Colorectal &Anal cancer

Dr .Tayseer Al-tawarah

Hepatobiliary &pancreatic surgeon

Assistant professor /Hashemite University

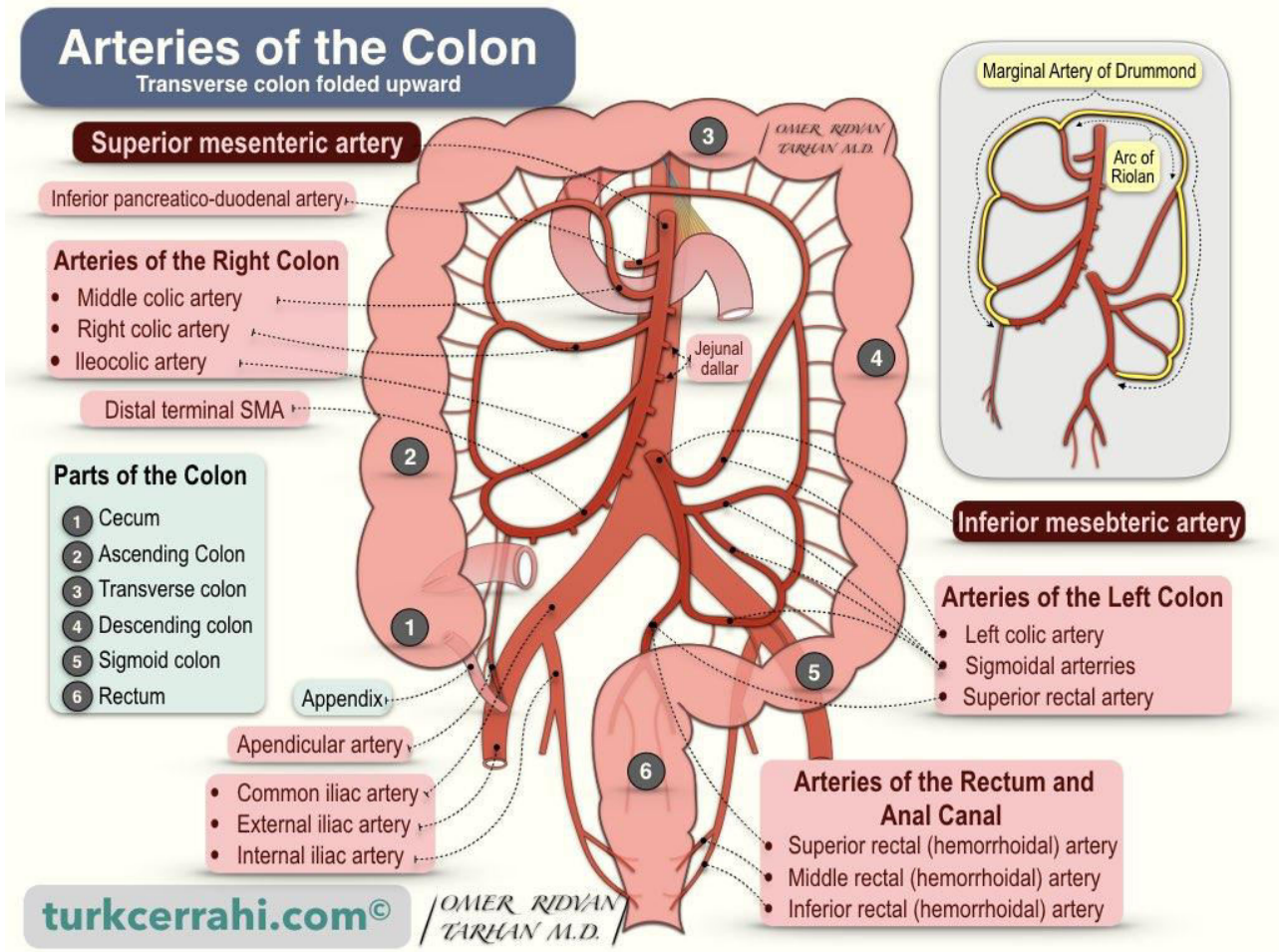
Definitions

- Although the colon comprises the large bowel proximal to the rectum, the definition of the rectum is unclear.
- Anatomical texts describe the top of the rectum as the point where the sigmoid mesocolon ends or that part of the large bowel level with the third sacral vertebra.
- Surgeons, on the other hand, prefer to think of the rectum as the segment of large bowel lying within the true pelvis

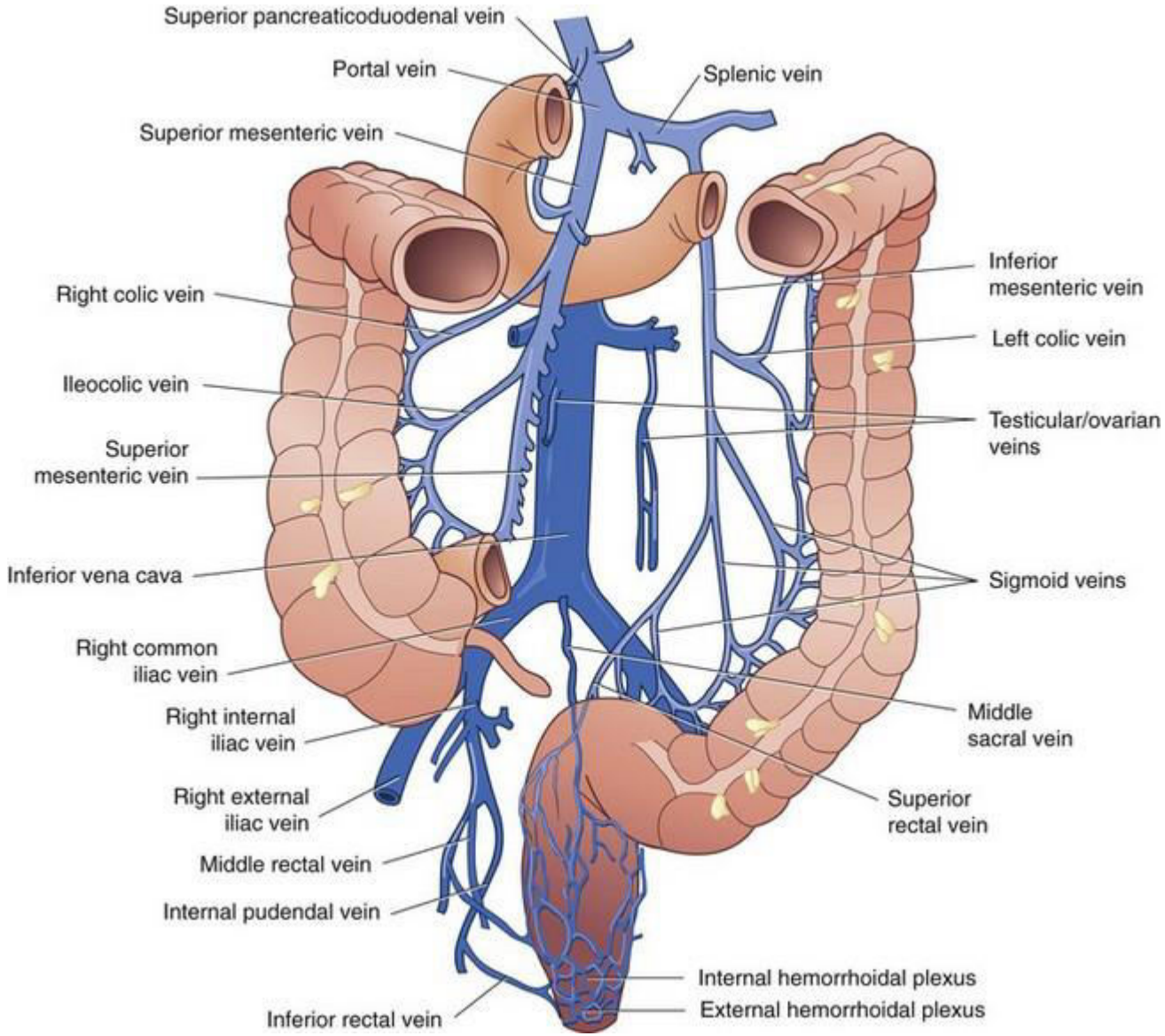
- the UK definition is a tumour within 15cm of the anal verge on rigid sigmoidoscopy, whereas authorities from the USA have preferred 11 or 12cm.
- Perhaps the simplest definition is the intraoperative identification of the fusion of the two antemesenteric taenia into an amorphous area where the true rectum begins
- These distinctions are important for two reasons. First, radiotherapy is not appropriate for colonic tumours and, secondly, comparisons between outcomes for colorectal cancer surgery are impossible unless uniform definitions are adopted

