrixoma
 - Congenital hypertrophy of the retinal pigment epithelium (CHRPE)
 - Brain tumours
- Mesodermal derivatives
 - Desmoid tumours
 - Osteomas
 - Dental problems

Hereditary non-polyposis colorectal cancer (Lynch syndrome)

Characterised by increased risk of colorectal cancer and also cancers of the endometrium, ovary, stomach and small intestines.

Accounts for about 5 – 10 % of all colon cancers .

Autosomal dominant condition caused by a mutation in one of the DNA mismatch repair genes(*MLH1* , *MSH2*).

The lifetime risk of developing colorectal cancer 80 %, and the mean age of diagnosis is 45 years.

Most cancers develop in the proximal colon.

30–50 % lifetime risk of developing endometrial cancer.

Diagnosed by genetic testing or the Amsterdam II criteria.

Patients with HNPCC are subjected to regular (every one to two years) colonoscopic surveillance.

Amsterdam II criteria

Three or more family members with an HNPCC-related cancer (colorectal, endometrial, small bowel, ureter, renal pelvis), one of whom is a first-degree relative of the other two

Two successive affected generations

At least one colorectal cancer diagnosed before the age of 50 years

FAP excluded

Tumours verified by pathological examination.

IBD



The risk of cancer in ulcerative colitis increases with duration of disease.



At ten years from diagnosis, it is around 1 %. This increases to 10–15 % at 20 years and may be as high as 20 % at 30 years.

Pathology

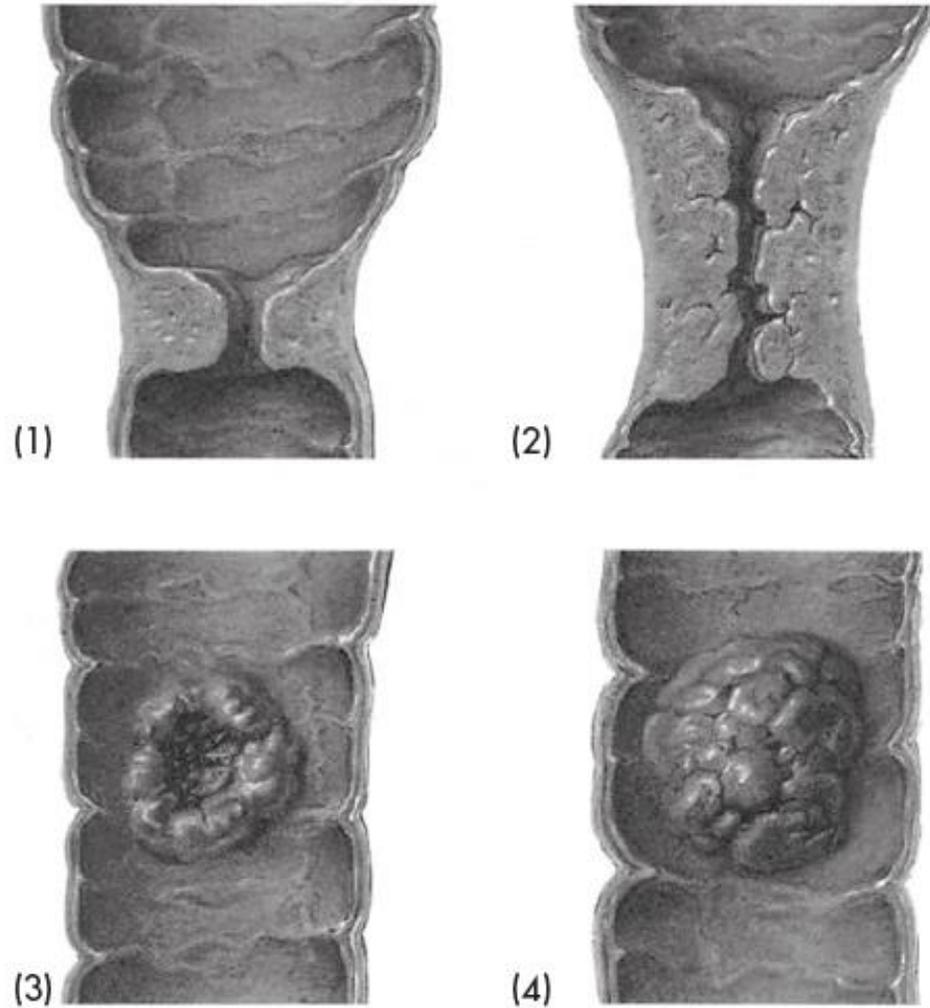
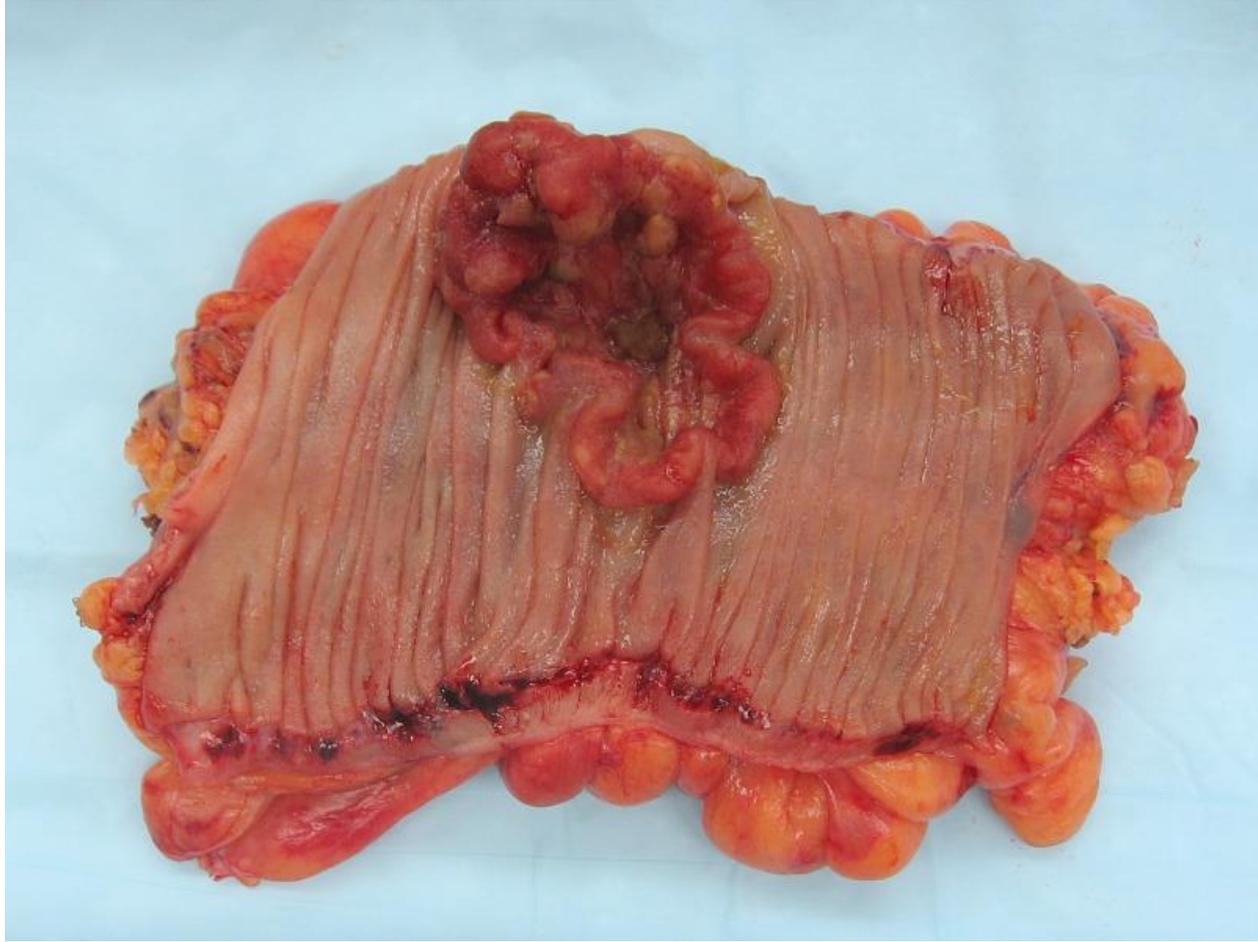


Figure 69.22 The four common macroscopic varieties of carcinoma of the colon. (1) Annular; (2) tubular; (3) ulcer; (4) cauliflower.





