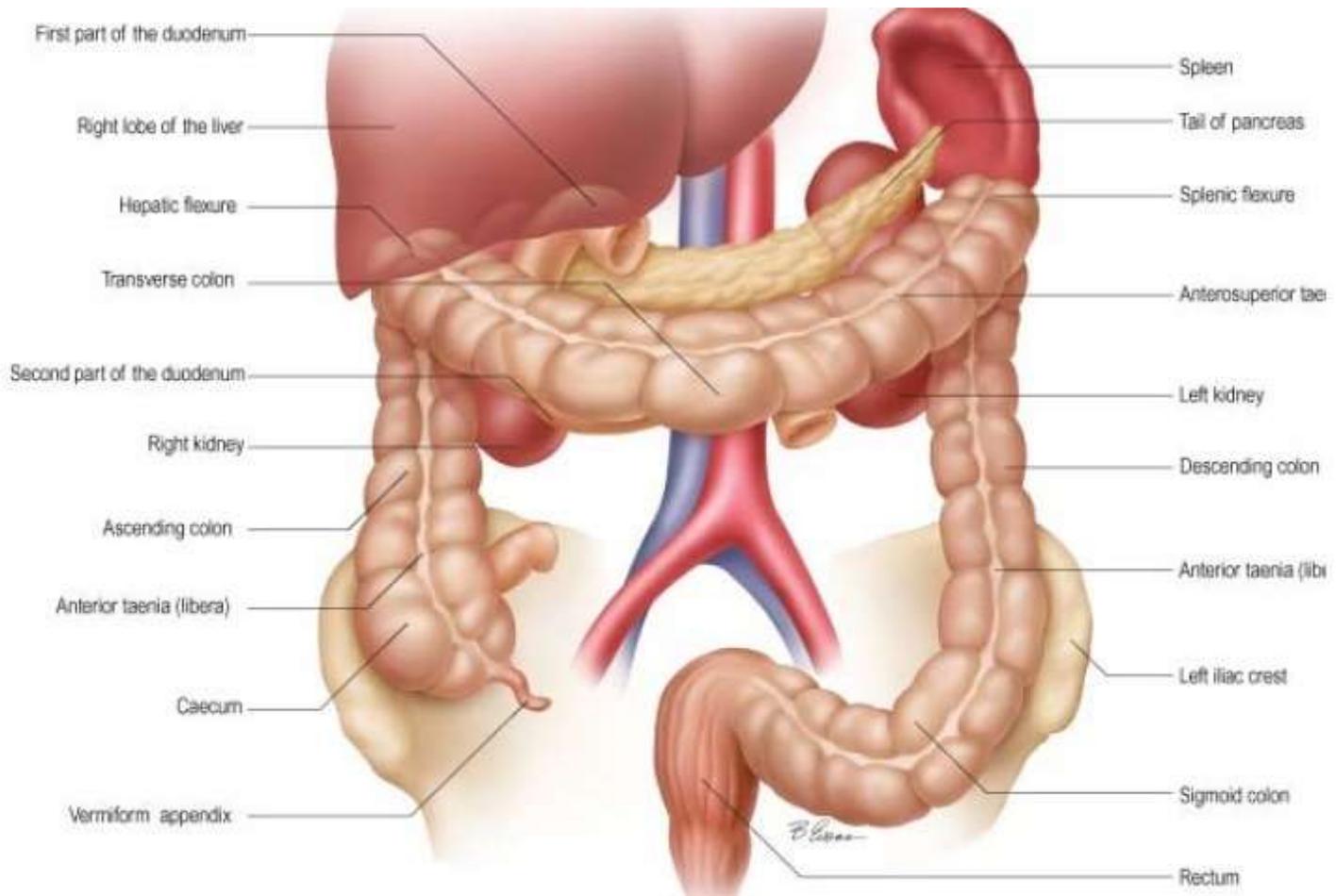


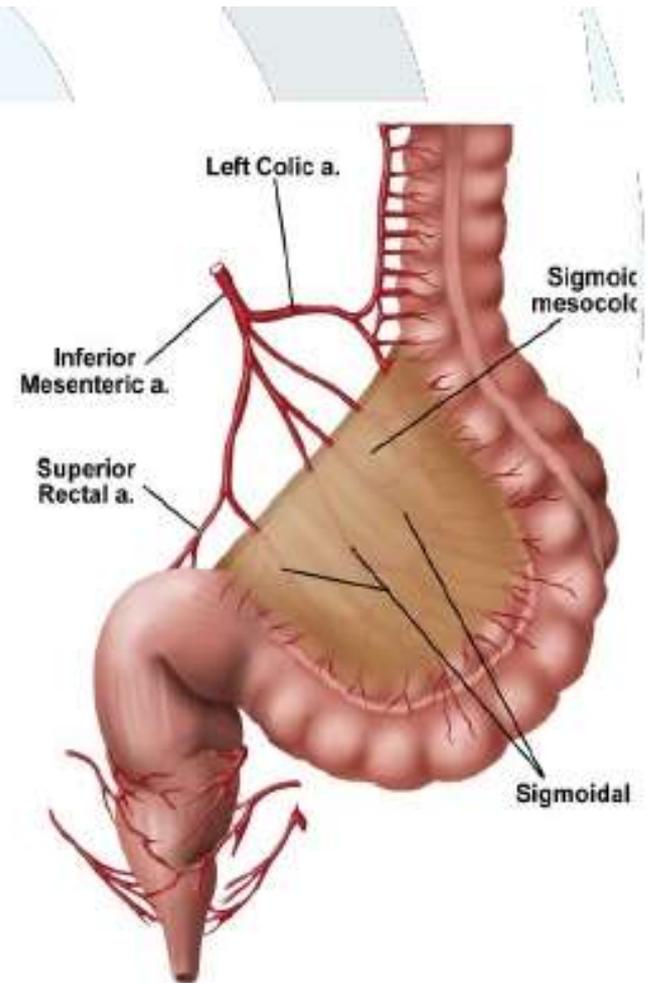
COLON CANCER

ABORAJOOH EMAD AREF
MD, General Surgery
GI and Minimally Invasive Surgery
IMRCS
JB and AB1



Blood Supply

- 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.

