Colorectal cancer

Objectives:

- **Definitions**
- **Polyps**
- **Basics of colorectal cancer**
- **Surgery**
- **Staging**

Resources:

- Davidson's.
- 435 Slides
- Surgical recall.
- 434 Teamwork

Done by: Sara AlQahtani & Balgees Alabbad
Sub-leader: Abdullah Alghizzi.
Leaders: Abdulrahman Alsayyari & Monerah Alsalouli
Reviewed by: Ahmad Alyahya & Luluh Alzeghayer

[Color index | Important | Notes | Extra]
[Editing file | Feedback | Share your notes | Shared notes]

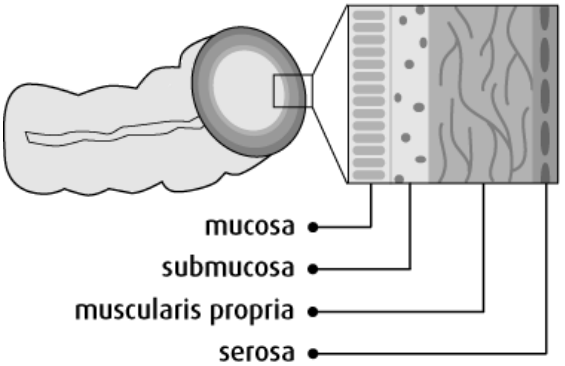
Once you stop learning
you start dying.

Basic review:

The rectum has the intraperitoneal and extraperotineal part, Same as colon but has an only difference is that the rectum has no serosa.

- Colon wall from an inner layer to outer layer:
  1. Mucosa
  2. Submucosa
  3. muscularis propria
  4. Serosa

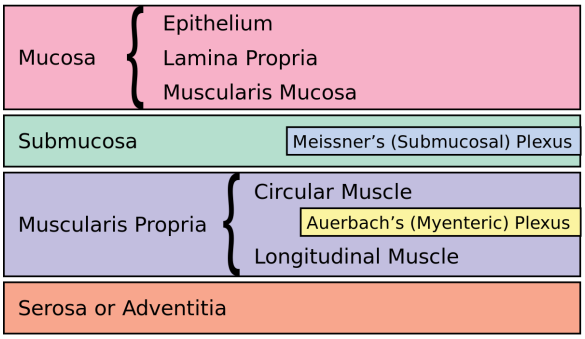
- Rectum wall:
  1. Mucosa
  2. Submucosa
  3. Muscularis propria
  4. mesorectal fat (no serosa so that's why in case of rectal cancer we give radiation because of the high recurrence which is within bony pelvis)



*serosa is not found on most of the rectum

So, T3 of the colon = T4 of the rectum

*You need to differentiate between Muscularis Propria and Muscularis Mucosa.



"Any growth above the **basement membrane** is benign, whenever it reaches the basement membrane it's considered as malignant tumor and it can metastasize (through lymphatic+blood vessels)"

Definitions:

- **Colon** = large bowel = large intestine. 150 cm in length
- **Rectum:** the terminal portion of the colon. 15 cm, most of the rectum is extra-peritoneal, has **no serosa** (that's how you can differentiate between rectum and colon)
- **Polyp:** benign growth (not invasive). (don't invade the basement membrane), benign polyps include: pseudopolyps, hyperplastic, Inflammatory, Adenomatous. All of them benign and will never develop cancer except **Adenomatous** with only 2% chance.

Polyp (benign) > invade basement membrane > malignant polyp (Carcinoma in situ) > invade submucosa > T1 cancer.

- **Adenoma:** type of polyp.
- **Cancer:** malignant growth (invasive[1]).
- **Stage:** where the cancer is growing. (the fist step we do when we know the pt has cancer)
- **Primary:** the original tumour, where it started.
- **Metastases:** where the tumour has spread to.

Cancer:

A cancer cell is **immortal**, multiplies uncontrollably, can live on its own without neighbors, and can live in other parts of the body.

