

430 SURGERY TEAM



Colorectal Cancer

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Green: Doctor's notes & explanation during the lecture.

Blue: Further explanation & team's notes.

Red: important notes.

Definitions:

- Colon = large bowel = large intestine
- Rectum - terminal portion of the colon
- Polyp: is a descriptive term used to describe any mass of tissue that bulges or projects outwards. Colonic polyps are mostly benign outgrowths.
- Adenoma - type of polyp and has chance to develop cancer but not all.
- Cancer - malignant growth; invasive (invades the basement membrane)
- Stage is an estimate to determine how large has the tumor grown.
- Primary - the original tumor, where it started.
- Metastases - where the tumor has spread to.

Colon and Rectum Anatomy and Cancer significance:

-The management and the characteristics of colon and rectal cancers are completely different

Cancer Development:

- Most cancers are acquired (sporadic), but some small percentage of cases arise from inherited diseases.
- Most cancers begin as adenomatous polyps, **however only a tiny percentage of adenomas become cancers (1 – 9% become malignant)**

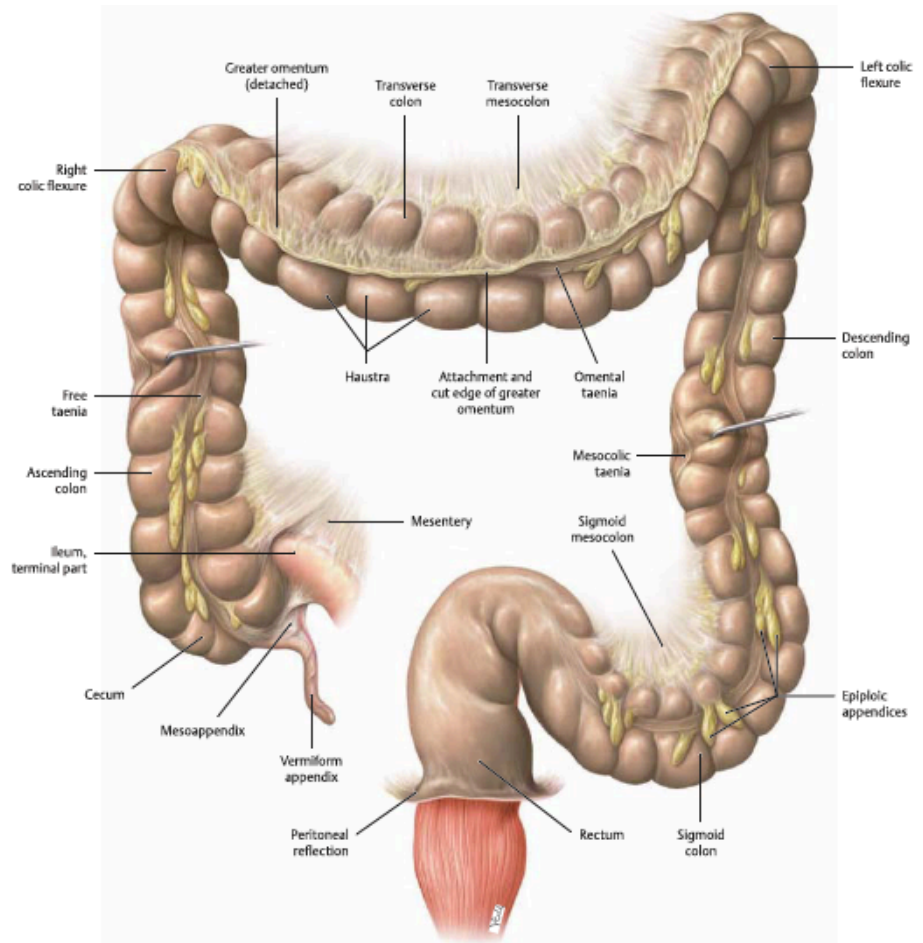
Polyps:

• *Non-neoplastic polyps:*

- The majority of polyps are non-neoplastic accounting for more than 90% of polyps. These arise as a result of inflammation or improper maturation. These include:
 - Hyperplastic polyps (most commonly seen)
 - Hamartomatous polyps (Juvenile & Peutz-Jeghers polyps)
 - Inflammatory polyps
 - Lymphoid polyps

• *Neoplastic polyps:*

- Account for less 10% of polyps and these are dysplastic polyps that have malignant potential.
- Adenoma