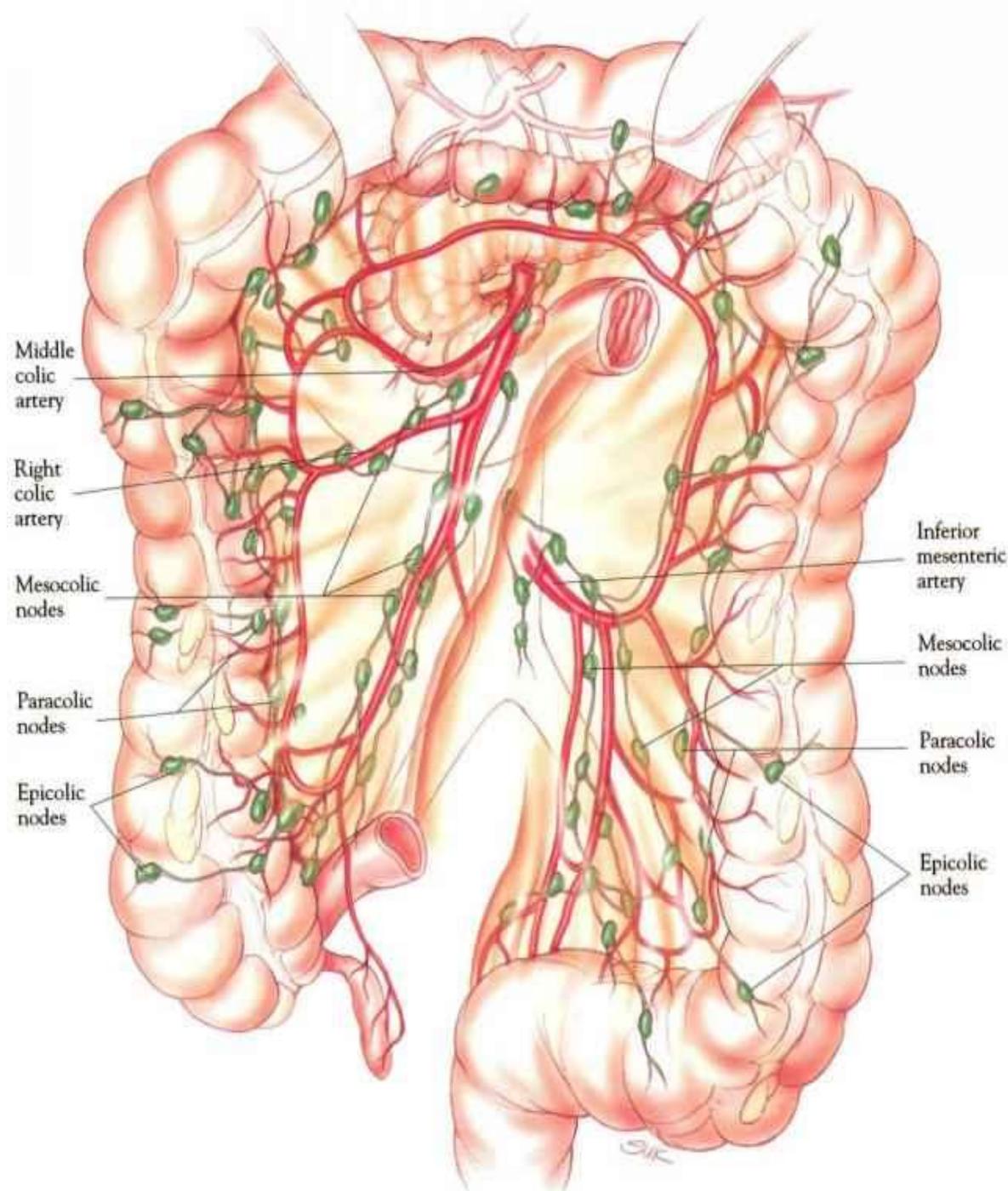
Lymphatic Drainage

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

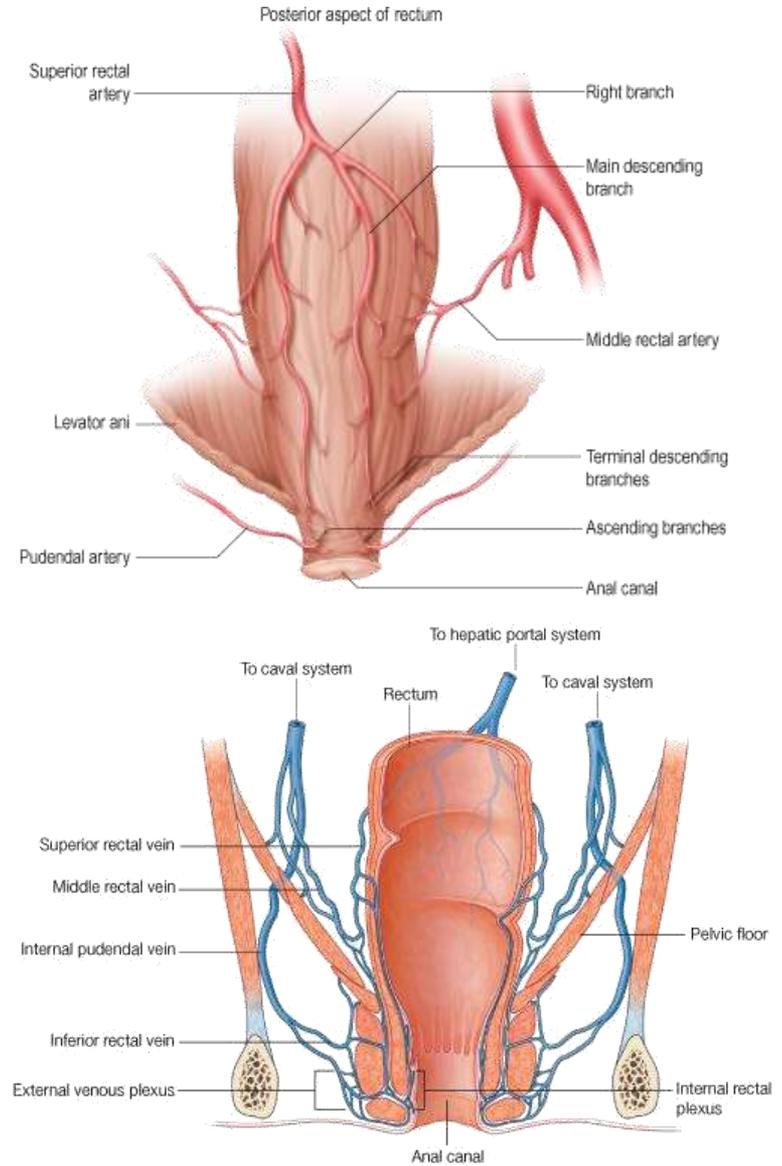
- Superior rectal A – fr. IMA; supplies upper and middle rectum
- Middle rectal A- fr. Internal iliac A. (supplies lower rectum)
- Inferior rectal A- fr. Internal pudendal A.

Venous drainage

- Superior rectal V- upper & middle third rectum
- Middle rectal V- lower rectum and upper anal canal
- Inferior rectal vein- lower anal canal

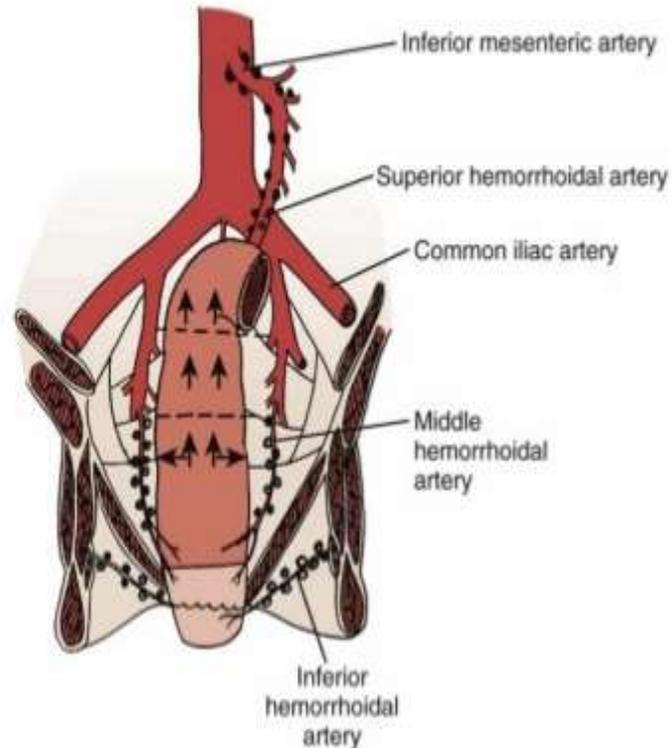
Innervations

- 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 fibre 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

- 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)