Arterial supply

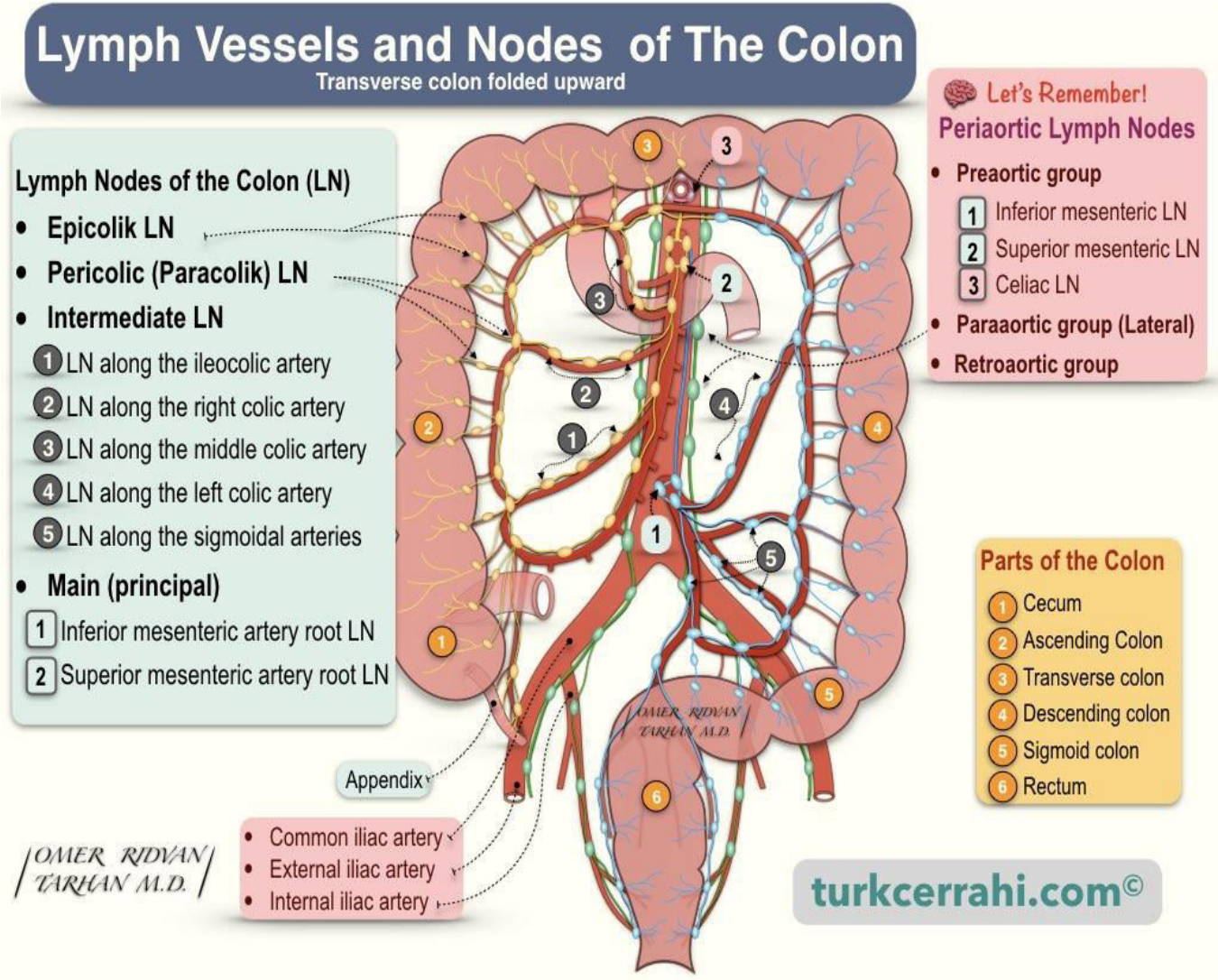
- Watershed area



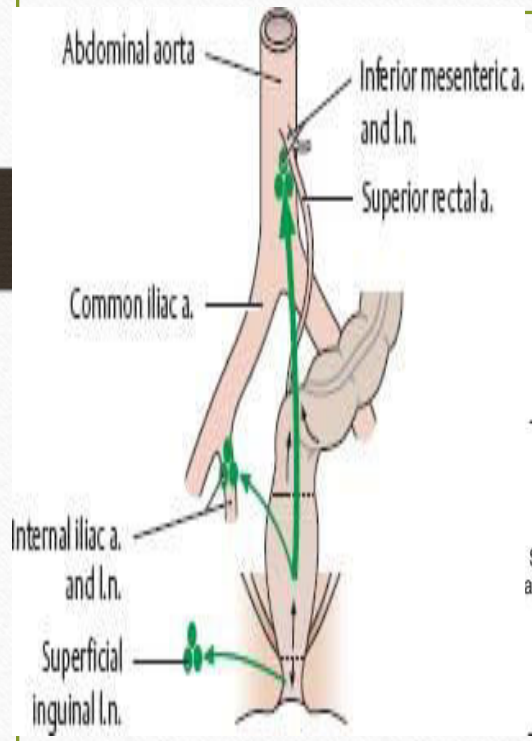
Venous drainage

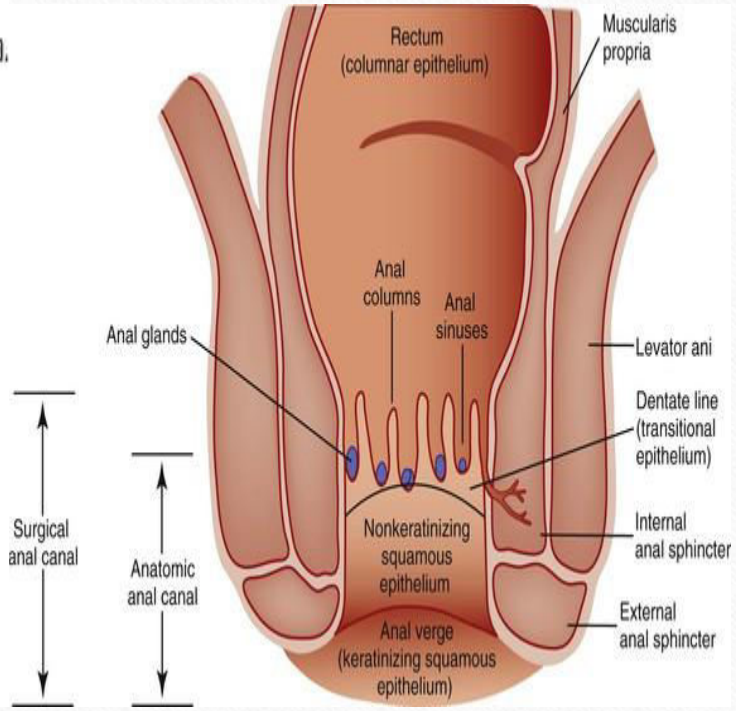


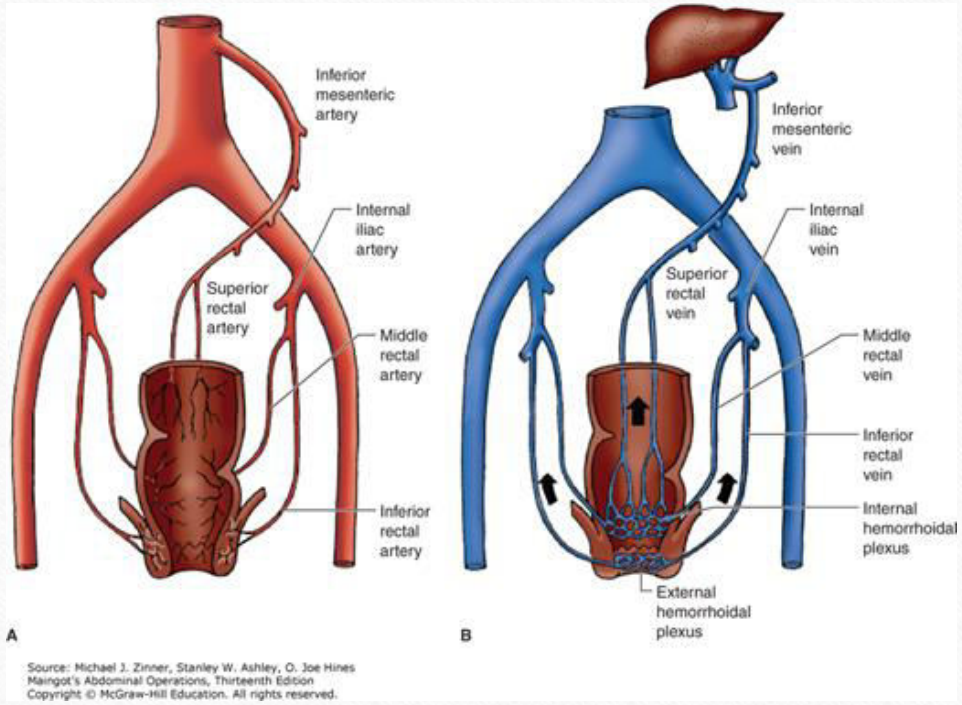
Lymphatic driange



Anal canal



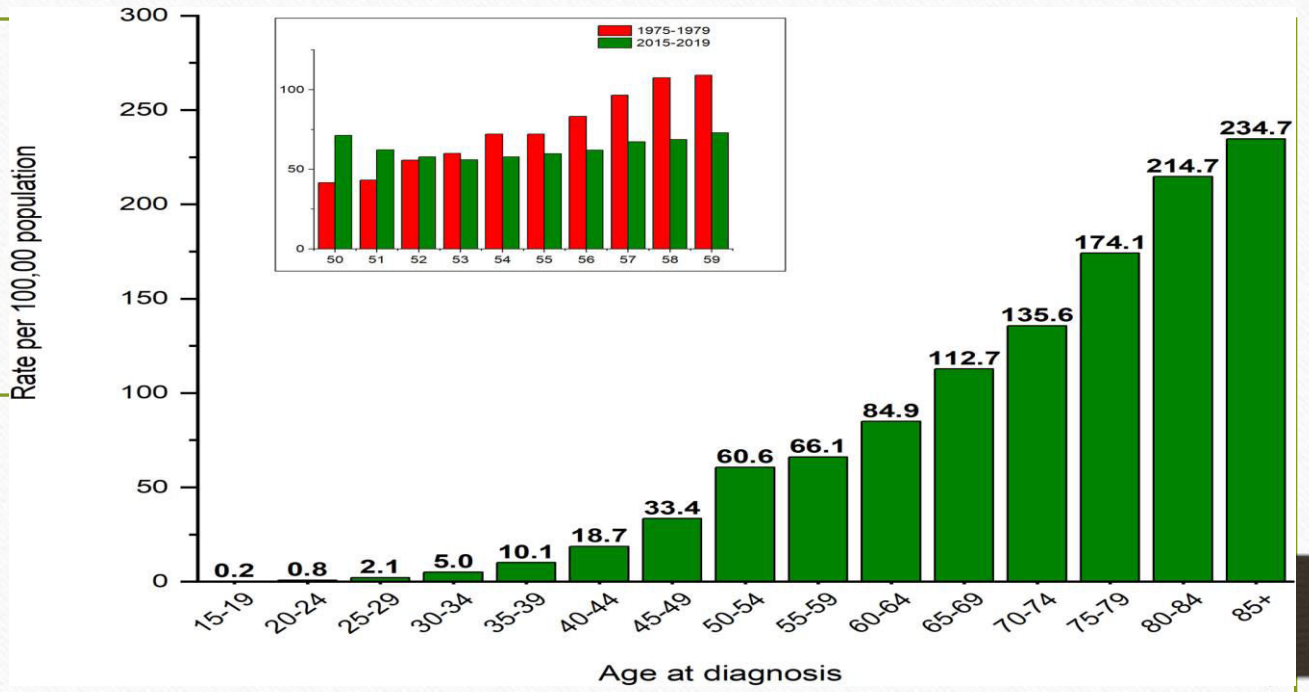




Statics

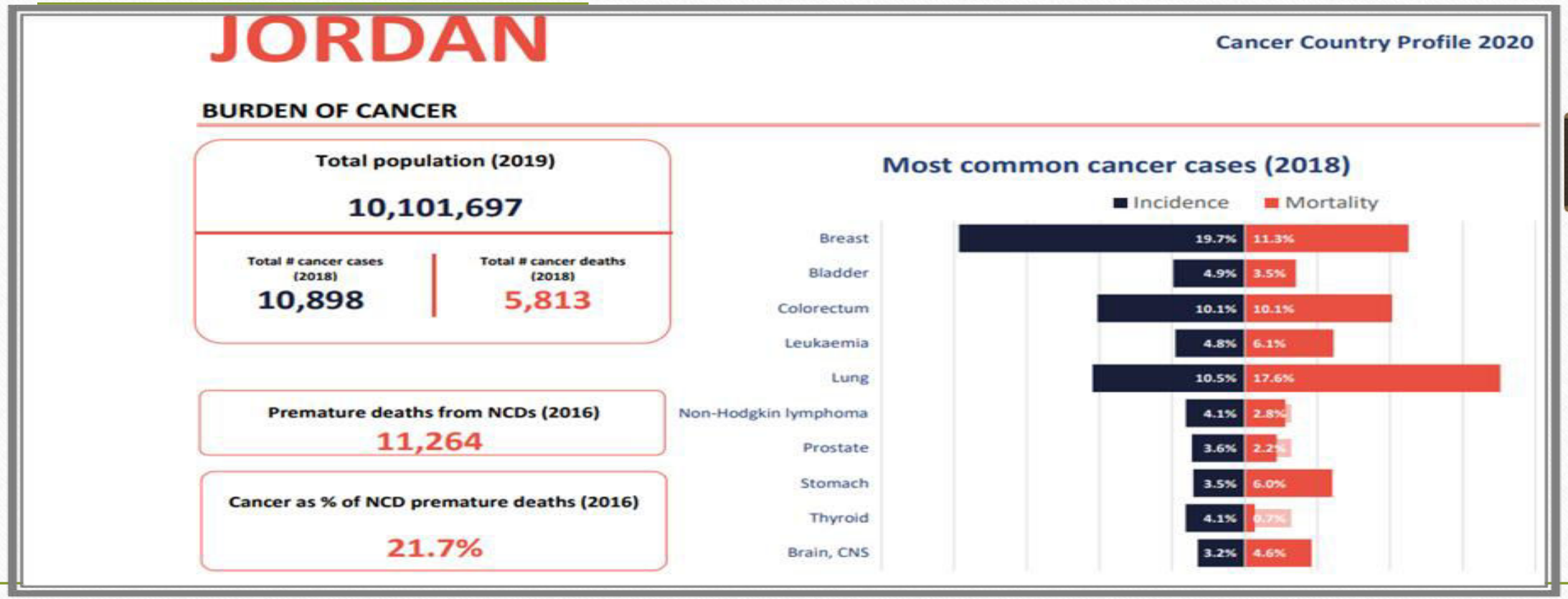
- Colorectal cancer is a major health problem.
- it is the second most common cause of cancer death
- The American Cancer Society estimates that 152,810 people in the U.S. will be diagnosed with colorectal cancer in 2024, and 53,010 will die from the disease.

