

# Colorectal cancer



## Objectives:

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

Lecturer: Dr.khayal alkhayal

Same as 436's lecture: yes

 Team leaders: Alanoud Almansour, Ghaida Al Musma , Muath Alhamoud and Mohammed Alquwayfli

 Done by: Raman mishal , Durrah alhamidi , Naser Alrashan , Tareq Alomaim and khalid Alshehri

 Revised by: Yazeed Al-Dossare

## Color Index:

● Important

● Doctor's Notes

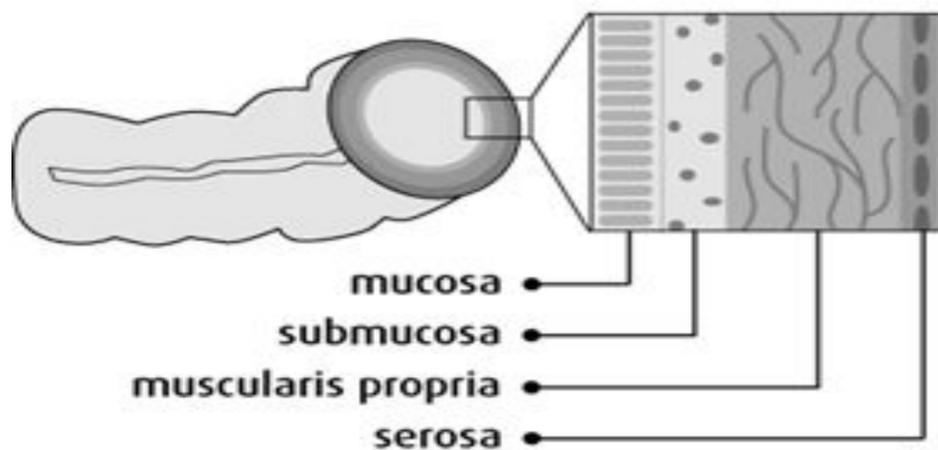
● Extra

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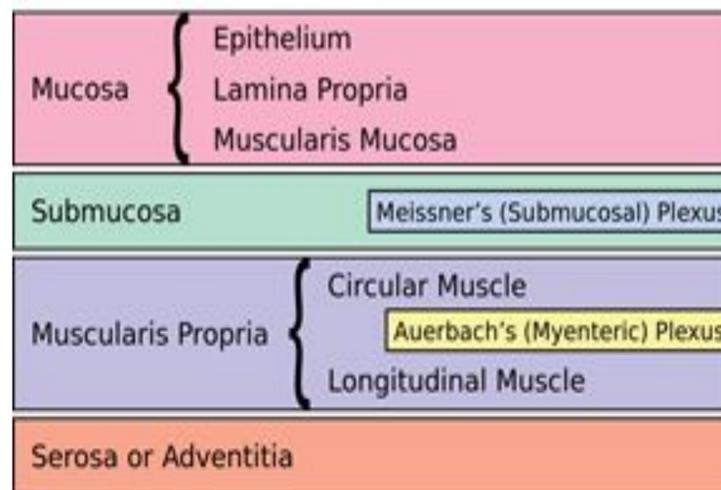
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# Basic review:



\*serosa is not found on most of the rectum



In the rectum the last layer is mesorectal fat (**no serosa**), so that's why in case of rectal cancer we give radiation because of the high local recurrence.

- So, T3 of the colon = T4 of the rectum
- Basement membrane = 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. 150cm, Functions: 1.excretion 2.water absorption.
  - Rectum: the terminal portion of the colon. 15cm, Function: 1.storage.
  - 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 1-2% chance. however most of the colon cancers arise from polyps

- Cancer: malignant growth (invasive).
- Stage: where the cancer is growing.
- 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 .

# 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 .
- 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) .
- Hereditary mutation of the APC gene is the cause of familial adenomatous polyposis (FAP), where affected individuals carry an almost 100% risk of developing colon cancer by age 40 years.
- What I want you to know about HNPCC that it's inherited colorectal cancer secondary to DNA mismatch gene repair.

## Polyp - Cancer Sequence:

- The process from benign polyp to cancer takes from **7 - 10 years** .
- The transformation into cancer is based on:
  1. The **type** of polyp **Adenomatous "sessile growth, and villous histology.**
  2. **Size** of polyp **>2cm**
  3. **Multiple** polyps = greater risk of cancer.