A brief intro to the lecture:
- ⅔ of all large bowel cancers occur in the rectum and sigmoid colon. the most clinical feature are change in bowel habit and blood per rectum.
- Diagnosis is done by colonoscopy and biopsy, CT colonography or barium enema "apple core sign"
- preoperative staging involves CT, MRI and PET CT scanning.

[1] invasion to basement membrane which located between Muscularis Mucosa and lamina propria contains lymphatics and Blood vessel

Colorectal Cancer

- Most cancers are acquired, some are inherited.
- Almost **all cancers begin as a benign polyp or adenoma**.
- Only a tiny percentage of adenomas become cancers.

بمعنى: كل الكانسرز تكون اديتوما في البداية، لكن مو شرط كل اديتوما تتحول لكانسر (فقط نسبة صغيرة منها).

- If I see 100 pt., **95 of them will be Sporadic** (no genetics background). They will be aged around 50 - 60 y.o, while the rest will be: some will have IBD, Hereditary Nonpolyposis Colorectal Cancer (HNPCC) or Familial adenomatous polyposis (FAP)[2].
- What I want you to know about HNPCC that it's inherited colorectal cancer secondary to DNA mismatch gene repair.

ايس مابيكم تضيعون

Polyp - Cancer Sequence:

- The process from benign polyp to cancer takes from **7 - 10 years**.
- The transformation into cancer is based on:
  - The type of polyp (Adenomatous, Villous, Sessile)
  - Size of polyp (>2cm)
  - Multiple polyps = greater risk of cancer.

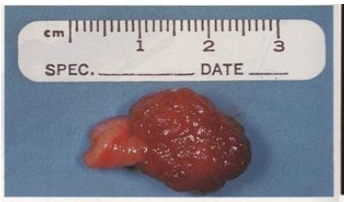


Fig. 22-7 Pedunculated polyp.

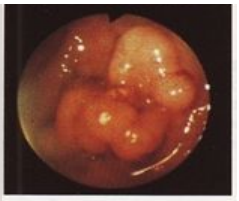


Fig. 22-8 Sessile polyp.

Adenomatous Polyp risk > other types
Villous type of adenomatous Polyp carries greater risk than tubular and tubulovillous.
Sessile polyp > Pedunculated polyp.
Size greater than > 2cm .

Future therapy: block one of those steps by gene therapy. (won't be asked about genes)

Removing polyps prevents cancer: **Colonoscopy**.


Sessile on Left
Pedunculated on the Right

Colorectal Carcinoma:

Classification:

- Adenocarcinoma[3]
- Carcinoid[4]
- Lymphoma
- Sarcoma
- Squamous cell carcinoma[5]

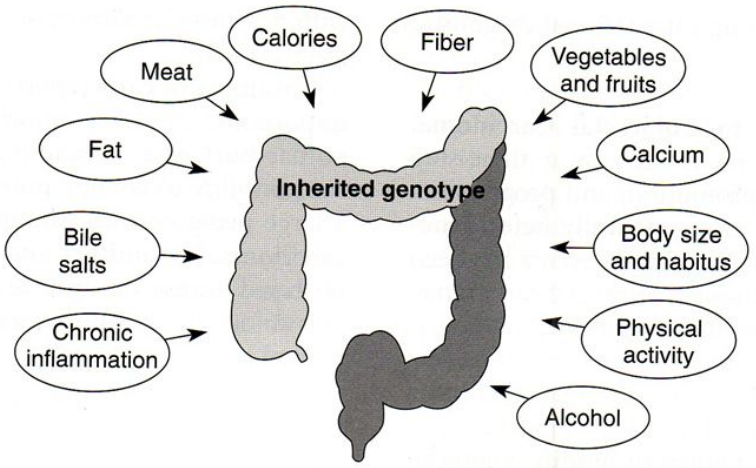
Epidemiology:

- 3th most common malignancy worldwide.
- 1st most common in Saudi males.
- 2nd to lung cancer as a cause of cancer death
- 21,500 new cases, 8900 will die (2008)
- risk of CRC – women 1/16 , men 1/14.
- peek incidence in 7th decade but it can occur at any age.