Colorectal cancer is the third most common cancer worldwide, accounting for approximately 10% of all cancer cases and is the second leading cause of cancer-related deaths worldwide.



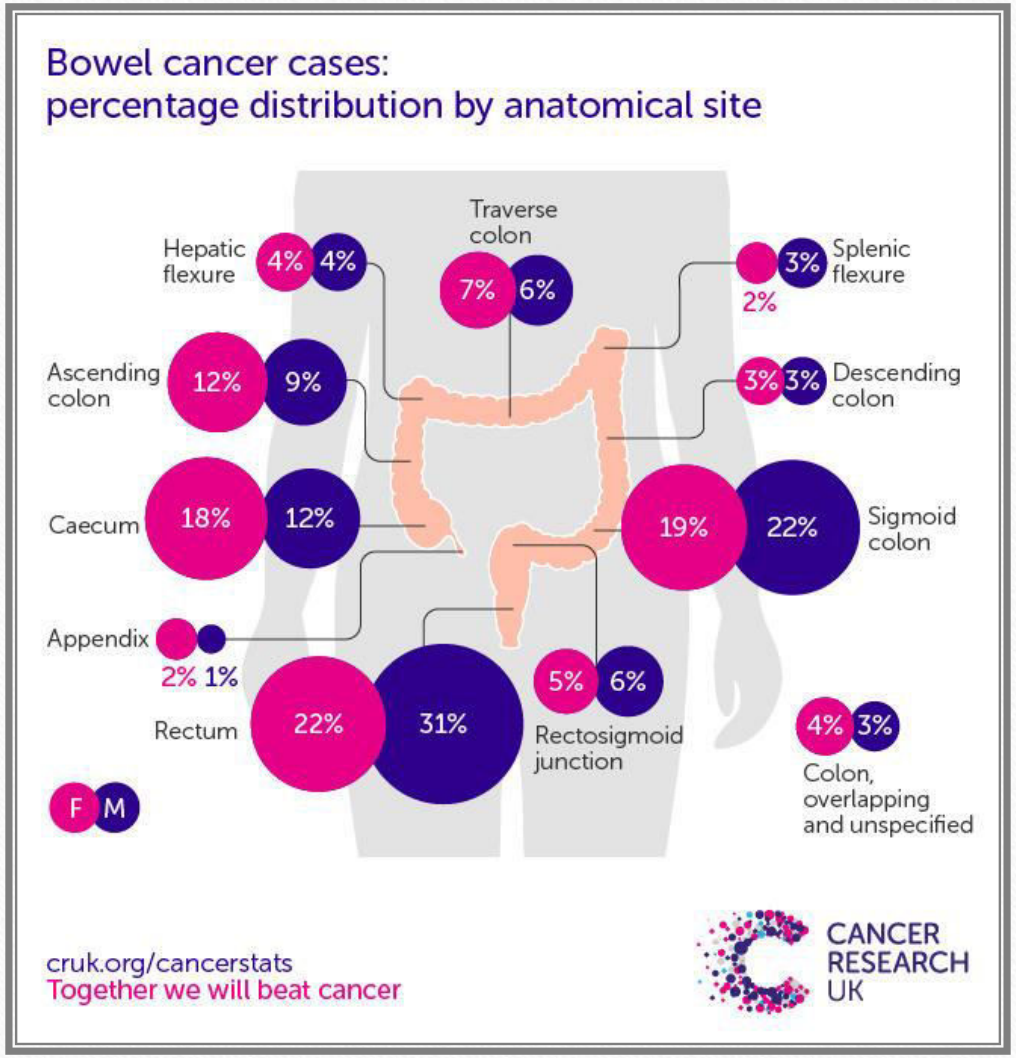
Age	U.S. colorectal cancer diagnoses in 2023	U.S. colorectal cancer deaths in 2023
0–49	19,550 (13%)	3,750 (7%)
50–64	48,210 (32%)	13,160 (25%)
65 and older	85,260 (56%)	35,640 (68%)
Total	**153,020**	**52,550**

Colorectal cancer in Jordan



- Cancer in the ascending or transverse colon is commonly referred to as proximal or right-sided, whereas cancer occurring in the descending or sigmoid colon or rectum is referred to as left-sided.
- Cancers of the appendix and anus are excluded from CRC statistics herein because, despite their proximity, they usually originate from different cell types and/or have different characteristics

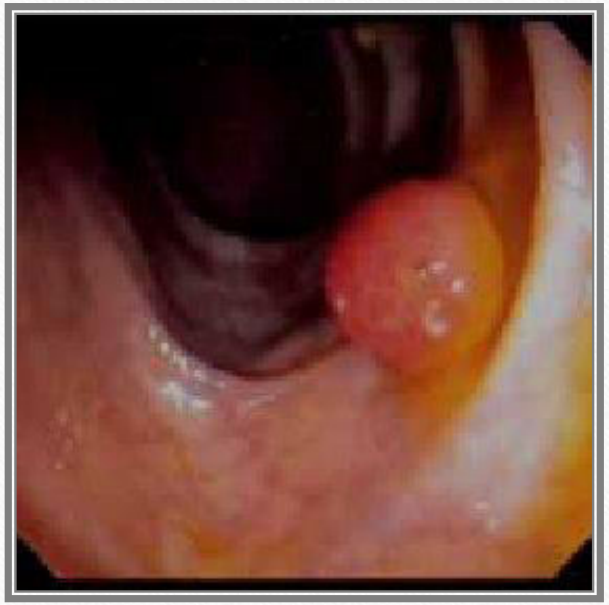
- Left colonic and rectum are more common than the right colon as primary site for colo-rectal cancer



- 80 % sporadic , 20 % familial
- Either Synchronous 5% or metachronous 3-5 %
- Synchronous means when the tumour diagnosed within 6 months of the primary
- Metachronous when the tumour develop after resection of the primary
- Genetically either activation of oncogene (K-ras) , or inactivation of tumour suppressor gene (P53 , APC)

Colorectal polyps

- It is now widely accepted that the majority of colorectal cancers arise from pre-existing adenomatous polyps, the supporting evidence being as follows:
- The prevalence of adenomas correlates well with that of carcinomas, the average age of adenoma patients being around 5 years younger than patients with carcinomas
- The distribution of adenomas throughout the large bowel is similar to that of carcinomas
- Adenomas are found in up to one-third of all surgical specimens resected for colorectal cancer.
- The incidence of colorectal cancer has been shown to fall with a long-term screening programme involving colonoscopy and polypectomy



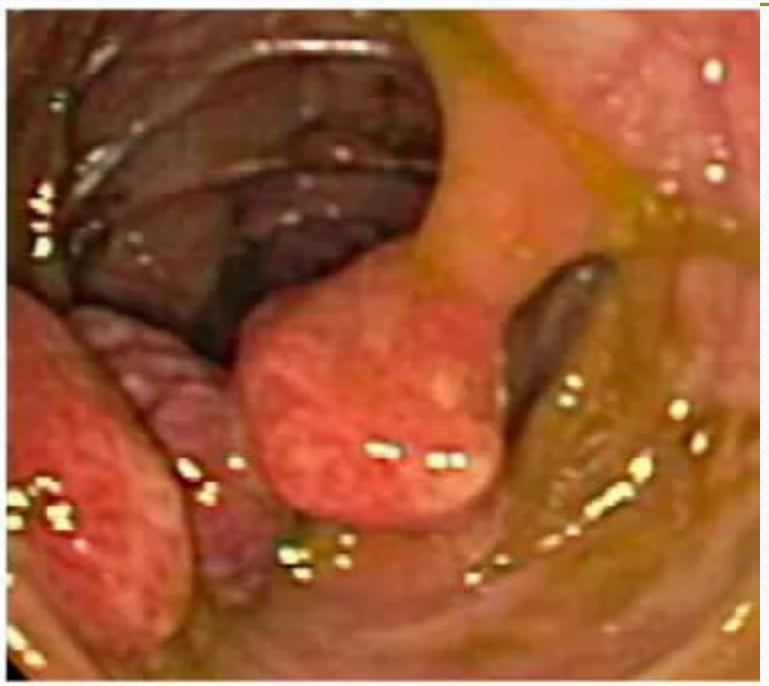
- Adenomatous tissue often accompanies cancer, and it is unusual to find small cancers with no contiguous adenomatous tissue
- Most sporadic adenomas are identical histologically to the adenomas of familial adenomatous polyposis (FAP), and this condition is unequivocally premalignant.
- Large adenomas are more likely to display cellular atypia and genetic abnormalities than small lesions

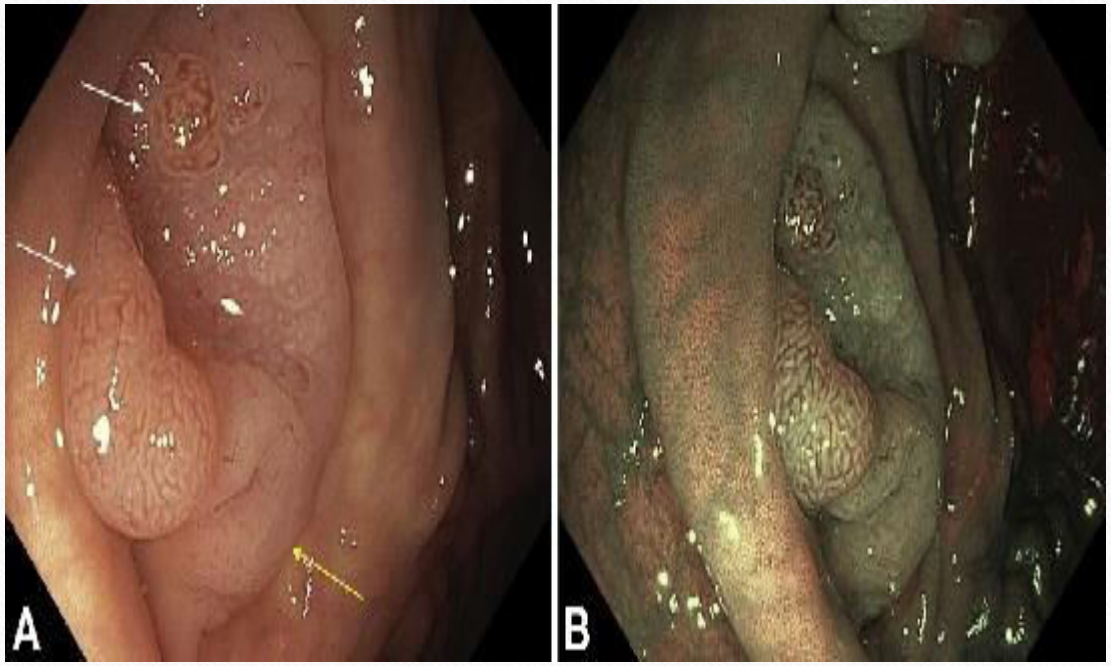
Polyps type

- Tubular and Tubulovillous are usually pedunculated but villous usually sessile
  - Usually asymptomatic but may presented with bleeding , intussusception or Most commonly detected during routine endoscopic surveillance

Histological Classification of Colorectal Polyps	
Neoplastic Polyps	**Non-neoplastic polyps**
Adenomatous polyps or Adenomas: • Tubular • Tubulovillous • Villous	1. Hyperplastic polyps 2. Hamartomatous polyps: – Juvenile polyps – PJS 3. Inflammatory polyps