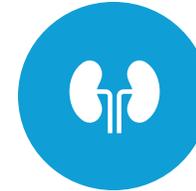
Clinical features



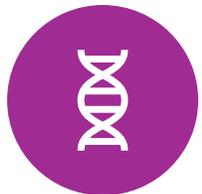
Occurs in patients over 50 years of age and is most common in the eighth decade of life



20% of cases present as an emergency with intestinal obstruction or peritonitis.



left sided colonic tumors which are far more common usually present with a change in bowel habit or rectal bleeding



While more proximal lesions typically present later with iron deficiency anaemia or a mass.



Patients may present for the first time with metastatic disease.



Lesions of the flexures may present with vague upper abdominal symptoms for many months before other, more specific symptoms suggestive of colonic disease appear.

Signs

Pallor

Abdominal mass

PR mass

Jaundice

Nodular liver

Ascites

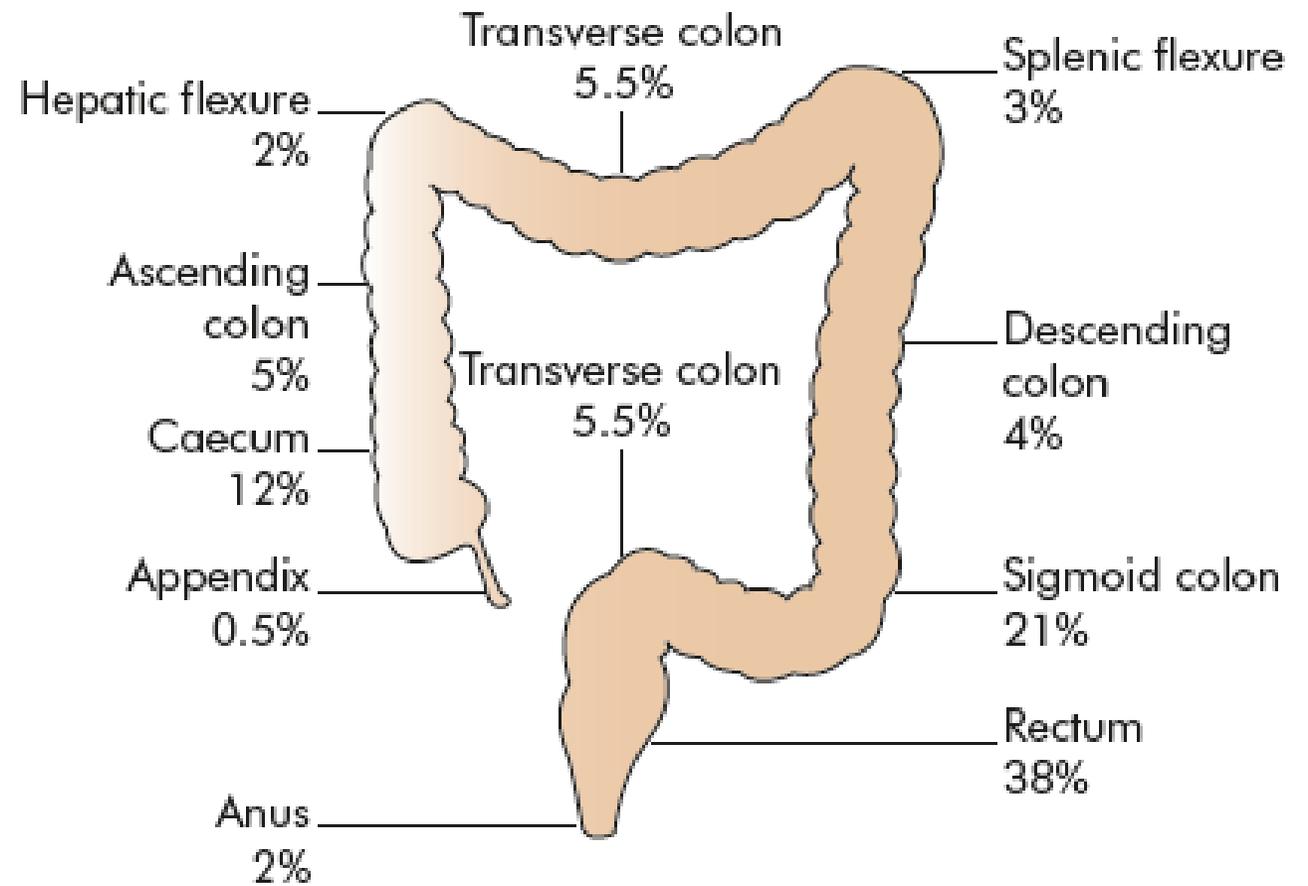


Figure 69.23 Distribution of colorectal cancer by site.

Diagnosis



Complete history



Physical examination /DRE



Routine investigations



Confirmatory- Biopsy

CXR

Barium enema



Staging workup

Colonoscopy

CT abdomen- pelvis

Virtual colonoscopy

MR



Gold standard- Colonoscopy+ Biopsy

- Others
- FOBT
- Stool cytology
- CEA
- IHC markers
- Molecular markers-
oncogenes

Screening Guidelines

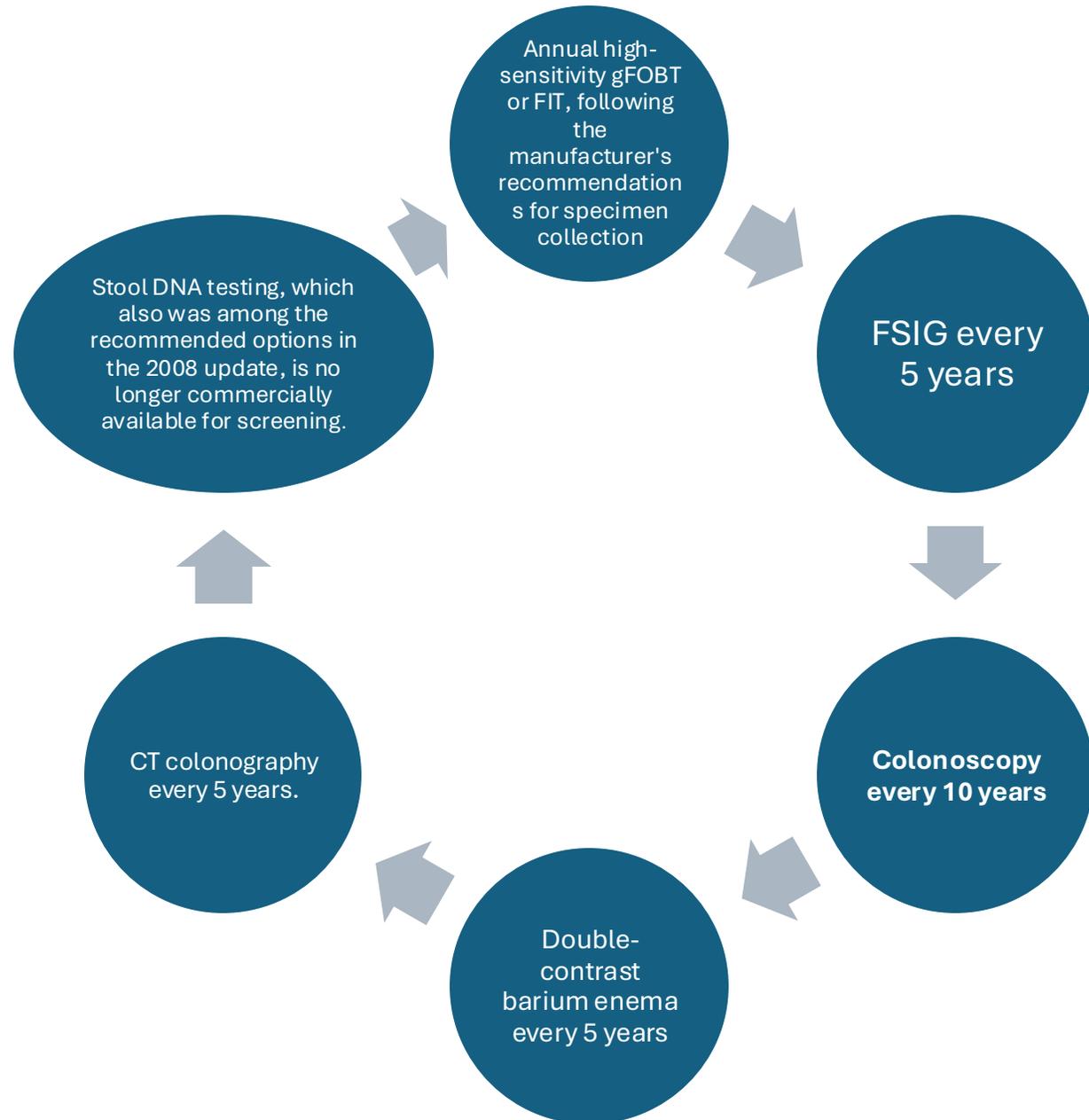
Screening for asymptomatic men and women at age 50, using a menu of screening options.