- Adenomatous Polyp risk > other types

- Villous type of adenomatous Polyp carries greater risk than tubular and tubulovillous.

- Sessile polyp (directly adhere to the wall of bowel) > Pedunculated polyp (has a stick)

**Future therapy:** block one of those steps by gene therapy .

**Removing polyps prevents cancer:** Colonoscopy. Screen with colonoscopy at 50 y of age if normal repeat after 10 y because cancer will develop after 10 y.

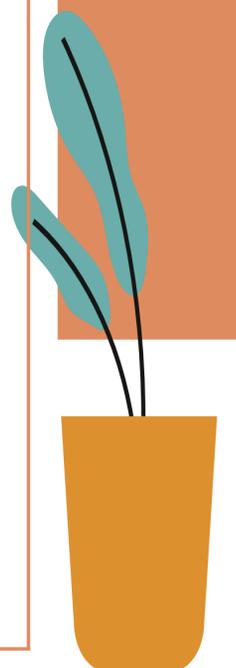
## Colorectal Carcinoma:

### Classification:

- Adenocarcinoma (95% of cases). ● Carcinoid ● Lymphoma ● Sarcoma ● Squamous cell carcinoma. **"more common in long standing ulcerative colitis"**

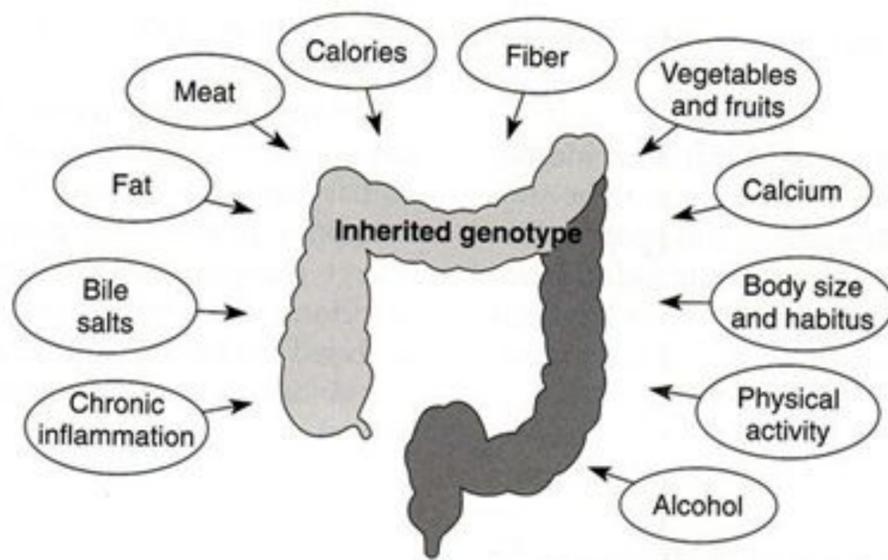
## Epidemiology:

- 3 th most common malignancy worldwide.
- **1 st 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.
- peak incidence in 7 th decade but it can occur at any age .



## 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. **Age and gender**
- 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
- Smoking , ETOH

### 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

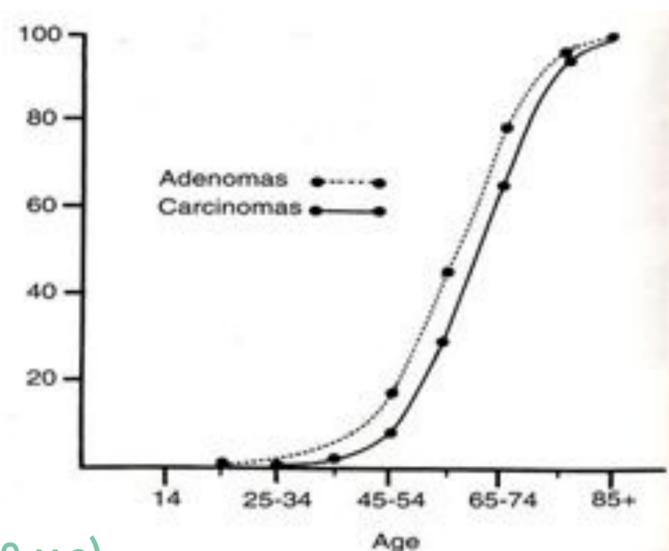
- The incidence of colorectal cancer start peaking at 50 y.o, polyps proceed the incidence by 10 years. So when I get a young pt. (25 y.o) complaining of bleeding per rectal it's most likely hemorrhoids, or other causes. We may get one case of colorectal of thousands in young patients. But when I get 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%
<u>One 1st degree CRC</u>	<u>2-3X* (12-18%)</u>
Two 1st degree CRC	3-4X*(18-24%)
One 1st degree CRC < 50 y	3-4 X*
One 2nd or 3rd CRC	1.5X(9%)
<u>2 2nd degree CRC</u>	<u>2-3X*</u>
1 first degree with polyp	2X*(12%)

