Lectures 6 & 7
Colonic Tumors & Polyp

PATHOLOGY TEAM 435

{ ومن لم يذق مرّ التعلُّمِ ساعةً.. تجرع ذلَّ الجهل طوال حياتهِ }

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Red: Important. Grey: Extra Notes Doctors Notes will be in text boxes

Objectives:

A. Know the classification of intestinal tumors (small intestine and colon)
B. Know the definition of a polyp.
C. Compare adenomatous polyps and hyperplastic polyps with respect to pathology (gross and microscopic features).
D. Know the three subtypes of adenomatous polyps, eg, tubular adenoma, villous adenoma, tubulovillous adenoma.
E. Describe the adenomatous polyp-cancer sequence and the features associated with risk of malignancy, eg, polyp size, histologic architecture, and severity of epithelial dysplasia.
F. Describe the classification of the hereditary syndromes involving the GI tract and the syndromes associated with an increased risk of cancer (Peutz-Jeghers syndrome, familial adenomatous polyposis, and hereditary nonpolyposis colorectal carcinoma)
G. Know common types of intestinal polyps
    A. Non-neoplastic polyps no dysplasia
        - *4 common types (hyperplastic, hamartomatous, inflammatory, lymphoid)*
    B. Neoplastic polyps there is dysplasia
        - *3 types (tubular, tubulovilous, villous)*

Colon cancer:

A. Describe the epidemiology of colon cancer.
B. Compare the pathology (gross and microscopic features) and clinical features of right-sided colonic adenocarcinoma and left-sided colorectal adenocarcinoma.
C. Describe the relationship between prognosis and the various stages of cancer of the colon and rectum as noted in the TNM (tumor-nodes-metastasis) classification and staging system.
D. Describe the relationship between carcinoembryonic antigen (CEA) and recurrence following resection of the primary tumor.
E. Mention the significant of carcinoid tumor and its features
H. Know the clinical presentation of left and right sided colon cancer, and the environmental factors that increase its risk
    C. Left colon: frank bleeding, obstruction
    D. Right colon: iron deficiency anaemia
    E. Tumor markers: CEA
I. Understand the pathogenesis of colon cancer
    F. Adenoma to Carcinoma Pathway
    G. Two genetic pathways APC/B-catenin and DNA mismatch repair genes
    H. Familial Polyposis Syndrome
J. Describe the Pathological features of colon cancer
    I. Adenocarcinoma most common: carcinoid tumor {neurosecretory granules}
    J. 70% are in the rectum and/or sigmoid
    K. Duke classification is used for staging

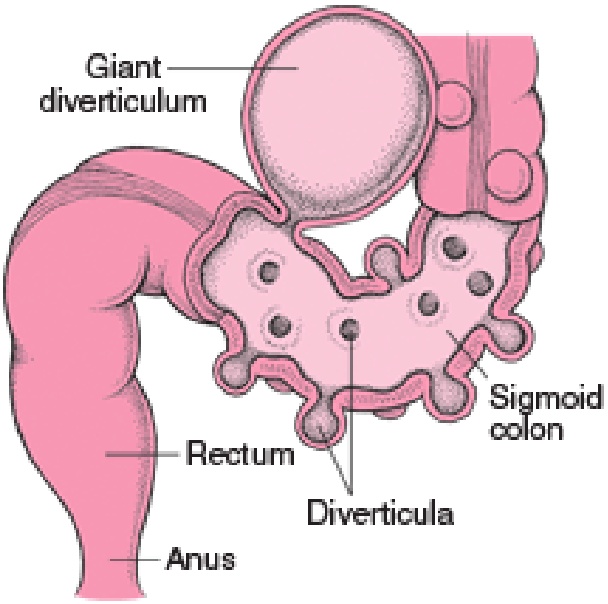
References: Lecture slides & Robbins

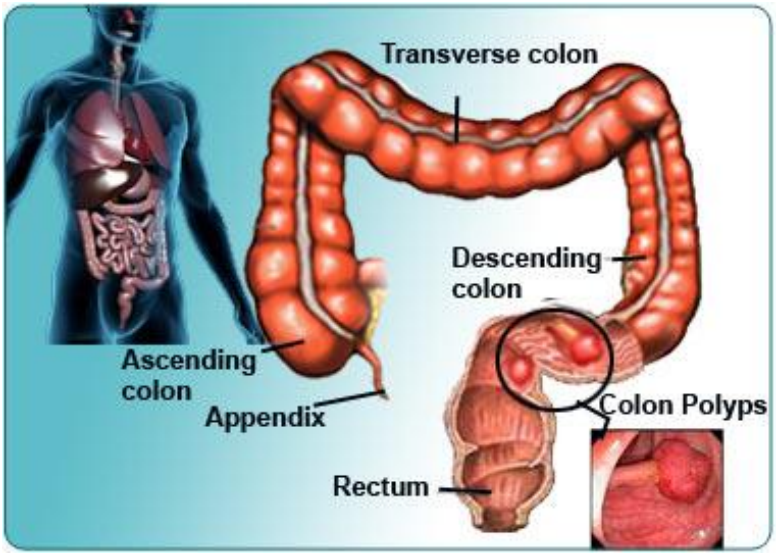
Tumors of the small and large intestines:

- Polyps
- Carcinoma
- Carcinoid tumor
- Lymphoma

- The majority of small and large intestine tumors appears as a polyp.
- Polyp: is protrusion or growth above the surface, which could be benign or malignant.
- If the polyp is big you can't discriminate from the morphology whether it's benign or malignant unless you examine it under the microscope, but if it's small like 2 mm it is benign.

Sigmoid Colon: Most common site of GI polyps, diverticula and cancer





The opposite of polyp is the diverticula which is out pouches in the wall of the colon, common in people who have chronic constipation, due to increased pressure on the wall and weakness of the muscle, but it's still lined by mucosa, & could lead to inflammation and sometimes to perforation, and it could be giant

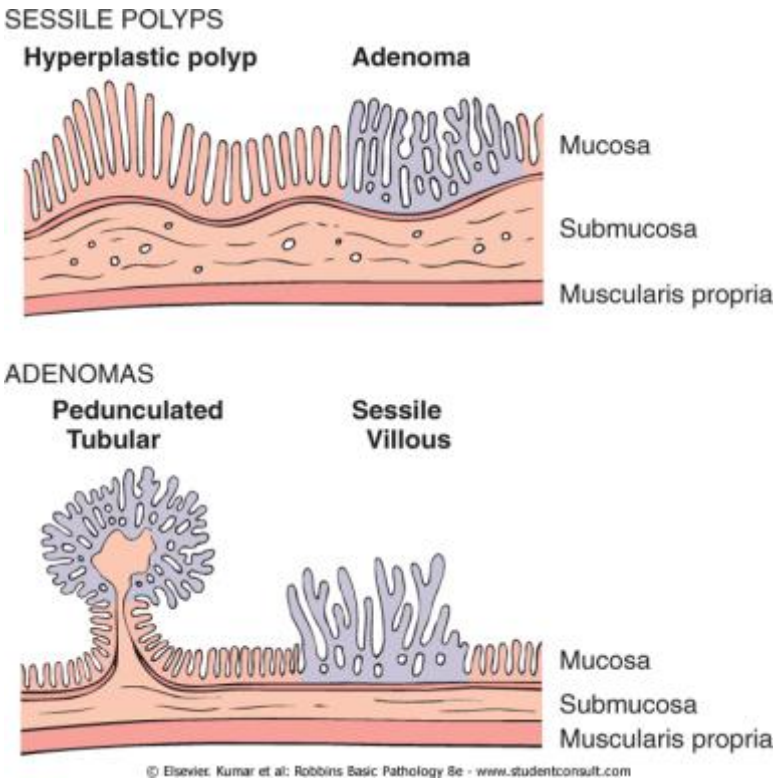
Introduction:

Polyps are most common in the colon but may occur in the esophagus, stomach, or small intestine. It has two types:

A. *Sessile:* without stalks, which is proliferation of cells adjacent to the polyp and the effects of traction on the luminal protrusion.

