

Colon Polyps & Cancers

Made by:

Pathology Team:

Moahammed Al-Harbi

Dona Barakah

Nujud Al-hejen

Nourhan El-Shamma'

Khuloud Al-Shuwarikh

Objectives

- Differentiate between the neoplastic and non-neoplastic polyps and to know common types of intestinal polyps
- Know the clinical presentation of left and right sided colon cancer, and the environmental factors that increase its risk
- Understand the Pathology and pathogenesis of colon cancer

Terminology

Polyps :

an abnormal growth of tissue projecting from a [mucous membrane](#)

Carcinoma :

An invasive [malignant tumor](#) consisting of transformed [epithelial cells](#).

Carcinoid tumor :

is a slow-growing type of [neuroendocrine tumor](#)

[are cancers of the interface between the endocrine (hormonal) system and the nervous system]

Lymphoma :

is a cancer in the lymphatic

Neoplastic :

Proliferation into NON-FUNCTIONAL cells (abnormal cells)

Non-Neoplastic:

Proliferation into FUNCTIONAL cells

Dysplasia:

Abnormal cell development

Polyps

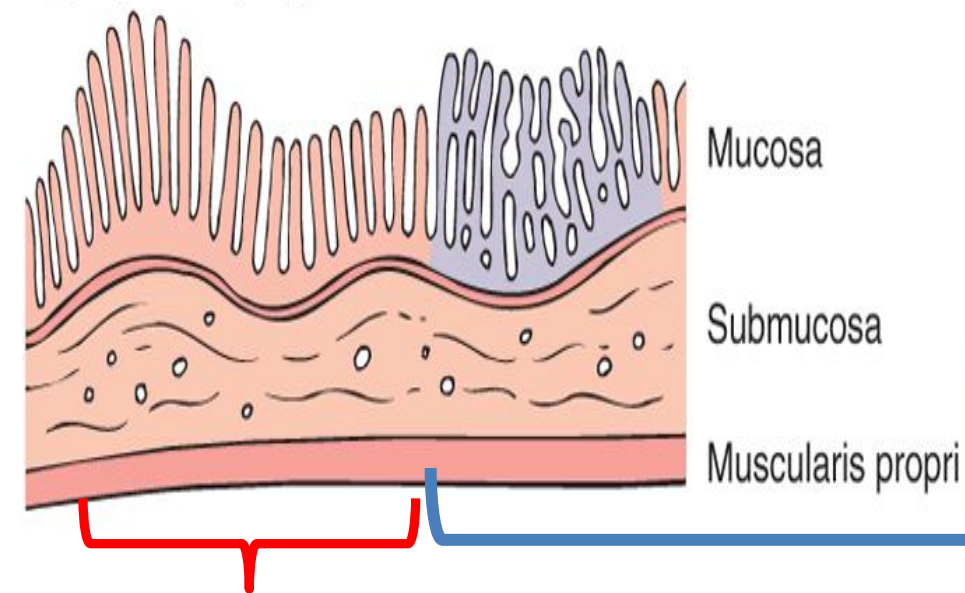
- ***Non-neoplastic polyps***
 - Hyperplastic polyps
 - Hamartomatous polyps (Juvenile & Peutz-Jeghers polyps)
 - Inflammatory polyps
 - Lymphoid polyps
- ***Neoplastic polyps***
 - Adenoma

The most common site for polyps is the rectosegmoid colon.

SESSILE POLYPS

Hyperplastic polyp

Adenoma

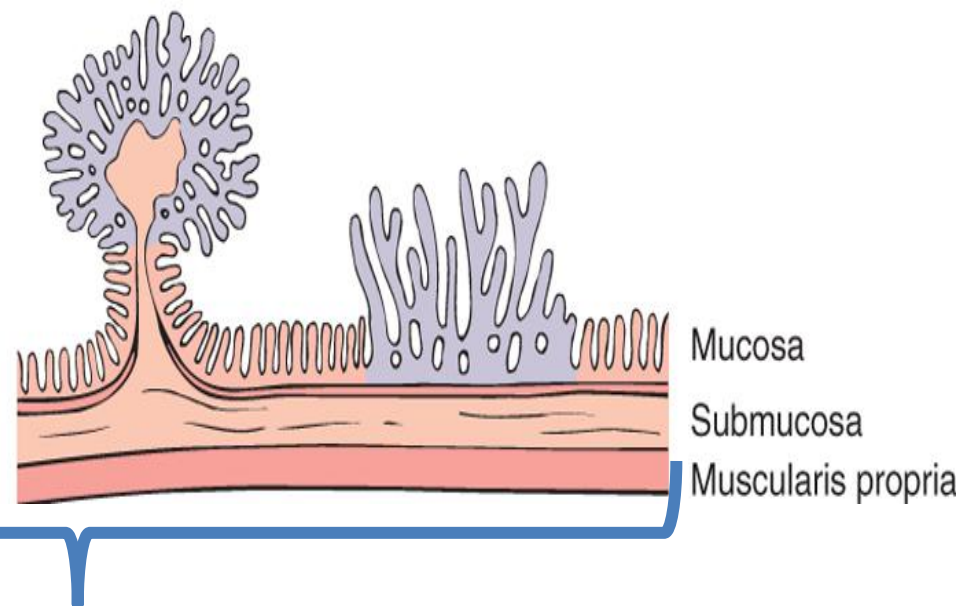


Non-Neoplastic polyp

ADENOMAS

Pedunculated
Tubular

Sessile
Villous

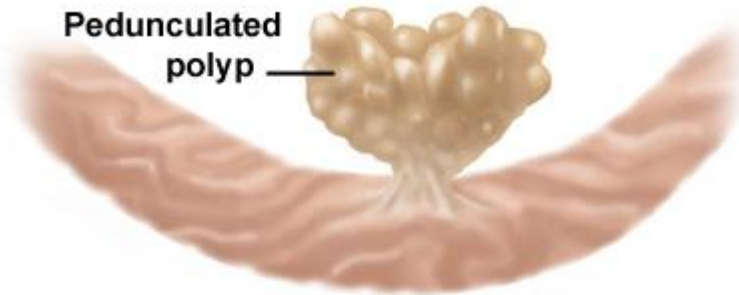


Neoplastic Polyp

In General , Polyps may be

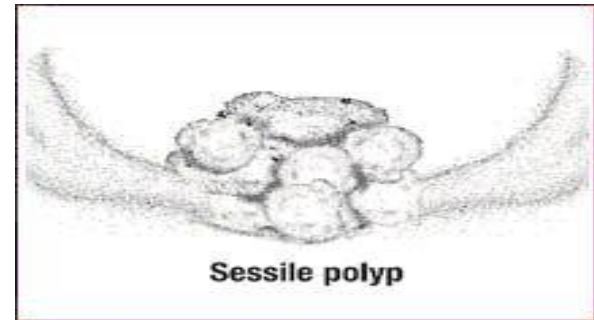
With Stalk (عنق)