## Clinical presentation:

Sign & Symptoms	Presentation
<b>Bleeding</b> Per rectum	gross, occult, <b>anemia</b> (37%) "mainly in right colon cancer"
Change in bowel habit	pain, diarrhea, constipation, alternating pattern "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".
<b>Obstruction</b>	more common with left sided lesions <b>most common cause of bowel obstruction in the elderly. Mostly sigmoid cancer,</b> (sigmoid is the narrowest portion of colon)
Vague abdominal pain	colicky in nature
Change in caliber of the stools	
Weight loss	
Abdominal mass	are especially in right sided colon cancer
<b>Asymptomatic</b>	

# Investigations:

## 1. General

- Complete history and physical examination (DRE)

## 2. Endoscopic

- To identify primary & synchronous lesions by:
  - Flexible sigmoidoscopy
  - Colonoscopy: **used to: 1-Diagnoses 2-take biopsy 3-exclude synchronous lesions**

## 3. Staging

- 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: **of used to :**
  - 1-assess the local extent of the disease
  - 2-roll out metastasis

## 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 gives two things:**
  - 1. Follow up (check for the recurrence) 2- idea about the prognosis



**Apple core lesion** \*AKA shouldering sign  
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): **grading**
  - 1-Well differentiated.
  - 2-Moderately differentiated.
  - 3-Poorly differentiated tumors have mucinous histology has a poor prognosis
- Lymph node involvement: **for staging**

# 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 according to the doctor it's **not that important** to know the principles

- Examine the entire abdomen **To make sure there is no metastasis.**

- 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**

- Open vs laparoscopic approach<sup>7</sup>

**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 sigmoid > Anterior resection**

- **Tumor in the Rectum > lower anterior resection (Sigmoidectomy).**

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

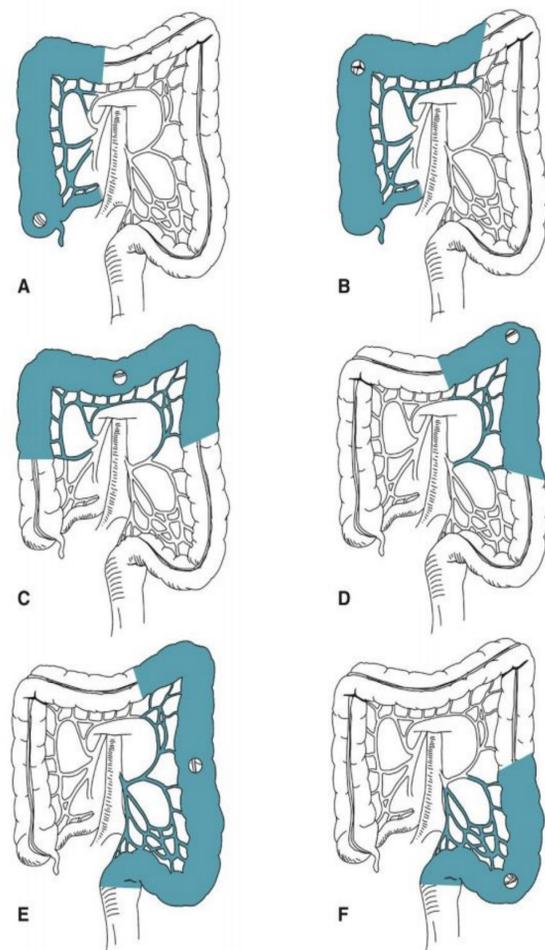
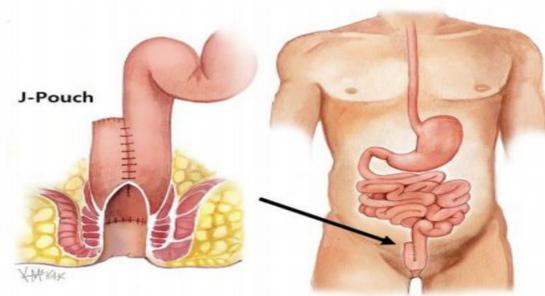
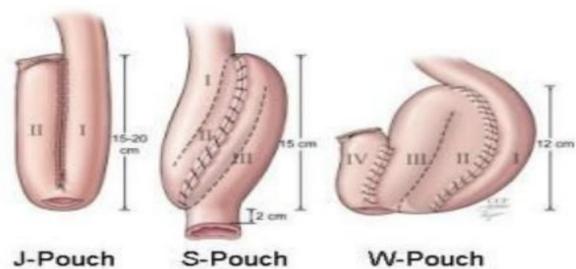