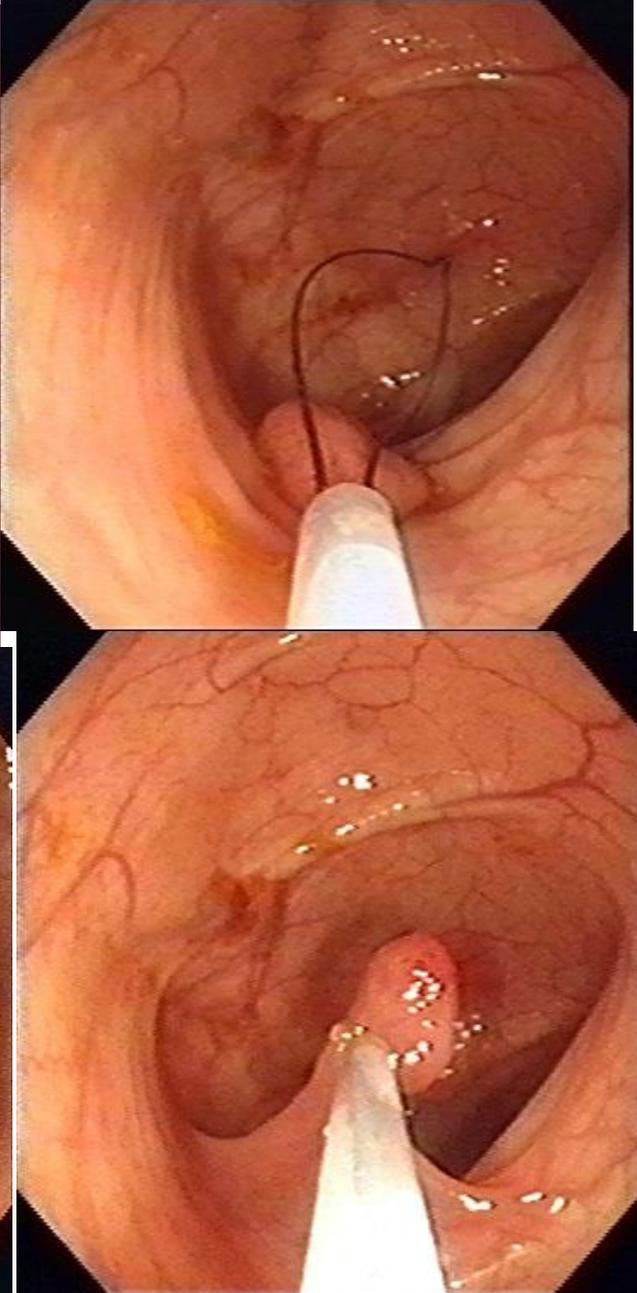
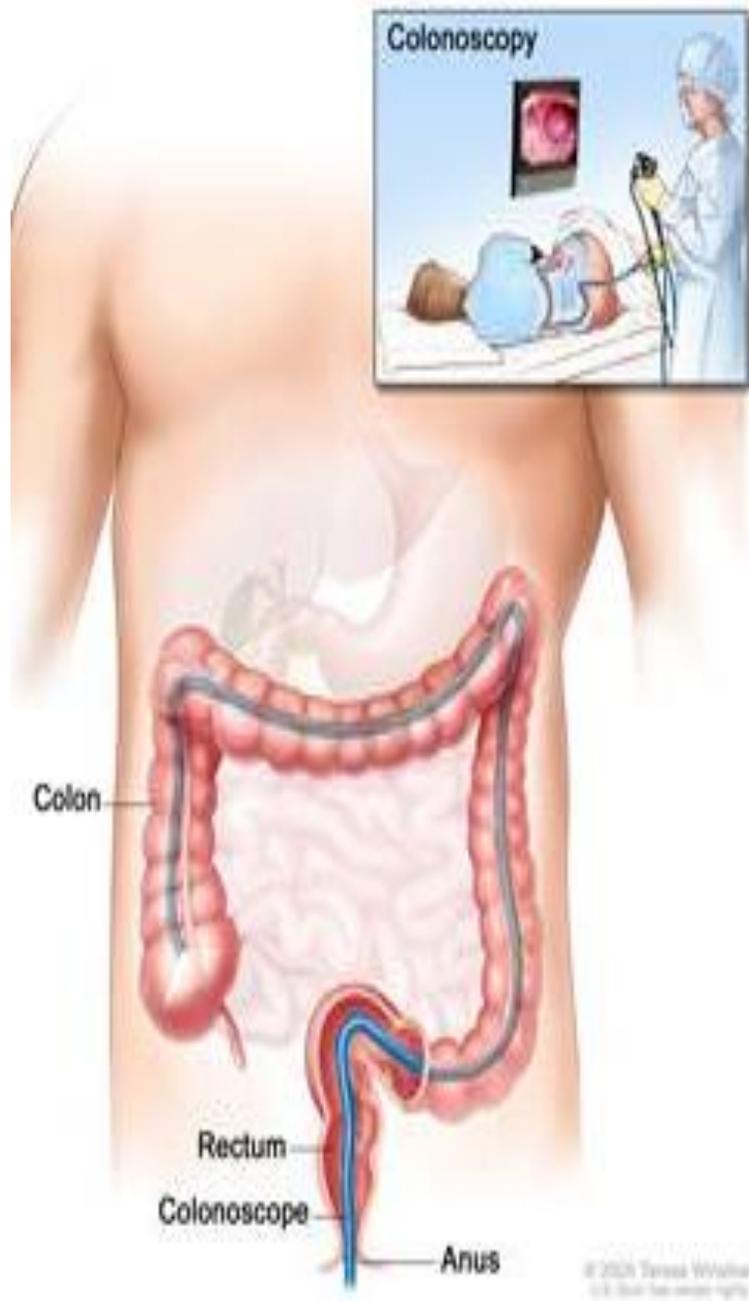


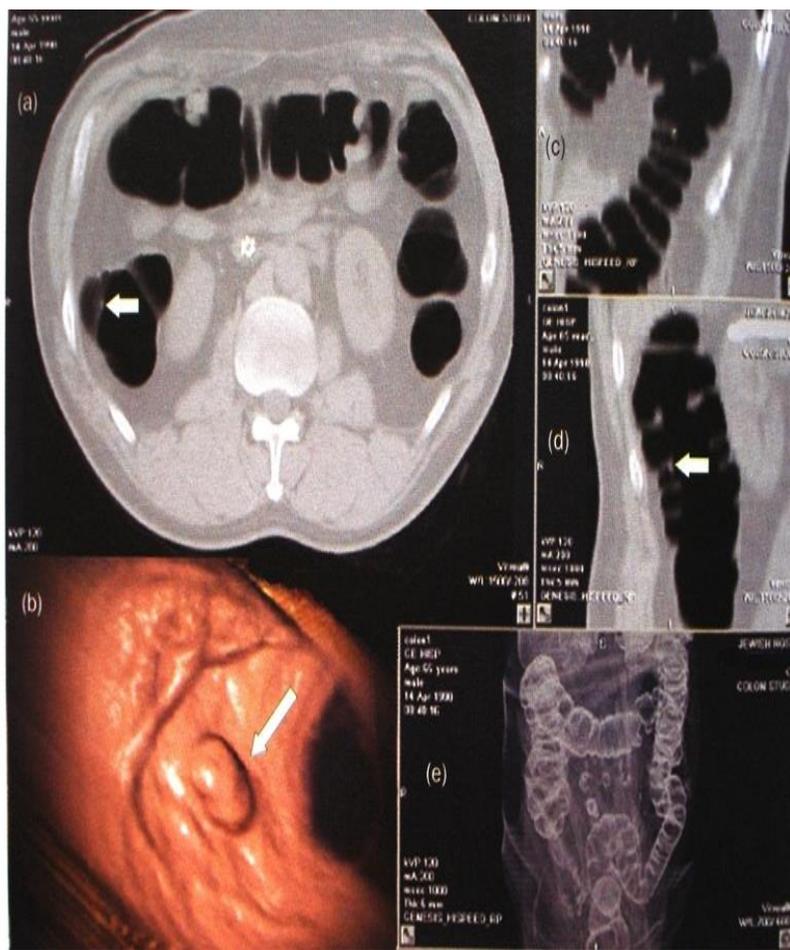
Mortality rates have been declining for the past 2 decades, largely attributable to the contribution of screening to prevention and early detection.