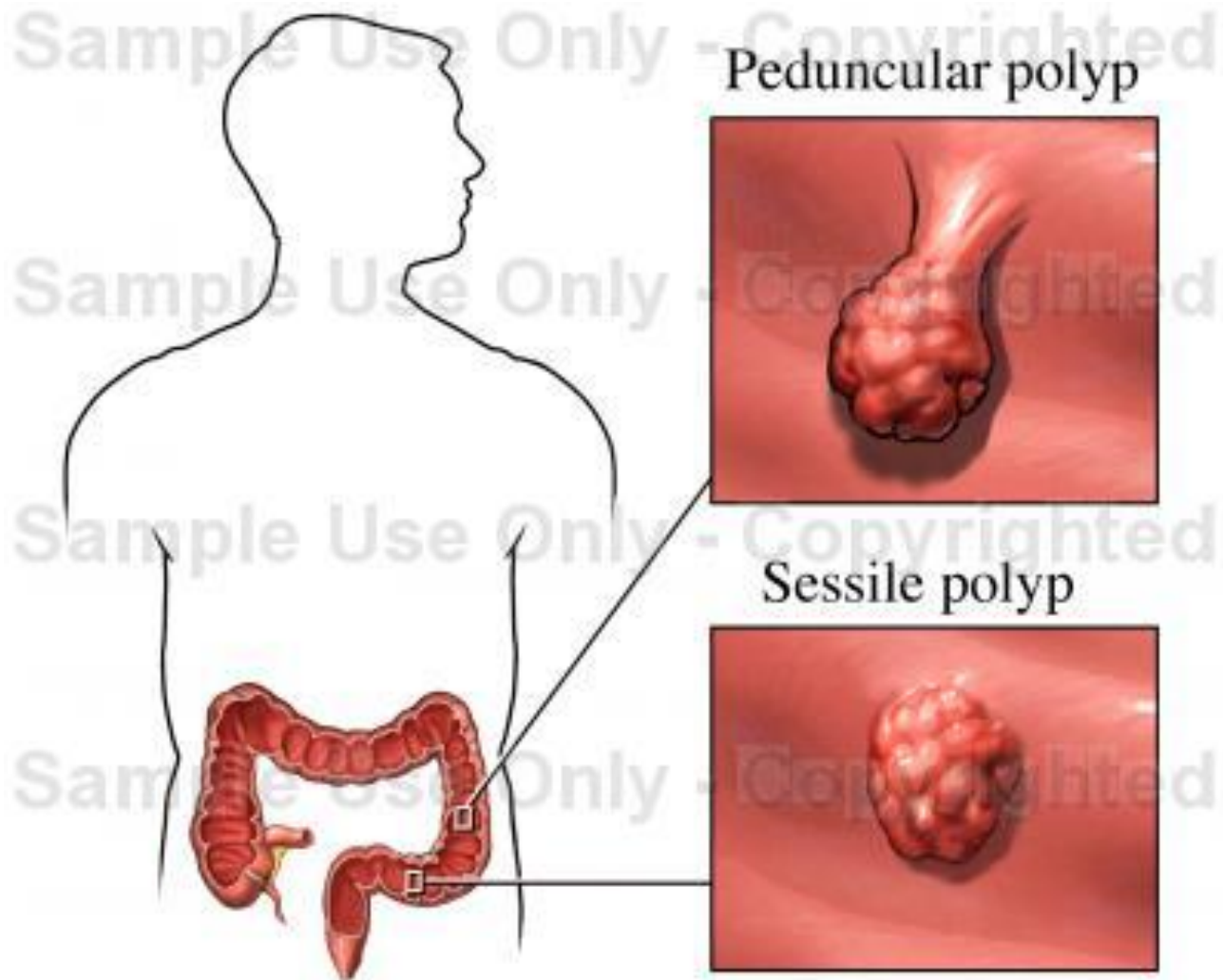
Called : **Pedunculated**



Without Stalk

Called : **Sessile**





Non-Neoplastic Polyp

Hyperplastic Polyp

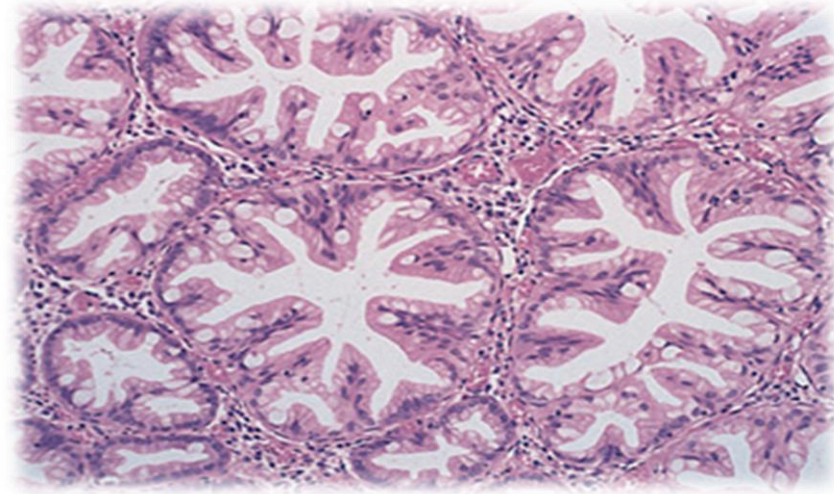
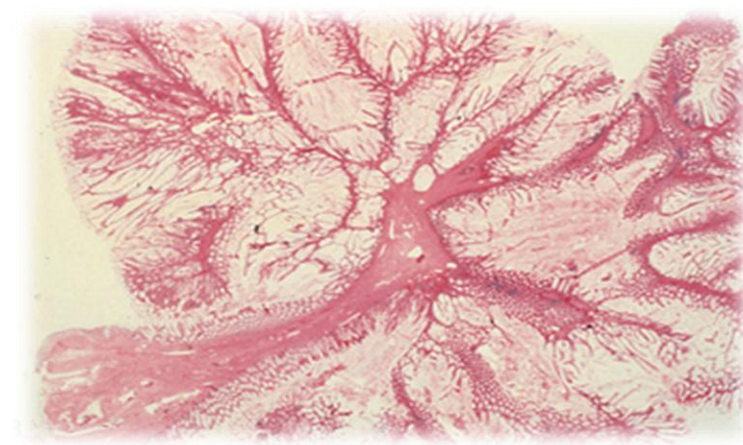
Proliferation in number of cells.