Jordan Cancer Registry

Web site: www.moh.gov.jo

Registry Email: jcr@moh.gov.jo

Department: Department of Cancer Prevention - Jordan Cancer Registry

Institution: Ministry of Health

P.O. Box: P.O Box 870

City: Amman

Zip Code: 11947

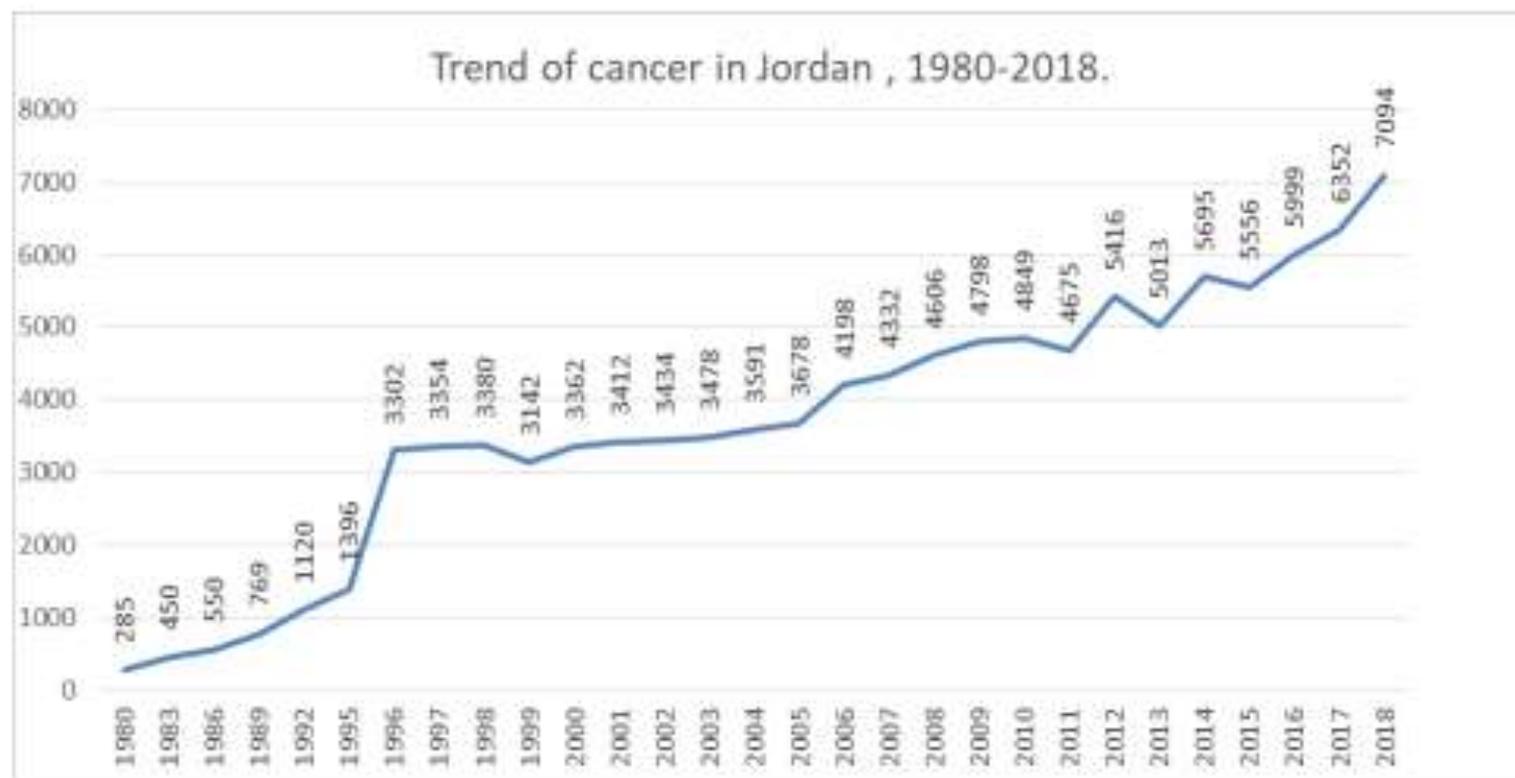
Country: Jordan

Phone #: (962) 6 5662067

Contact: Dr. Omar Nimri

Email: onimri@gmail.com

Figure 2: Trend of cancer in Jordan, 1980-2018



Ten most common cancers among Jordanians both genders, 2018

Rank	Cancer	No	%
1	Breast	1474	20.8
2	Colorectal	750	10.6
3	Lymphoma	477	6.7
4	Lung	458	6.5
5	Thyroid	359	5.1
6	Bladder	349	4.9
7	Leukemia	299	4.2
8	Prostate	253	3.6
9	Stomach	214	3.0
10	Brain, Nervous System	198	2.8

N.B: The total of the top Ten cancers accounted, 4831 (68.1%)

Table 8: Ten most common cancers among Jordanian Males, 2018



Rank	Site	Frequency	Percent
1	Colorectal	435	13.1
2	Trachea, bronchus, lung	365	11.0
3	Bladder	308	9.2
4	Prostate	253	7.6
5	NHL	179	5.4
6	Leukemia	164	4.9
7	Stomach	136	4.1
8	Brain, Nervous system	125	3.8
9	Kidney	122	3.7
10	Hodgkin disease	106	3.2

N.B: The total of the top Ten male cancers accounted, 2193(65.8%)

Table 9: Ten most common cancers among Jordanian Females, 2018



Rank	Site	Frequency	Percent
1	Breast	1463	38.9
2	Colorectal	315	8.4
3	Thyroid	272	7.2
4	Corpus Uteri	186	4.9
5	Leukemia	135	3.6
6	NHL	102	2.7
7	Ovary	101	2.7
8	Trachea, Bronchus, Lung	93	2.5
9	Hodgkin Disease	90	2.4
10	Stomach	78	2.1

N.B: Total top ten female cancers accounted for 2835 (75.4%)

Table 10: Number of cancer cases and crude incidence rates, by governorates and sex, 2018.

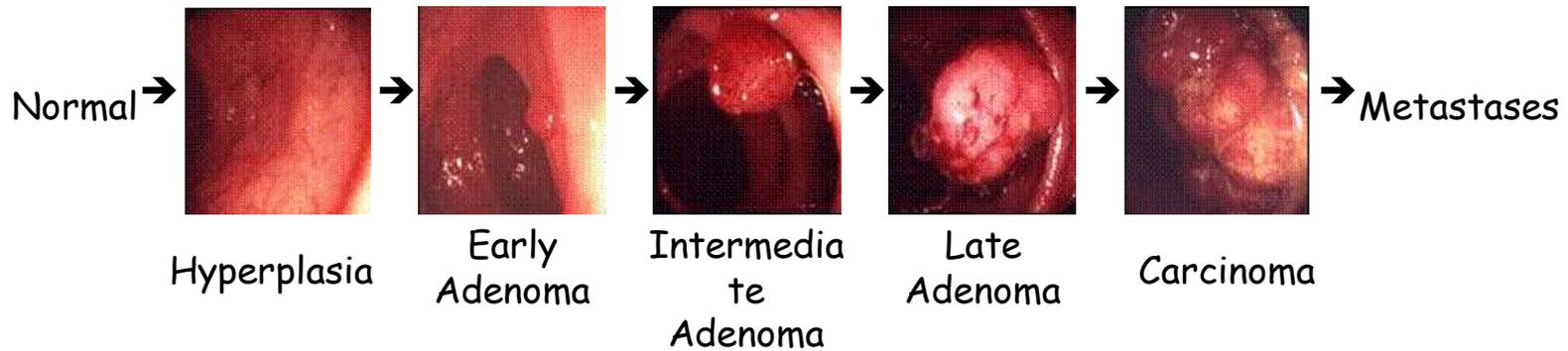
Governorate	Male		Female		Total		
	N	CR*	N	CR	N	CR	%
Amman	1971	140.9	2125	156.4	4096	148.5	57.7
Zarka	330	64.6	421	86.7	751	75.4	10.6
Balqa	185	85.2	201	95.3	386	90.2	5.4
Madaba	48	55.6	89	107.6	137	81.0	1.9
Central Region -CR	2534	114.5	2836	132.7	5370	123.4	75.7
Irbid	392	54.0	448	64.6	840	59.2	11.8
Jarash	61	65.7	73	83.0	134	74.1	1.9
Ajloun	64	74.1	67	80.6	131	77.3	1.8
Mafraq	84	48.4	91	55.1	175	51.7	2.5
North Region CR	601	55.7	679	65.9	1280	60.7	18.0
Karak	93	62.7	115	79.0	208	70.8	2.9
Aqaba	38	50.6	50	70.9	88	60.4	1.2
Maan	34	48.3	25	30.8	59	38.9	0.8
Tafiela	22	44.3	42	88.6	64	65.9	0.9
South Region- CR	187	54.4	232	67.3	419	60.9	5.9
Not Resident	11		14		25		0.4
Total- CR	3333	91.7	3761	107.4	7094	99.4	100.0

*(CR, crude rate)

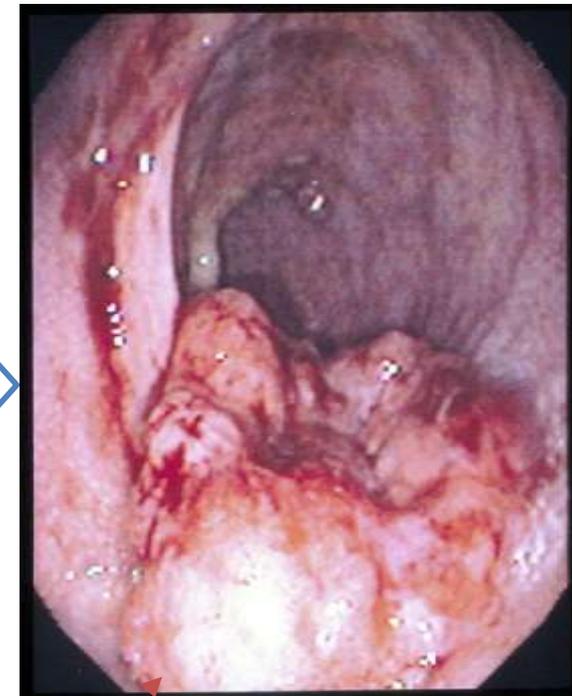
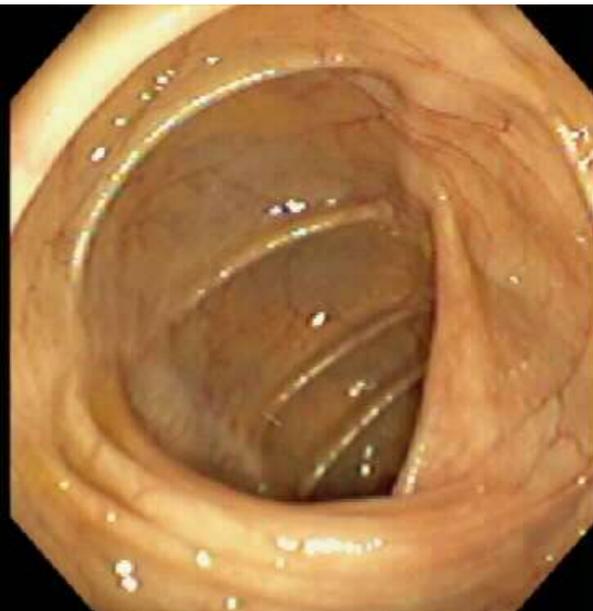
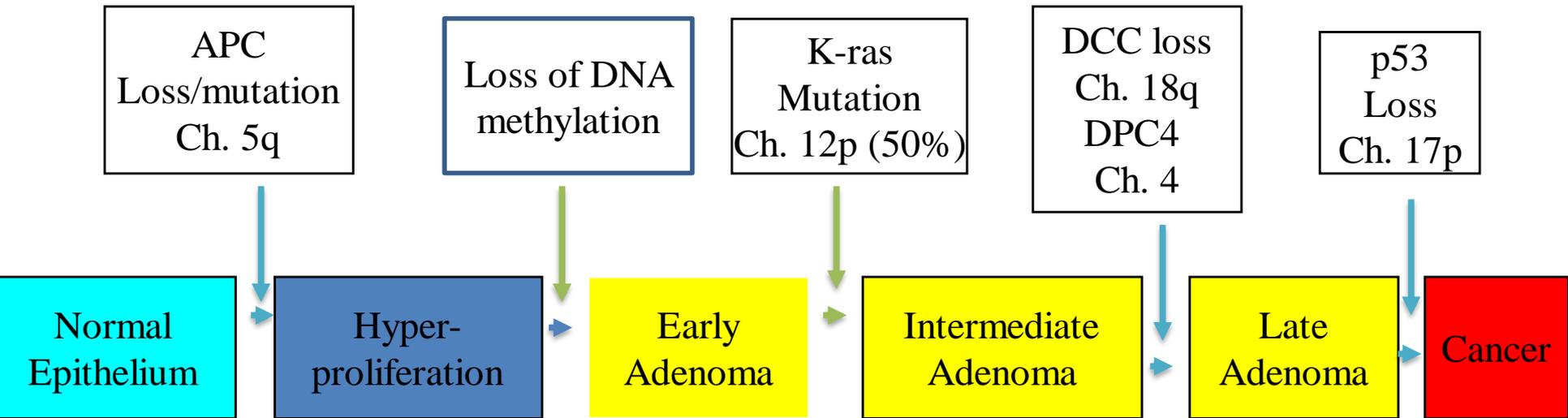
Aetiology