Colonoscopy view of pedunculated and sessile polyps



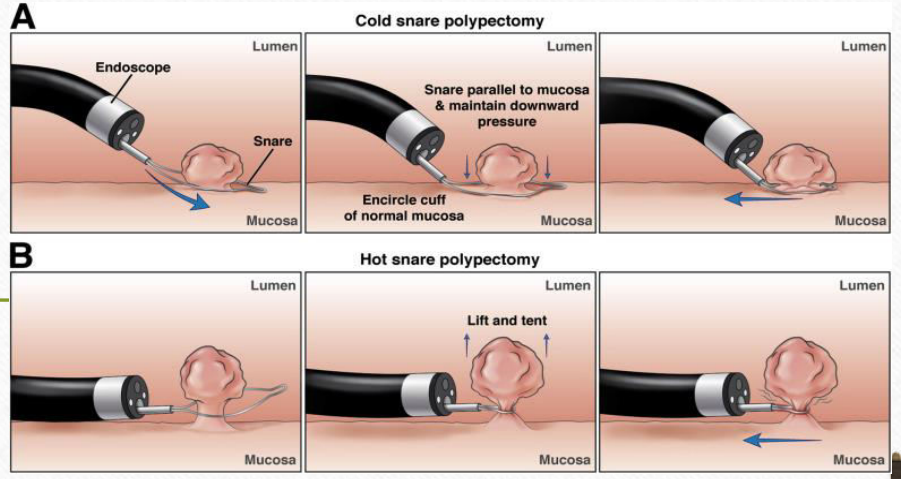


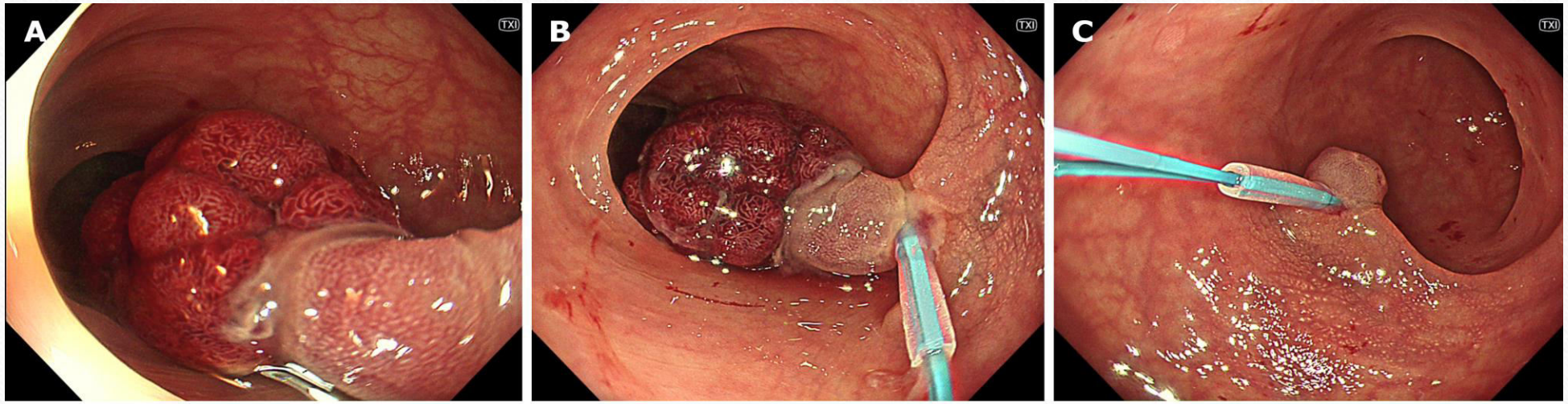
Adenomatous polyp's

- The most common type is the tubular type, but the villous type carries high malignant potential
- 80 % of villous polys located in rectosigmoid but 20% of tubular are in rectosigmoid
- endoscopic resection is the treatment except if the lesion cant be safely removed then biopsy should be done and further segmental
- Resection should be planned in case of villous type or if the lesion is dysplastic or indurated

Adenomatous Polyps			
Types	**Incidence**	**Villous tissue**	**Risk of Malignancy**
Tubular	65-80%Q	<25%	5%
Tubulovillous	10-25%	25-75%	20%
Villous	5-10%	>75%Q	40%Q

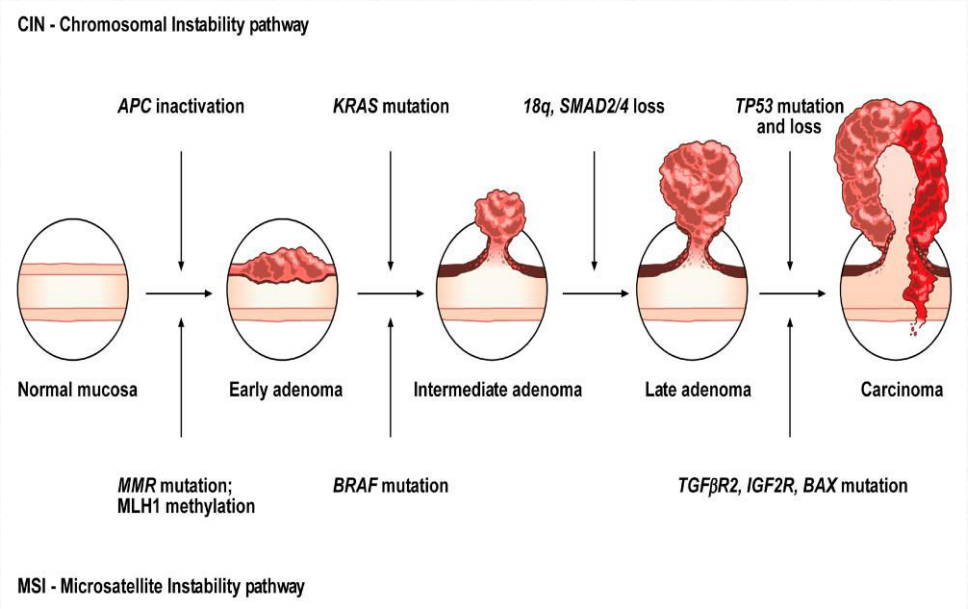
Probability of development of malignancy depends upon		
Gross Appearance of lesion	**Histology**	**Size**
• Pedunculated • **Sessile (Increased risk)**Q	• **Tubular (MC)**Q • Tubulovillous • **Villous (Highest risk)**Q	• <1 cm • 1-2 cm • **>2 cm (Increased risk)**Q

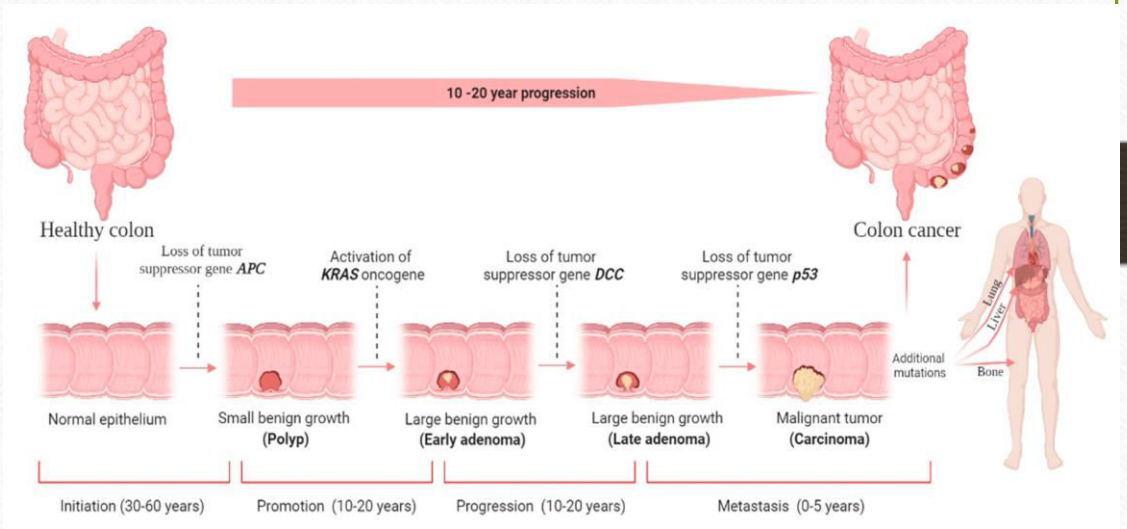




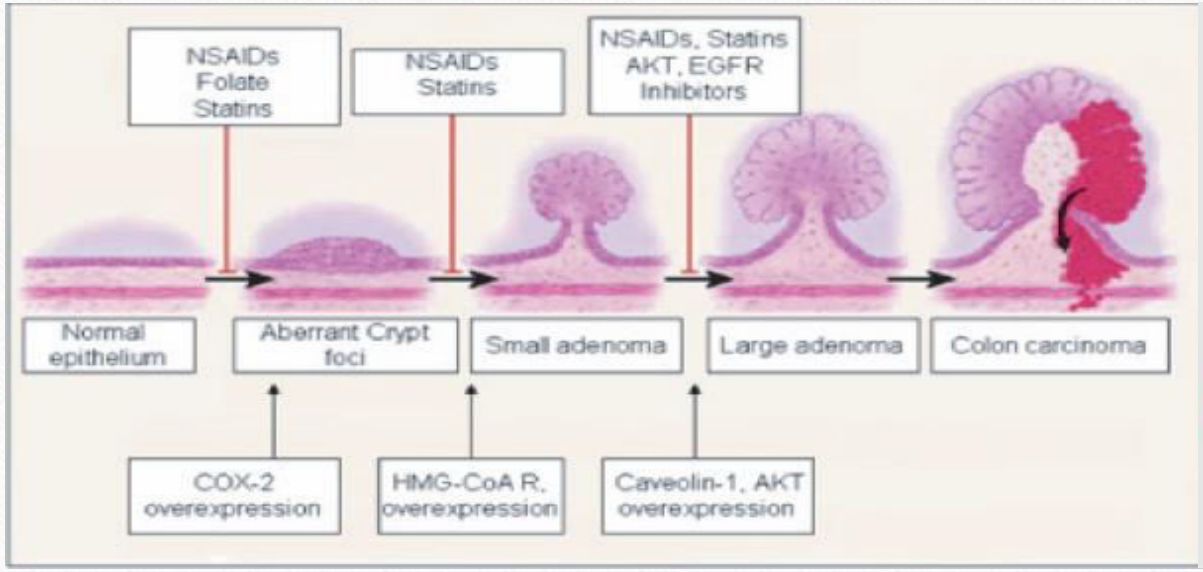
DOI: 10.3748/wjg.v29.i17.2600

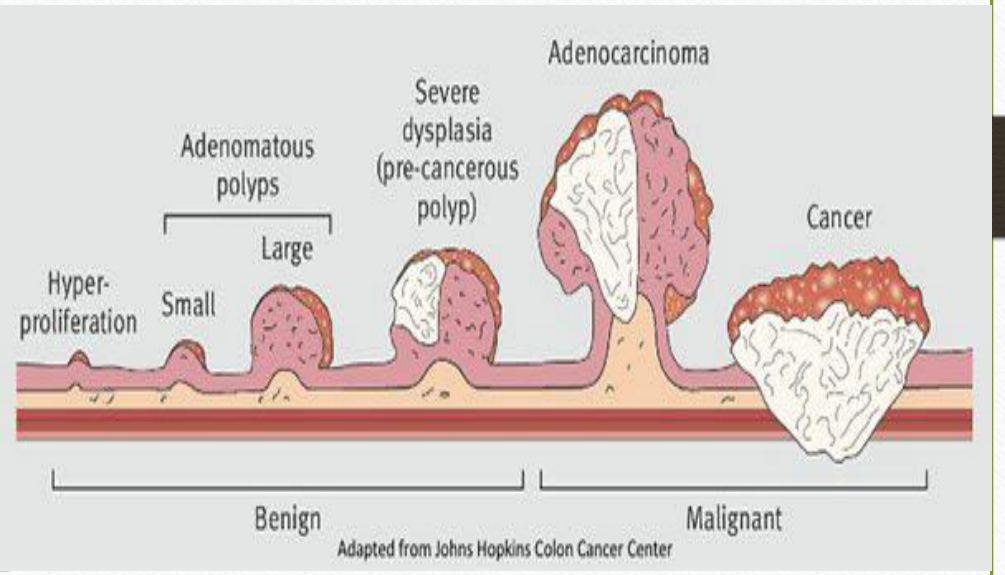
Adenoma- carcinoma sequence





polyp -cancer sequence





Hyperplastic Polyps

MC colorectal polyp, >90% of all colorectal polyps, mostly found in the rectosigmoid

→

Histologic appearance of these polyps is serrated (saw-toothed appearance).