- Asymptomatic.
- > 50% are located in the [rectosigmoid](#)
- **Histopathology:**
 - **Glands:** well-formed
 - **Crypts:** lined by differentiated: *goblet* or *absorptive* cells.

Low incidence of transforming into cancer

Because 1- Nuclei Are Normal.
+ there's only 2- proliferation of cells.

Pure Hyperplastic polyp



If it's Mixed :

Hyperplastic polyp + Adenomatous polyp



Serrated (blade-like) adenoma
(develop into cancer)

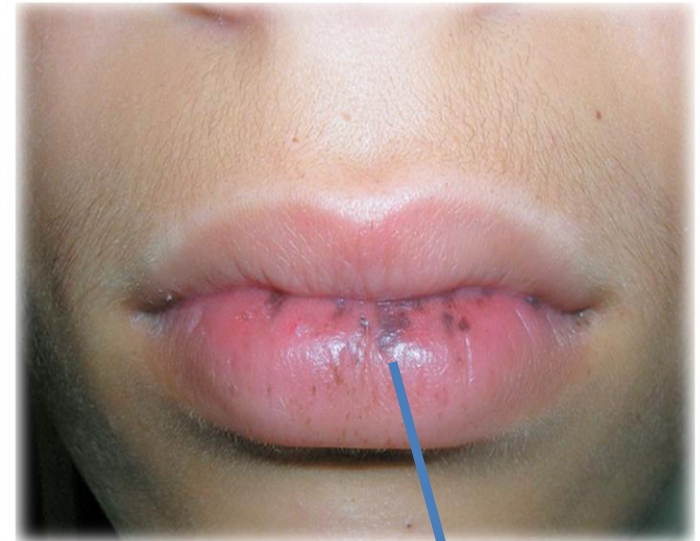
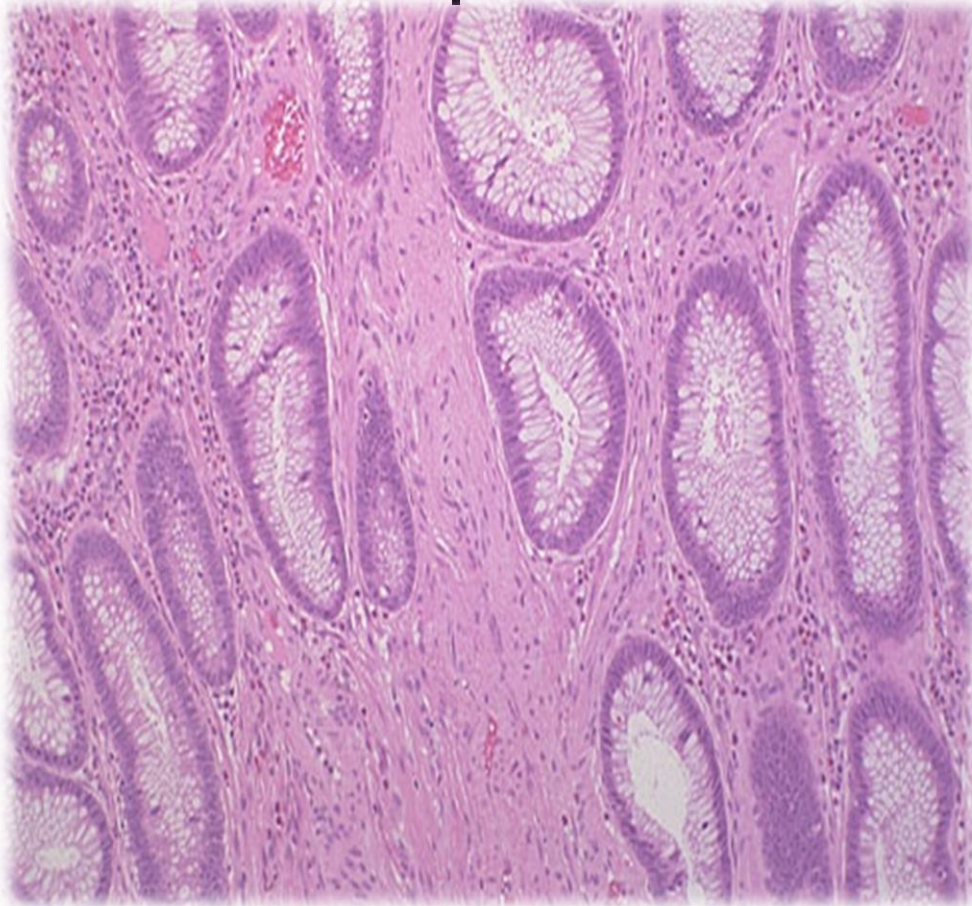
Hamartomatous polyp

Characteristics : Dilated Glands + Smooth muscles in lamina propria.

1. May come as Juvenile Polyps (in children)-retention polyp(in adults)
 - Developmental malformations affecting the glands and lamina propria
 - Commonly occur in children under 5 years old in the rectum.
 - In adult called retention polyp. (less common in adults)

2. It may be apart of a syndrome : Peutz-Jehgers syndrome
 - Rare-autosomal dominant
 - accompanied by mucosal and cutaneous pigmentation around the lips, oral mucosa, face and genitalia (genitalia: sex organ).
 - Polyps tend to be large and pedunculated.
 - Increased risk of developing carcinoma of the pancreas, breast, lung, ovary and uterus