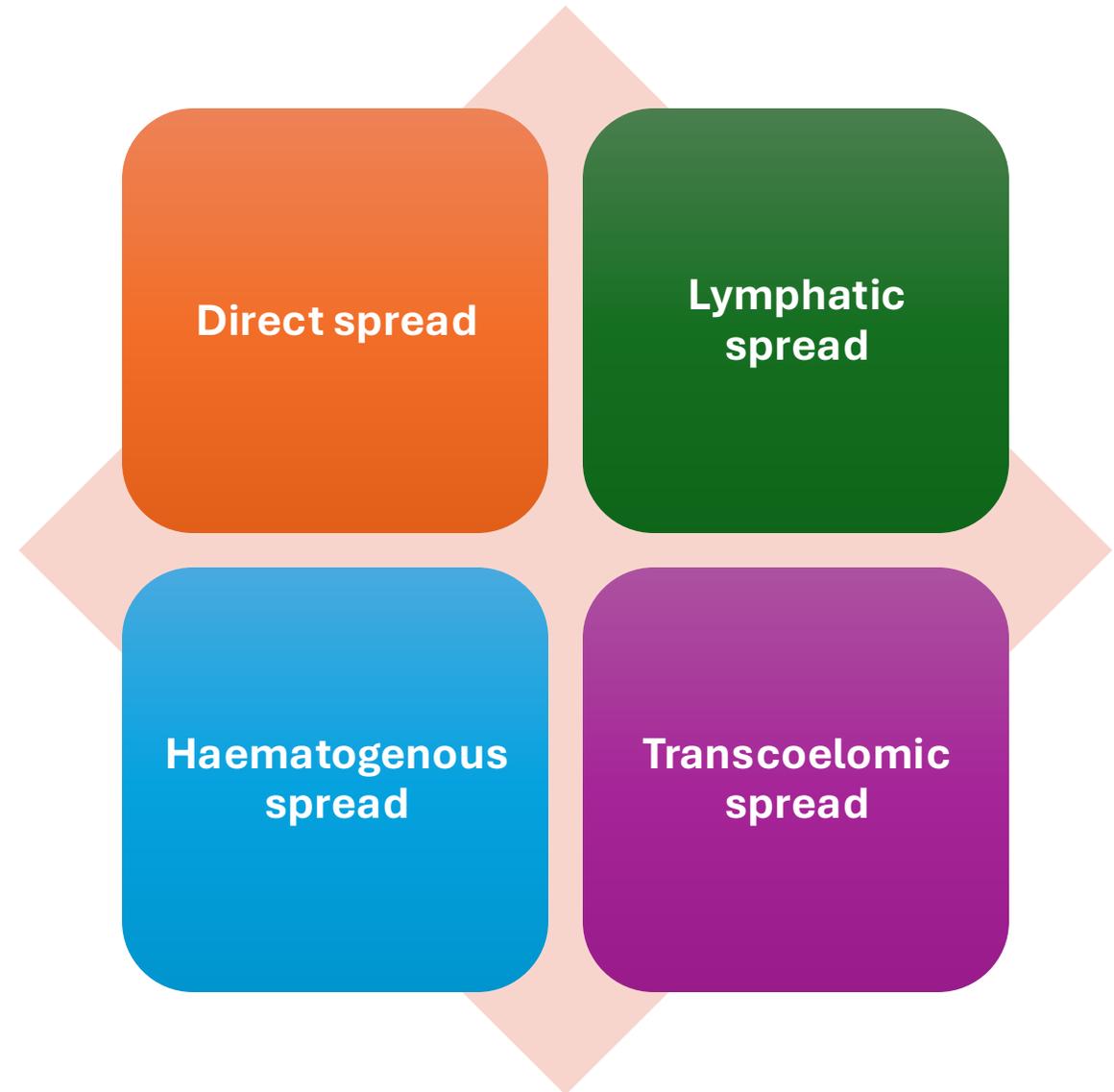
Recommended CRC screening tests







SPREAD OF CARCINOMA OF THE COLON



Classifications

TNM classification for colonic cancer

- T, Tumour stage
 - T1, Into submucosa
 - T2, Into muscularis propria
 - T3, Into pericolic fat or sub-serosa but not breaching serosa
 - T4, Breaches serosa or directly involving another organ
- N, Nodal stage
 - N0, No nodes involved
 - N1, 1–3 nodes involved
 - N2, Four or more nodes involved
- M, Metastases
 - M0, No metastases
 - M1, Metastases

Dukes' staging for colorectal cancer

- 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

Dukes classification-

Dukes A: Invasion into but not through the bowel wall.

Dukes B: Invasion through the bowel wall but not involving lymph nodes.

Dukes C: Involvement of lymph nodes

Dukes D: Widespread metastases

Modified astler coller classification-

Stage A : Limited to mucosa.

Stage B1 : Extending into muscularis propria but not penetrating through it; nodes not involved.

Stage B2 : Penetrating through muscularis propria; nodes not involved

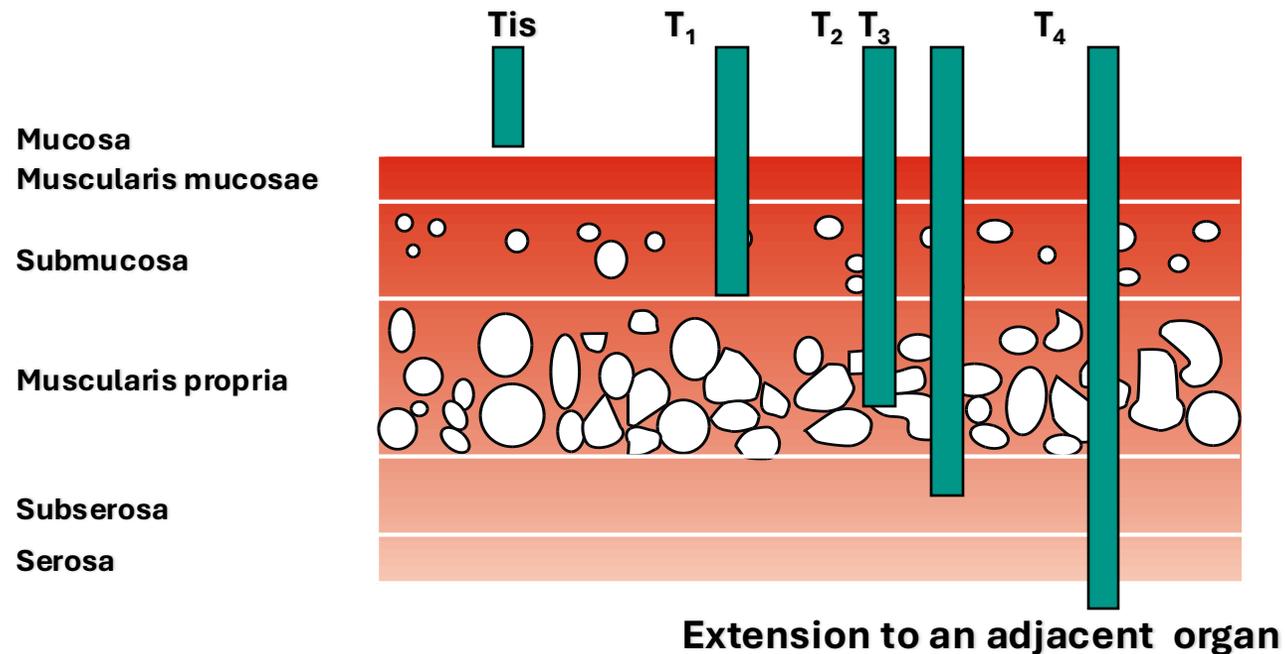
Stage C1 : Extending into muscularis propria but not penetrating through it. Nodes involved

Stage C2 : Penetrating through muscularis propria. Nodes involved

Stage D: Distant metastatic spread

TNM Classification

T _x	Primary tumor cannot be assessed
T ₀	No evidence of primary tumor
T _{is}	Carcinoma <i>in situ</i> : intraepithelial or invasion of lamina propria
T ₁	Tumor invades submucosa
T ₂	Tumor invades muscularis propria
T ₃	Tumor invades through the muscularis propria into pericolorectal tissues
T _{4a}	Tumor penetrates to the surface of the visceral peritoneum
T _{4b}	Tumor directly invades or is adherent to other organs or structures