[2] FAP: Defect in APC gene > grow thousands of polyps > increase risk of developing cancer at the age of 30 y.o.
[3] 95% of cases.
[4] common in rectal can be found by DRE
[5] more common in long standing ulcerative colitis.

Etiology of Colorectal Cancer:

Causes are pure molecular genetics but those are predisposing factors.



Risk Factors:

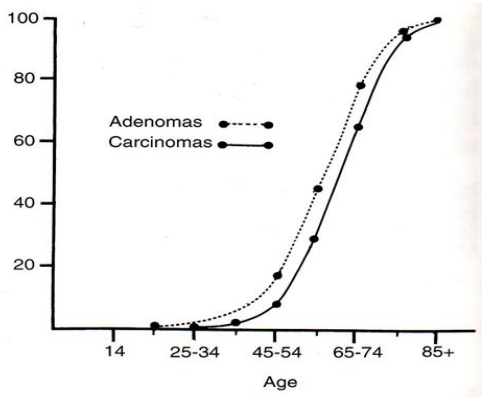
1. **Family history, Genetics**:
   - Previous personal history increases the risk of recurrence, Increasing in age & being a Male.
   - First degree family member history **doubles** the risk.
   - Hereditary colorectal cancer syndromes.

   Let's say a father diagnosed with CRC at 55 y.o, his son should be screened at 45 y.o for polyps since it proceeds CRC by 10 years, and keep screening every 5 years
2. Polyps
3. Inflammatory bowel disease
4. Others:
   - Diet and Nutrients "risk factor was high fat, red meat and low dietary ca and vit D deficiency" on the other side high fiber diet is a protective factor.
   - Smoking, ETOH alcohol
   - Lack of physical exercises.

Protective agents:
- Aspirin, NSAID
- Dietary Ca
- vit D supplement
- high fiber diet

This chart shows the effect of age on the incidence of colorectal cancer and colorectal Polyps

The incidence of colorectal cancer start peaking at 50 y.o, polyps proceed the incidence by 10 years.
So when I get a young pt. (25 y.o) complaining of bleeding per rectal it's most likely hemorrhoids, or other causes. We may get one case of colorectal of thousands in young patients.
But when I get 50 y.o patient with per rectal bleeding you immediately think of colorectal cancer even if you see hemorrhoids, do colonoscopy!



Why Screening is important?
- Common
- Treatable
- Preventable
- Cost effective

For whom?
- Average risk group (every 10 years starting from age 50 y.o)
- High risk group (IBD, Polyps, 1st degree relative history of CRC)

Colorectal Cancer Risk Based on Family History:

General population	6%
One 1st degree CRC	2-3X* (12-18%)
Two 1st degree CRC	3-4X*
One 1st degree CRC < 50 y	3-4 X*
One 2nd or 3rd CRC	1.5X
2 2nd degree CRC	2-3X*
1 first degree with polyp	2X*

Clinical presentation:

Sign & Symptoms	Presentation
Bleeding	gross, occult, anemia (37%)
Change in bowel habit	pain, diarrhea, constipation, alternating pattern Most common presentation: abdominal pain, bleeding per rectal, change in bowel habits (Diarrhea + Constipation), why? Narrowed lumen because of the tumor will cause constipation and the feces will build up pressure then diarrhea will result.
Obstruction	more common with left sided lesions most common cause of bowel obstruction in the elderly "mostly Sigmoid cancer"
Vague abdominal pain	"colicky"
Change in caliber of the stools	
Weight loss	
Abdominal mass	especially in right sided colon cancer
Tenesmus	over 50% occur with low rectal cancer
Asymptomatic	

Investigations:

Colon:

Hx > PEx (mass, cachexia, LN adenopathy) > CBC + CEA > Radiology CT CAP if contrast contraindicated do CXR, U/S > only do MRI if you find something in the liver.