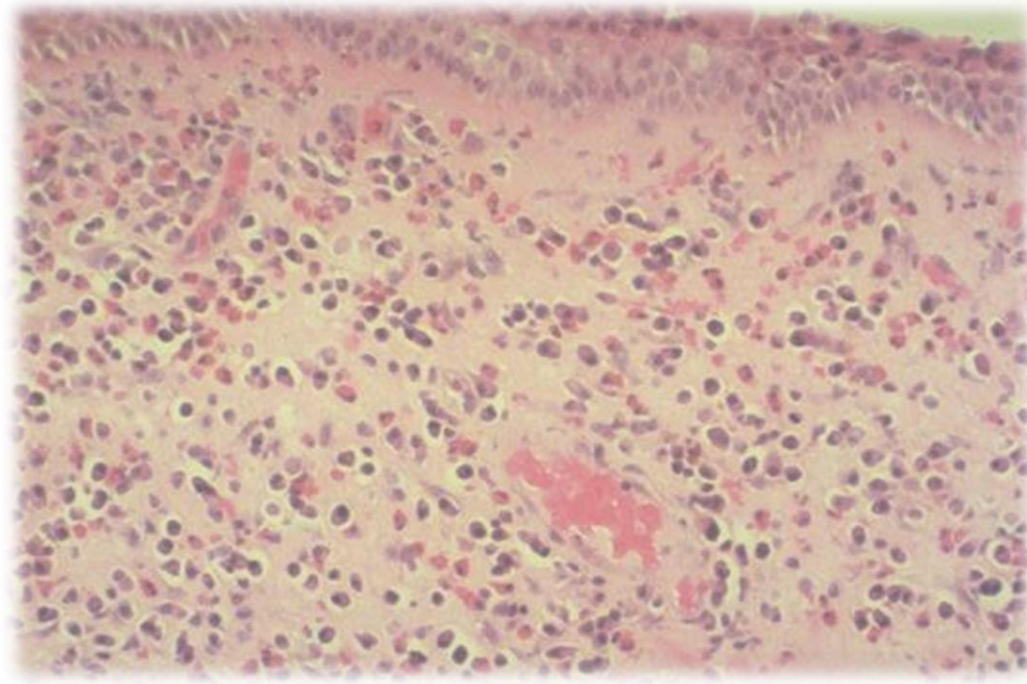
Hamartomatous Polyps



Peutz-Jehgers syndrome
Pigmented lips.

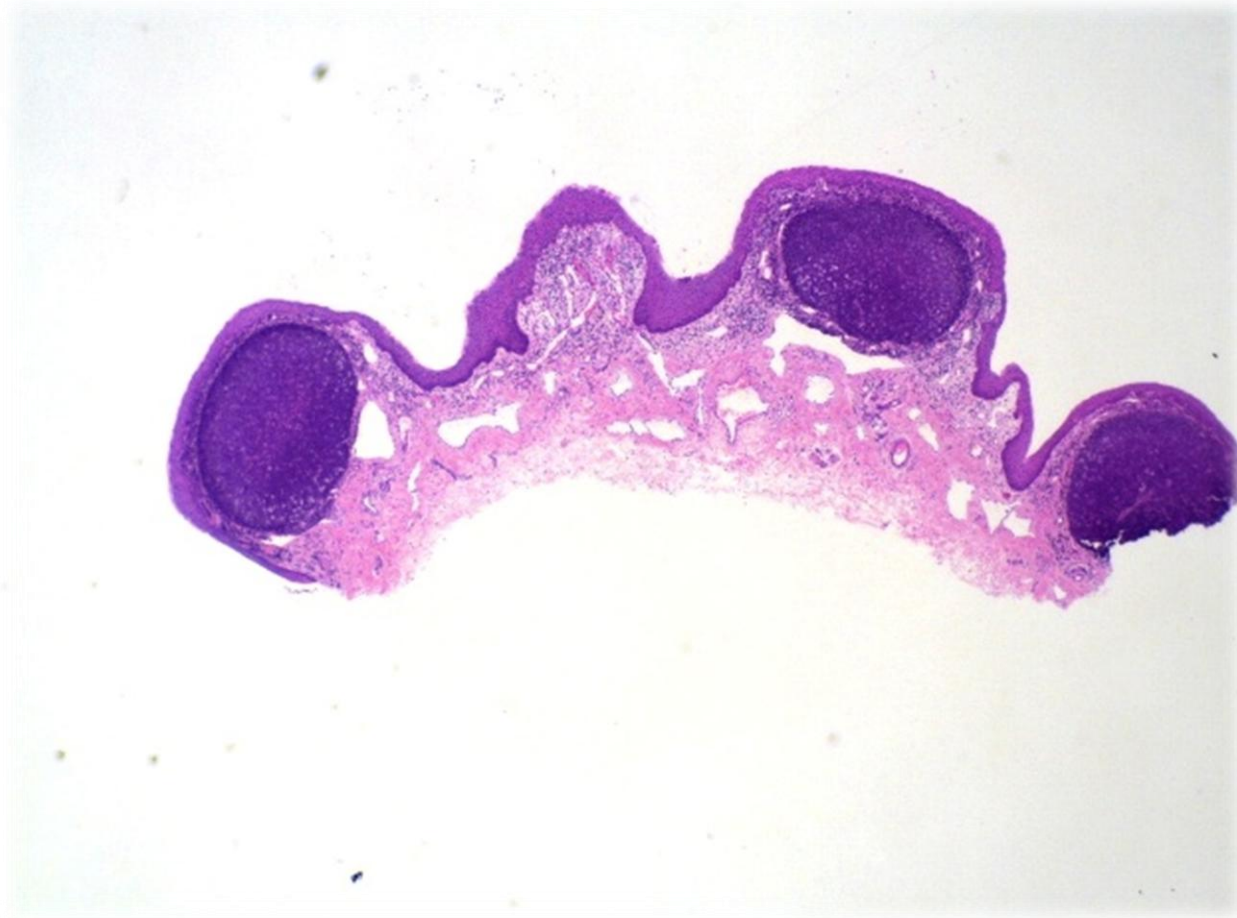
Inflammatory Polyps

- longstanding **Inflammatory Bowel Disease**, especially in **chronic ulcerative colitis**.
- Represent an exuberant reparative response to longstanding mucosal injury called pseudopolyps (characteristics : inflammatory exudate + edema)
- Increase risk of developing into cancer .



Lymphoid polyps

when **Peyers patches** [organized lymphoid nodules usually found in the ileum] enlarge and protrude into the wall and produce a polyp.