- 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





METRIC 1 2 3 4 5 6

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

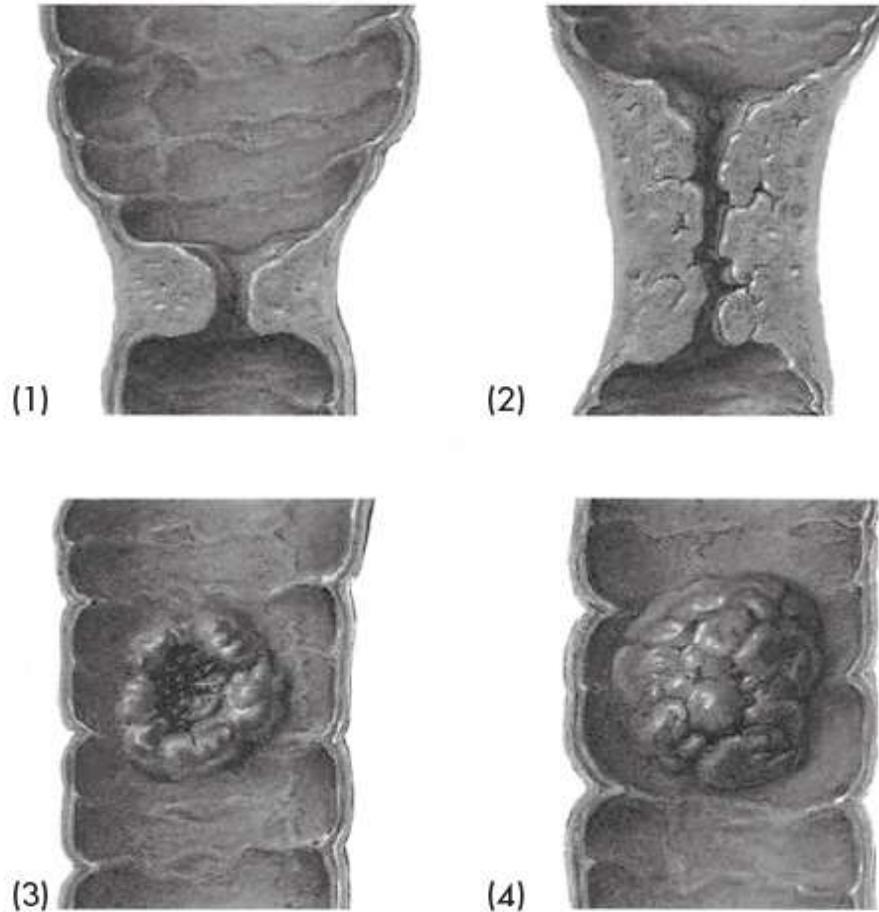
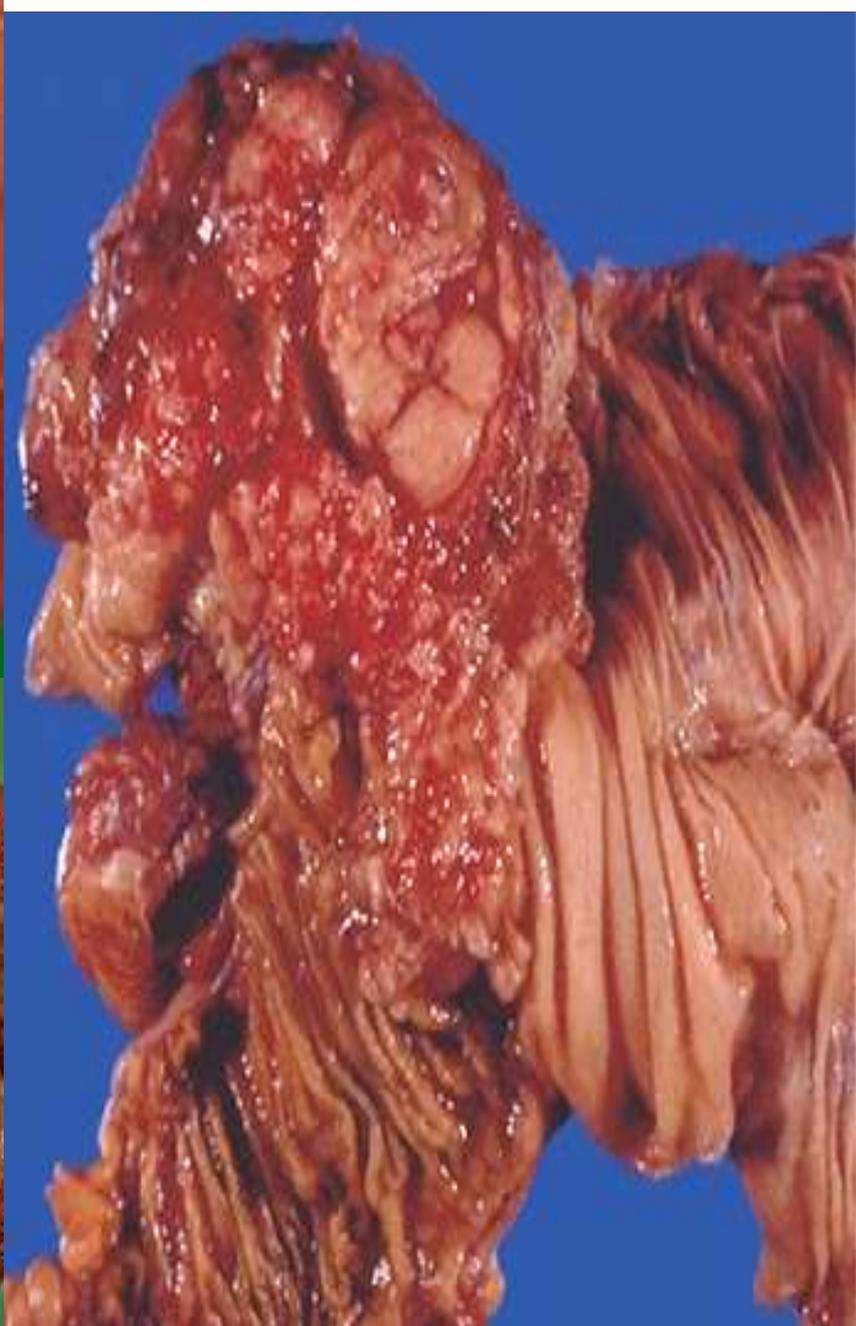


Figure 69.22 The four common macroscopic varieties of carcinoma of the colon. (1) Annular; (2) tubular; (3) ulcer; (4) cauliflower.