B. *Pedunculated:* may combine to create a stalk.

Sessile polyp usually has a wide base with finger like projections above the surface, appears velvety under the microscope.
Pedunculated polyp: like mushroom.

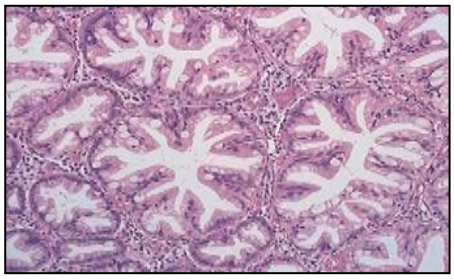


Polyps:

In general, intestinal polyps can be classified as neoplastic or non- neoplastic.

- Non-neoplastic polyps (90%)
  - Hyperplastic polyps
  - Hamartomatous polyps (Juvenile & Peutz-Jeghers polyps)
  - Inflammatory polyps
  - Lymphoid polyps
- Neoplastic polyps (10%)
  - Adenoma: The most common neoplastic polyp is the adenoma

The most common type that Dr. Maha saw in the clinic is the neoplastic one because they do not take biopsy from hyperplastic polyps.



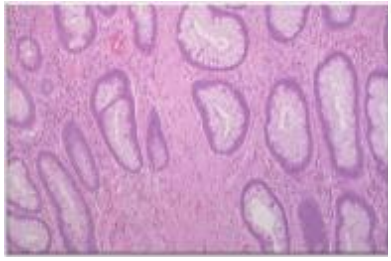
Hyperplastic Polyps:

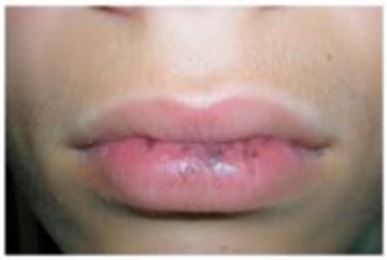
- Asymptomatic.
- > 50% are located in the **rectosigmoid.**
- **Sawtooth** surface.
- **Star shaped** crypts.
- Composed of well-formed glands and crypts lined by differentiated goblet or absorptive cells.

Hyperplastic polyp: no stalk, only increases the number of cells (goblet cells and enterocytes) in the lining epithelium (because of more mitosis and less apoptosis) without any premalignant changes (no dysplasia).
- The elongation of the crypts with the folds of cells gives the sawtooth appearance.
- It could be 2 or three but not polyposis (polyposis: more than a hundred polyps).

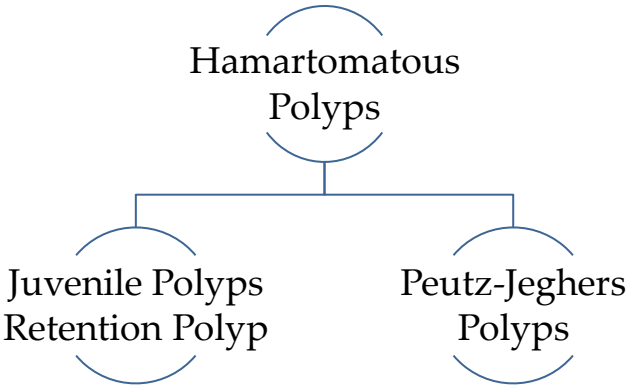
Hamartomatous polyps:

Hamartoma is a tumour composed of tissue elements normally found at that site of the organ, but which are growing in a disorganized mass. not a malignant tumor.





Hamartoma: normal tissue in disorganized manner, such as pulmonary hamartoma (usually it is congenital anomaly)



In addition to the dilated glands there is smooth muscles in the lamina propria which start to branch.
- That's why it's called hamartoma.

Juvenile Polyps (retention polyp)

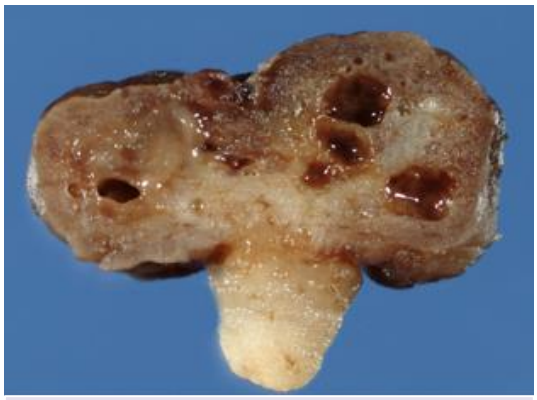
- Developmental malformations affecting the glands and lamina propria.
- Commonly occur in children under 5 years old in the rectum.
- In adult called retention polyp.
- No malignant potential.

- Could cause abdominal pain and rectal bleeding.
- Could lead to polyposis in the colon or stomach.
-Juvenile POLYPOSIS could lead to malignancies, notice not juvenile POLYPs!
- Cronkhite-Canada syndrome: it is related to auto immune disorders not mutations, the patients have high risk of rheumatoid arthritis and other autoimmune disorders.

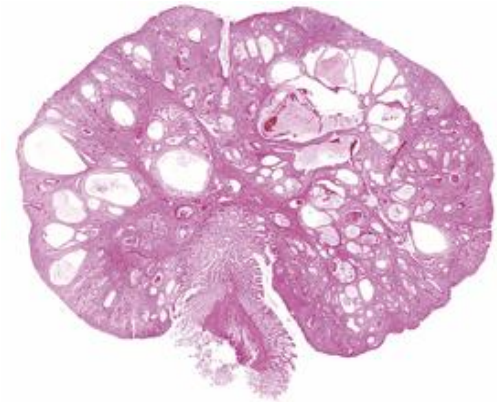
Peutz-Jeghers syndrome

- Rare, autosomal dominant
- Hamartomatous polyps accompanied by mucosal and cutaneous pigmentation around the lips, oral mucosa, face and genitalia, present with red blood in stool.
- On gross evaluation, Polyps tend to be large and pedunculated. with a lobulated contour
- Increased risk of developing carcinoma of the **pancreas, breast, lung, ovary and uterus**.

Patient requires CT screening every year
Important ↓
Mainly it's dilated glands + smooth muscles in the lamina propria, blood in stool, pigmentation in oral mucosa + gentile skin + face and lips.
Large pedunculated polyps
بما انها كبيرة ففيه خطر سرطان



Juvenile Polyps (retention polyp): Pedunculated polyp, the stroma is edematous with cystic dilatation.



Under the microscope you will see a dilated gland containing mucus, and surrounded by stroma, this stroma has inflammatory cells & the surface is slightly ulcerated

Smooth eroded surface with numerous mucus retention cysts, typical of sporadic juvenile polyps.

it's the normal tissue between two ulcers, it gets inflamed and projects like polyp so it's called pseudopolyps, there's a risk of cancer.

Inflammatory Polyps:

- Longstanding IBD, especially in **chronic ulcerative colitis**.
- Represent an exuberant reparative response to longstanding mucosal injury called **pseudopolyps.**

Multiple ulcers, in between these ulcers the mucosa is inflamed, edematous and protrudes so it appears like a polyp, so it's the normal tissue and surrounded by ulcers (pseudopolyps)

Lymphoid polyps:

It's a normal polyp

Stimulation and activation of Peyer's patch, lead to enlargement of it.