Neoplastic Polyps

Adenomatous Polyp

- Occur mainly in large bowel.
- Sporadic [several in number] and familial [hundreds in number]
- **It Vary:** from small pedunculated to large sessile
[it may be small peduncualted with stalks or large sessile without a stalk]
- Epithelium proliferation and dysplasia [mitosis]
- Divided into:
 1. **Tubular adenoma:** less than 25% villous architecture (↓Villous)
 2. **Villous adenoma:** villous architecture over 50% (↑Villous)
 3. **Tubulovillous adenoma:** villous architecture between 25 and 50%.
(Average Villous)

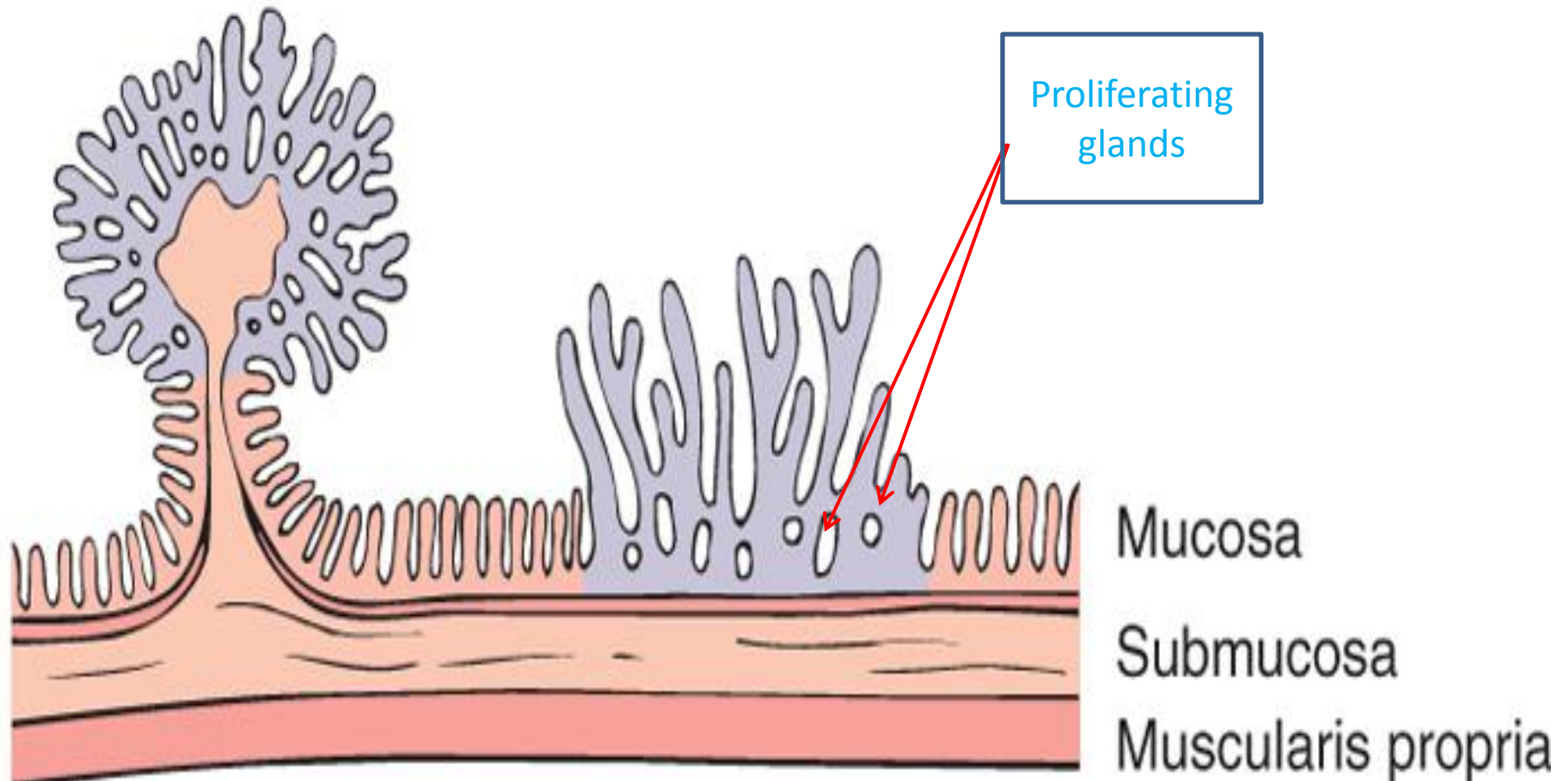
Sporadic: acquired from environment. Not present previously in family members.

Familial: born with it. Present previously in family members (due to genes).

ADENOMAS

Pedunculated Tubular

Sessile Villous



Adenomatous polyps:

1]Villous Adenoma : (The least common)

Lies directly on the mucosa and has a finger like projection (see figure the slide before)

Large in size

- Most ominous of (most malignant) epithelial polyps
[Higher chances of developing cancer]
- Age: 60 to 65 years .
- Present with **rectal bleeding** or **anemia**.
- large ones may secrete High amounts of mucoid material rich in protein. (may cause **osmotic diarrhoea**)
- **75% located in rectosigmoid area.**



2] *Tubular adenoma* : (most Common)

It has a stalk

Small in size

- Represents 75% of all neoplastic polyps.
- **75 % occur in the**
- **distal colon and rectum.**



3] *Tubulovillous adenoma* :

It has a stalk (like tubular adenoma) and 25-50% of villous projection (like villous adenoma)

Intermediate in size

- degree of dysplasia and malignant potential between tubular and villous adenomas.