→

No malignant potential

→

Observation vs endoscopic removal

Hamartomata's Polyps

A hamartomata's polyp is a localized overgrowth of normal, mature intestinal epithelial cells.

Usually lined with normal epithelium over a submucosal core.

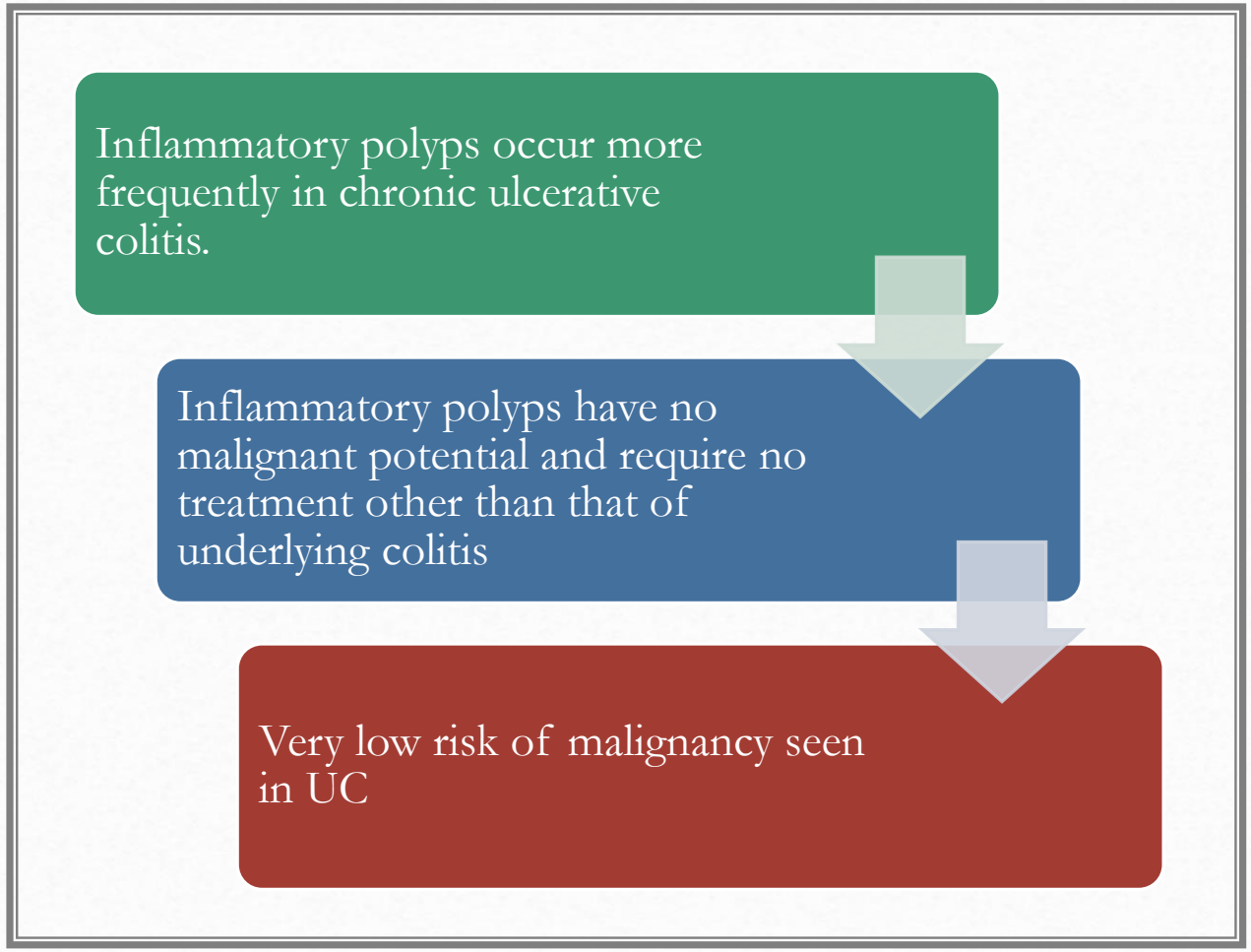
Juvenile polyps are the MC type of colorectal hamartomas

Other form seen in Peutz–Jeghers polyp

Seen commonly in small bowel

Excise for bleeding or obstruction

Inflammatory Polyps



Aetiology of colorectal cancer

Genetic factors

- The most commonly inherited forms of colorectal cancer are Lynch syndrome, caused by mutations to the DNA mismatch repair genes, and familial adenomatous polyposis (FAP), caused by germline mutations in the APC gene
- However, any family history can confer a degree of risk, which is presumably accounted for by a combination of shared environmental factors and inherited genetic polymorphisms

Diet and lifestyle

- With respect to colorectal cancer, evidence for decreased risk was found for physical exercise, dietary fibre, calcium, garlic, non-starchy vegetables and pulses.
- Evidence for increased risk was uncovered for obesity, red meat, processed meat, alcohol, animal fat and sugar.
- Being overweight and underactive stand out as major risk factors, and governments worldwide have recognised this as an area for action.
- Smoking is also important and long-term smoking is associated with relative risks of between 1.5 and 3.
- Aspirin may also provide protective effect when it usually taken on regular base as it lower the risk of polyp's formation significantly

Predisposing conditions

- Long-standing inflammatory bowel disease, both ulcerative colitis and Crohn's disease, increases the risk of colorectal cancer.
- Previous gastric surgery has also been implicated, and although the association is controversial, the risk may be about twofold.
- Altered bile acid metabolism may play a role in this process, both after gastrectomy and after vagotomy.
- The risk after ureterosigmoidostomy is well established, although this operation has now been largely superseded using an isolated ileal conduit for urinary diversion

Presentation.

Peak incidence around 70

Presentation.

- Colorectal cancer can present as an emergency or with chronic symptoms that are well recognised
- Right sided cancer typically presents with anaemia, as the liquid nature of the faeces and the wider diameter of the colon make obstructive symptoms unusual, palpable mass in advance disease
- When the tumour is situated in the descending or sigmoid colon, change of bowel habit, colicky abdominal pain and blood in the stool are the commonest symptoms , obstruction .
- In the rectum, bleeding is predominant, and with a large tumour, tenesmus is common, obstruction .
- Occasionally, the patient may notice the primary tumour as a mass and even more rarely a sigmoid cancer may cause pneumaturia and urinary infection by fistulation into the bladder

Guidelines have been developed to classify those at high risk warranting urgent investigation based on change in bowel habit, rectal bleeding in the absence of anal symptoms, palpable abdominal or rectal masses and anaemia

- Other symptoms : change in stool calibre , obstruction , perforation and symptoms related to anaemia

Box 3.1 • UK Department of Health criteria for high and low risk of colorectal cancer

Higher risk

- Rectal bleeding with a change in bowel habit to looser stools or increased frequency of defecation persisting for 6 weeks (all ages)
- Change in bowel habit as above without rectal bleeding and persisting for 6 weeks (>60 years)
- Persistent rectal bleeding without anal symptoms* (>60 years)
- Palpable right-sided abdominal mass (all ages)
- Palpable rectal mass (not pelvic) (all ages)
- Unexplained iron deficiency anaemia (all ages)

Low risk

- Patients with no iron deficiency anaemia, no palpable rectal or abdominal mass
- Rectal bleeding with anal symptoms and no persistent change in bowel habit (all ages)
- Rectal bleeding with an obvious external cause, e.g. anal fissure (all ages)
- Change in bowel habit without rectal bleeding (<60 years)
- Transient changes in bowel habit, particularly to harder or decreased frequency of defecation
- Abdominal pain as a single symptom without signs and symptoms of intestinal obstruction (all ages)

Investigation

Bloods

- CBC (anaemia)
- LFT, Renal profile , coagulation test
- Tumour marker – CEA : not for screening or diagnosis but to monitor the recurrence
- Malignant cause of elevated CEA :
- Benign condition causing raised CEA :

CEA

- In the case of colorectal cancer, it varies with the tumour stage, grade, location, and spread to the liver. Several studies have shown that patients with high preoperative concentrations of CEA have a worse outcome than those with low concentrations of the marker
- Medullary thyroid cancer can cause elevated CEA

Nonmalignant	Malignant
Smoking	Tumors associated with high CEA expression
Infections	Colorectal[a]
Peptic ulcer disease	Ovarian[a]
Inflammatory bowel disease	Cervical[a]
Pancreatitis	Lung
Hypothyroidism	Oesophageal
Liver cirrhosis, hepatitis	Gastric
Benign breast conditions	Small intestinal
Other benign tumors usually	Hepatobiliary
in organs where the	Pancreatic
cancers are associated	Breast
with raised CEA	Medullary
	Other CEA-expressing tumors
	Choriocarcinoma
	Osteosarcoma
	Retinoblastoma
	Hepatoma
	Melanoma
	Lymphoma
	Urinary bladder, prostate and renal cell carcinoma

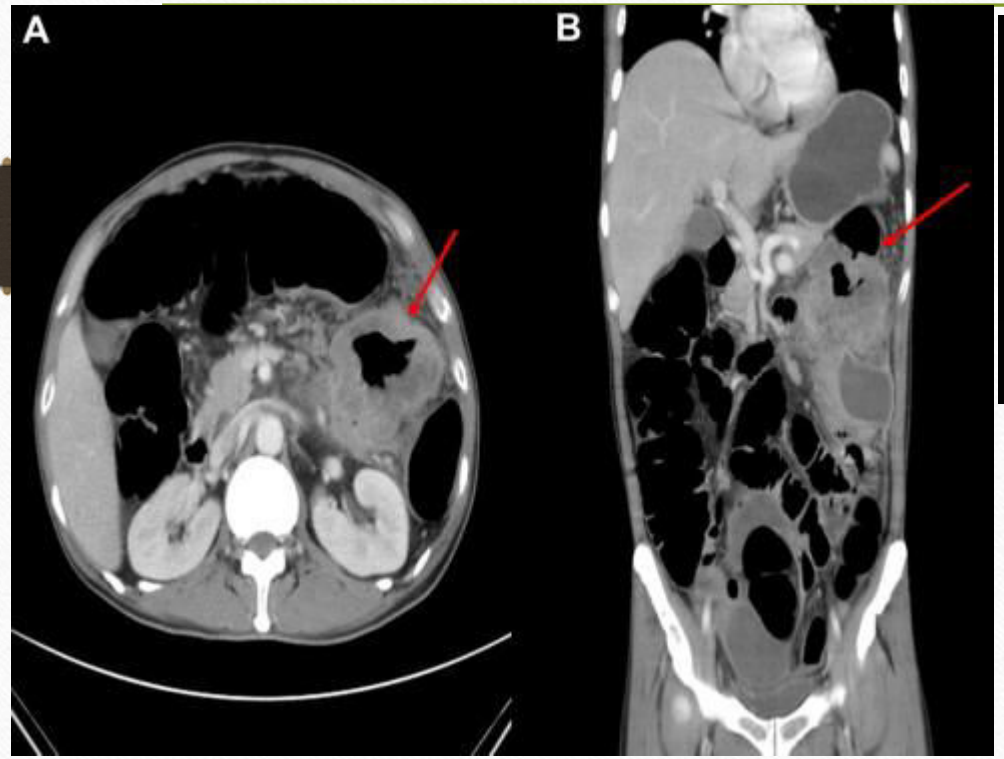
CEA, carcinoembryonic antigen.
[a]CEA monitoring used clinically.