Rectum:

Hx > PEx (mass, cachexia, LN adenopathy) > CBC + CEA > Radiology CT CAP if contrast contraindicated do CXR, U/S > must do MRI pelvis + endoscopy, why? To see invasion to give neoadjuvant before surgery to reduce local recurrence.

ليش ما اسوي MRI في الـ colon؟ لأني شايله شايله ما راح أعطي neoadjuvant اساسا!

1. General

- Complete history and physical examination (DRE)

  -Look for signs of advanced disease such as cachexia, ascites or jaundice.

  -Digital rectal exam > used to detect low cancer.

2. Endoscopic

- To identify primary & synchronous lesions by:
  - Flexible sigmoidoscopy
  - Colonoscopy used to: 1. Diagnose, 2. Take biopsy, 3. Exclude synchronous lesions.

3. Staging (more details below)

- Endorectal ultrasound (rectal cancer).
- Chest x-ray (metastases).
- Liver ultrasound (metastases).
- Abdominal CT scan (metastases).
- **CT CAP (chest, abdomen, pelvis) scan is the investigation of choice.**

  CT colonography used to:

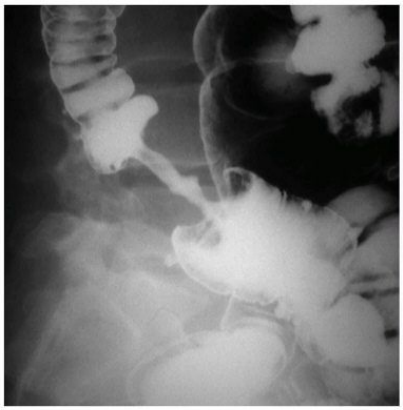
  1. Assess the local extent of the disease,
  2. Roll out Metastasis.

  (Colon or rectal cancer should undergo CT of the chest and abdomen and pelvis.)

4. Bloodwork

- CBC electrolytes.
- CEA - Carcinoembryonic antigen (tumour marker). Don't use CEA as screening as well as diagnostic. Use it only for monitoring the pt . CEA give us two things:

1. Idea about the prognosis (response to treatment). 2. Follow up every 3 months (check for recurrence)



Apple core lesion
By constriction of the lumen of the colon by a stenosing colorectal carcinoma

Colorectal Cancer Pathology

- Macroscopic: 2/3 **ulcerating**, other types are: polypoidal and stenosing
- Microscopic (differentiation):

  1-Well differentiated.

  2-Moderately differentiated.

  3-Poorly differentiated tumors have mucinous histology has a poor prognosis

- Lymph node involvement: via the portal blood to the liver or by transperitoneal seeding, low rectal tumours may involve the inguinal node

Treatment:

1st: Surgical therapy

- Surgery is the most important variable in the treatment of colorectal cancer.
- Radiation and chemotherapy alone cannot cure any stage of colorectal cancer.
- The site of tumour dictates the basic procedure.

Principles of Surgery

- Examine the entire abdomen.
- Remove the appropriate segment of the colon with adequate margins (5cm to the left of the tumor & another 5cm to the right in the draining Blood supply+adequate number of LN)
- Remove the corresponding lymph nodes

(Before surgery you can't determine LN infiltration. Thus you must resect 12 lymph nodes to make sure there is no infiltration and metastasis)[6] (important)

- Open vs laparoscopic approach[7].