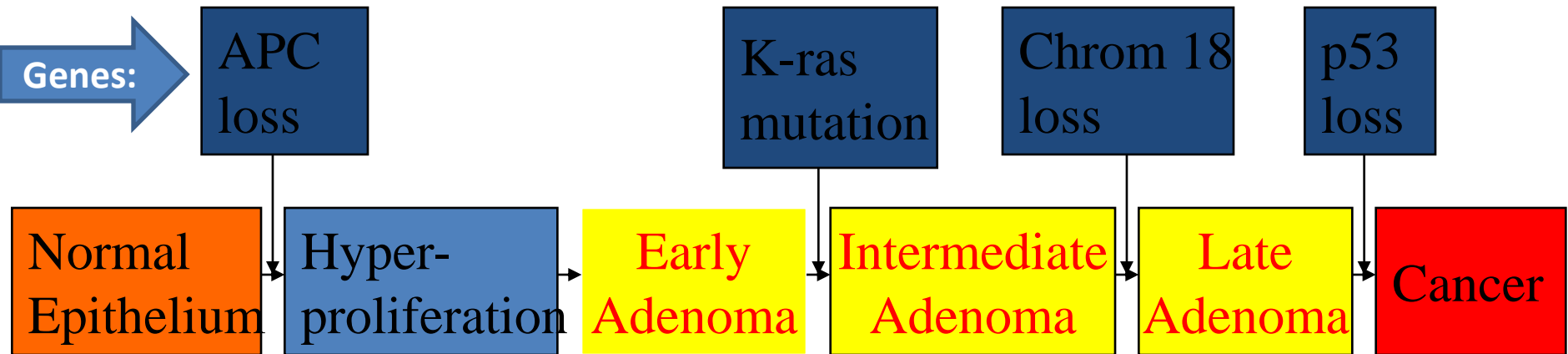
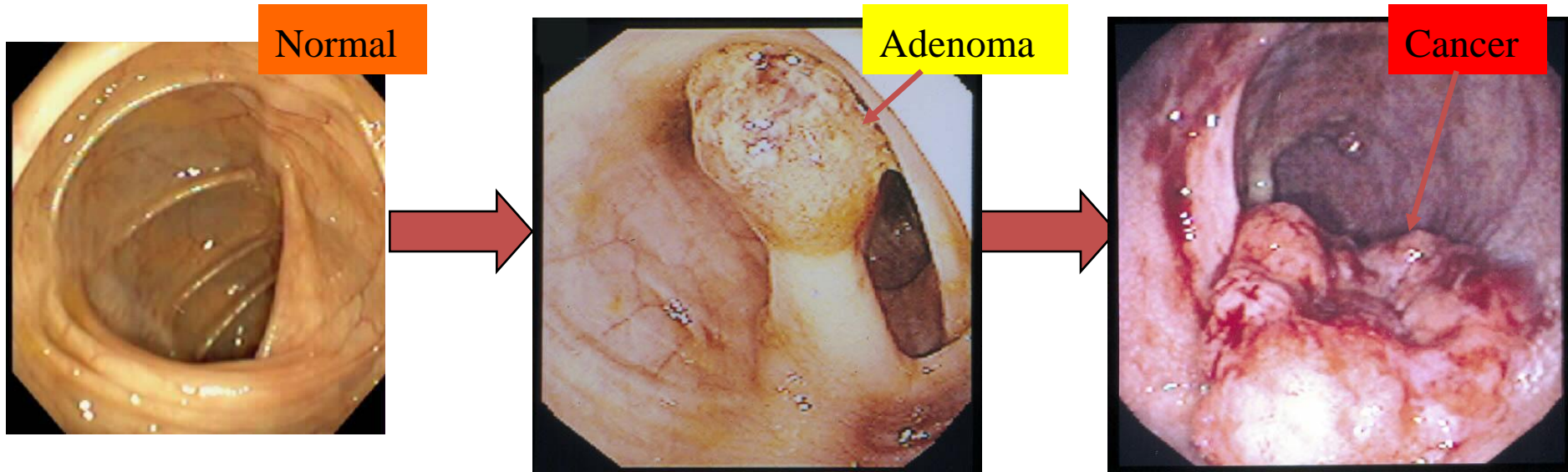
Keep in mind !!

- Most common → **tubular adenoma**
- Less common → **Villous Adenoma**
- Higher incidence to develop cancer → **Villous Adenoma**
- Lower incidence to develop cancer → **Tubular Adenoma**

Relationship of Neoplastic Polyps to Carcinoma

- ***Adenoma-to-carcinoma*** sequence is documented by several ***genetic*** alterations (described in next slide).
- The probability of carcinoma occurring in a neoplastic polyp is related to:
 1. The size of the polyp. [↑ size ↑ develop cancer]
 2. The relative proportion of its villous features.
[↑ villous feature ↑ developing of cancer]
 3. The presence of significant *cytologic atypia* (dysplasia) in the neoplastic cells.
[↑ dysplasia ↑ developing of cancer]

Adenoma to Carcinoma Pathway



Familial Polyposis Syndrome

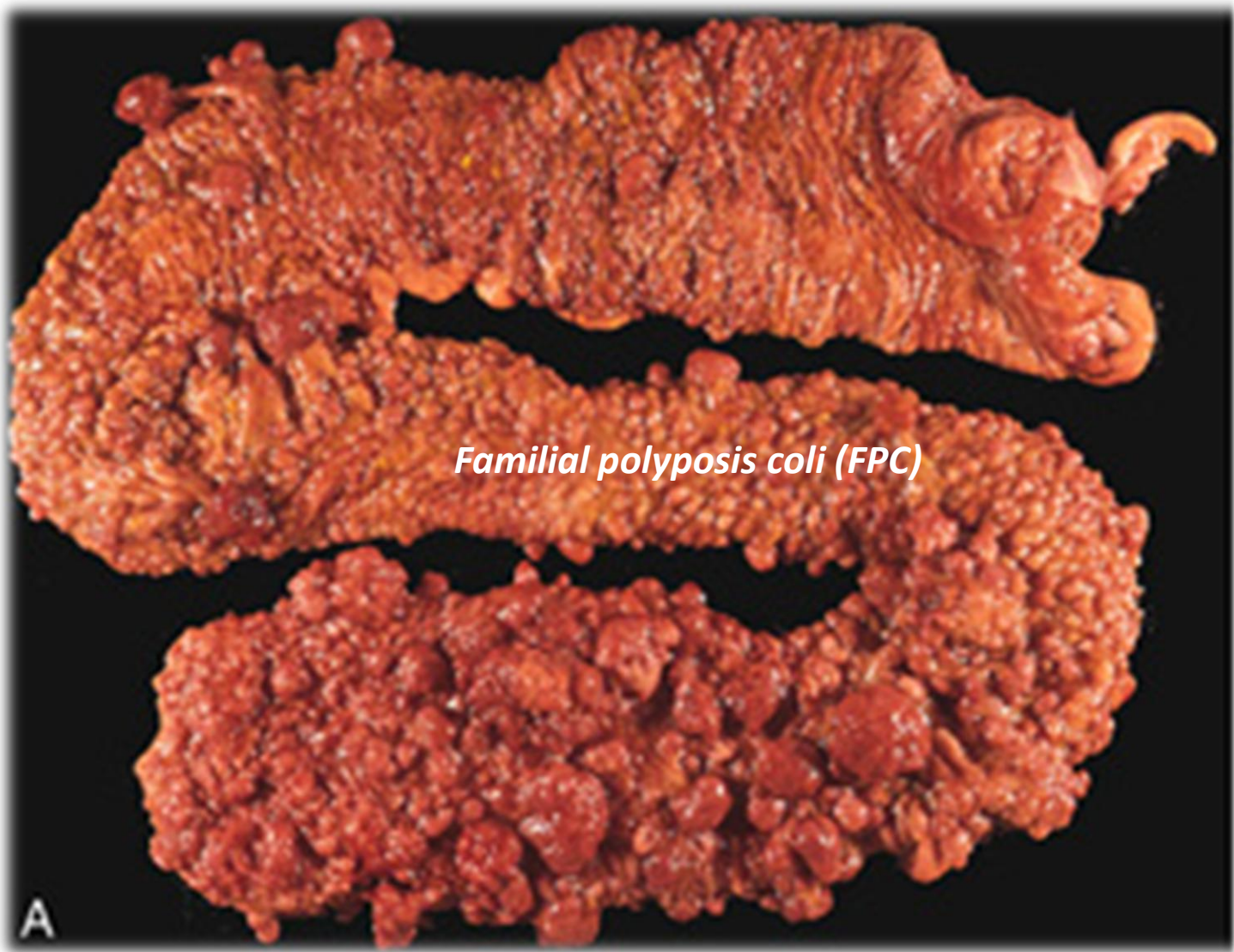
- Patients have genetic tendencies to develop neoplastic polyps.
Called: Familial polyposis coli (FPC)
- Genetic defect ch5 q21.
- Innumerable (high numbers all over the colon) neoplastic polyps in the colon (500 to 2500)
- Polyps are also found elsewhere in alimentary tract
- Most polyps are tubular adenomas
- The risk of colorectal cancer is 100% by midlife.