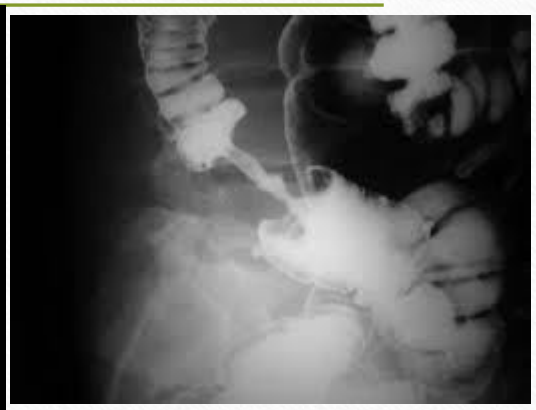
Images

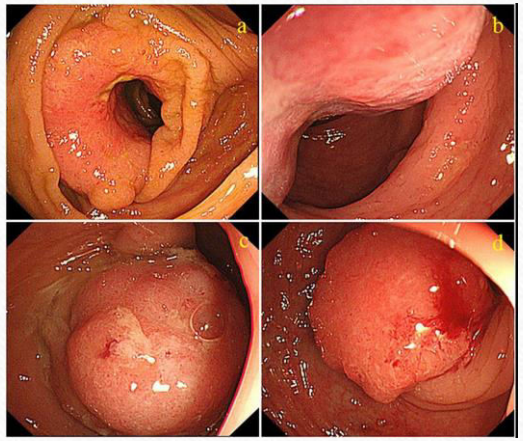
- Currently, the main investigative techniques include sigmoidoscopy, colonoscopy and computed tomography (CT) colonography.
- Barium enema, formerly the mainstay of investigation, has fallen out of favour owing to false-positive and false negative results occurring in up to 1% and 7% of cases, respectively
- CT as a primary investigative modality is now coming to the fore with the widespread introduction of CT colonography or 'virtual colonoscopy', which is effective in detecting polypoid lesions down to 6mm in diameter and superior to barium enema for the detection of cancers and significant polyps

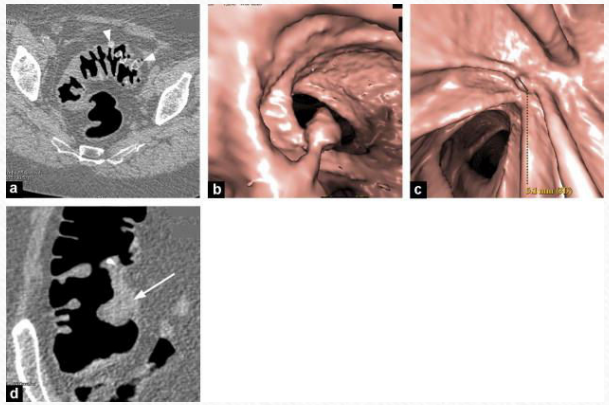
Images

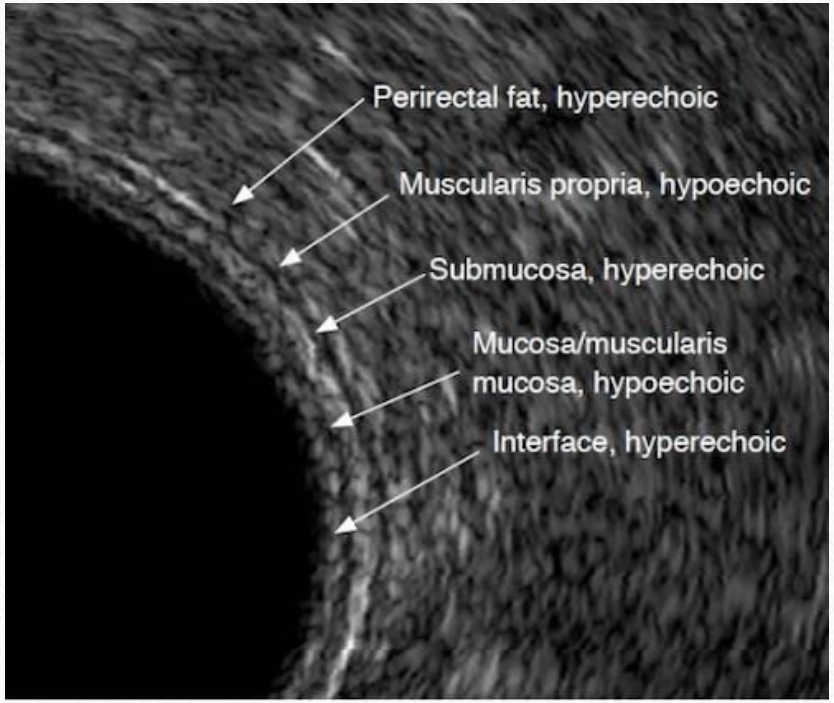
- Capsule endoscopy, until recently used only to visualise the small bowel, has now been modified to allow examination of the large bowel, and may become a very important tool in the investigation of colorectal symptoms and in screening and surveillance
- Chest , abdomen and pelvic CT to detection of metastasis and pre op staging
- Endorectal EUS to detect the depth of invasion in rectal cancer


A
B




a
b
c
d


a
b
c
d


Perirectal fat, hyperechoic
Muscularis propria, hypoechoic
Submucosa, hyperechoic
Mucosa/muscularis
mucosa, hypoechoic
Interface, hyperechoic

Role of images in CRC staging

- CT of the chest and abdomen is now regarded as the staging modality of choice.
- In a patient with a rectal cancer, MRI of the rectum is now considered mandatory to allow accurate preoperative staging and treatment planning.
- Endorectal ultrasound is used in some centres to assist with the assessment of early rectal cancer as it is reasonably accurate in distinguishing T1 from T2 tumours, but it is highly operator-dependent and not universally employed.
- PET-CT scanning has a limited role, but is recommended when surgical resection of metastases is being considered in order to exclude occult disease.

Screening

- Used for asymptomatic patient
- Patients with suspicious symptoms should be investigated with either endoscopic visualisation of the whole of the large colon by total colonoscopy or CT colonography
- For patients with average risk, the guidelines recommend that, beginning at age 50

Low risk

- 1. no personal history of bowel cancer; and 2. no first-degree relative (i.e. parent, sibling or child) with bowel cancer; or 3. one first-degree relative with bowel cancer diagnosed at age 50 years or older.
- The risk of bowel cancer even in these individuals may be up to twice the average risk
- There is no evidence to support invasive surveillance in this group

Moderate-risk group

- There is a three- to sixfold relative risk for individuals in this category,2 but probably only a marginal benefit from surveillance

- If the patient has intermediate risk, the screening should begin at age 40 and be done more frequently than every 10 years (e.g., every 3 to 5 years)

Low-moderate risk

This group comprises:

1. those with one affected first-degree relative diagnosed under 50 years; or
2. two affected first-degree relatives diagnosed at age 60 years or older.

High-moderate risk

This group comprises those with:

1. three or more affected relatives in a first-degree kinship (none under 50 years); or
2. two affected relatives diagnosed under 60 years (or with a mean age at diagnosis under 60 years) in a first-degree kinship.

High risk

- There is up to a 1 in 2 chance of inheriting a lifetime risk in excess of 50% of developing bowel cancer in this group, and referral to a clinical genetics service is essential
- patients who have had Ulcerative or Crohn's colitis for more than 10 years fall in this Groupe

High-risk group

This category encompasses Lynch syndrome and the various polyposis syndromes. Criteria for inclusion include:

1. member of a family with known familial adenomatous polyposis (FAP) or other polyposis syndrome; or
2. member of a family with known Lynch syndrome; or
3. pedigree suggestive of autosomal dominantly inherited colorectal (or other Lynch syndrome-associated) cancer; or
4. pedigree indicative of autosomal recessive inheritance, suggestive of MYH-associated polyposis (MAP).

Screening

- The ideal screening test should detect the majority of tumours without a large number of false positivity .
- In addition, it must be safe and acceptable to the population offered screening

UC and CRC

- Prolonged duration, continuously active disease, severity of inflammation, PSC and diffuse involvement (pancolitis) are cumulative risk factors for the development of colorectal cancer in the setting of UC
- Incidence rates for the development of cancer correspond to cumulative probabilities of 2% by 10 years, 8% by 20 years and 18% by 30 years.
- As a general rule, beginning 10 years after the diagnosis of UC, the incidence of colorectal cancer increases by approximately 1% per year as long as the patient has their colon

- The relative risk for cancer in relation to ulcerative proctitis has been estimated to be 1.7, left-sided colitis 2.8 and pancolitis 14.8. In relation to the general population, there is an overall eightfold higher risk of colorectal cancer, with a 19-fold higher risk in patients with extensive colitis
- Patients with PSC and UC have an increased risk of colorectal cancer in comparison to those without PSC

- The American Gastroenterological Association and British Society of Gastroenterology share international guidelines recommending surveillance colonoscopy every 1–2 years starting 8–10 years after a diagnosis of pancolitis, or 15 years after left sided colitis.
- Recommendations are also advocated for random non-targeted biopsies performed every 10cm in all four quadrants, equating to 20–40 biopsies per colon.

Screening tools

- Guaiac-based fecal occult blood test (gFOBT)
- test that detects the peroxidase-like activity of haematin in faeces.
- Because this activity is diminished as haemoglobin travels through the gastrointestinal tract,15 upper gastrointestinal bleeding is less likely to be detected than colonic bleeding.
- On the other hand, false-positive results may be produced by ingestion of animal haemoglobin or vegetables containing peroxidase, and because of the intermittent nature of bleeding from tumours, the sensitivity of Haemoccult is only about 50–70%

faecal immunological testing (FIT)

- is not affected by dietary peroxidase or animal haemoglobin and is therefore more accurate than the indirect guaiac test.
- It is also associated with higher uptake, as, unlike the guaiac test, only one sample is required, and the collection device is more hygienic.
- Of particular interest is the use of quantitative FIT, which is automated and therefore not subject to human observational error, and provides the user with the facility to set the performance characteristics to suit the screening programme
- FIT-DNA test
- Theses test done once a year and colonoscopy should be done if these test are positive

- flexible sigmoidoscopy
- Colonoscopy
- CT Colonography
- In the UK, flexible sigmoidoscopy is being introduced as part of the national bowel screening programme, and the guaiac test is being replaced by FIT.