Figure 19-1. Resection of colon cancer. Right colectomy (A), right hemicolectomy with division of middle colic pedicle (B), transverse colectomy (C), resection of splenic flexure sparing left colic artery (D), left hemicolectomy (E), sigmoid colectomy sparing left colic artery (F). (Reproduced, with 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.)

<sup>7</sup>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.

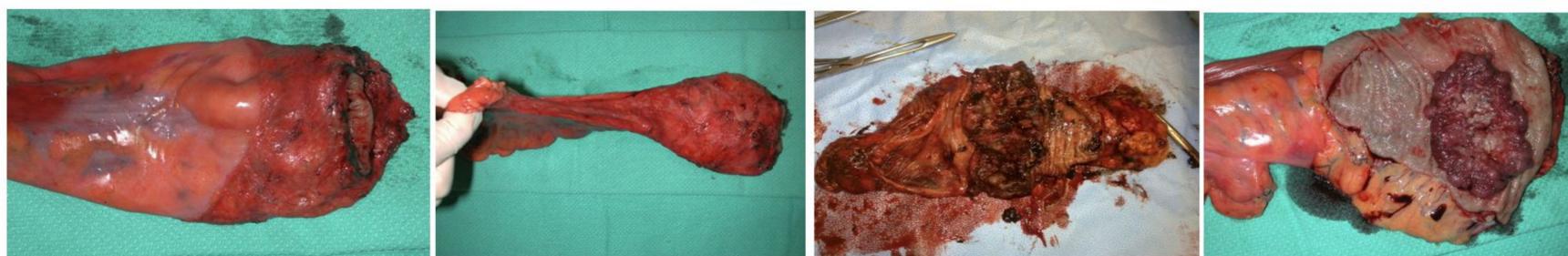


### Preparation for surgery :

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:

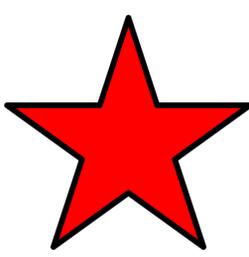
- All stage 3 patients (positive nodes) - chemotherapy.
- High risk stage 2 patients (9)

### 2. RECTUM:

- All stage 2 and stage 3 patients should get radiation Before surgery and chemo

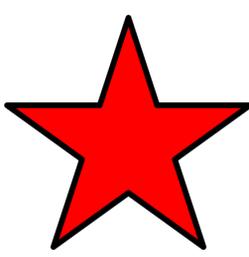
<sup>9</sup>who are high risk stage 2 ? • poorly differentiated • perineural/ perivascular invasion,  
 • inadequate retrieval of LN during resection. **Less than 12** • obstruction/ perforation

Difference between staging and grading: Grading -> under microscopy is it poor or well differentiated. staging-> position of the tumor is it metastasize to the liver or lymph node ..etc.



## TNM staging system :

T stage: How far into the wall has it grown? tumor growth "depth"	
Tis Carcinoma in situ	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 (Bladder)
N stage: How many lymph nodes have been involved?	
N0	No lymph nodes involvement
N1	1-3 lymph nodes
N2	>3 lymph nodes 4 and more
N3	distant lymph nodes
M stage: Are there distant organ metastasis?	
M0	No distant organ mets
M1	Distant organ (liver, lung)



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.**

# 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. 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	
<b>Type</b>	Multiple non-neoplastic
<b>What is it</b>	autosomal recessive
<b>Chance of malignancy</b>	very high risk
<b>Diagnosis</b>	Histologically, has a sawtooth pattern
<b>Management</b>	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.