Adenomatous Polyp (adenoma): (Compare it with hyperplastic)

- Occur mainly in large bowel.
- Sporadic and familial.
- Vary from small pedunculated to large sessile.
- Epithelium proliferation and **dysplasia.**

Benign tumor, it's epithelium proliferation + Dysplasia (so important!!!)

Villous: (highest possibility of developing carcinoma).
Tubular: (lowest possibility of developing carcinoma)

Divided into:

- Sporadic (1 or 2 polyps especially in old age)
- Familial (> 500 polyps)

1. Tubular adenoma: less than 25% villous architecture

- Represents 75% of all neoplastic polyps.
- 75 % occur in the distal colon and rectum
- Sigmoid colon most common site.

Tubular adenoma has a smooth surface unlike the villous adenoma which has finger like projections.
In adenoma, you will see dysplasia (nuclear enlargement, hyperchromatism, pleomorphism and abnormal mitosis)

2. Villous adenoma: villous architecture over 50%

- The least common, largest and most ominous of epithelial polyps (most likely to undergo malignant transformation).
- Age: 60 to 65 years, 75% located in rectosigmoid area.
- Present with rectal bleeding or anemia, large ones may secrete copious amounts of mucoid material rich in protein and potassium.
- Large tumors can produce hypoalbuminemia and hypokalemia.

Thin core + dysplasia, finger like projection without stalk, least common but largest
وبما انها اكبر وحده فهي أخطر وحدة وممكن تسبب لنا سرطان .
we will see: Diarrhea, hypoalbuminemia and hypokalemia

3. Tubulovillous adenoma: villous architecture between 25 and 50%.

- 20%–30% of polyps
- Intermediate in size, degree of dysplasia and malignant potential between tubular and villous adenomas.

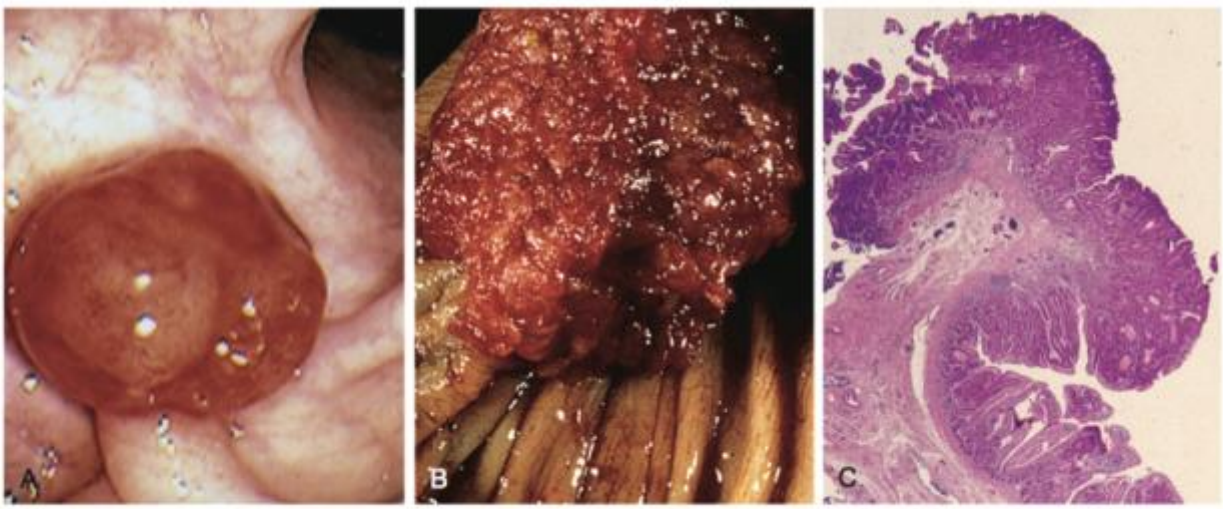
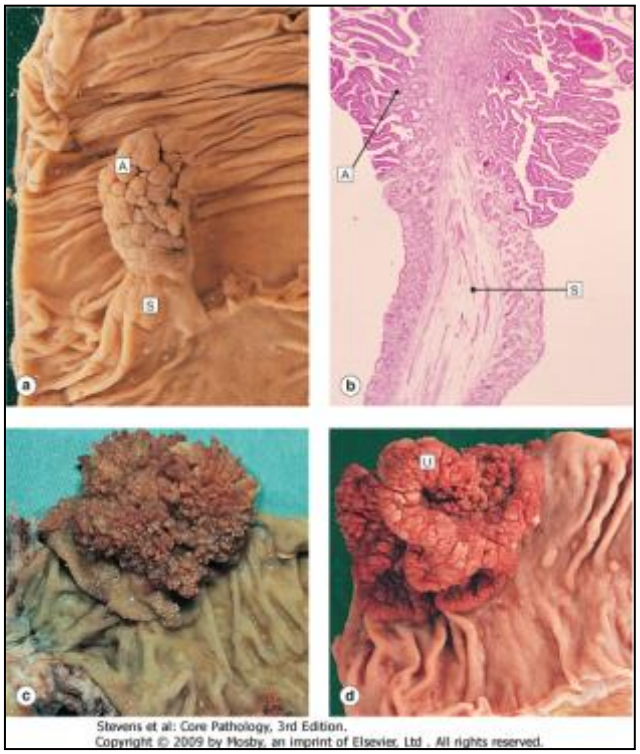
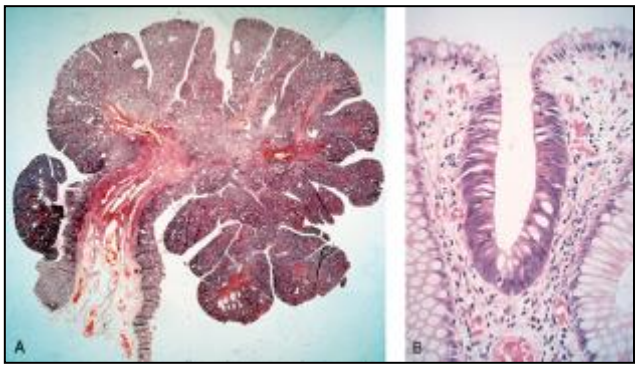


Figure 14–33 Colonic adenomas. **A,** Pedunculated adenoma (endoscopic view). **B,** Adenoma with a velvety surface. **C,** Low-magnification photomicrograph of a pedunculated tubular adenoma.