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

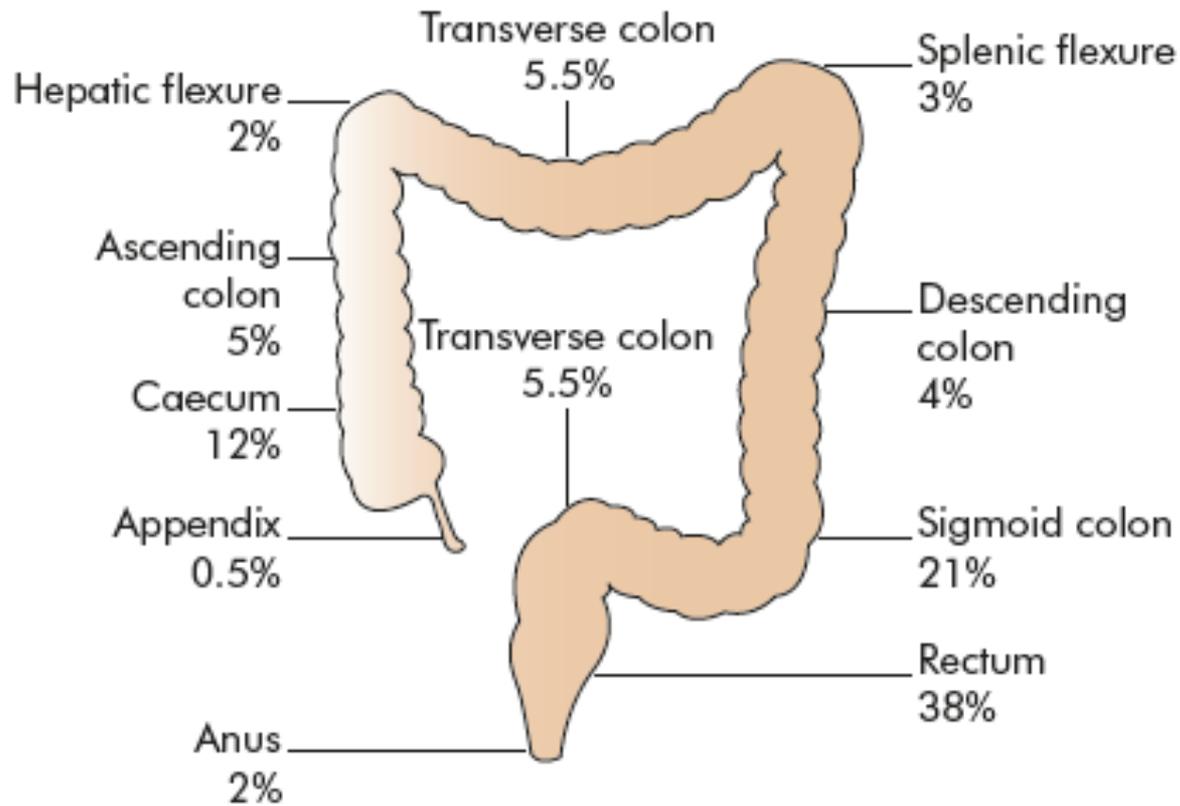


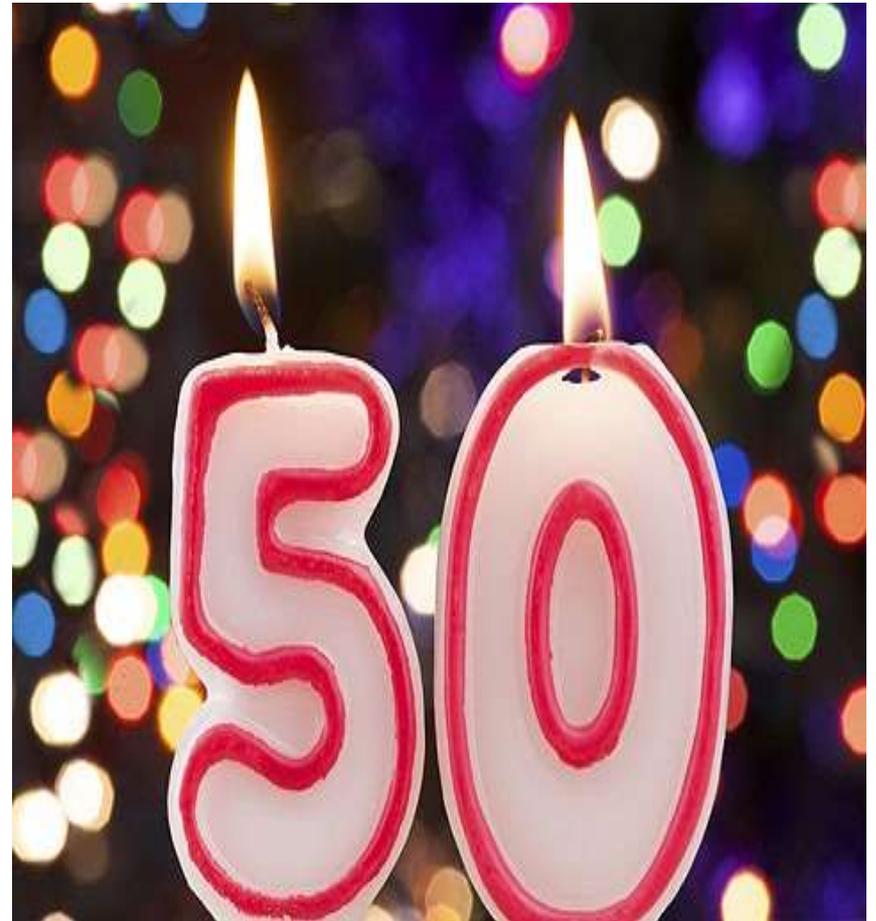
Figure 69.23 Distribution of colorectal cancer by site.

Diagnosis

- Complete history
- Physical examination /DRE
- Routine investigations
- Confirmatory- Biopsy
- Staging workup
 - CXR
 - Barium enema
 - Colonoscopy
 - CT abdomen- pelvis
 - Virtual colonoscopy
 - MRI
 - PET
- Gold standard- Colonoscopy+ Biopsy
- Others
- FOBT
- Stool cytology
- CEA
- IHC markers
- Molecular markers- oncogenes

Screening Guidelines

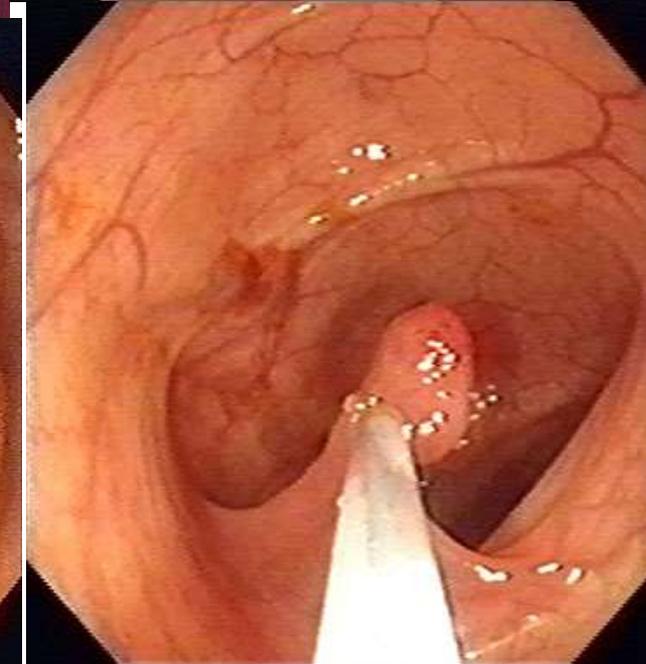
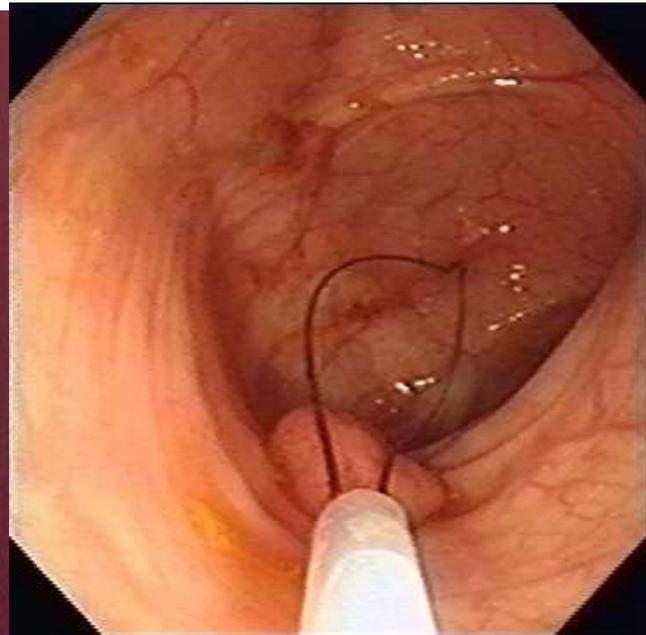
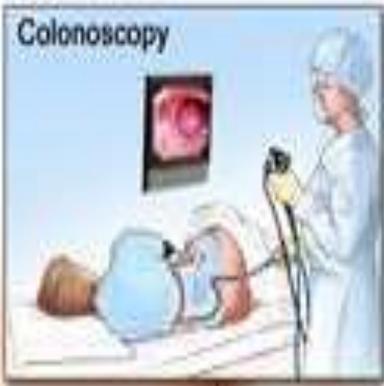
- Screening for asymptomatic men and women at age 50, using a menu of screening options.
- Mortality rates have been declining for the past 2 decades, largely attributable to the contribution of screening to prevention and early detection.



Recommended CRC screening tests

1. Annual high-sensitivity gFOBT or FIT, following the manufacturer's recommendations for specimen collection
2. FSIG every 5 years
3. Colonoscopy every 10 years
4. Double-contrast barium enema every 5 years
5. CT colonography every 5 years.

Stool DNA testing, which also was among the recommended options in the 2008 update, is no longer commercially available for screening.