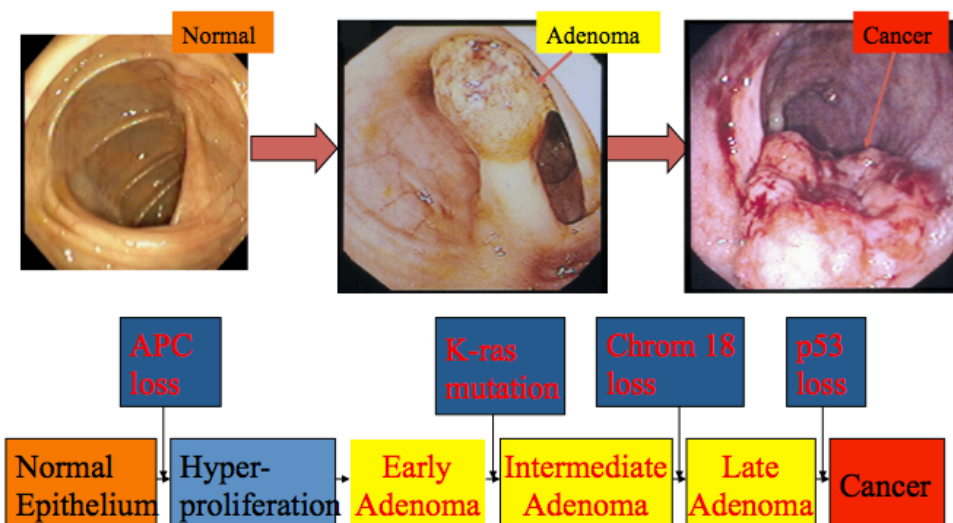
Adenomatous Polyp (adenoma):

- Occur mainly in large bowel.
- Sporadic and familial
- Vary from small pedunculated to large sessile.
- Epithelium proliferation and **dysplasia**
- Divided into:
 1. Tubular adenoma: less than 25% villous architecture
 2. Villous adenoma villous architecture over 50%
 3. Tubulovillous adenoma: villous architecture between 25 and 50%.

Cancer Sequence:

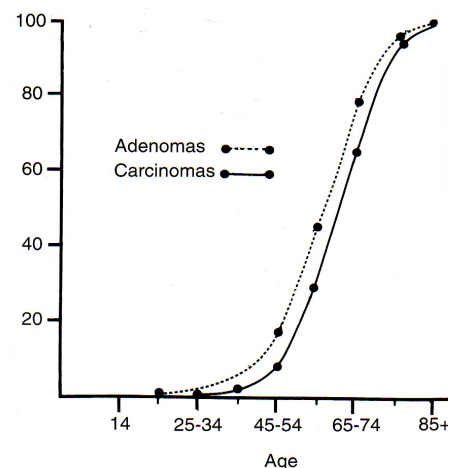
- The process from benign polyp to cancer takes from 7 - 10 years
- The transformation risk into cancer is based on:
 - Size of polyp
 - the histologic subtype of the polyp. They are organized in descending order for cancer development risk: Villus, Tubulovillous, Tubular polyps
 - Severity of epithelial dysplasia
 - Number of polyps, with multiple polyps holding a greater risk of developing cancer
- The transformation from normal mucosa to cancer undergoes some important steps as the following:

Adenoma to Carcinoma Pathway



The Effect of Age on the Incidence of Colorectal Cancer and Colorectal Polyps:

- As seen on the graph, the incidence of CRC increases tremendously after the age of 50.
- Colonoscopy is advised to be performed at the age of 50 for people with no significant risk factors, and younger than that if the person has individual risk factors.
- Colonoscopy can detect and remove adenomas and thus prevent cancer occurrence.



Classification of Colorectal Carcinoma:

1. Adenocarcinoma (>95%)
2. Carcinoid
3. Lymphoma
4. Sarcoma
5. Squamous cell carcinoma

Epidemiology of CRC:

- 3th most common malignancy worldwide.
- Most common in Saudi males.
- Second 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
- Mean age of diagnosis was 60 according to the

Risk Factors:

1. Medical and Family history:
 - A. Hereditary colorectal cancer syndromes: **this group of syndromes include hereditary non-polyposis colorectal cancer (HNPCC) syndrome and Familial adenomatous polyposis (FAP). In typical FAP, numerous colonic adenomas appear during childhood. Symptoms appear at a very early age and colonic cancer occurs in 90 percent of untreated individuals by age 45. These patients will have to undergo prophylactic colectomy.**
 - B. Personal history: previous polyps (**relative risk of 3.5 to 6**), occurrence of previous CRC (**relative risk of 2 in the first two years**)
 - C. Family history: first-degree family member doubles risk. Further detail to follow. **When a member of the family diagnosed with colorectal cancer, it is recommended to screen them at 10 years younger from their relative's diagnosis.**
2. Inflammatory bowel disease (**mainly for cases of disease that extensively involve the colon and pancolitis, these conditions hold a relative risk of around 2.6 – 2.8**)
3. Other: Diet, nutrients, smoking, alcohol consumption

Colorectal Cancer Risk Based on Family History:

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

Clinical presentation:

1. Bleeding (melena/hematochezia) - gross, occult, anemia: Hematochezia is more often caused by rectal than colon cancer. Iron deficiency anemia from unrecognized blood loss is more common with right sided CRCs and is frequently associated with a delayed diagnostic evaluation.
2. Change in bowel habit – pain, diarrhea, constipation, alternating pattern
3. Abdominal pains: partial obstruction, peritoneal dissemination, or intestinal perforation leading to generalized peritonitis.

4. Obstruction – more common with left sided lesions, because fecal contents are liquid in the proximal colon and the lumen caliber is larger, and they are therefore less likely to be associated with obstructive symptoms. CRC is most common cause of bowel obstruction in the elderly.
5. Change in caliber of the stools
6. Weight loss
7. Abdominal mass
8. Asymptomatic.

Some symptoms give clues on the location of the tumor:

- Sigmoid colon: obstruction and change in bowel habits.
- Rectum: bleeding and tenesmus
- Cecum: pain and melena
- Metastasis: weight loss.

Note:

- Symptoms of CRC are typically due to growth of the tumor into the lumen or adjacent structures. As a result, symptomatic presentation is often a manifestation of relatively advanced CRC.
- In a series of Meta analyses: the previous first three symptoms were the most common upon presentation.
- Sensitivity of individual symptoms for the diagnosis of CRC was poor, but Dr.AIKhayal mentioned it in the lecture and I thought I should add it.

Investigations:

- A. General: Complete history and physical examination including a DRE
- B. Endoscopic: (identify primary, synchronous lesions)

Synchronous lesions: defined as two or more distinct primary tumors separated by normal bowel and not due to direct extension or metastasis. In other words: two or more cancers occurring at the same time.

- Flexible sigmoidoscopy
- Colonoscopy “to roll out other lesions”: it is the most accurate diagnostic test in symptomatic individuals, since it can localize and biopsy lesions throughout the large bowel, detect synchronous neoplasms, and remove polyps.

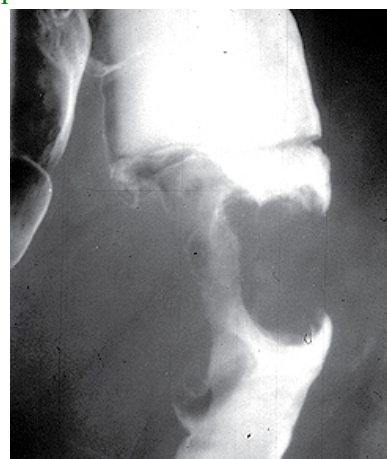
- **Staging:**

- o Endorectal ultrasound (rectal cancer)
- o Chest x-ray (metastases)
- o Liver ultrasound (metastases)
- o Abdominal CT scan (metastases)

Note: when colorectal cancer is diagnosed, it is practically protocol to perform CT scans of the chest, abdomen, and pelvis to detect or rule out any metastasis.

Extra notes:

- CRC can spread by lymphatic and hematogenous dissemination, as well as by contiguous and transperitoneal routes.
- The most common metastatic sites are the regional lymph nodes, liver, lungs, and peritoneum.
- Because the venous drainage of the intestinal tract is via the portal system, the first site of hematogenous dissemination is usually liver, followed by lungs, bone, and many other sites, including brain.
- tumors arising in the distal rectum may metastasize initially to the lungs because the inferior rectal vein drains into the inferior vena cava rather than into the portal venous system.



Double contrast barium enema shows an apple-core lesion surrounding the lumen of the descending colon.