Tubulovillous adenoma



Tubular adenoma

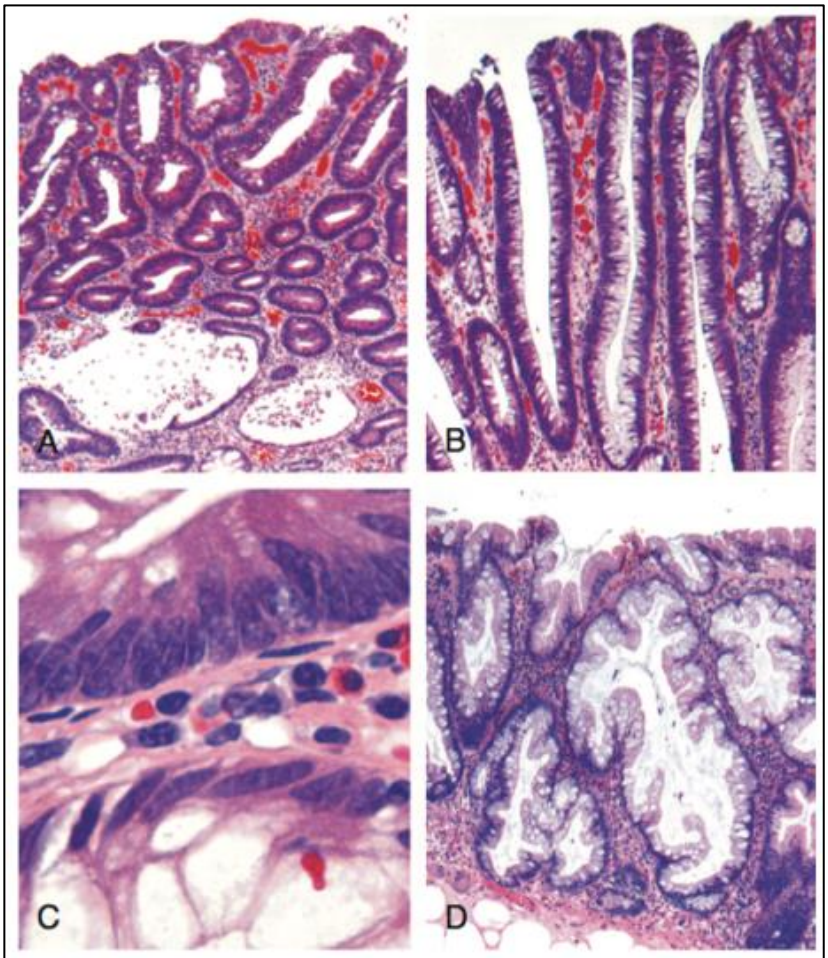
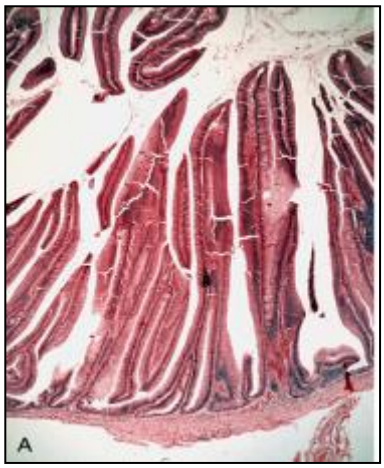
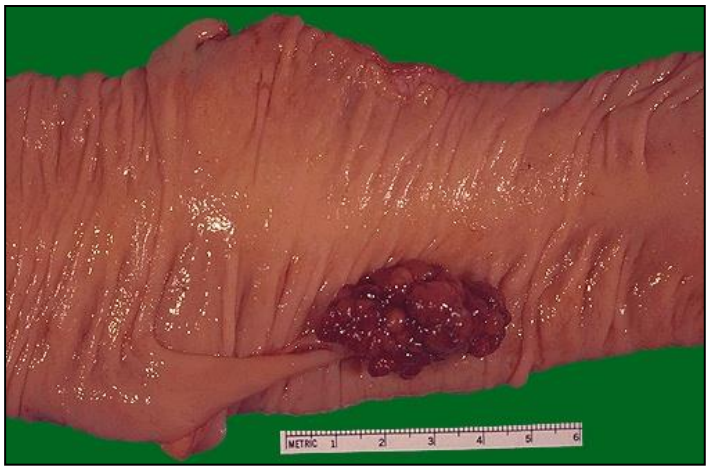


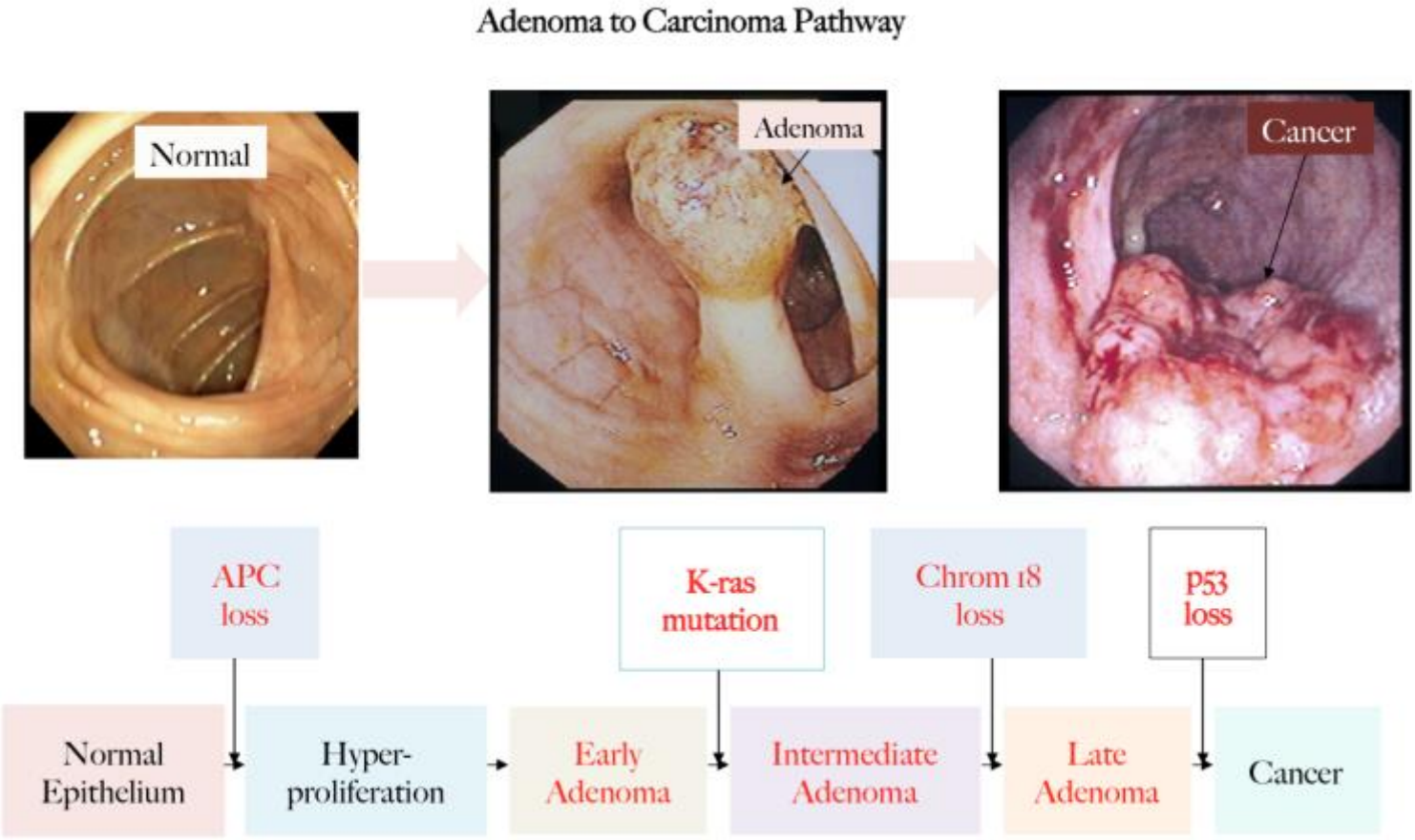
Figure 14–34 Histologic appearance of colonic adenomas. **A,** Tubular adenoma with a smooth surface and rounded glands. In this case, crypt dilation and rupture, with associated reactive inflammation, can be seen at the bottom of the field. **B,** Villous adenoma with long, slender projections that are reminiscent of small intestinal villi. **C,** Dysplastic epithelial cells (*top*) with an increased nuclear-to-cytoplasmic ratio, hyperchromatic and elongated nuclei, and nuclear pseudostratification. Compare with the nondysplastic epithelium below. **D,** Sessile serrated adenoma lined by goblet cells without typical cytologic features of dysplasia. This lesion is distinguished from a hyperplastic polyp by involvement of the crypts. Compare with the hyperplastic polyp in Figure 14–32.