SPREAD OF CARCINOMA OF THE COLON

- **Direct spread**
- **Lymphatic spread**
- **Haematogenous spread**
- **Transcoelomic spread**

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

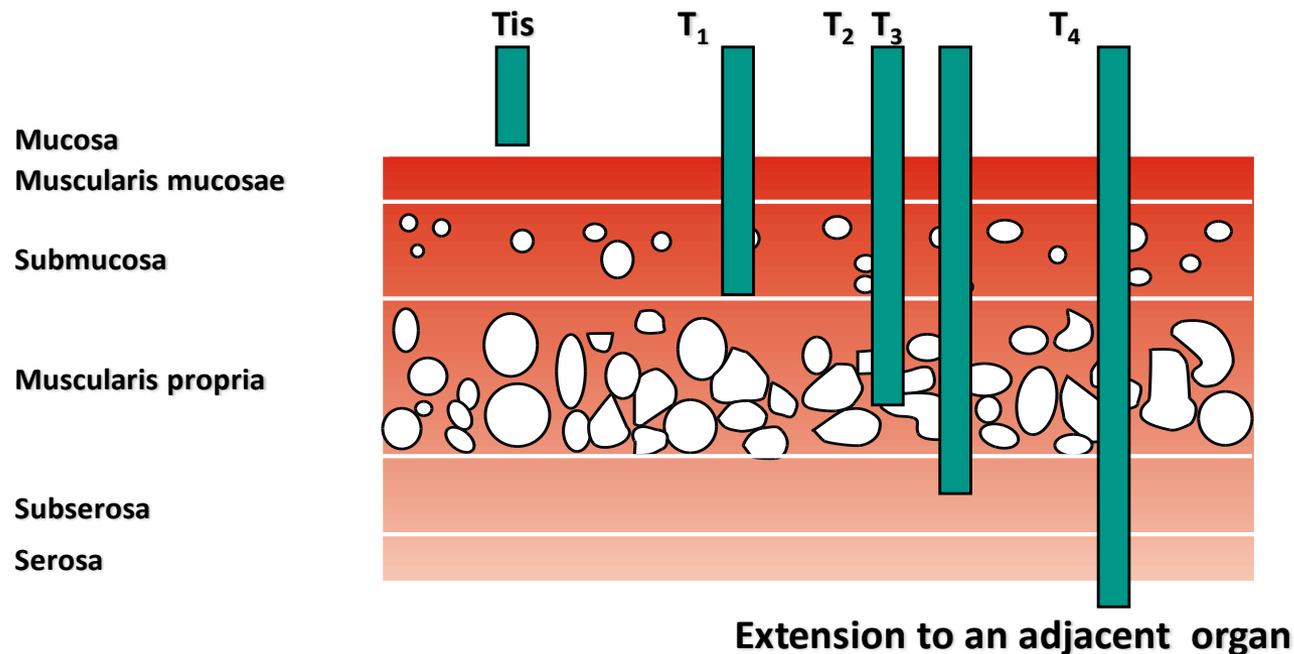
Stage C1 : Extending into muscularis propria but not penetrating through it. Nodes involved

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

Regional Lymph Nodes (N)

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

Distant Metastasis (M)

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.

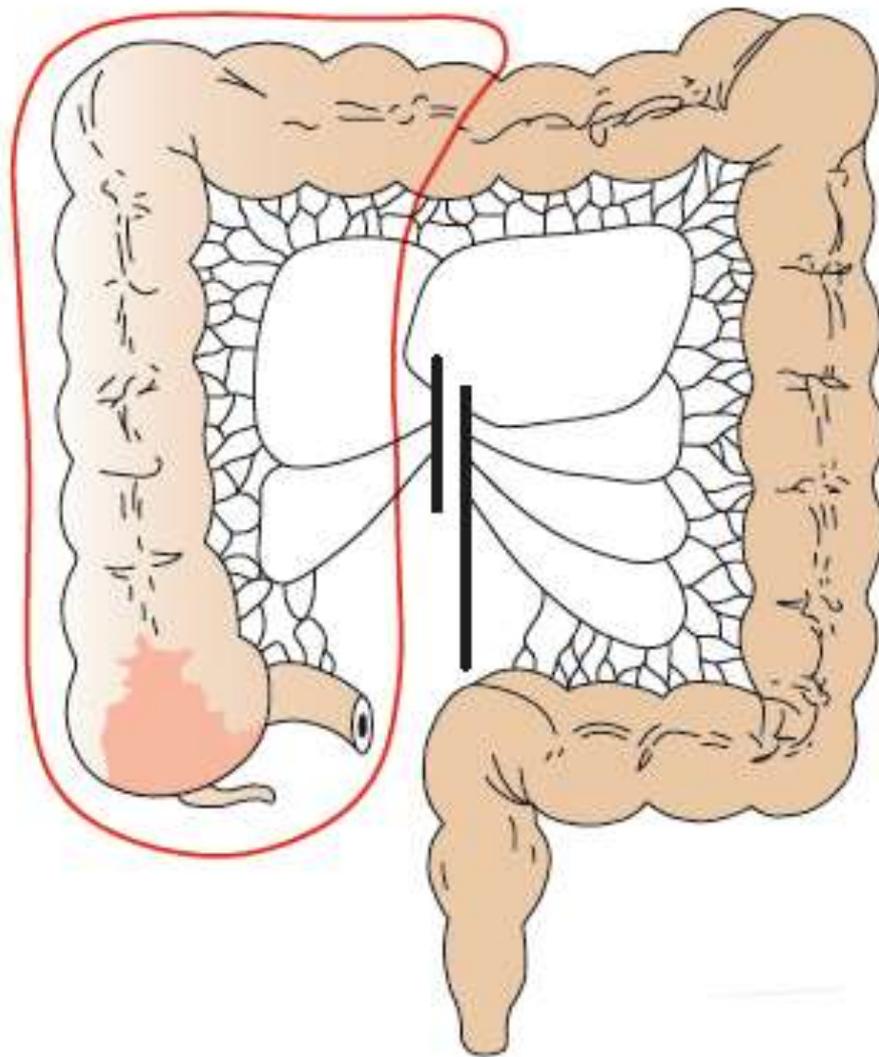


Figure 69.28 Schematic showing right hemicolectomy.