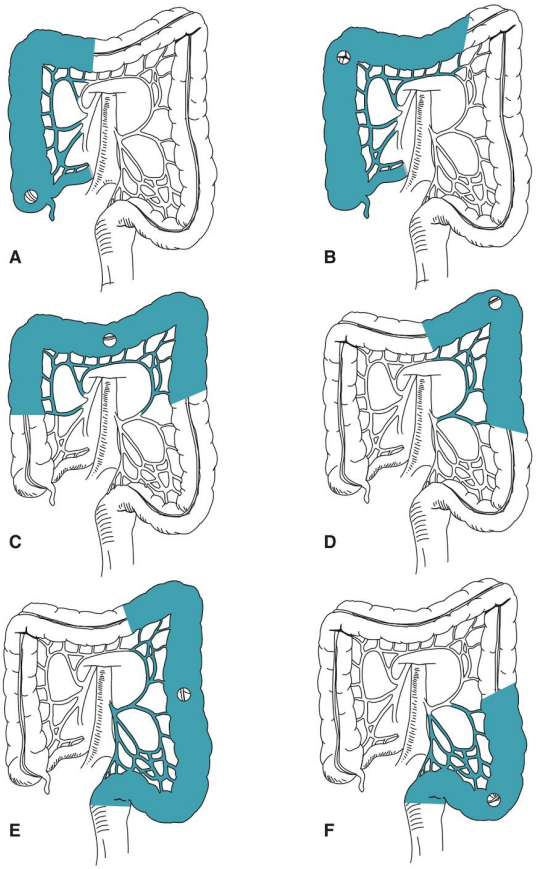


Figure 19–1. Resection of colon cancer. Right colectomy (**A**), right hemicolectomy with division of middle colic pedicle (**B**), transverse colectomy (**C**), resection of splenic flexure sparing left colic artery (**D**), left hemicolectomy (**E**), sigmoid colectomy sparing left colic artery (**F**). *(Reproduced, with permission, from Niederhuber JE, ed.* Fundamentals of Surgery. *Stamford, CT: Appleton & Lange; 1998:322 as modified from Schwartz SI, Ellis H.* Maingot's Abdominal Operations. *10th ed. Norwalk, CT: Appleton & Lange; 1989:1053.)*

- In resection we depend on blood supply

- Tumor in Right colon > Right hemicolectomy (all the ascending colon and part of transverse).

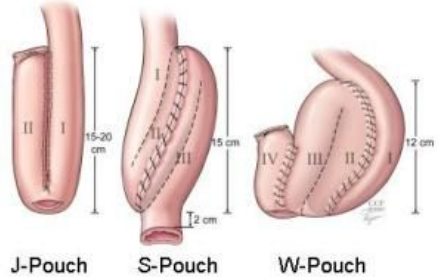
- Tumor in Left colon > Left hemicolectomy (all the Descending colon and part of transverse).

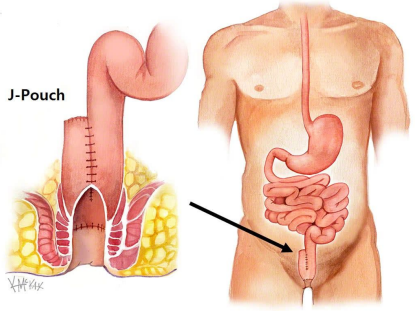
- Tumor in Transverse Colon > Extended Right or Left hemicolectomy.

- Tumor in the Rectum > Anterior resection (Sigmoidectomy).

- Tumor in Lower Rectum > Abdominoperineal resection (APR).

Surgery for rectal cancer:
is excision of the entire **mesorectum** by using **transanal endoscopic microsurgery** (TEM) colonic J pouch 'ileoanal" may formed to improve defecation functions. - surgical procedure called a total proctocolectomy and ileal **pouch** anal anastomosis (IPAA), the entire **colon** and rectum are removed. A reservoir is created from the distal small bowel (called the ileum), which is then joined to the anal canal.