Villous adenoma

Relationship of Neoplastic Polyps to Carcinoma: Very important (Memorize the genes) Adenoma to carcinoma sequence is documented by several genetic alterations.



Polyp removal leads to CRC prevention; Polyp is surrogate marker.

The probability of carcinoma occurring in a neoplastic polyp is related to:

- **The size of the polyp. Size is the most important characteristic that correlates with risk of malignancy.**
- The relative proportion of its villous features.
- The presence of significant cytologic atypia (dysplasia) in the neoplastic cells.
- Multiple polyps.
- Accumulation of genetic mutation.

Familial Polyposis Syndrome:

Patients have genetic tendencies to develop neoplastic polyps.

Familial polyposis coli (FPC):

A. Genetic defect of Adenomatous polyposis coli (*APC*).

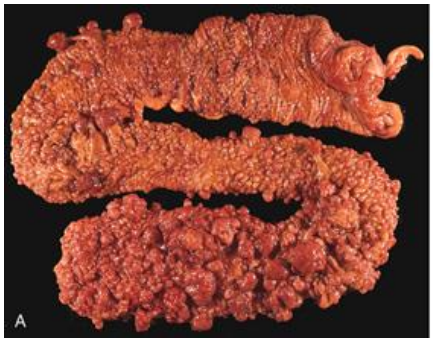
B. *APC* gene located on the long arm of chromosome 5 (5q21).

C. *APC* gene is a tumor suppressor gene.

D. Innumerable neoplastic polyps in **the colon** (Need ≥ 100 for diagnosis, 500 to 2500).

E. Polyps are also found elsewhere in alimentary tract

F. The risk of colorectal cancer is 100% by midlife.



Familial adenomatous polyposis (FAP) is an autosomal dominant disorder marked by the appearance of numerous **colorectal adenomas (will be discussed below)** by the teenage years. Except for their remarkable numbers, these growths are *morphologically indistinguishable from sporadic adenomas.* Colorectal adenocarcinoma develops in 100% of patients with untreated FAP, often before age 30. Thus, **prophylactic colectomy** is standard therapy for persons carrying *APC* mutations. However, patients remain at risk for *extraintestinal manifestations,* including neoplasia at other sites.

Usually they do for them prophylactic colectomy

Gardener's syndrome:

Polyposis coli, multiple osteomas, epidermal cysts, and fibromatosis.

Turcot syndrome: Polyposis coli, glioma and fibromatosis

After the removal of colon one of the complication is fibromatosis which is tumor of the fibrous tissue at the site of the surgery

Adenocarcinoma:

- Adenocarcinoma of the colon is the most common malignancy of the GI tract and is a major cause of morbidity and mortality worldwide.
- The small intestine, accounts for 75% of the overall length of the GI tract, is an uncommon site for benign and malignant tumors.
- It represents nearly 15% of all cancer-related deaths, second only to lung cancer.
- Constitutes 98% of all cancers in the large intestine.
- Incidence peaks at 60 to 70 years of age.
- Males are affected slightly more often than females.
- Most prevalent in the developed countries.

Predisposing factors

- **IBD, adenomas, polyposis syndrome.**
- **Diet appears to play an important role in the risk for colon cancer:**
  - Low fiber diet.
  - High fat content.
  - Alcohol.
  - Reduced intake of vit A, C & E.

Table 14–7 Common Patterns of Sporadic and Familial Colorectal Neoplasia

Etiology	Molecular Defect	Target Gene(s)	Transmission	Predominant Site(s)	Histology
Familial adenomatous polyposis (70% of FAP)	APC/WNT pathway	*APC*	Autosomal dominant	None	Tubular, villous; typical adenocarcinoma
Familial adenomatous polyposis (<10% of FAP)	DNA mismatch repair	*MUTYH*	None, recessive	None	Sessile serrated adenoma; mucinous adenocarcinoma
Hereditary nonpolyposis colorectal cancer	DNA mismatch repair	*MSH2, MLH1*	Autosomal dominant	Right side	Sessile serrated adenoma; mucinous adenocarcinoma
Sporadic colon cancer (80%)	APC/WNT pathway	*APC*	None	Left side	Tubular, villous; typical adenocarcinoma
Sporadic colon cancer (10% to 15%)	DNA mismatch repair	*MSH2, MLH1*	None	Right side	Sessile serrated adenoma; mucinous adenocarcinoma

Carcinogenesis

Two pathogenetically distinct pathways for the development of colon cancer, both seem to result from accumulation of multiple mutations:

The APC/β-catenin pathway (85%)

* Figure 14-36

- The classic adenocarcinoma sequence.
- Chromosomal instability that results in stepwise accumulation of mutations in a series of oncogenes and tumor suppressor genes.
- Account for **80% of sporadic colon tumors**.
- *TP53* → mutated later.
- Mutation in *APC* tumor suppressor gene → Early stage.

Beta catenin induces cancer
APC INHIBIT OR SUPRESS beta catenin

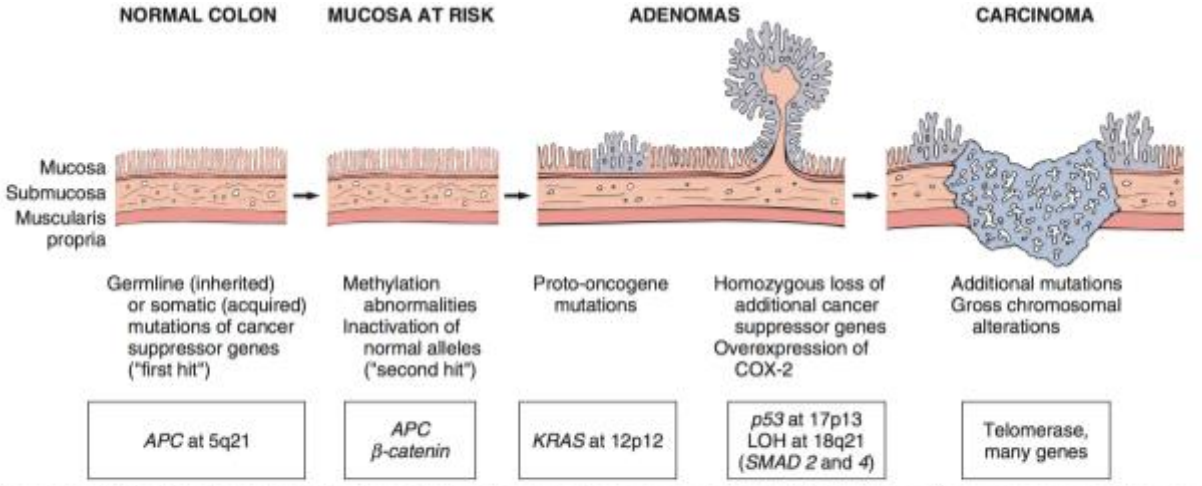


Figure 14–36 Morphologic and molecular changes in the adenoma-carcinoma sequence. It is postulated that loss of one normal copy of the tumor suppressor gene *APC* occurs early. Persons may be born with one mutant allele, making them extremely prone to the development of colon cancer, or inactivation of *APC* may occur later in life. This is the "first hit" according to Knudson's hypothesis. The loss of the intact copy of *APC* follows ("second hit"). Other mutations involving *KRAS*, *SMAD2*, and *SMAD4*, and the tumor suppressor gene *TP53*, lead to the emergence of carcinoma, in which additional mutations occur. Although there may be a preferred temporal sequence for these changes, it is the aggregate effect of the mutations, rather than their order of occurrence, that appears most critical.