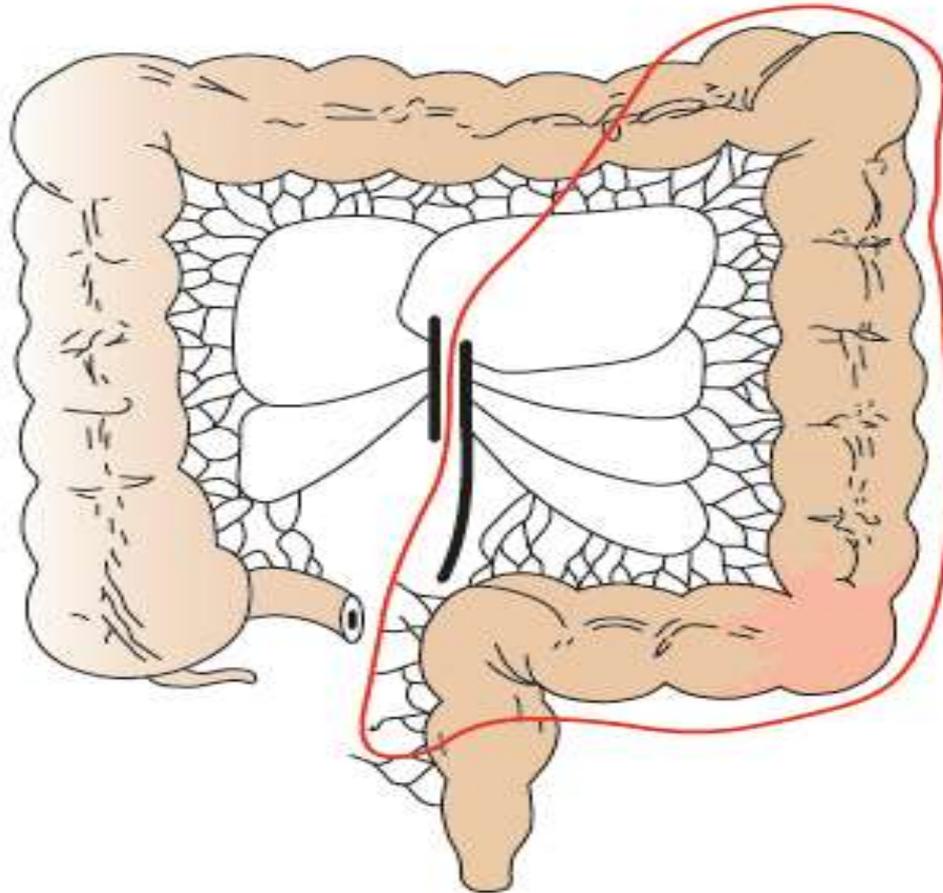
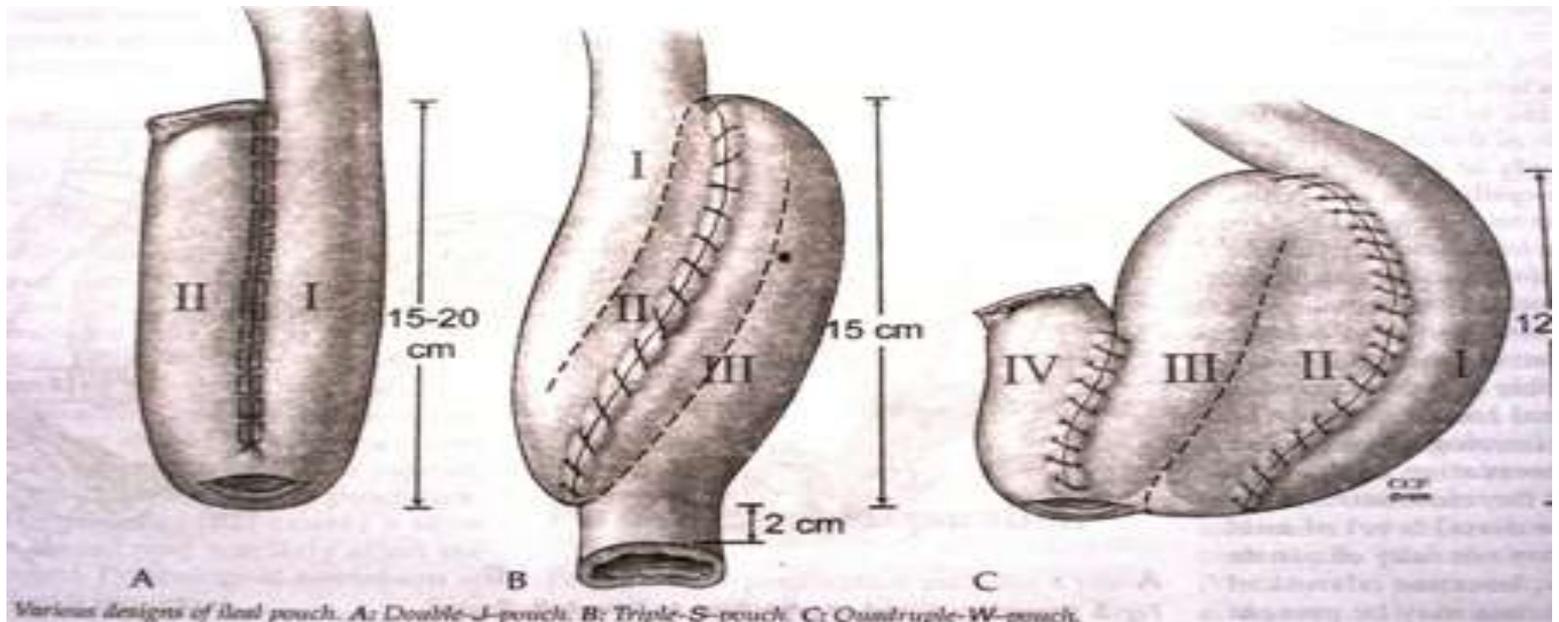
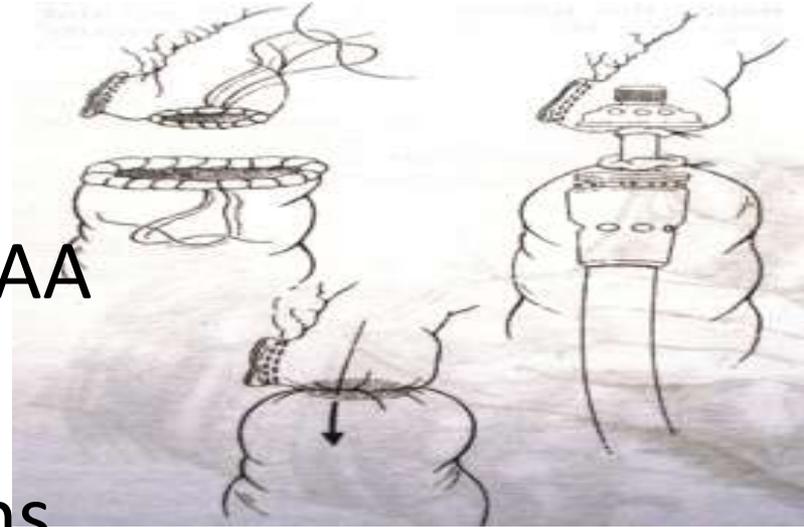


Figure 69.29 Schematic showing left hemicolectomy.

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



T1N0M0

T2N0M0

T3N0M0



Stage I

80-95%

Stage II

70-75%

Node +

TxN1M0

Stage III

30-65%

Distant Mets

TxNxM1

Stage IV

<5%

- 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.

CA COLON

STAGE I

STAGE IIA

STAGE IIB

STAGE III

**Stage IV/
Metastatic**



**PRIMARY
SURGERY**

**PRIMARY SX+/-
ADJUVANT
CCT**

**PRIMARY SX+ ADJUVANT
CCT ± ADJUVANT RT
? ADJUVANT
IMMUNOTHEARPY**

**RESECTION OF LOCAL/ METS
PALLIATIVE CCT
ADJUVANT IMMUNOTHEARPY**

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**
 - Bleeding per rectum
 - Altered bowel habit
 - Mucus discharge
 - Tenesmus
 - Prolapse

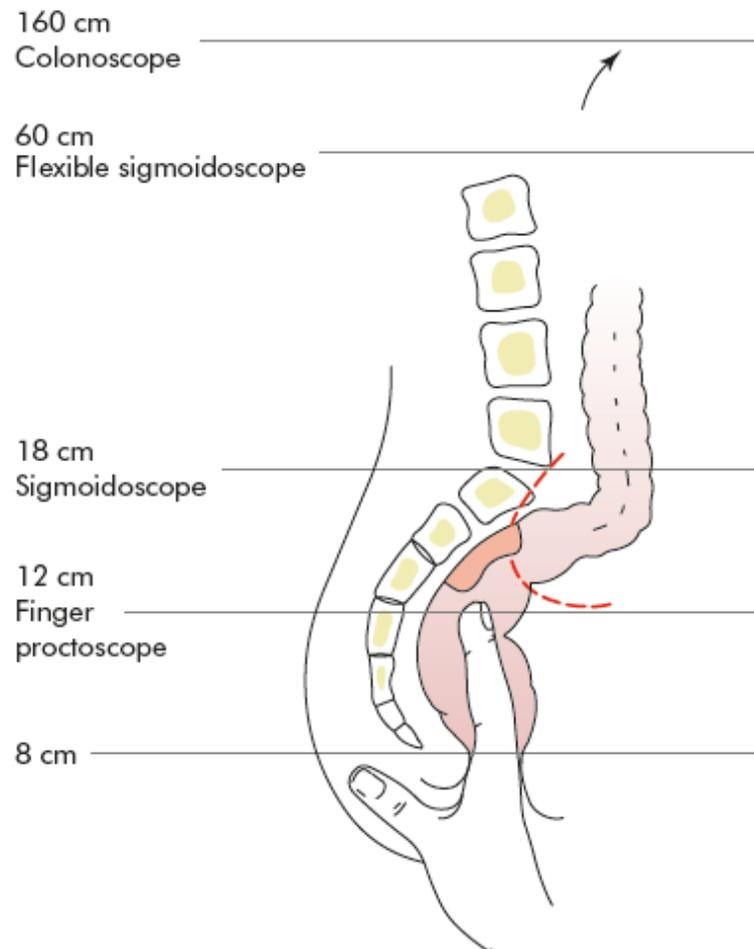
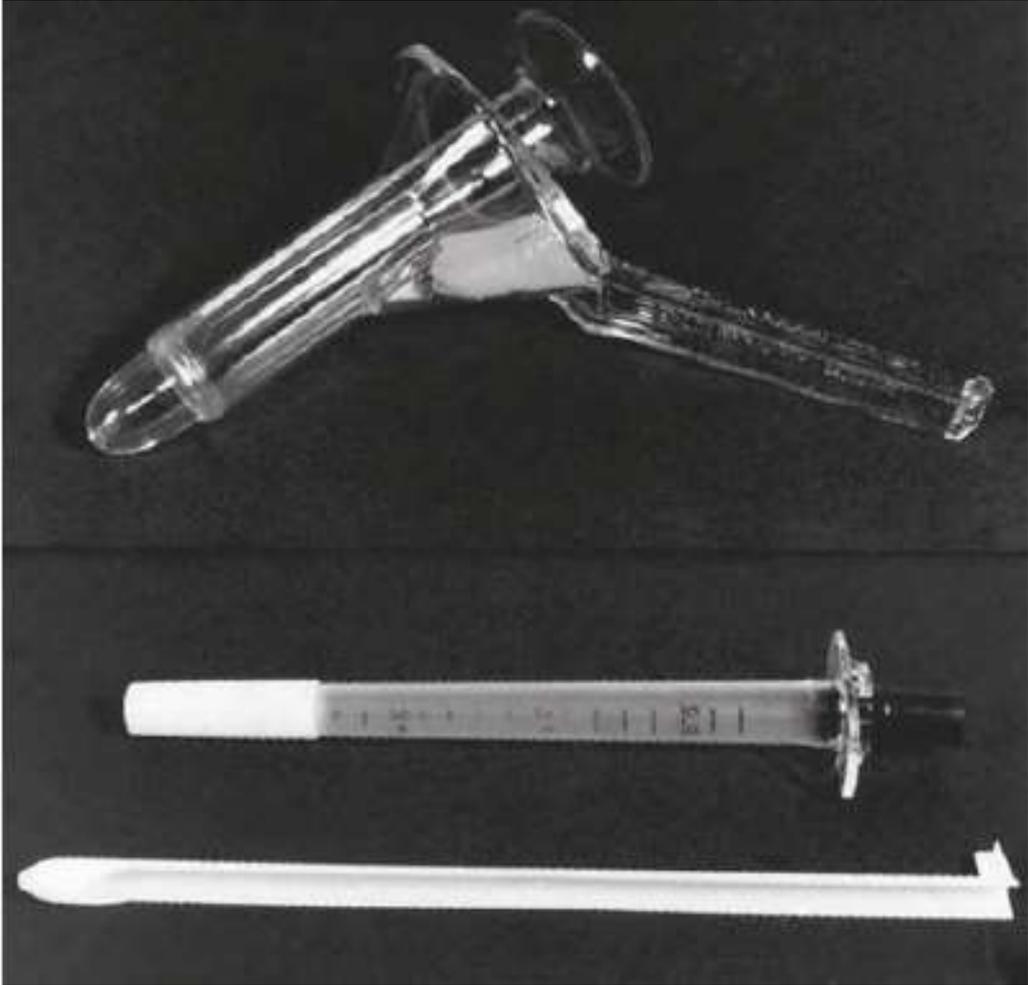