- Bloodwork
 - o CBC, electrolytes, and other function tests
 - o CEA (CarcinoEmbryonic Antigen) is protein molecule known that is produced in high levels by CRC cells.
 - o It is not a specific marker, and can be elevated in many benign conditions like smoking! and other malignant cases like pancreatic cancer; therefore, can never be used as a screening test.
 - o However, CEA maybe used as a prognostic factor for evaluation of CRC management.

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 tumor dictates the basic procedure

Treatment indications for different stages:

-Stage I and II: surgery

-High risk stage II and stage III: surgery + chemo/radiotherapy

-Stage IV: chemotherapy \pm Surgery, depending on whether or not the tumor is resectable and on other factors.

Preoperative preparation:

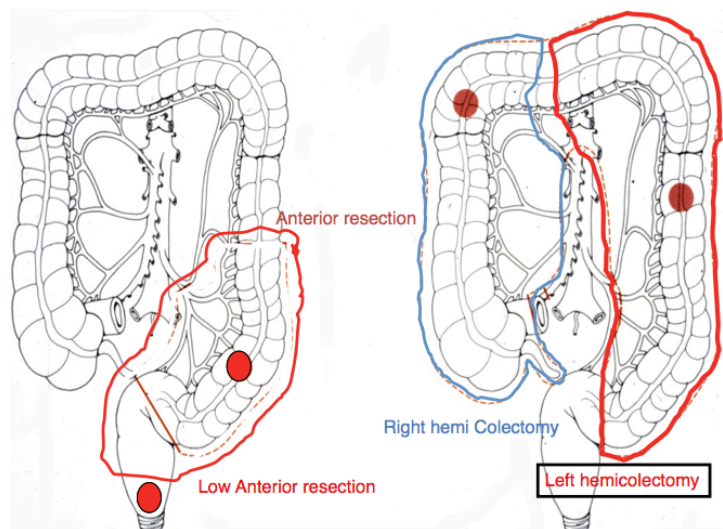
- Evaluation of medical problems. This is especially important with patients who have **cardiopulmonary disease**, as these patients must be evaluated by concerned specialists.
- Mechanical bowel preparation (bowel cleansing by laxatives)
 - Colyte, Oral fleet
- IV antibiotics
- DVT prevention
 - Heparin shots
 - Compression stockings
- Foley catheter
- Epidural catheter

Principles of Surgery:

- Examine the entire abdomen
- Remove the appropriate segment of the colon with adequate margins
- Remove the corresponding lymph nodes: **a minimum of 12 lymph nodes have to be removed in a proper colectomy.**
- Open vs laparoscopic approach

Ostomy insertion:

- The intestine is brought out through a hole in the abdominal wall
- Colostomy (colon on the skin)
- Permanent when the rectum is removed
- Temporary when it is unsafe to make a join



- Ileostomy (ileum on the skin)
- Temporary when the join needs time to heal

Recovery:

- Surgery 2 to 4 hours
- Hospital stay 4 to 10 days
- IV, urine catheter, compression stockings, intravenous pain killers, blood thinner
- Discharge when ambulating, eating, bowel function, good pain control
- Recovery 4 weeks

Follow up:

- Office visit every 3 months for two years then every 6 months for 3 years
- Regular blood work (CEA)
- Colonoscopy at year 1 and 4 and every 5 years
- CT scan yearly

Some points on CEA:

- CEA used to detect the prognosis: higher CEA levels indicate a worse prognosis.
- It is used to detect recurrence: (CEA levels are usually around 2.5 – 5 ng/ml).
- If CEA was 50 then after surgery it becomes 5 then after some time it raised to 50 again. Here we suspect recurrence.
- If CEA was 100 and after a surgery it is still 100 it can indicate 2 things A) There is another mass, i.e. metastasis and it hasn't been removed or B) the initial mass was not excised properly.

Staging: (very important)

Staging of CRC is now achieved with the TNM classification and not the modified Duke classification, as studies have shown that the 2010 modification of the TNM classification had better results.

1. How far into the wall has it grown?

T stage:

- Tis – invasion of mucosa only
- T1 – Invasion of submucosa
- T2 – Invasion of muscularis propria
- T3 – Full thickness/perirectal fat
- T4 – Invasion into adjacent organs.
- Take note that adjacent organs does not mean distant metastasis, as that is a different component in the score. Adjacent organs mean structures like: the urinary bladder, uterus, and even the abdominal wall.