The DNA mismatch repair genes pathway

- These are referred to as MSI (microsatellite instability) high, or MSI-H, tumors.
- Defect results in **microsatellite instability pathway**.
- **10% to 15% of sporadic cases**.
- There is accumulation of mutations (as in the *APC/B-catenin schema*)
- Five DNA mismatch repair genes (**MSH2, MSH6, MLH1,** PMS1 & PMS2)
- Give rise to the ***hereditary non-polyposis colon carcinoma (HNPCC) syndrome.***

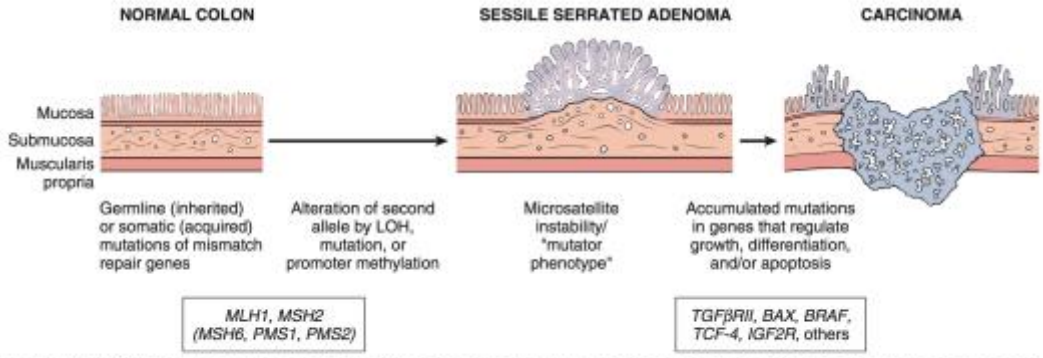


Figure 14–37 Morphologic and molecular changes in the mismatch repair pathway of colon carcinogenesis. Defects in mismatch repair genes result in microsatellite instability and permit accumulation of mutations in numerous genes. If these mutations affect genes involved in cell survival and proliferation, cancer may develop. LOH, loss of heterozygosity.

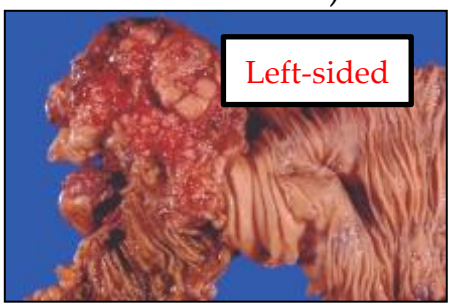
These genes check the DNA to repair any mutations, so if there's mutation in those genes we will have accumulation of mutations thus carcinoma could develop.
HNPCC وراثي لكن غير متعدد وممكن يسمى Lynch syndrome

Colorectal Carcinoma:

Hereditary mutation of the APC gene is the cause of familial adenomatous polyposis (FAP) is a major cause.

Morphology:

- 70% are in the rectum, rectosigmoid and sigmoid colon.
- Left-sided carcinomas tend to be annular, encircling lesions with early symptoms of **obstruction**.
- Right-sided carcinomas tend to grow as polypoid, fungating masses, obstruction is uncommon. (Mostly presents with anemia).



Colorectal carcinomas metastasize mainly to regional lymph nodes and liver, less commonly developing other systemic metastases such as brain, bone and lung.

- Mucinous adenocarcinoma secret abundant mucin that may dissect through cleavage planes in the wall.

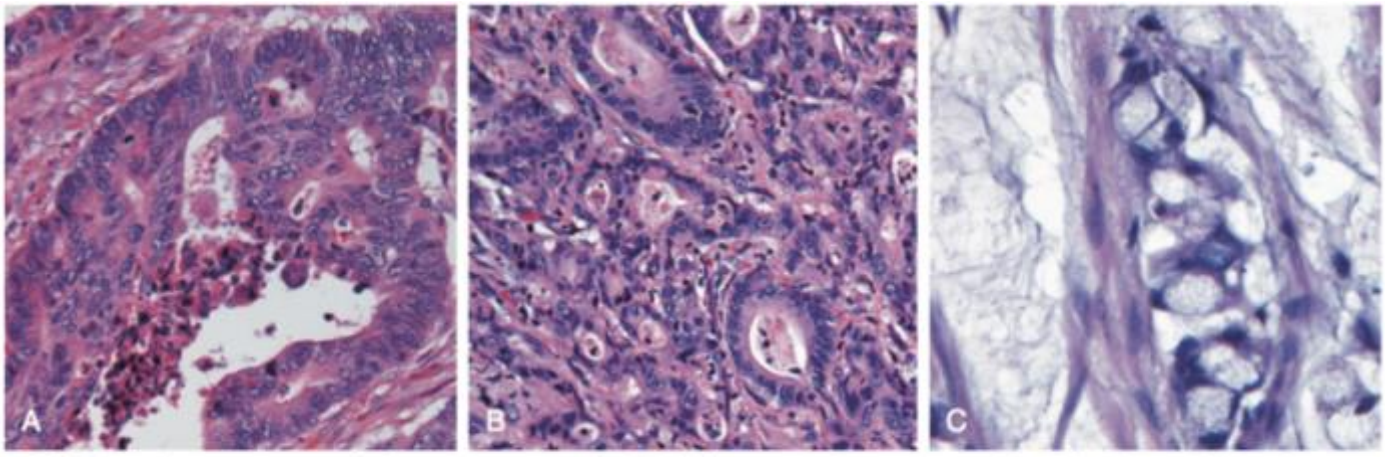


Figure 14–39 Histologic appearance of colorectal carcinoma. **A,** Well-differentiated adenocarcinoma. Note the elongated, hyperchromatic nuclei. Necrotic debris, present in the gland lumen, is typical. **B,** Poorly differentiated adenocarcinoma forms a few glands but is largely composed of infiltrating nests of tumor cells. **C,** Mucinous adenocarcinoma with signet ring cells and extracellular mucin pools.

We have to differentiate between each side:
Left: Fast, obstruct colon, severe colic pain, more invasive, annular encircling (يعني كل المحيط فيه سرطان وهذا أخطر) it will lead to constriction + obstruction
Right: ulcers, bleeding (black stool), iron deficiency & better prognosis than left side

Signs and symptoms:

- If located closer to the anus: change in bowel habit, feeling of incomplete defecation, PR bleeding.
- A tumor that is large enough to fill the entire lumen of the bowel may cause bowel obstruction.
- Right-sided lesions are more likely to bleed while left-sided tumors are usually detected later and could present with bowel obstruction.
- Serum levels of carcinoembryonic antigen (CEA) are related to tumor size and extent of spread. They are helpful in monitoring for recurrence of tumor after resection.

TNM Staging of Colon Cancers is used for staging:

Duke classification is used for staging.

Tumor markers:

A **tumor marker** is a substance found in the blood, urine or body tissues that can be elevated in cancer, among other tissue types.

- Carcinoembryonic antigen **(CEA) & Carbohydrate antigen (CA19-9)** are **Useful to assess disease recurrence (late stage)**
- **Elevated in:**

CEA	Some **non-neoplastic** conditions like ulcerative colitis pancreatitis, cirrhosis COPD, Crohn's disease as well as in smokers.
CA19-9	Colon cancer, pancreatic cancer, esophageal cancer and hepatocellular carcinoma. Apart from cancer, pancreatitis, cirrhosis.