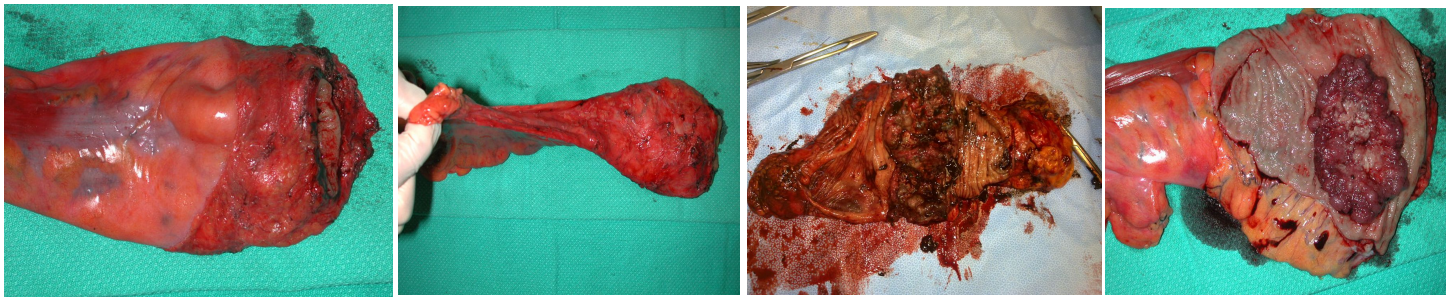


[6] Studies showed that if you get 12 LN and all of them were negative the chance of positive LN are less than 1%. If Some are positive or if you didn't get 12 LN you should give chemotherapy.
[7] Laparoscopic resections has shown some short-term benefits, less pain & shorter hospital stay (rapid recovery). However, there's no evidence of improved long-term outcomes over open surgery.

- Preparation for surgery :
    1. Patient: should be fasted prior to surgery.
    2. Comorbidity: should be addressed.
    3. Pre-operative: Give broad spectrum antibiotic.
    4. Thromboprophylaxis: “LMWH “ to reduce risk of DVT and PE.

- Emergency colorectal resection:

  In case of **perforation** or **obstruction** of colorectal cancer.



2nd: Follow Up

- Office visit every 3 months for two years then every 6 months for 3 years (total 5 years).
- Regular blood work (**CEA**). (when CEA starts to increase we should do colonoscopy & CT to check for recurrence)
- Colonoscopy: to check for recurrence: after 1 year of surgery, then after 3 years (4th year), then every 5 years.
- CT scan every year.

Who Gets Additional Treatment?

1. **COLON:**
    - All **stage 3 patients** (positive nodes) - **chemotherapy.**
    - **High risk stage 2** patients[8]
2. **RECTUM:**
    - All **stage 2 and stage 3** patients should get **radiation and chemo**

[8] **who are high risk stage 2 ?** مهم
- poorly differentiated
- perineural/ perivascular invasion,
- inadequate retrieval of LN during resection
- obstruction/ perforation

TNM staging system imp :

T stage: How far into the wall has it grown?	
Tis[9]	invasion of mucosa only
T1	Invasion of submucosa
T2	Invasion of muscularis propria
T3	Full thickness (Serosa) in case of colon cancer. Perirectal fat and adjacent organs (as T4) in rectal cancer
T4	Invasion into adjacent organs
N stage: How many lymph nodes have been involved?	
N0	No lymph nodes involvement
N1	1-3 lymph nodes
N2	>3 lymph nodes
N3	distant lymph nodes
M stage: Are there distant organ metastasis?	
M0	No distant organ mets
M1	Distant organ (liver, lung)

*Very important (don't mix Tumor stage with TNM)

Based on the TNM classification, we have 4 stages of Colorectal Cancer:		5 Year Survival chance
Stage 0	Tis Tumors	
Stage 1	T1 and T2 tumors (No nodes nor mets)	90%
Stage 2	T3 and T4 tumors (No nodes nor mets) / ^T3N0 tumors	80%^
Stage 3	Any lymph node involvement (+ve node/s with any T) * (depends on number of nodes involved)	27-69%*
Stage 4	Distant metastases (+ve mets with any T)	8%

In colon cancer we should use:

- Chemotherapy in Stage 3 & 4 .
- Chemotherapy in Stage 2 if: poorly differentiated, perineural invasion, perforated sigmoid cancer .

Keep in mind:
Tis - Invades BM
T1 - Submucosa
T2 - Muscularis Propria
T3 - Serosa
T4 - Adjacent organs
* T4 in colon = T3 in rectum
Rectum has no Serosa.