TNM Classification

<i>Regional Lymph Nodes (N)</i>	
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in 1 to 3 regional lymph nodes
N1a	Metastasis in 1 regional lymph node
N1b	Metastasis in 2-3 regional lymph nodes
N1c	Tumor deposit(s) in the subserosa, mesentery, or non-peritonealized pericolic or perirectal tissues without regional nodal metastasis
N2	Metastasis in 4 or more regional lymph nodes
N2a	Metastasis in 4 to 6 regional lymph nodes
N2b	Metastasis in 7 or more regional lymph nodes
<i>Distant Metastasis (M)</i>	
M0	No distant metastasis (no pathologic M0; use clinical M to complete stage group)
M1	Distant metastasis
M1a	Metastasis confined to one organ or site (e.g. liver, lung, ovary, non-regional node).
M1b	Metastases in more than one organ/site or the peritoneum

Stage Grouping

Clinical					
Group	T	N	M	Dukes*	MAC*
0	Tis	N0	M0		-
I	T1	N0	M0	A	A
	T2	N0	M0	A	B1
IIA	T3	N0	M0	B	B2
IIB	T4a	N0	M0	B	B2
IIC	T4b	N0	M0	B	B3
IIIA	T1-T2	N1/N1c	M0	C	C1
	T1	N2a	M0	C	C1
IIIB	T3-T4a	N1/N1c	M0	C	C2
	T2-T3	N2a	M0	C	C1/C2
	T1-T2	N2b	M0	C	C1
IIIC	T4a	N2a	M0	C	C2
	T3-T4a	N2b	M0	C	C2
	T4b	N1-N2	M0	C	C3
IVA	Any T	Any N	M1a	-	-
IVB	Any T	Any N	M1b	-	-
*Dukes B is a composite of better (T3 N0 M0) and worse (T4 N0 M0) prognostic groups, as is Dukes C (Any TN1 M0 and Any T N2 M0). MAC is the modified Astler–Coller classification.					
Stage unknown					

SURGERY

SURGERY is the GOLD STANDARD and principle therapy of primary and non metastatic ca colon

Curative

Palliative

Accurate disease staging

Guides adjuvant treatment

Likelihood of cure is greater when disease is detected at early stage

AIM

To excise the primary lesion with adequate margin ~5 cm of normal bowel proximal and distal to the tumor

To reconstitute bowel continuity

- The operations described are designed to remove the primary tumour and its draining locoregional lymph nodes.

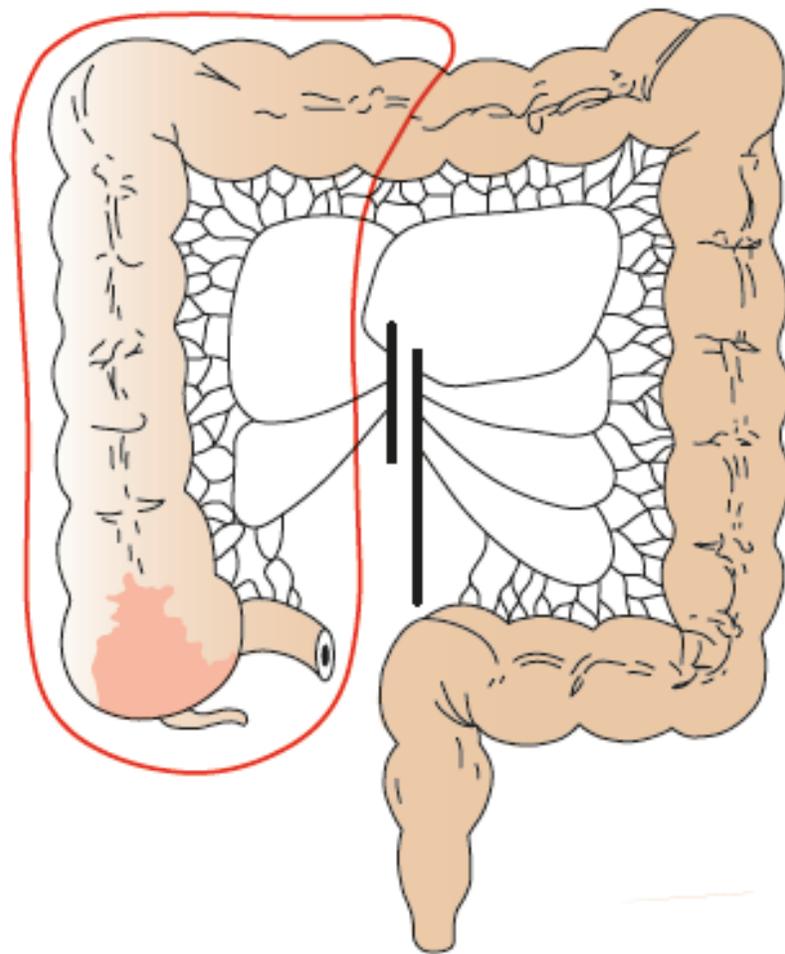


Figure 69.28 Schematic showing right hemicolectomy.

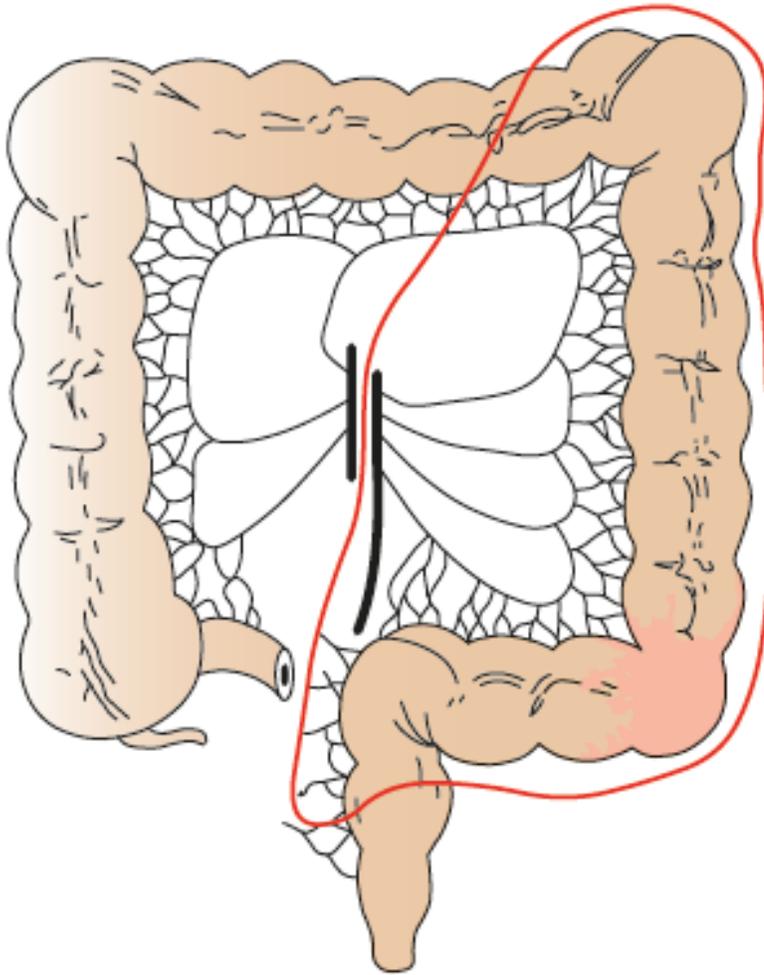
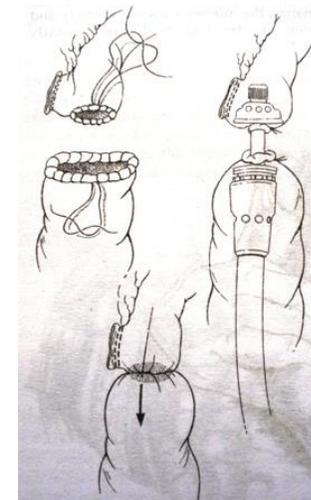
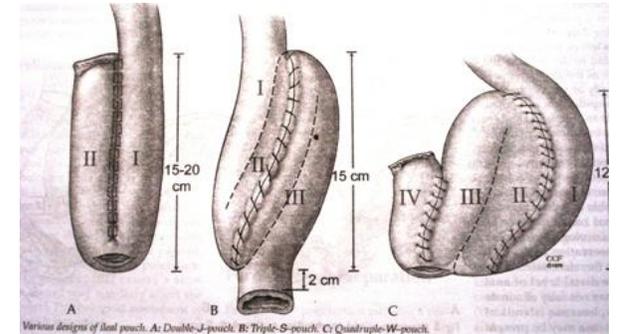


Figure 69.29 Schematic showing left hemicolectomy.