- **Tissue inhibitor of metalloproteinases 1 (TIMP1) = Early as well as late stage disease.**

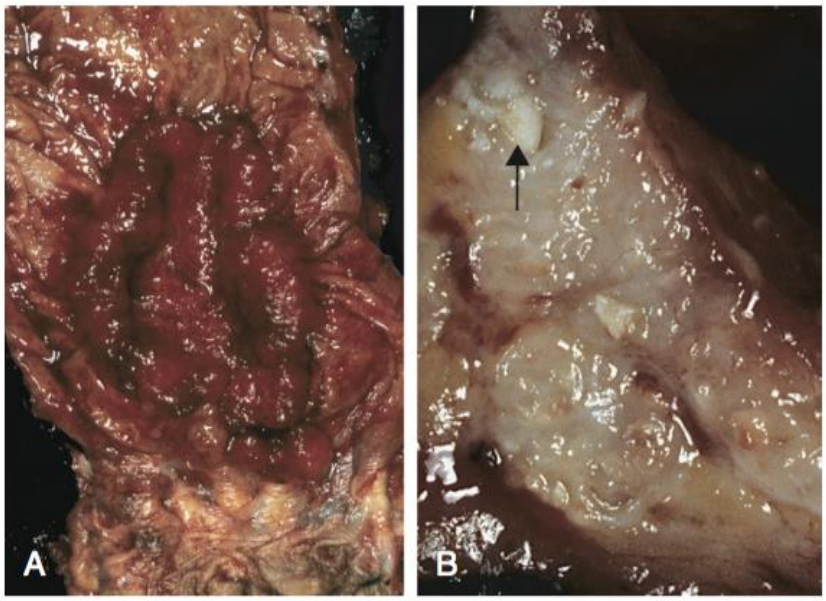


Figure 14–38 Colorectal carcinoma. **A,** Circumferential, ulcerated rectal cancer. Note the anal mucosa at the bottom of the image. **B,** Cancer of the sigmoid colon that has invaded through the muscularis propria and is present within subserosal adipose tissue (*left*). Areas of chalky necrosis are present within the colon wall (*arrow*).

Malignant Small Intestinal Neoplasms:

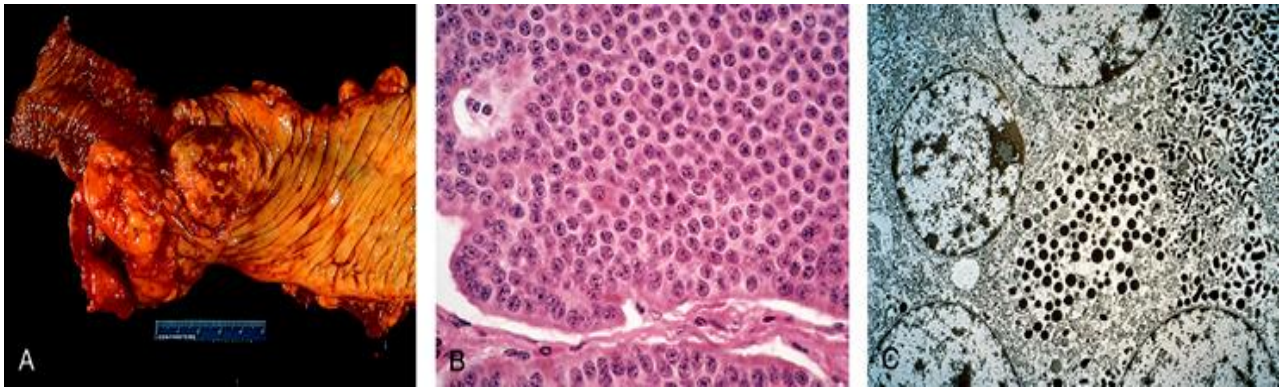
In descending order of frequency:

- Carcinoid.
- Adenocarcinomas.
- Lymphomas.
- Leiomyosarcomas.

Carcinoid Tumors:

These tumors were called "carcinoid" because they are slower growing than carcinomas.

- Neoplasms arising from **endocrine cells** found along the length of GIT mucosa.
- The peak incidence: sixth decade, but they may appear at any age.
- They compose less than 2% of colorectal malignancies.
- Almost half of small intestinal malignant tumors:
  - 60 to 80% appendix and terminal ileum.
- 10 to 20% rectum.



Local tumor of endocrine cells that secrete serotonin (vasoactive amine), it's more malignant in ileum, benign in rectum.
Carcinoid tumor is asymptomatic, **why?** Because secreted serotonin goes to the liver through the portal vein and gets detoxified, it does not enter the systemic circulation thus it's asymptomatic.
Morphology: Low grade tumor, cells have the same size (coin cells) & neurosecretory vesicles contain serotonin

Ultrastructural features: neurosecretory electron dense bodies in the cytoplasm

Clinical features:

- Asymptomatic.
- May cause obstruction, intussusception or bleeding.
- May elaborate hormones: Zollinger-Ellison (Gastrin secretion), Cushing's carcinoid or other syndromes.

Cushing's secretes: ACTH like hormone
increases the cortisone

Carcinoid syndrome:

- 1% of carcinoid tumor & in 20% of those of widespread metastasis.
- Paroxymal flushing, episodes of asthma-like wheezing, right-sided heart failure, attacks of watery diarrhea, abdominal pain.
- The principal chemical mediator is **serotonin.**
- The syndrome is classically associated with ileal carcinoids with **hepatic metastases.**

Syndrome means that the tumor metastasized to liver which means that serotonin will get out to the circulation through hepatic vein > thus symptoms appear.

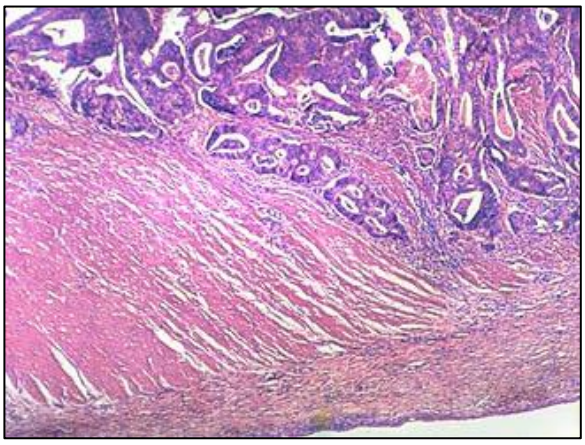
Symptoms:
Flushing, abdominal pain, asthma like, watery diarrhea (because serotonin will increase the motility of the intestine.)

Serotonin and Diarrhea:

Patients with carcinoid syndrome often suffer from diarrhea, which has both a secretory and a motor component. The secretory component of carcinoid diarrhea is attributable to excessive serotonergic stimulation of submucosal secretomotor neurons; the motor component includes faster small bowel and colon transit and an exaggerated tonic response of the colon to ingestion of a meal.

Lymphoma: the doctors said that it's not important

- Most often low-grade lymphomas arising in mucosal-associated lymphoid tissue (MALT) lymphoma or high-grade non-Hodgkin's lymphomas of B cell type.
- May occur in any part of the intestine; particularly the stomach
- The ileocecal region is a favored site for Burkitt's lymphoma.



Malignant glands of an adenocarcinoma of the colon infiltrating the muscularis propria.

What is the mode of spread of this cancer?

Colonic carcinomas spread by local extension to adjacent structures. The favored sites of metastases are regional lymph nodes, liver, lungs, and bones.