2. Is it growing in other places?

N stage: lymph node involvement, M stage: presence of metastasis

- N1 – 1-3 lymph nodes
- N2 - >4 lymph nodes
- N3 – distant lymph nodes
- M1 – Distant organ (mostly to the liver, lung)

TNM staging:

- Stage 0 – Tis tumors

Invasion of mucosa

- Stage 1 – T1 and T2 tumors

Invasion of sub mucosa & muscularis propria

- Stage 2 – T3 and T4 tumors

Invasion of full thickness & adjacent organ

- **Stage 3 – Any lymph node involvement**
- Stage 4 – Distant metastases

Who gets additional therapy?

- COLON
 - All stage 3 patients (positive nodes) - chemotherapy
 - High risk stage 2 patients. **These patients include: Cancers with the mucinous subtype, patients with bowel obstructions; perforation, and who have undergone resection with less than 12 resected nodes.**
- RECTUM
 - All stage 2 and stage 3 patients should get radiation and chemo
 - Note: in the rectum there are no serosa layer so the stage 2 receive chemotherapy

Survival and TNM staging:

<u>STAGE</u>	<u>5-Year Survival</u>
1	90%
2	80%^
3	27-69%*
4	8%

^for T3N0 tumors

*depends on # of nodes involved

Summary:

1. Common Cancer
2. Can be prevented through screening and resection of polyps
3. Surgery is the primary treatment
4. Slow but steady improvement in survival

MCQs:

1) How should a patient who had Dukes C colon cancer two years previously be followed for recurrence of liver metastasis?

- A. liver enzymes
- B. CEA
- C. U/S
- D. CT
- E. Radionuclide imaging

2) An 80-year-old man is admitted to the hospital complaining of nausea, abdominal pain, distention, and diarrhea. A cautiously performed transanal contrast study reveals an “apple core” configuration in the rectosigmoid. Appropriate management at this time would include:

- A. Colonoscopic decompression and rectal tube placement
- B. Saline enemas and digital disimpaction of fecal matter from the rectum

- C. Colon resection and proximal colostomy
- D. Oral administration of metronidazole and checking a *Clostridium difficile* titer
- E. Evaluation of an electrocardiogram and obtaining an angiogram to evaluate for colonic mesenteric ischemia

3) Correct statements regarding carcinoembryonic antigen (CEA) and colorectal tumors include which of the following?

- a. Elevated CEA is indicative of a tumor of gastrointestinal origin
- b. A low CEA level after resection of a colon tumor is a poor marker of disease control
- c. Ninety percent of colorectal tumors produce CEA
- d. There is a high likelihood of liver involvement if the CEA level is high (greater than 100 ng/mL)
- e. CEA levels are unusually low in cigarette smokers

4) A definite increased risk of colon cancer is associated with:

- A. Diet high in fiber.
- B. Diet low in animal fat and protein.
- C. Diet low in fiber.
- D. Ulcerative Colitis
- E. Prior cholecystectomy.

5) A 52 year-old female diagnosed to have sigmoid cancer invading the uterus with no evidence of metastasis based on CT scan and colonoscopy, she underwent sigmoidectomy and hysterectomy, the histopathology report revealed invasive moderately differentiated adenocarcinoma involving the entire bowel wall and invading the myometrium, perinural and lymphovascular invasion, 6 out of 15 lymph nodes were positive for metastasis. The TNM classification for this patient will be:

- A. T3 N1 M0
- B. T3 N2 M1
- C. T4 N2 M0
- D. T4 N2 M1

6) For the above patient, she recovered well from surgery and visited you in clinic. The action that should be taken at this stage is?

- A. Referral to medical oncology for adjuvant chemotherapy
- B. Referral to radiation oncology for adjuvant radiotherapy
- C. Referral to medical radiation oncology for both chemo-radiation
- D. Referral to medical oncology for surveillance only

7) A 39 year-old male presented to the clinic for medical checkup because of significant family history of colon cancer, detailed family history revealed that three of his second degree relatives were diagnosed with colon cancer at age of 50, you counseled him for screening because:

- A. He as average risk
- B. He as double risk
- C. He has 5 times greater risk
- D. He has 10 times greater risk

8) Which one of the following factors is most likely to be associated with development of colorectal cancer?

- A. Increase Calcium intake
- B. Increase fat intake
- C. Smoking
- D. History of Colonic polyps

Answer key: (1.B) (2.C) (3.D) (4.D) (5.C) (6.C) (7.) (8.D)

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