FAP

Total proctocolectomy and
IPAA

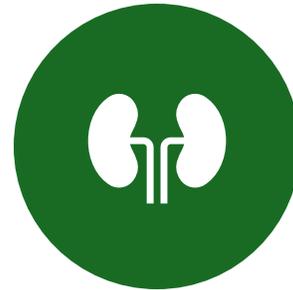
Various designs of ileal
pouches



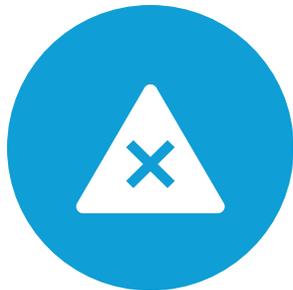
Emergency surgery



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; this can be facilitated by decompressing the bowel at the start of the operation



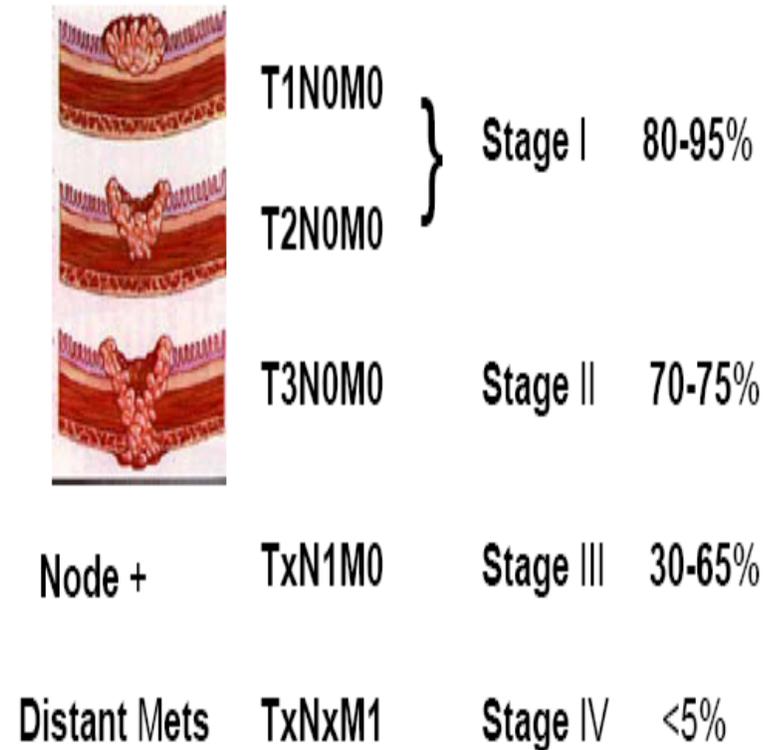
Perforation with substantial contamination or if the patient is unstable, it may be advisable to bring out an ileo/colostomy rather than anastomosing bowel in these circumstances.



For a left-sided lesion, the decision-making process is similar to that in diverticular disease between a **Hartmann's** procedure and resection and anastomosis

Stage	Mean 5 yr survival rate (%)
T ₁ N ₀	97
T ₂ N ₀	90
T ₃ N ₀	78
T ₂ N ₊	74
T ₄ N ₀	63
T ₃ N ₊	48
T ₄ N ₊	38

5 yr survival after curative resection of CRC





The most important determinant of prognosis is tumour stage and, in particular, lymph node status.



Overall five-year survival for colorectal cancer is approximately 50 %.



Follow up aims to identify synchronous bowel tumours that were not picked up at original diagnosis due to emergency presentation or incomplete assessment

Chemotherapy

- 5Fu
- Leucovorin
- Oxaliplatin
- Irinotecan
- Bevacizumab
- cetuximab

Combinations

- FOLFOX
- FOLFIRI
- Leucovorin/5FU
- Capecitabine
- Bevacizumab in combination with the above regimens.

Rectum

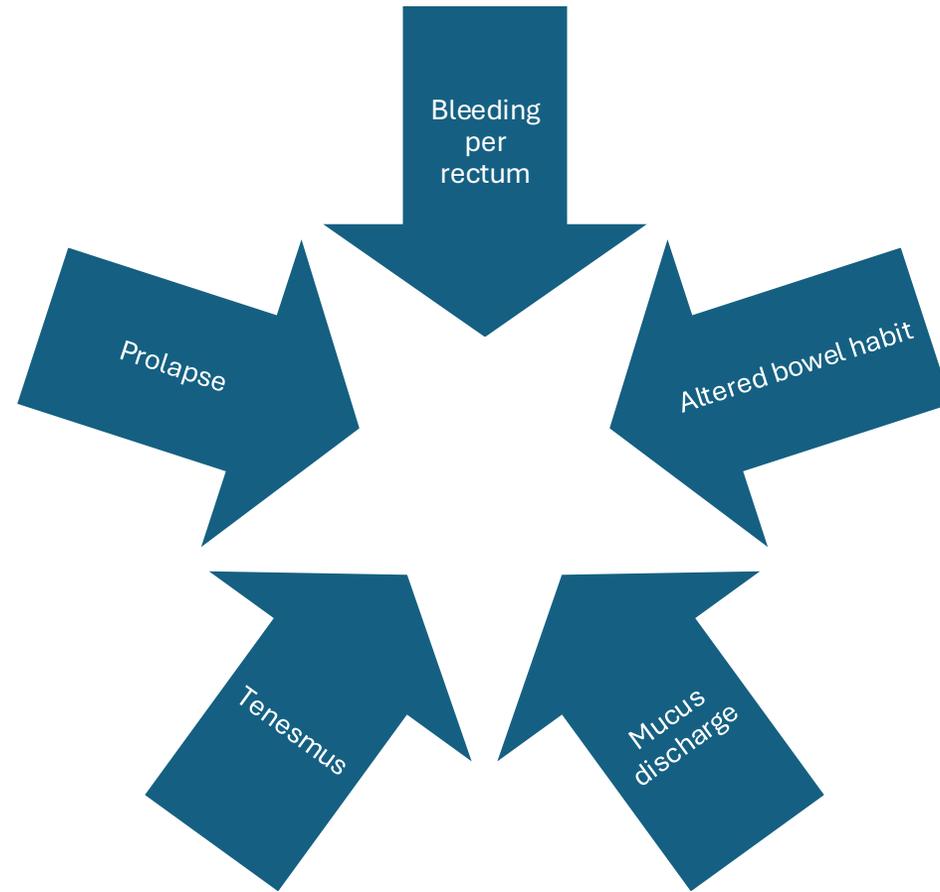
The rectum measures approximately 15 cm in length

It is divided into lower, middle and upper thirds

The blood supply consists of superior, middle and inferior rectal vessels

Although the lymphatic drainage follows the blood supply, the principal route is upwards along the superior rectal vessels to the para-aortic nodes