[9] Carcinoma in situ

Polyps: "Extra from Davidson"

Colorectal adenoma	
Type	solitary neoplastic
What is it?	classified as tubular, tubulovillous or villous adenomas
Chance of Malignancy	Villous adenomas has 30% chance of malignancy. tubular adenoma is around 10%. Multiple adenomas are 24%.
Diagnosis	The majority are asymptomatic, but symptoms include rectal bleeding or large bowel colic, polyp may prolapse through the anus, Patients with giant villous adenoma of the rectum may present with severe watery diarrhea which lead to hypokalemia
Management	Colonoscopic polypectomy. Follow up: colonoscopy is recommended after 6–12 months and 2–3 year.
Familial adenomatous polyposis	
Type	multiple neoplastic
What is it?	inherited as an autosomal dominant trait.It's single gene disorders. the gene responsible is APC, which is located on the long arm of ch.5
Chance of Malignancy	Adenomatous polyps usually develop during teenage years and early adulthood, with > 90% chance of colorectal cancer
Diagnosis	Clinicopathological diagnosis: requires the presence of > 100 adenomatous polyps of the large bowel established by sigmoidoscopy biopsy. Gene analysis
Management	Prophylactic surgical resection of the large bowel is indicated for familial adenomatous polyposis
Juvenile polyposis syndrome	
Type	Multiple non-neoplastic
What is it?	Autosomal dominant genetic disorder
Diagnosis	Causal mutations of the SMAD4 or BMPR1A/ALK3 genes
Metaplastic associated polyposis	
Type	Multiple non-neoplastic
What is it?	autosomal recessive
Chance of Malignancy	very high risk
Diagnosis	Histologically, has a sawtooth pattern
Management	Prophylactic colectomy and ileorectal anastomosis

Recall:

What is the lifetime risk of colorectal cancer?
6%
What is the incidence of rectal cancer?
Comprises 20% to 30% of all colorectal cancer
What Other risk factors for colorectal cancer?
Family history is important when taking history: FAP, Lynch's syndrome⇒ HNPCC Hereditary NonPolyposis Colon Cancer—autosomal dominant inheritance of high risk or development of colon cancer.
What signs/symptoms are associated with the following conditions:

Right sided lesions	Left sided lesions
Right side of bowel has a large luminal diameter, so a tumor may attain a large size before causing problems. Microcytic anemia, occult/melena more than hematochezia(left sided) PR, postprandial discomfort, fatigue	Left side of bowel has smaller lumen and semisolid contents. Change in bowel habits (small caliber stools), colicky pain, signs of obstruction, abdominal mass, heme(+) or gross red blood. Nausea, vomiting, constipation.

What unique diagnostic test is helpful in patients with rectal Cancer?
Endorectal ultrasound (probe is placed transanally and depth of invasion and nodes are evaluated).
What are the signs/ symptoms of rectal cancer?
Most common symptom is hematochezia (passage of red blood stool) or mucus; also tenesmus, feeling of incomplete evacuation of stool (because of the mass), and rectal mass.
What disease does microcytic anemia signify until proven otherwise in a man or postmenopausal woman?
Colon cancer.
What are the current recommendations for colorectal cancer screening if there is a history of colorectal cancer in a first degree relative less than 60 years old?
Colonoscopy at age 40, or 10 years before the age at diagnosis of the youngest first degree relative, and every 5 years thereafter.
What are the white lines of Toldt?
Lateral peritoneal reflections of the ascending and descending colon.
What is the blood supply to the rectum:

Arteries	Veins
Proximal: Superior hemorrhoidal (or superior rectal) from the IMA. **Middle:** Middle hemorrhoidal (or middle rectal) from the hypogastric (internal iliac). **Distal:** Inferior hemorrhoidal (or inferior rectal) from the pudendal artery (a branch of the hypogastric artery).	**Proximal:** Via the IMV to the splenic vein, then to the portal vein. **Middle:** Via the iliac vein to the IVC. **Distal:** Via the iliac vein to the IVC.