Figure 72.4 Illustration showing how the various methods of examining the rectum reach different levels. Note that even cancers in the upper part of the rectum can be felt with the index finger, especially if the patient is asked to 'strain down' (courtesy of CV Mann).



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)

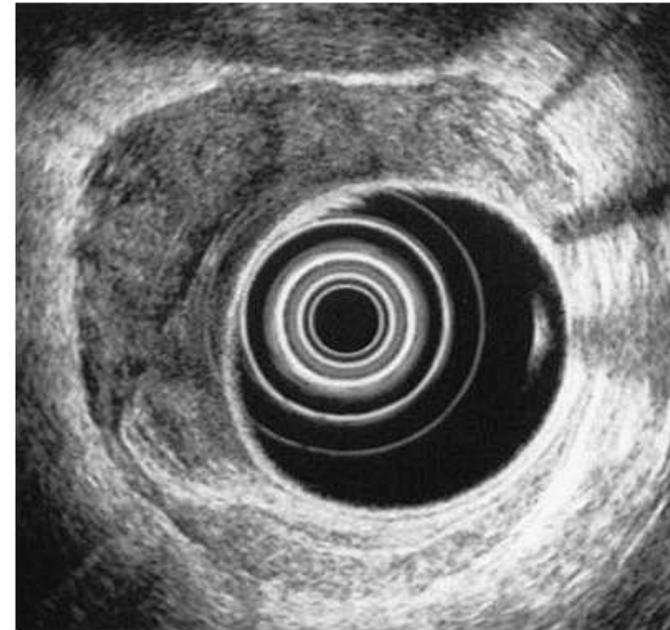
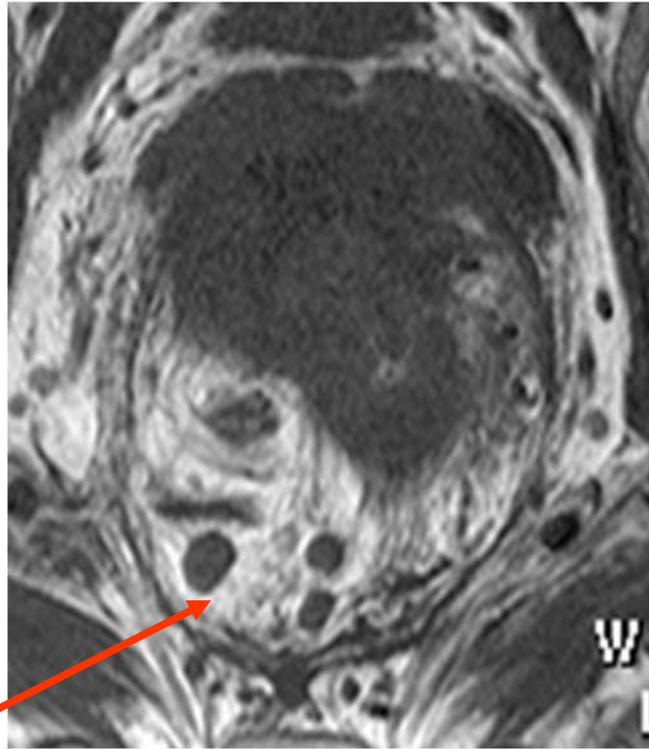


Figure. Endorectal ultrasound of a T3 tumor of the rectum, extension through the muscularis propria, and into perirectal fat.

MRI



Circumferential Resection
Margin (CRM)

Management

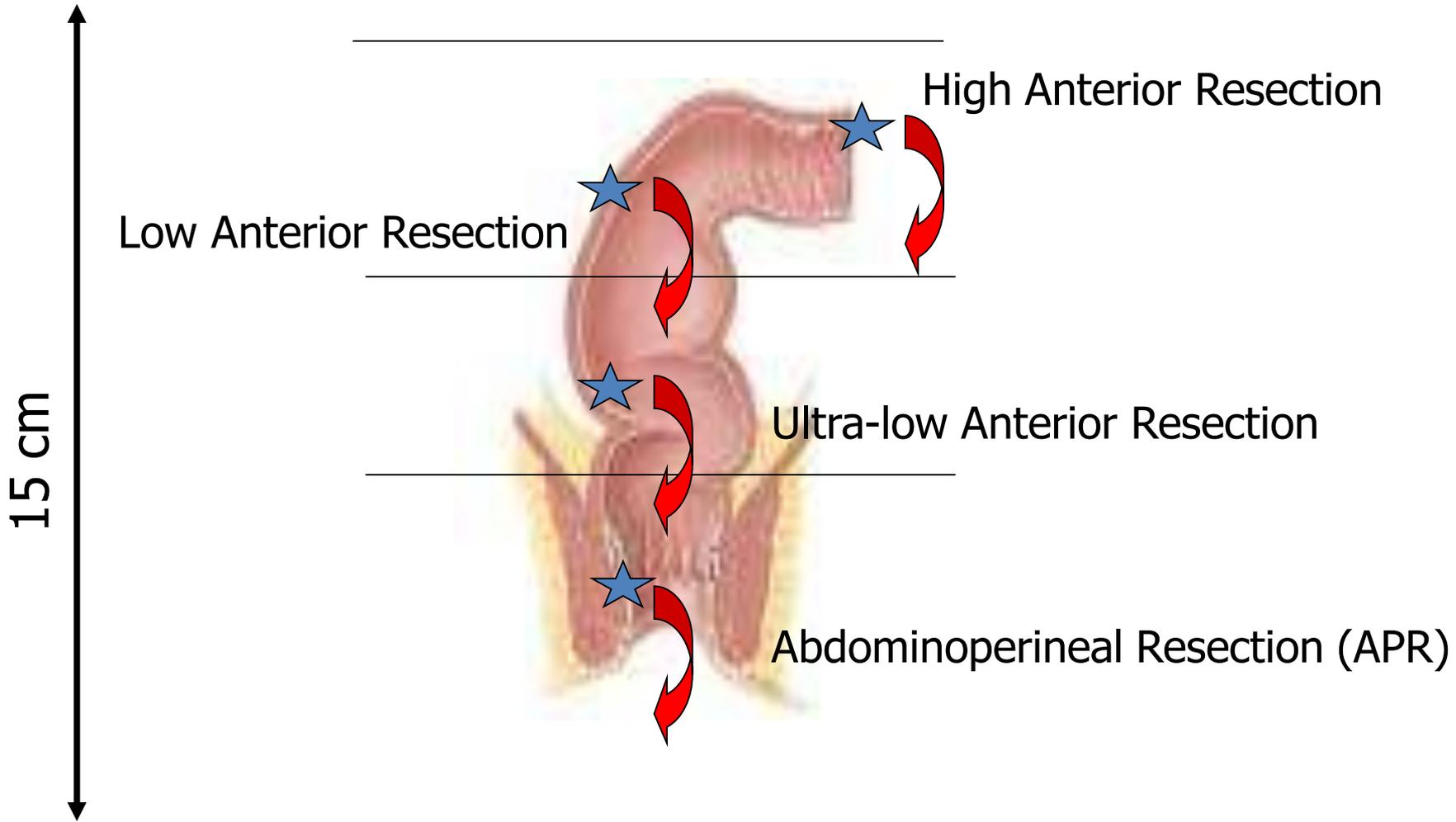
- Management of rectal cancer has become increasingly complex, because of the various surgical, neoadjuvant and adjuvant options available, and is best delivered in a multidisciplinary setting.
- Before treatment can be planned, it is necessary to assess:
 - Fitness of the patient
 - Extent of spread

- 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

- 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