Main symptoms of rectal disease



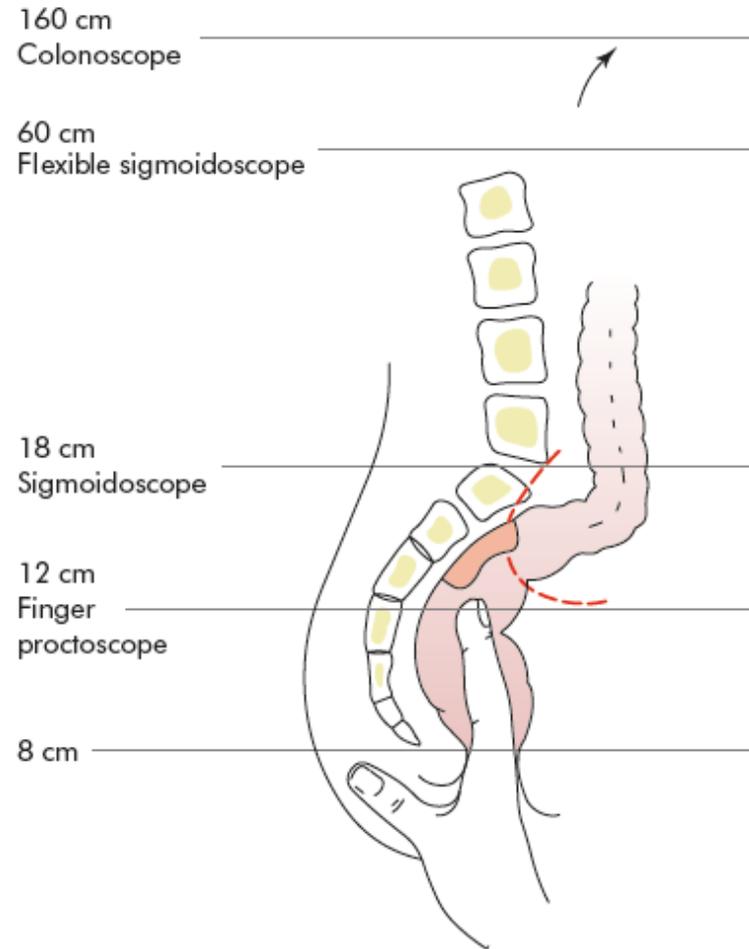
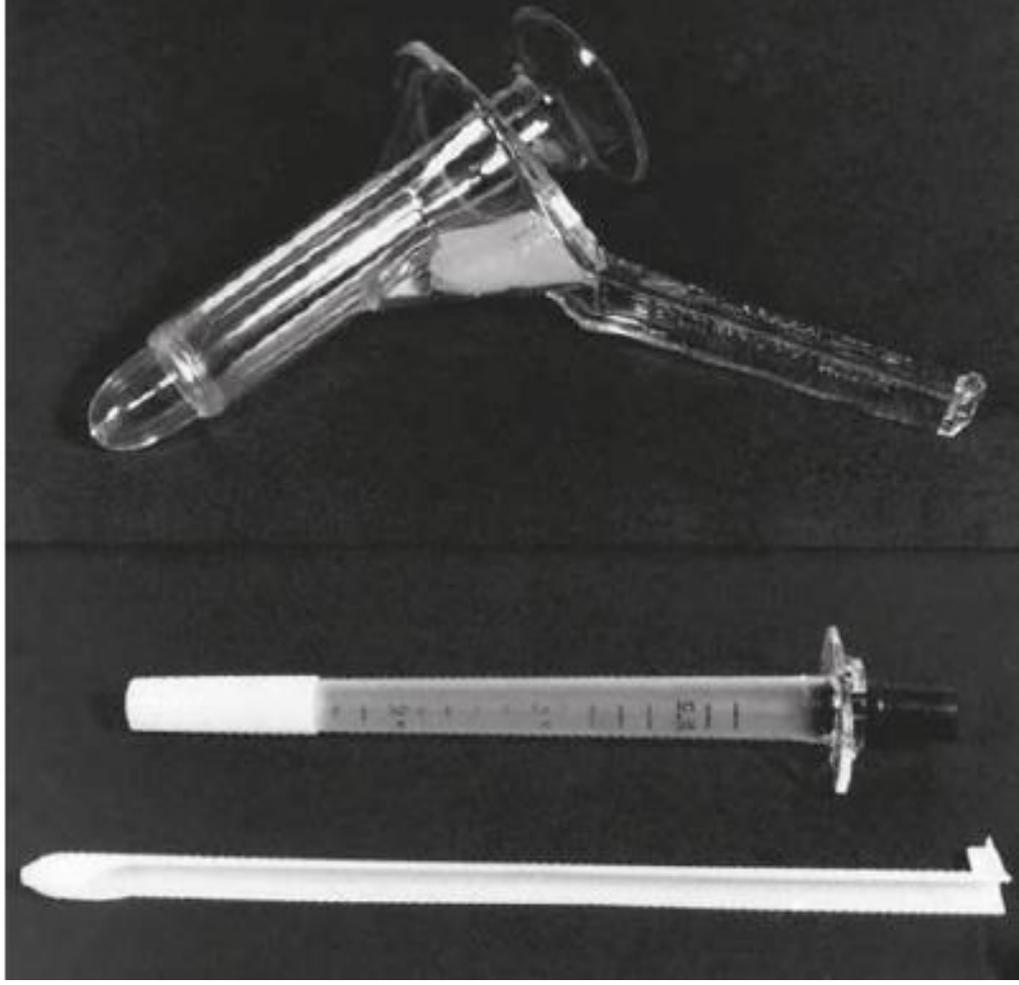


Figure 72.4 Illustration showing how the various methods of examining the rectum reach different levels. Note that even cancers in the upper part of the rectum can be felt with the index finger, especially if the patient is asked to 'strain down' (courtesy of CV Mann).



Rectal polyps

- Either single or multiple
- Adenomas are the most frequent histological type
- Villous adenomas may be extensive and undergo malignant changes
- All adenomas must be removed to avoid carcinomatous change
- All patients must undergo colonoscopy to determine whether further polyps are present
- Most polyps can be removed by endoscopic techniques, but sometimes major surgery is required

Workup

- CT of the chest and abdomen to exclude distant metastases
- PET scanning can be helpful in identifying metastases if imaging is otherwise equivocal
- Endoluminal ultrasound, performed using a probe placed in the rectal lumen, can be used to assess the local spread of the tumour
- MRI

Transrectal ultrasound –EUS

use for clinical staging.

80-95% accurate in tumor staging

70-75% accurate in mesorectal lymph node staging

Very good at demonstrating layers of rectal wall

Use is limited to lesion < 14 cm from anus, not applicable for upper rectum, for stenosing tumor

Very useful in determining extension of disease into anal canal (clinical important for planning sphincter preserving surgery)

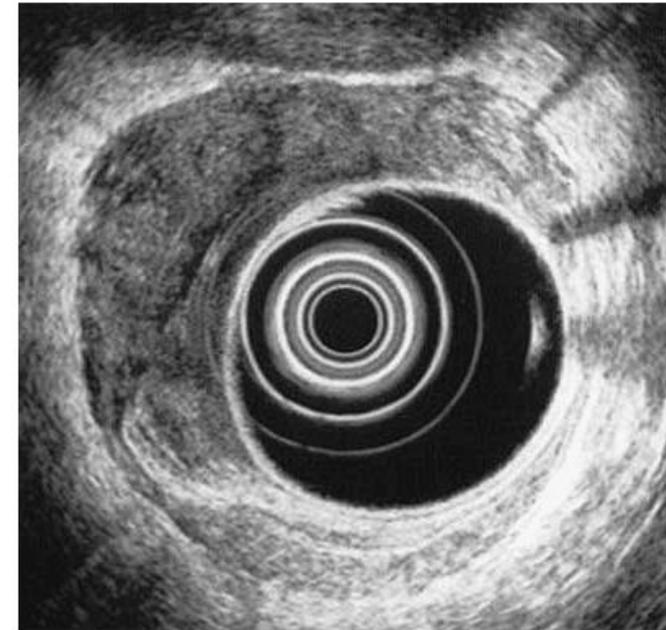
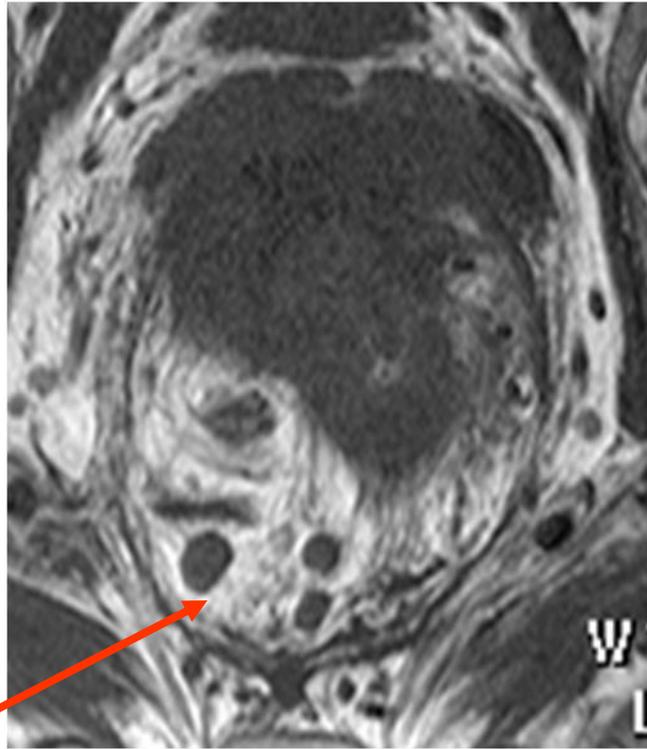


Figure. Endorectal ultrasound of a T3 tumor of the rectum, extension through the muscularis propria, and into perirectal fat.

MRI



Circumferential Resection
Margin (CRM)

Management

Management of rectal cancer has become increasingly complex, because of the various surgical, neoadjuvant and adjuvant options available, and is best delivered in a multidisciplinary setting.

The diagram consists of two blue circles connected by two light blue arrows. The top arrow points from the left circle to the right circle, and the bottom arrow points from the right circle to the left circle, indicating a bidirectional relationship between the two concepts.

Before treatment can be planned, it is necessary to assess:

- Fitness of the patient
- Extent of spread

Radical excision of the rectum, together with the mesorectum and associated lymph nodes, should be the aim in most cases.