Gardener's syndrome

- Polyposis coli, multiple osteomas (benign bone tumor), epidermal cysts, and fibromatosis.

Turcot syndrome

- Polyposis coli, glioma and fibromatosis



Malignant Tumors of the Large Intestine

Malignant Tumors of Large Intestine

Adenocarcinoma

- The most common malignancy of the GI tract
- It's a major cause of morbidity and mortality worldwide.
- Constitutes 98% of all cancers in the large intestine.

- Predisposing factors:

1. Inflammatory Bowl Disease

- 2. adenomas**

3. polyposis syndrome.

4. Diet :

- Low content of non-absorbable vegetable fibers.
- High fat content.
- Reduced intake of vitamin A, C & E.

- Risk factors :

1. Age

- 2. Adenomas**, Polyps

3. Sedentary lifestyle, Diet, Obesity

4. Family History of CRC


5. Inflammatory Bowel Disease

6. Hereditary Syndromes

(familial adenomatous polyposis → FAP)


Dietary factors implicated in colorectal carcinogenesis

increased risk



- consumption of red meat
- animal and saturated fat
- refined carbohydrates
- alcohol

decreased risk



- dietary fiber
- vegetables
- fruits
- antioxidant vitamins
- calcium
- folate (B Vitamin)

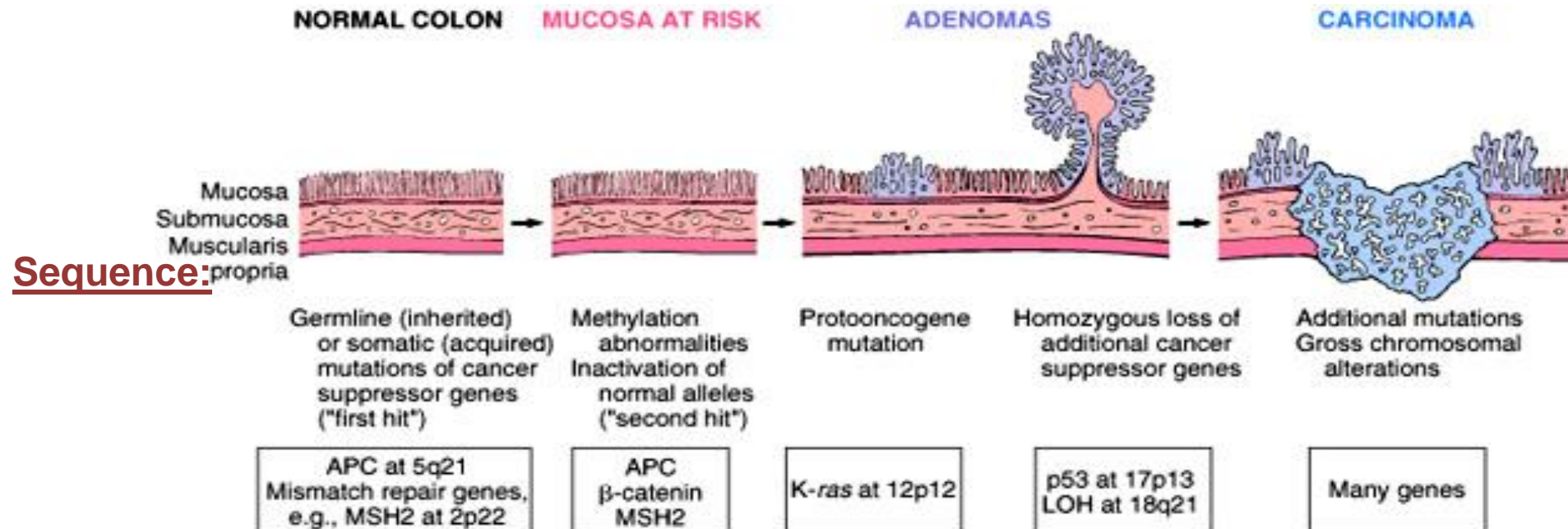
Adenocarcinoma of Large Intestine

Carcinogenesis

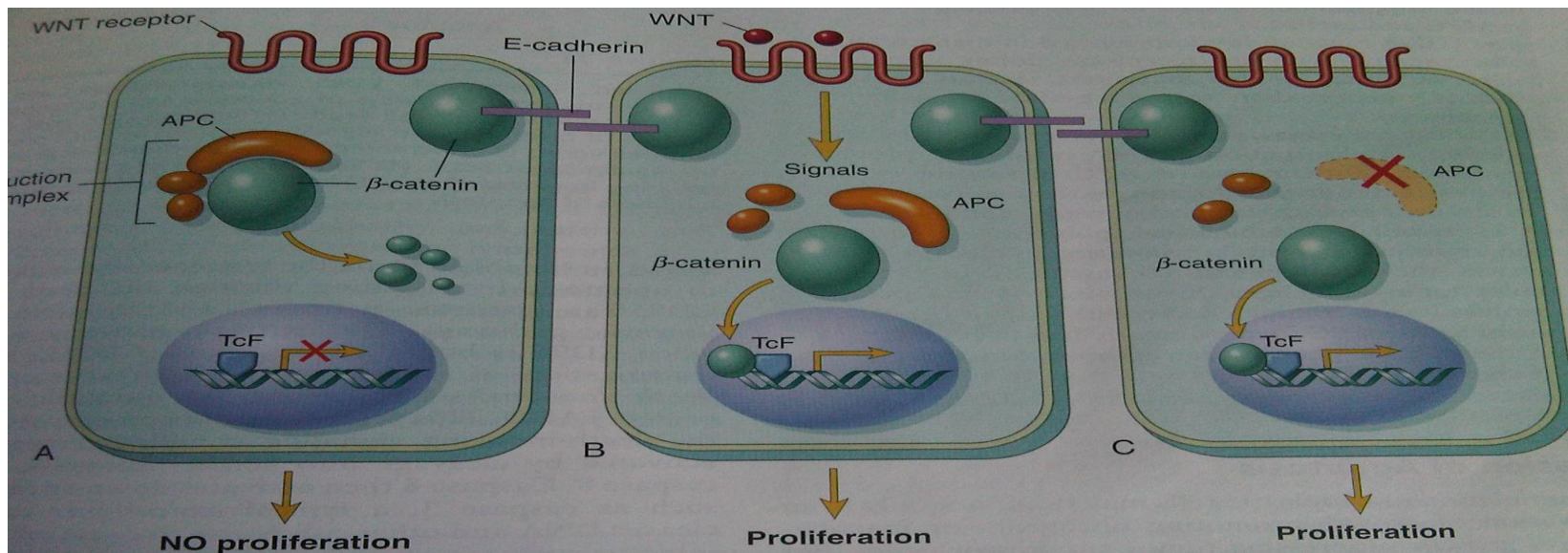
- Two pathogenetically distinct pathways for the development of colon cancer, both seem to result from **accumulation of multiple mutations**:

1- The APC/B-catenin pathway (85 %) [most common]

- chromosomal instability that results in stepwise accumulation of mutations in a series of oncogenes and tumor suppressor genes.



- **APC** is a tumor suppressor gene & an antiproliferative.
- **B-catenin** is responsible for proliferation of cells.
- Normally, APC is attached to B-catenin to control its function (B-catenin's function) by degrading it.
- B-catenin is stimulated by a NORMAL stimulant which allows it to be translocated into the DNA and cause proliferation of cells.
- IN COLON CANCER, APC (the preventer) is absent or mutated, so nothing can stop B-catenin from translocating into the DNA and cause uncontrollable proliferation of cells.



Role of APC in regulating the stability and function of β -catenin. APC and β -catenin are components of the WNT signaling pathway. In resting cells (not exposed to WNT), β -catenin forms a macromolecular complex containing the APC protein. This complex targets β -catenin for degradation, and intracellular levels of β -catenin are low. When cells are stimulated by secreted WNT molecules, the destruction complex is deactivated, β -catenin degradation does not occur, and cytoplasmic levels increase. β -catenin translocates into the nucleus where it binds to TcF, activating several genes involved in the cell cycle. When APC is mutated, the destruction complex is inactive, leading to constitutively high levels of β -catenin and uncontrolled proliferation.