Frequency

- Flexible sigmoidoscopy every 5 years*
- 2. Colonoscopy every 10 years
- 3. Double-contrast barium enema every 5 years*
- 4. CT colonography (virtual colonoscopy) every 5 years

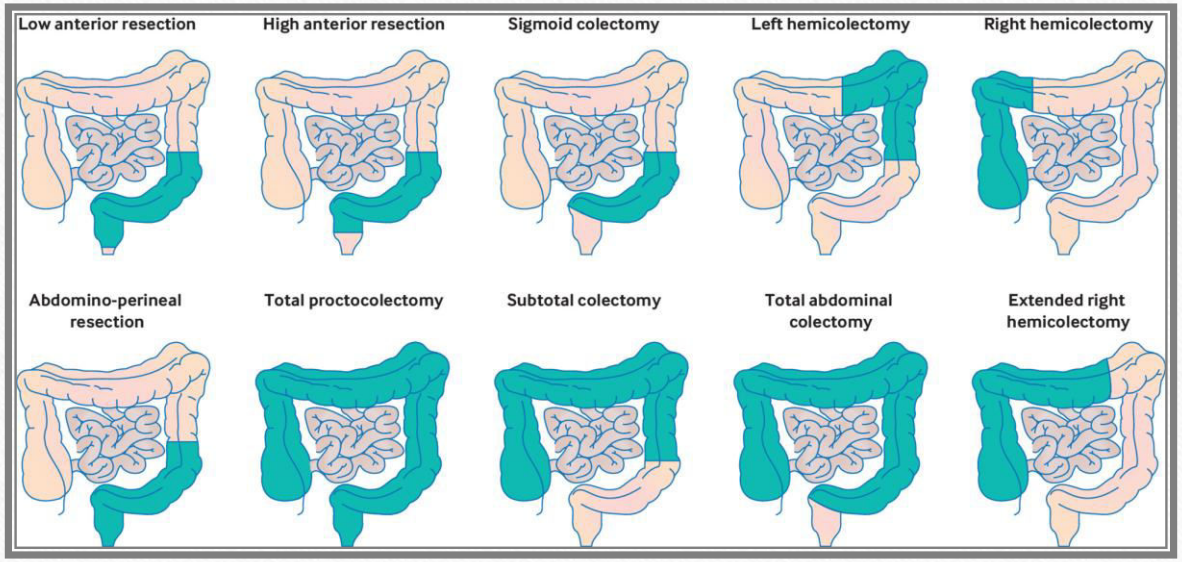
Management

- Depending on a lot of factors

1. Elective Vs Emergency presentation
2. Location (Rectal vs colon – R vs L)
3. Presence of metastasis
4. Patient fitness for surgery

Surgery

- Surgical excision remains the mainstay of treatment for colorectal cancer
  - Elective
  - right hemicolectomy for any tumour involving the caecum, right colon or right transverse colon
  - Transverse colectomy
  - When a tumour is present at the splenic flexure a ‘segmental left colectomy
- In virtually all patients with left colon cancer distal to the ascending left colic artery, a left hemicolectomy
  - Sigmoidectomy



- At least 12 LN should be taken for proper staging
- 5 cm is the margin

Rectal cancer

- Transanal endoscopic microsurgery (TEMS) shown to successfully treat selected early rectal cancers (ERC) with favourable pathology (pT1, <3cm , well differentiated, no lymph vascular invasion)
- Neo adjuvant chemo radio therapy
- Surgical treatment depending on the location from the anal verge

Neo adjuvant

- the advantages of preoperative therapy include increased sphincter preservation, less small intestinal radiation injury, and improved bowel function.
- Typically, preoperative therapy is reserved for those tumors with evidence of nodal or transmural disease.
- The combined chemoradiation is given for six weeks, followed by a break of 4–10 weeks before surgery.
- An additional four months of chemotherapy is given postoperatively

Surgical option

Treatment Options for Carcinoma Rectum	
Low Anterior Resection	• **Sphincter saving operation**[Q] • Performed for the **cancers** of **proximal third** to **two third of** the **rectum** (Located **> 5 cm above**[Q] the **anal verge**) • Descending colon is anastomosed with the distal rectum
Abdominoperineal Resection (APR or Miles Procedure)	• **Complete excision** of **rectum** and **anus**, by concomitant dissection through the abdomen and perineum with **creation of permanent colostomy**[Q]. • Performed for carcinoma of **lower rectum** (**at** or **below 5 cm** from **anal verge**)
Hartmann's Procedure	• When there is **too much destruction** or **sepsis** to allow a safe anastomosis[Q] • For **elderly** or **severely unstable patients**[Q] who would not stand a lengthy anterior resection or APR procedure

Staging

Modified Duke's (Modified Astler-Collar) Classification	
Stage	**Description**
A	**Confined to the mucosa**
B1	**Partially penetrated** the **muscularis propria**[Q]
B2	**Fully penetrated**[Q] the muscularis propria
C1	**Lymph node invasion without penetration** of the entire bowel wall[Q]
C2	**Lymph node invasion with penetration**[Q] **of the entire bowel wall**
D	**Distant metastasis**[Q]

<4 LN involved for C1 ,

C2 : 4 or more LN involved

TNM

8th AJCC (2017) TNM Classification of Colorectal carcinoma	
Tis: Carcinoma in situ: intraepithelial or invasion of lamina propria	**N1:** Metastasis in **1-3** regional LNs **N1a:** Metastasis in **1** regional LN **N1b:** Metastasis in **2-3** regional LN **N1c: Tumor deposits** in in the **subserosa, mesentery,** or **nonperitonealized pericolic** or **perirectal tissues without regional LN metastasis**[Q]
T1: Tumor invades **submucosa**[Q]	
T2: Tumor invades **muscularis propria**[Q]	
T3: Tumor **invades subserosa or into non-peritonealized pericolic or perirectal tissues**[Q]	
T4a: Tumor **penetrates** the surface of **visceral peritoneum**[Q]	**N2a:** Metastasis in **4-6** regional LN[Q] **N2b**: Metastasis in **7 or more** regional LN[Q]
T4b: Tumor directly **invades** or is **adherent** to other **organs** or **structures**[Q]	**M1a:** Metastasis confined to **one organ or site** (e.g. Liver, lung, ovary, non-regional node) without peritoneal metastases[Q] **M1b**: Metastasis to **more than one organ**[Q] **M1c:** Metastasis to **peritoneum with or without other organ involvement**[Q]

Stage Grouping					
I	**II**	**IIIA**	**IIIB**	**IIIC**	**IV**
T1N0 **T2**N0	**IIA: T3**N0 **IIB: T4a**N0 **IIC: T4b**N0	**T1-T2, N1** **T1, N2a**	**T1-T2, N2b** **T2-T3, N2a** **T3-T4a, N1**	**T3-T4a, N2b** **T4a, N2a** **T4b, N1-N2**	**IVa:** Tany Nany **M1a** **IVb:** Tany Nany **M1b** **IVC:** Tany Nany **M1c**

Table 4: **Colon cancer 5-year survival rates**

Stage	%
Stage I	93
Stage IIA	85
Stage IIB	72
Stage IIIA	83
Stage IIIB	64
Stage IIIC	44
Stage IV	8

I, T1-2 N0M0; IIA, T3 N0M0; IIB, T4N0M0; IIIA, T1-2N1M0;

Adjuvant therapy for colon cancer

- Because of the high risk of radiation enteritis affecting adjacent small bowel, adjuvant radiotherapy is not recommended for primary colon cancer
- Systemic chemotherapy for all patient with stage III, hight risk group in stage II(pT4 primary tumor or two or more other high-risk features (fewer than 12 sampled lymph nodes in the surgical specimen, perineural or lymphovascular invasion, poorly differentiated or undifferentiated histology, clinical intestinal obstruction, tumor perforation).
- Genetic study required in stage II to decide about the chemotherapy
- Biological therapy in metastatic or advance disease
- **Chemotherapy has improved survival in colon cancer patients both with resectable and unresectable disease**
- FOLFOX (5-FU, leucovorin and oxaliplatin) is the standard treatment regimen currently.

Adjuvant therapy for colon cancer

- Genetic study required in stage II to decide about the chemotherapy
- Biological therapy in metastatic or advance disease
- **Chemotherapy has improved survival in colon cancer patients both with resectable and unresectable disease**
- FOLFOX (5-FU, leucovorin and oxaliplatin) is the standard treatment regimen currently.

Adjuvant therapy for Rectal cancer

- Postoperative chemotherapy combined with radiation therapy has been shown to improve outcomes in patients with transmural or node positive rectal cancers.
- Combined chemotherapy and radiation improve local control and increase overall survival.
- This combined therapy is the standard of care for patients with Stage II and III rectal cancers.
- Radiation therapy is typically administered with chemotherapy for a six-week period. Chemotherapy alone is then administered for an additional four months

Management of advanced disease

- In advanced colon cancer, bypass surgery may be appropriate, but multi-organ en bloc resection may be curative, and suitable patients should be given this option
- Likewise, in rectal cancer, although palliative radiotherapy with or without a defunctioning stoma may produce a degree of symptom control, consideration should always be given to pelvic exenteration, particularly in younger, fitter patients
- In patients with peritoneal spread alone, or with easily operable liver metastases, peritonectomy combined with heated intraperitoneal chemotherapy (HIPEC) may result in long-term survival
- Inoperable disseminated disease : chemotherapy , bevacizumab(Anti VEGF)

Histological

HISTOPATHOLOGIC TYPE

Adenocarcinoma *in situ*
Adenocarcinoma
Medullary carcinoma
Mucinous carcinoma (colloid type; >50% extracellular mucinous carcinoma)
Signet ring cell carcinoma
Squamous cell (epidermoid) carcinoma
Adenosquamous carcinoma
High-grade neuroendocrine carcinoma (small cell carcinoma and large cell neuroendocrine carcinoma)
Undifferentiated carcinoma
Carcinoma, NOS

Spreading and metastasis

- Direct spread
- Lymphatic spread
- Blood-borne spread:
- The most common site for blood-borne spread of colorectal cancer is the liver, presumably arriving by the portal venous system. Up to 37% of patients may have occult liver metastases at the time of operation, and around 50% of patients may be expected to develop overt disease at some time.
- The lung is the next most common site, with around 10% of patients developing lung metastases at some stage; other reported sites include ovary, adrenal, bone, brain and kidney
- Trans coelomic spread- associated with development of malignant ascites

Operable mets

- Hepatic resection for colorectal cancer metastases is now widely practised
- Pulmonary metastases may also be amenable to resection, but as only 10% of patients develop such metastases and only 10% of these have disease confined to the lung

Prognostic factor

Stage and grade (size , depth)
Positive Surgical margins
lymph node involvement (the most important)
High preoperative CEA levels
People who have a bowel obstruction or perforation at the time of diagnosis have a poorer prognosis.
Mucinous adenocarcinoma, signet ring cell carcinoma and small cell carcinoma have a poorer prognosis than other types of colorectal tumours.
Microsatellite instability (MSI)- high MSI good prognosis
KRAS gene mutation : bad prognosis as it will not respond to the target therapy
BRAF gene mutation: aggressive disease
PERITONEAL INVOLVEMENT

Emergency surgery

- In case of perforation or obstruction (closed loop obstruction)
- The overall mortality for emergency/urgent surgery should be 20% or less.
- Role of colonic stent : for obstruction left colon cancer as definitive palliative treatment or bridging before surgery , not used for rectal cancer

Follow up post surgery
It aim to detect the recurrence that usually occur in the first 18to 24 months

clinic visit :every 3 months for 2 years, every 6 months for 3 years, and then yearly until 5 or 10 years postresection

CEA : its level and progressive raise in its level which mandate further investigation with CT , colonoscopy , PET It is currently the most sensitive test to detect recurrent colorectal cancer.