When a tumour appears to be locally advanced, the administration of a course of neoadjuvant chemoradiotherapy over approximately 6 weeks may reduce its size and make curative surgery

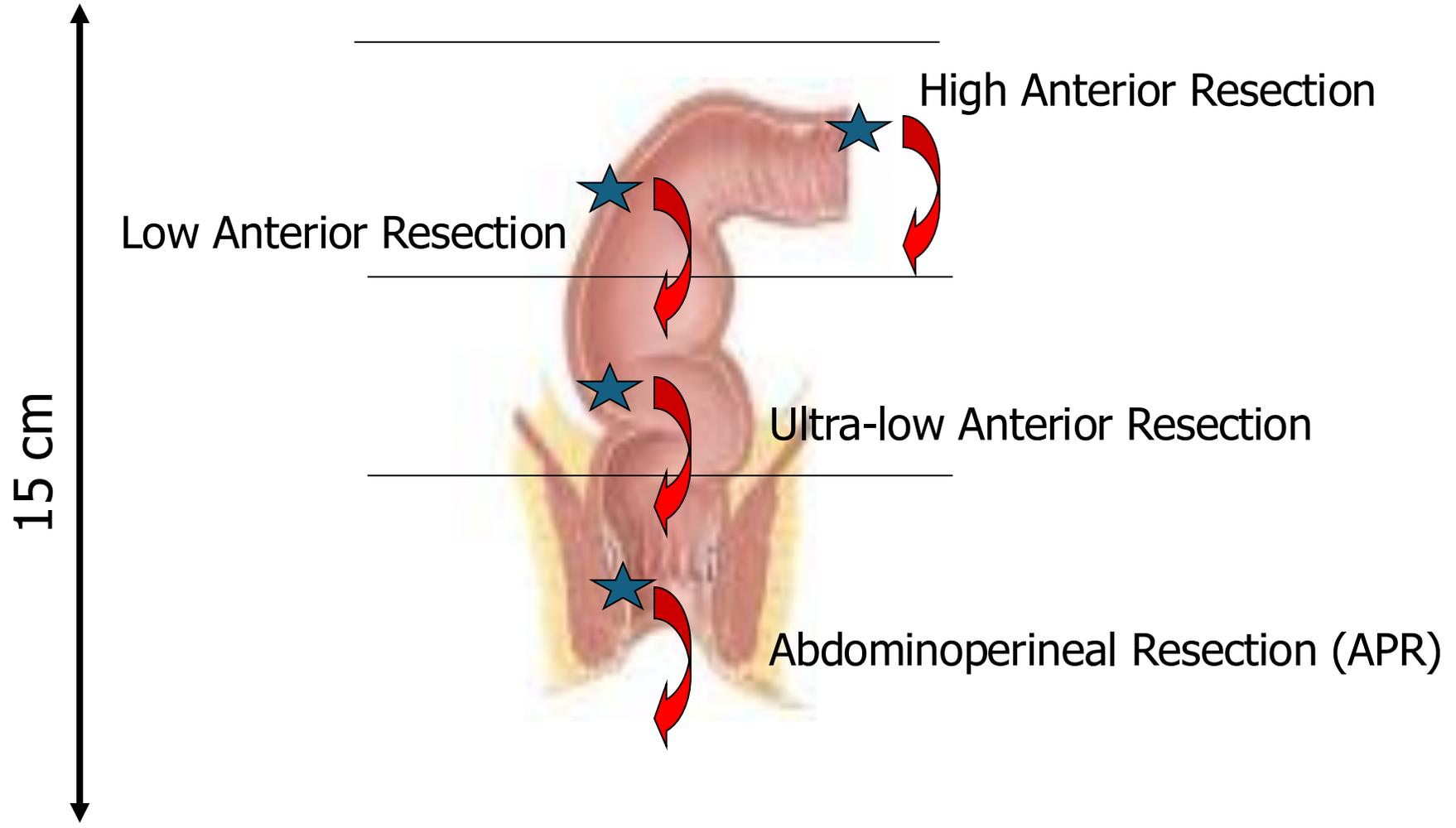
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graph LR; A((For patients who are unfit for radical surgery, who have very early tumours or who have widespread metastases, a local procedure such as transanal excision, laser destruction or interstitial radiation should be considered)) --> B((Sphincter-saving operation (anterior resection) is usually possible for tumours whose lower margin is 2 cm above the anal canal.))
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For patients who are unfit for radical surgery, who have very early tumours or who have widespread metastases, a local procedure such as transanal excision, laser destruction or interstitial radiation should be considered

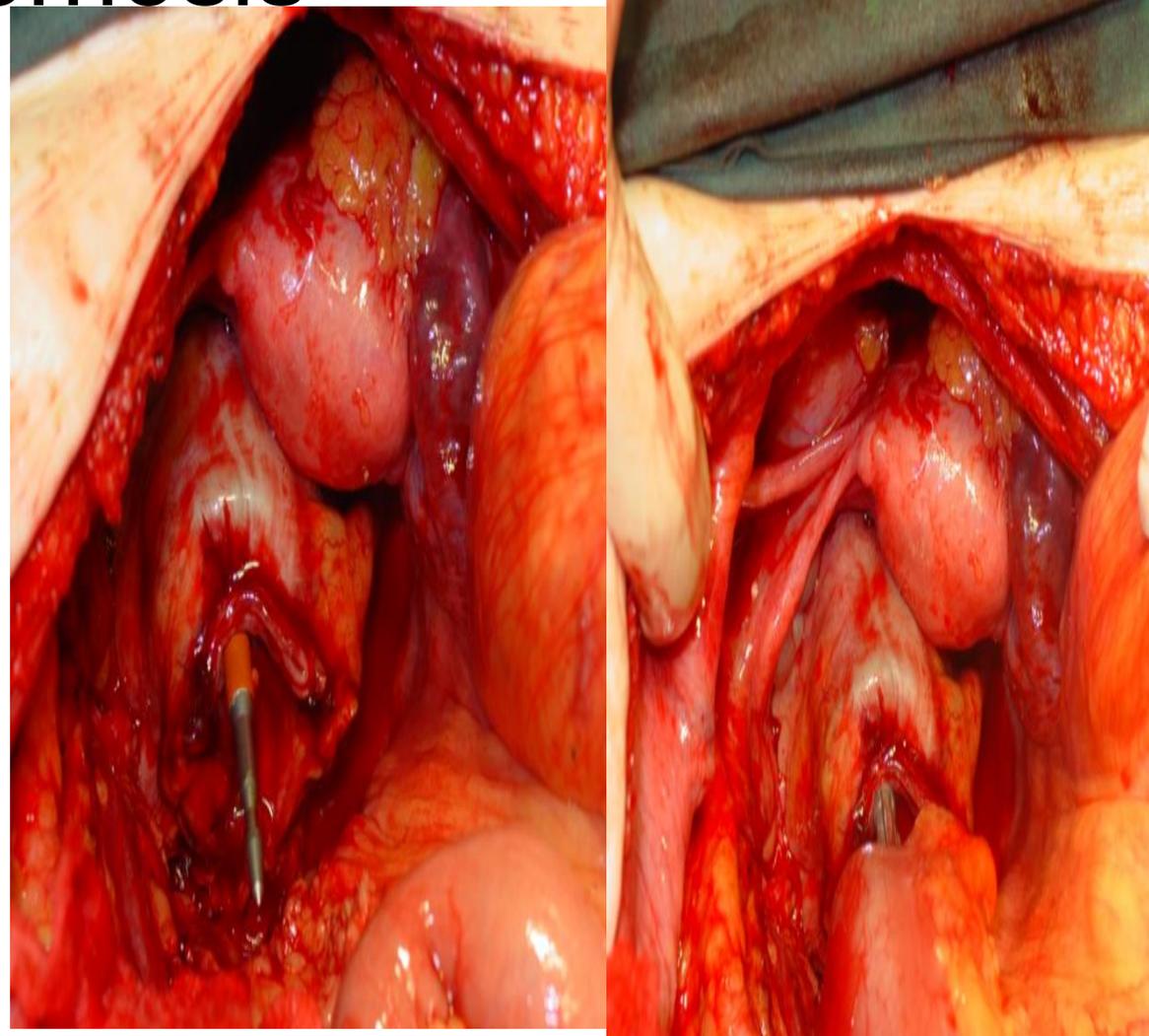
Sphincter-saving operation (anterior resection) is usually possible for tumours whose lower margin is 2 cm above the anal canal.

Operative Position





Mid-rectal Anastomosis





Thank you