Right sided lesions	Left sided lesions
<p>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</p>	<p>Left side of bowel has smaller lumen and semisolid contents.</p> <p>Change in bowel habits (small caliber stools), colicky pain, signs of obstruction, abdominal mass, heme(+) or gross red blood.</p> <p>Nausea, vomiting, constipation.</p>

**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 Toltd?**  
 Lateral peritoneal reflections of the ascending and descending colon.

**What is the blood supply to the rectum:**

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

**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.

# Summary

## Colorectal Cancer

### 1. Classification

1. Adenocarcinoma 2. Carcinoid 3. Lymphoma  
4. Sarcoma 5. Squamous cell carcinoma

### 2. Etiology

**Causes are pure molecular genetics but those are predisposing factors:**  
1. Meat 2. chronic inflammation 3. Bile salt 4. fat 5. calories 6. Fibers  
7. vegetables & fruits 8. calcium 9. Alcohol 10. physical activity 11. body size and habitus.

### 3. Risk Factors

1. Family history, Genetics 2. Polyps 3. Inflammatory bowel disease  
4. smoking & alcohol 5. Diet and Nutrients

### 4. Clinical presentation

1. Bleeding 2. Change in bowel habit 3. Obstruction  
4. Vague abdominal pain 5. Abdominal mass

### 5. Investigations

1. **General** "history physical examination"  
2. **Endoscopic** "To identify primary & synchronous lesions"  
3. **Staging**  
4. **Blood work** "CBC & CEA"

### 6. Treatment

**1st: Surgical therapy:**  
**A. Remove the appropriate segment of the colon with adequate margins**  
B. Remove the corresponding lymph nodes  
C. In resection we depend on blood supply  
D. Open vs laparoscopic approach  
**2nd: Follow Up:**  
1. Office visit every 3 months for two years then every 6 months for 3 years (total 5 years)  
2. Regular blood work (CEA)  
3. Colonoscopy CT scan every year

### TNM staging system:

	(is)	(0)	(1)	(2)	(3)	(4)
<b>N</b>	-----	No lymph nodes involvement	1-3 lymph nodes	>3 lymph nodes	distant lymph nodes	-----
<b>M</b>	-----	No distant organ mets	Distant organ (liver, lung)	-----	-----	-----
<b>T</b>	Invasion of mucosa only	-----	Invasion of submucosa	Invasion of muscularis propria	Full thickness (Serosa) in case of colon cancer. Perirectal fat and adjacent organs (asT4) in rectal cancer	Invasion into adjacent organs

**Based on the TNM classification, we have 4 stages of Colorectal Cancer:**

Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
Tis Tumors	T1 and T2 tumors (No nodes nor mets)	T3 and T4 tumors (No nodes nor mets) / ^T3N0 tumors	Any lymph node involvement (+ve node/s with any T) (depends on number of nodes involved)	Distant metastases (+ve mets with any T)

**Apple core appearance is Adenomatous polyp**

# Questions

Q1: Patient came with colon cancer what is the first thing you do

- A- Staging
- B- Endoscopy
- C- Blood work
- D- Start treatment

Q2: On histology the rectum is lack of which of the following

- A- Mucosa
- B- Sub mucosa
- C- Muscularis Propria
- D- Serosa

Q3: Which of the following carries the highest risk of transforming to colon cancer?

- A- Villous adenomatous polyp.
- B- Tubular adenomatous polyp.
- C- Tubulovillous adenomatous polyp.
- D- Inflammatory polyp.

Q4: Regarding to colon cancer staging, which of the following is correct?

- A- N3 indicates more than 3 lymph nodes are positives.
- B- T4 indicates metastasis to distant organs.
- C- N0 indicates less than 3 lymph nodes are positives.
- D- N3 indicates distant lymph node involvement.

Q5: A 58-year-old male was diagnosed to have colon cancer and went for colectomy. Unfortunately, the surgeon could not excise more than 9 lymph nodes. The Histopathologist reported that all lymph nodes are free of cancerous cells. Which of the following is your next step in managing this patient?

- A- Assure the patient and ask him for annual checkup.
- B- Ask the patient to comeback after 6 months to do CT.
- C- Re-operate and try to excise more lymph nodes.
- D- Give the patient prophylactic chemotherapy.

Answers

1-A

2-D

3-A

4-D

5-D