Colonoscopy: at 1 and 2 years postoperatively and then every 2 to 3 years

Lynch syndrome

- autosomal dominant fashion, is responsible for about 3% of colorectal cancers and is the commonest of the inherited bowel cancer syndromes.
- Also known as hereditary non-polyposis colorectal cancer (HNPCC) to distinguish it from the polyposis syndromes and to highlight the absence of the large numbers of colorectal adenomas found in FAP. However, scanty adenomatous polyps are a feature of Lynch syndrome

- Lynch syndrome is characterised by early onset of colorectal cancer, the average age at diagnosis being 45 years.
- These tumours have certain distinguishing pathological features. There is a predilection for the proximal colon, and tumours are frequently multiple (synchronous and metachronous).
- They tend to be mucinous, poorly differentiated and of 'signet-ring' appearance, with marked infiltration by lymphocytes and lymphoid aggregation at their margins.
- The prognosis of these cancers tends to be better than in the same tumours arising sporadically.

germline mutations in MMR genes

- The prognosis of these cancers tends to be better than in the same tumours arising sporadically

- germline mutations in MMR genes(DNA mismach repair gene)
  - The most commonly affected genes are MLH1 and MSH2

Table 4.1 • Cancers associated with Lynch syndrome

Site	Frequency (%)
Large bowel	30–75
Endometrium	30–70 (of women)
Stomach	5–10
Ovary	5–10 (of women)
Urothelium (renal pelvis, ureter, bladder)	5
Other (small bowel, pancreas, brain)	<5

Diagnosis

- Also genetic testing are used

Box 4.3 • Outcomes of genetic testing

Mutation detected
Test at-risk family members (predictive testing): if positive, surveillance and/or other management (e.g. surgery); if negative, no surveillance required

Mutation not detected
Keep all at-risk members under surveillance

Box 4.1 • Amsterdam criteria II

- At least three relatives with a Lynch syndrome-associated cancer (colorectal, endometrial, small bowel, ureter, renal pelvis), one of whom should be a first-degree relative of the other two
- At least two successive generations should be affected
- At least one cancer should be diagnosed before age 50 years
- FAP should be excluded
- Tumours should be verified by pathological examination

Surveillance

- Colonoscopy every 1–2 years from age 25 years (or 5 years younger than the youngest affected relative, whichever is the earlier)11 is recommended for Lynch syndrome. Surveillance should continue until about 75 years or until the causative mutation in that family has been excluded

Box 4.4 • Extracolonic surveillance in Lynch syndrome

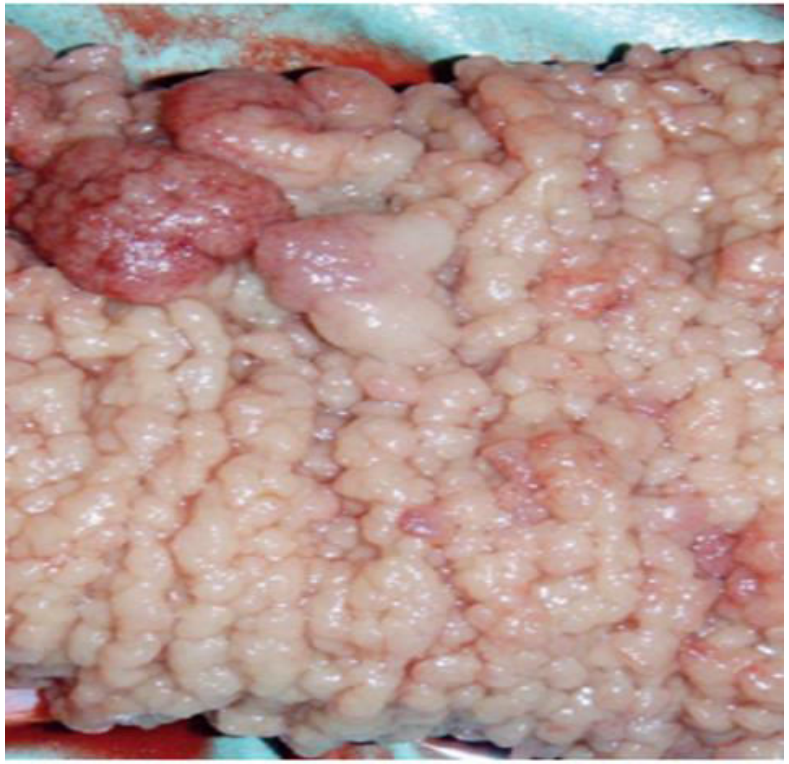
- Annual transvaginal ultrasound ± colour flow Doppler imaging ± endometrial sampling
- Annual CA125 level and clinical examination (pelvic and abdominal)
- Upper gastrointestinal endoscopy every 2 years
- Annual urinalysis/cytology
- Annual abdominal ultrasound of renal tracts, pelvis, pancreas
- Annual liver function tests, CA19–9, CEA

Management

- Prophylactic subtotal colectomy if rectum spared or might take the form of a restorative proctocolectomy. In mutation carrier should be discussed carefully
- Surgery as a treatment when colon cancer develop
- prophylactic hysterectomy and bilateral salpingooophorectomy in women who have completed their families.
- MC extraintestinal feature: Endometrial cancer

Peutz-Jegher's Syndrome (AD)

- mucocutaneous pigmentation together with multiple gastrointestinal hamartomatous polyps.
- The gene responsible in some patients is STK11 (LKB1) on chromosome 19p13
- significantly increased risk of gastrointestinal malignancy, although the risk has not been well defined.
- Other areas at increased risk include the breasts (female), ovaries, cervix, pancreas and testes.



Familial Adenomatous Polyposis

- autosomal dominant inherited syndrome
- hundreds of colorectal adenomatous polyps at a young age (second or third decade of life)
- mutation in the tumour-suppressor adenomatous polyposis coli (APC) gene on chromosome 5q up to 80%
- duodenal adenomatous polyps and small bowel polyps and cancer can develop
- <1% of CRC
- If left untreated, colorectal cancer develops in nearly 100% of these patients by age 40 years
- >80% positive family history.

- If an individual has symptoms attributable to the large bowel (anaemia, rectal bleeding or change in bowel habit),colonoscopy should be performed.
- Otherwise annual flexible sigmoidoscopy starting at 13–15 years of age is recommended. If no polyps are detected, 5-yearly colonoscopy should be started at the age of about 20 years, with annual flexible sigmoidoscopy in the intervening years

Box 4.5 • Extracolonic manifestations in FAP

Ectodermal origin
- Epidermoid cysts
- Pilomatrixoma
- Tumours of central nervous system
- Congenital hypertrophy of the retinal pigment epithelium

Mesodermal origin
- Connective tissue: desmoid tumours, excessive adhesions
- Bone: osteoma, exostosis, sclerosis
- Dental: dentigerous cyst, odontoma, supernumerary teeth, unerupted teeth

Endodermal origin
- Adenomas and carcinomas of duodenum, stomach, small intestine, biliary tract, thyroid, adrenal cortex
- Fundic gland polyps
- Hepatoblastoma

If the diagnosis has been made on the basis of flexible sigmoidoscopy, colonoscopy should be performed to assess the colonic polyp burden.

Gardner's Syndrome (AD)

The combination of FAP with:

• Bony lesions (osteomas, cortical thickening of long bones & ribs) •

Benign lymphoid polyposis of ileum

• CHRPE

• Dental anomalies (impacted tooth, supernumerary tooth, dental cyst) •

Desmoid tumors & sebaceous cyst

Turcot's Syndrome (AR)

- MC brain tumours are medulloblastoma & particularly glioblastoma.
- • It is a phenotypic variant of FAP and is transmitted by an autosomal recessive gene.
- •Medulloblastoma in FAP & Glioblastoma multiforme in HNPCC

Surgery in FAP

- Prophylactic Vs Treatment
- Options (colectomy and ileorectal anastomosis (IRA); restorative proctocolectomy (RPC) with an ileal pouch–anal anastomosis; total proctocolectomy and end ileostomy)
- post-surgery flexible endoscopic for pouch surveillance and bx examination are mandatory, at intervals of up to 12 months, depending on findings
- Duodenal adenomas occur in nearly all patients with FAP but are severe in only 10%, with malignant change occurring in 5%

FAP

- Surveillance usually begins in the third decade of life (in the asymptomatic patient), with endoscopies at intervals of between 6 months and 5 years depending on the severity of duodenal polyposis with gastroscopies
- After the CRC is eliminated by surgery, periampullary tumors are MC cause of death among individuals with FAP
- complications of desmoid tumours have reduced life span

Anal cancer

- Anal cancer is rare, accounting for approximately 2–4% of large bowel malignancies
- Most anal cancers arise from the squamous epithelium of the anal margin or anal canal, although a few arise from anal glands and ducts.
- anal margin is variously described as the visible area external to the anal verge, or as the area below the dentate line. Anal margin tumours are said to be within a 5-cm radius of the anal orifice.
- Other definitions of anal canal are discussed in slide 7

Histology

- 80 % are squamous cell carcinoma arising from the squamous epithelium of the anal canal and perianal region
- 10 % adenocarcinoma arising from glandular mucosa of the upper anal canal, the anal glands and ducts
- Very rare and particularly aggressive tumour is anal melanoma.
- Lymphomas and sarcomas of the anus are even less common but have increased in incidence in recent years, particularly among patients with human immunodeficiency virus (HIV) infection.

- Tumours arising at the anal margin tend to be well differentiated and keratinising, occurring more in men, whereas those arising in the canal are more commonly poorly differentiated and are commoner in women.
- Lymph node metastases occur frequently, especially in tumours of the anal canal initially to the perirectal group of nodes and thereafter to inguinal, haemorrhoidal and lateral pelvic lymph nodes.
- Haematogenous spread tends to occur late and is usually associated with advanced local disease.
- The principal sites of metastases are the liver, lung, paraaortic nodes and bones

Most cases underreported due to misclassification as low rectal tumour

- 1300 cases of anal cancer diagnosed each year in the United Kingdom
- Over 50 000 new cases and 19 000 deaths have been estimated worldwide in 2020.
- he incidence of anal cancer is increasing in both males and females with a greater increase in females
- In Jordan according to the Jordan cancer registry 2018 the incidence was 0.2% equally between male and female

Risk factor

- human papillomavirus (HPV) infection (anal-genital warts)-HPV-16;-MC HPV-18, 31, 33
- history of receptive anal intercourse or sexually transmitted disease
- history of cervical, vulvar, or vaginal cancer
- immunosuppression after solid organ transplantation or human immunodeficiency virus (HIV) infection
- hematologic malignancies
- smoking.
- Certain autoimmune disease (SLE, IBD)

Clinical presentation

- Most patients present with rectal bleeding & pain in 50 %, most commonly is the bleeding
- Mass protruding felt by the patient in 25%-30%
- Pruritus and discharge
- Fistula , fissure
- Incontinence in advance tumours invading the sphincter
- Invasion of the posterior vaginal wall may cause a fistula
- Cancer of the anal margin usually has the appearance of a malignant ulcer, with a raised, everted, indurated edge.

Investigation

- The most important investigation in the management of anal cancer is a detailed clinical examination under anaesthetic. EUA
- Examination under anaesthesia permits optimum assessment of the tumour in terms of size, involvement of adjacent structures and nodal involvement, and also provides the best opportunity to obtain a biopsy for histological confirmation
- CT (CAP), MRI for staging and assessment of distant and locoregional involvement respectively .
- Other , PET –CT, endo-anal US

Treatment

- The current standard of care for anal cancer is chemoradiotherapy with in all cases except those where local excision is complete or there are contraindications to radiotherapy.
- This achieves equivalent survival rates to surgery but with the advantage of stoma avoidance in the majority of cases.
- Nigro PROTOCOL
- Gynaecologic examination including screening for cervical cancer is suggested for women, due to its association with anal cancer and HPV

Role of surgery

- Four situations may require surgery after chemoradiation for anal cancer treatment: residual tumour, complications of treatment, incontinence or fistula after tumour resolution, and subsequent tumour recurrence
- Inguinal metastases Inguinal lymph nodes are enlarged in up to a third of patients with anal cancers. Inguinal lymph node involvement is now treated by chemoradiotherapy; if this is contraindicated then block dissection
- Usually in form of APR