What parts of the GI tract do not have a serosa?
Esophagus, middle and distal rectum.
How are they anatomically classified?
Sessile (flat), Pedunculated (on a stalk)
What are the histologic classifications of the following types:
Inflammatory (pseudopolyp): As in Crohn's disease or ulcerative colitis
Hamartomatous: Normal tissue in abnormal configuration
Hyperplastic: Benign - normal cells - no malignant potential
Neoplastic: Proliferation of undifferentiated cells; premalignant or malignant cells.

MCQs (extra)

Taken from *Case Files Surgery*

1) Which of the following patients has the highest risk of developing colorectal cancer?

A. A 45-year-old man whose younger brother has a history of colon cancer.

B. A 30-year-old woman with a BRCA1 mutation .

C. A 55-year-old man with a 15-year history of ulcerative colitis .

D. A 50-year-old man with a history of resected adenomatous colonic polyps.

E. A 44-year-old man with FAP syndrome (polyposis coli).

2) Which of the following is the most appropriate treatment for a 40-year-old man with a T3 N1 carcinoma of the cecum?

A. Preoperative chemoradiation therapy followed by right hemicolectomy.

B. Right hemicolectomy and postoperative chemotherapy with 5-FU, leucovorin, and oxaliplatin.

C. Endoscopic removal of the tumor followed by chemoradiation therapy.

D. Right hemicolectomy and postoperative tamoxifen therapy.

E. Definitive treatment with six cycles of FOLFOX and remove the colon only if the patients develops symptoms.

3) Which of the following is the most appropriate follow-up for a 60-year-old man who underwent a colonoscopy and complete endoscopic removal of a 2-cm adenomatous polyp from the sigmoid colon?

A. Annual colonoscopy.

B. Repeated colonoscopy at 3 years and, if the results are negative, repeated every 5 years.

C. CT scan and repeated colonoscopy at 3 years and, if the results are negative, repeated every 5 years.

D. Repeated colonoscopy every 2 years.

E. Examine the stool for occult blood every 6 months.

4)A 58-year-old woman with a history of stage III colon cancer that was treated with primary colectomy and adjuvant FOLFOX therapy develops a rise in serum CEA and is found on CT scan to have a 2-cm localized lesion in the greater omentum. Biopsy of the lesion reveals metastatic carcinoma. Which of the following is the most appropriate treatment?

A. Radiation therapy .

B. Operative resection of the mass.

C. Additional systemic chemotherapy.

D. Immunotherapy.

E. Completion colectomy and omentectomy.

Answer key:
1 (E) | 2 (B) | 3 (B) | 4 (C)

Not convinced? Check out the next page :)

Q_1: E.
BRCA1 does not confer an increased risk of colon cancer, whereas BRCA2 does. The other conditions are associated with increased risks of developing colorectal cancer, but a patient with FAP syndrome (the colon is filled with thousands of polyps) has nearly a 100% risk of developing colon cancer.

Q_2: B.
Right hemicolectomy with postoperative adjuvant chemotherapy using FOLFOX4 (5-FU, leucovorin, and oxaliplatin) is indicated for this patient with stage III colon cancer. Radiation therapy is generally indicated for patients with rectal carcinoma. Tamoxifen therapy is not useful for colorectal carcinoma. Definitive systemic treatment for colorectal cancer without surgery is indicated only in patients with relative asymptomatic stage IV disease.

Q_3: B.
The current recommendations for colonic polyp follow-up are as follows: Once the colon is cleared of polyps, repeated colonoscopy at 3 years and, if the results are negative, repeated colonoscopy every 5 years. A CT scan is not recommended for the follow-up of patients with polyps. Occult blood screening has not been shown to be an effective strategy for the early identification of colorectal cancers.

Q_4: C.
This patient has an intraperitoneal recurrence that signifies stage IV disease. Local or radical resections of intraperitoneal recurrences generally do not improve survival and should be done only to palliate significant symptoms. Additional systemic chemotherapy or targeted molecular therapies could be considered at this time. Alternatively, the patient can be observed for disease progression and treated if the tumor grows.