Colonic Polyps, Adenomas, and Adenocarcinomas Summary:

- *Intestinal polyps* can be classified as non-neoplastic or neoplastic. The non-neoplastic polyps can be further defined as inflammatory, hamartomatous, or hyperplastic.
- *Inflammatory polyps* form as a result of chronic cycles of injury and healing.
- *Hamartomatous polyps* occur sporadically or as a part of genetic diseases. In the latter case, they often are associated with increased risk of malignancy.
- *Hyperplastic polyps* are benign epithelial proliferations most commonly found in the left colon and rectum. They are not reactive in origin, in contrast with gastric hyper- plastic polyps; have no malignant potential; and must be distinguished from *sessile serrated adenomas.*
- Benign epithelial neoplastic polyps of the intestines are termed *adenomas*. The hallmark feature of these lesions, which are the precursors of colonic adenocarcinomas, is cytologic dysplasia.
- In contrast with traditional adenomas, *sessile serrated adenomas* lack cytologic dysplasia and share morphologic features with hyperplastic polyps.
- *Familial adenomatous polyposis* (FAP) and *hereditary nonpolyposis colorectal cancer* (HNPCC) are the most common forms of familial colon cancer. FAP is caused by *APC* mutations, and patients typically have over 100 adenomas and develop colon cancer before the age of 30.
- HNPCC is caused by mutations in DNA mismatch repair genes. Patients with HNPCC have far fewer polyps and develop cancer at an older age than that typical for patients with FAP but at a younger age than in patients with sporadic colon cancer.
- FAP and HNPCC are examples of two distinct pathways of neoplastic transformation, both of which contribute to sporadic colon cancer.
- The vast majority of colonic cancers are adenocarcinomas. The two most important prognostic factors are *depth of invasion* and the presence or absence of *lymph node metastases.*

Table 14–8 AJCC Tumor-Node-Metastasis (TNM) Classification of Colorectal Carcinoma

Designation	Description
Tumor	
Tis	In situ dysplasia or intramucosal carcinoma
T1	Tumor invades submucosa
T2	Tumor invades into, but not through, muscularis propria
T3	Tumor invades through muscularis propria
T4	Tumor invades adjacent organs or visceral peritoneum
Regional Lymph Nodes	
NX	Lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in one to three regional lymph nodes
N2	Metastasis in four or more regional lymph nodes
Distant Metastasis	
MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis or seeding of abdominal organs

AJCC, American Joint Committee on Cancer.

Table 14–9 AJCC Colorectal Cancer Staging and Survival

Stage*	Tumor-Node-Metastasis (TNM) Criteria			5-Year Survival (%)
	T	N	M	
I	T1, T2	N0	M0	74
II				
IIA	T3	N0	M0	67
IIB	T4	N0	M0	59
III				
IIIA	T1, T2	N1	M0	73
IIIB	T3, T4	N1	M0	46
IIIC	Any T	N2	M0	28
IV	Any T	Any N	M1	6

*Colorectal cancer staging is based on the TNM classification (Table 14–8). For example, a T3 tumor without nodal or distant metastases is classified as stage IIA and is associated with a 5-year survival rate of 67%.
AJCC, American Joint Committee on Cancer.

Summary
(Focus on 1st three, read the rest if you have time)

Syndrome	Mean age at presentation years	Mutated gene	GI lesion	Selected Extragastrointestinal manifestation
Peutz-Jeghers syndrome	10-15	LKB1/STKII	Arborizing polyps-small intestine>colon>stomach; colonic adenocarcinoma	Mucocutaneous pigmentation; increased risk of thyroid, breast, lung, pancreas, gonadal and bladder cancer
Juvenile polyposis	<5	SMAD4, BMPR I A	Juvenile polyps; increased risk of gastric, small intestine, colonic and pancreatic adenocarcinoma	Pulmonary arteriovenous malformations, digital clubbing
Familial adenomatous polyposis (FAP) Classic FAP Attenuated FAD Gardner syndrome Turcot syndrome	 10-15 40-50	APC, MUTYH	Multiple adenomas	Congenital RPE hypertrophy Osteomas, desmoids, skin cysts CNS tumors, medulloblastoma
Cowden syndrome, Bannayan-Ruvalcaba-Riley syndrome	<15	PTEN	Hamartomatous polyps, lipomas, ganglioneuromas, inflammatory polyps; increase risk of colon cancer	Benign skin tumors, Benign and malignant thyroid and breast lesions
Cronkhite-Canada syndrome	>50	Nonhereditary	Hamartomatous colon polyps, crypt dilatation and edema in nonpolypoid mucosa	Nail atrophy, hair loss, abdominal skin pigmentation, cachexia, anemia
Tuberous sclerosis	Infancy to adulthood	TSCI, TSC2	Hamartomatous polyps (rectal)	Facial angiofibroma, cortical tubers, renal angiomyolipoma

Check Your Understanding

MCQs:

1. **Which one of the following is a neoplastic polyp:**
   A. Adenoma
   B. Hyperplastic polyps
   C. Lymphoid polyps
   D. Inflammatory polyps
2. **Which one of the following has ectodermal abnormalities of the nails?**
   A. Juvenile Polyps
   B. Peutz-Jehgers syndrome
   C. Hyperplastic polyps
   D. Adenoma
3. **What is the most common site of GI polyps, diverticula and cancer?**
   A. Ascending colon
   B. Sigmoid colon
   C. Transverse colon
   D. Descending colon
4. **What is the most common polyps type in adults?**
   A- Hyperplastic polyps
   B- Hamartomatous polyps
   C- Inflammatory polyps
   D- Lymphoid polyps
5. **Patient came to the clinic with a history of pallor, weight loss, intermittent diarrhea. clinical investigation revealed positive stool guaiac test, increased serum CEA, microcytic anemia. doctor revealed that he has a colon cancer, which is the second leading cause of death caused by malignancy. which one of the following the patient had?**
   A. Familial Adenomatous Polyps
   B. Sporadic colon cancer
   C. Adenocarcinoma
   D. Hereditary Nonpolyposis Colorectal Cancer
6. **Which one of the following abnormalities associated with adenocarcinoma of the colon?**
   A. Over stimulation of ACP gene.
   B. Increase activity of β-catenin.
   C. Increase activity of TP53.
   D. Non of the above choices.

1:A 2:A 3:B 4:A 5:C 6: B

7. **Which one of the following mechanisms is associated with morphological identifiable changes in adenocarcinoma of the colon?**
   A. APC mutation\ β-catenin mechanism.
   B. The microsatellite instability pathway.
8. **An early symptom of left-sided carcinoma (Colorectal carcinoma)?**
   A. Fibrosis
   B. Obstruction
   C. Bleeding
   D. Stricture
9. **Right-sided carcinoma (Colorectal carcinoma) associated with?**
   A. Sickle cell anemia
   B. Hypochromic microcytic anemia
   C. Iron deficiency anemia
   D. Bleeding
10. **Survival is decreased in Colorectal carcinoma in case of?**
   A. lymph node metastases
   B. lung metastases
   C. mucosal gland metastases
   D. brain metastases
11. **Most common site of metastatic lesions?**
   A. Heart
   B. spleen
   C. Pancreas
   D. liver
12. **Under the microscope we found a polyp which is 0.4 cm in diameter, the type of it is:**
   A- Hyperplasic polyp.
   B- Adenomatous polyp.
   C- The diameter cannot guide us in this case.
13. **The hall mark of adenomatous polyps:**
   1- Epithelial dysplasia.
   2- mature goblet and absorptive cells
   3- nuclear hyperchromasia
14. **Which one of these polyps will result because the epithelium fails to mature as cells migrate out of the crypt?**
   A- Hyperplasic polyp.
   B- Adenomatous polyp.
   C- Both.

7: A 8:B 9:C 10:A 11:D 12:C 13:A 14:B

Q12: The explanation:
Hyperplastic polyps are less than 0.5 cm
adenomatous polyps range from 0.3 – 10 cm

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قال صلى الله عليه وسلم: {من سلك طريقًا يلتمس فيه علمًا سهَّل الله له بهِ طريقًا إلى الجنة}

دعواتنا لكم بالتوفيق