2- The DNA mismatch repair genes pathway [MMR]:

(10% to 15%)

- Sporadic cases.
- There is accumulation of mutations (as in the *APC/B-catenin*)
But the involved genes are different .

[Inherited mutation in one of Five DNA mismatch repair genes

(*MSH2*, *MSH6*, *MLH1*, *PMS1*, AND *PMS2*)

give rise to the hereditary non polyposis colon carcinoma (HNPCC)]

- **MLH1 gene is the one most commonly involved in sporadic colon carcinomas**
- **Normally** , MMR Checks the DNA sequence during transcription .
- **In Colon cancer** , MMR are mutated or loss which will cause microsatellites (simple repetitive DNA sequences) to be unstable during DNA replication Giving rise to alteration in genes involved in regulation of cell growth which will cause colorectal carcinoma .

Hereditary Colorectal Carcinoma

Molecular Pathway	Adenocarcinoma sequence	Microsatellite instability
Clinical Phenotype	Familial adenomatous polyposis	Hereditary nonpolyposis colorectal cancer
Histopathology	<ol style="list-style-type: none"> 1. Innumerable adenomatous polyps 2. Moderately differentiated adenocarcinomas 	<ol style="list-style-type: none"> 1. Mucinous * 2. poorly differentiated carcinomas with 3. lymphocytic infiltrates
Genetics	Germ-line APC inactivation	Germ-line inactivation of mismatch repair (<i>MLH1</i> or <i>MSH2</i> DNA) genes

* **Mucinous** :means that something has a lot of mucus

Sporadic Colorectal Carcinoma

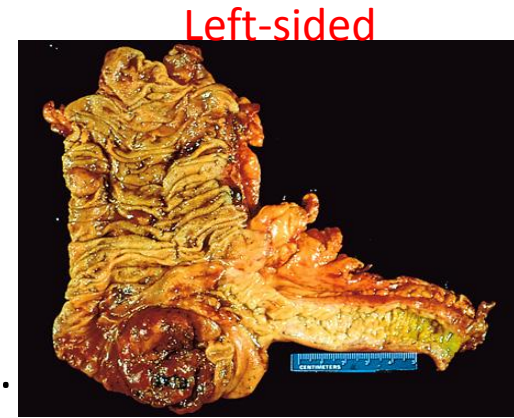
Molecular Pathway	Adenocarcinoma sequence	Microsatellite instability
Clinical Phenotype	Left-sided predominant cancers	Right-sided predominant cancers
Histopathology	<ol style="list-style-type: none"> 1. Tubular, tubulovillous, and villous adenomas 2. Moderately differentiated adenocarcinomas 	No precursor lesions <ol style="list-style-type: none"> 1. Sessile serrated adenoma 2. Large hyperplastic polyps 3. Mucinous carcinomas
Genetics	Somatic inactivation or mutation of multiple genes	Somatic inactivation of mismatch repair (<i>MLH1</i> or <i>MSH2</i> DNA) genes

Morphology

70% are in the rectum, rectosigmoid and sigmoid colon.

- **Left-sided carcinomas:**

1. Tend to be annular (occupies the whole diameter of the colon) .
2. encircling lesions with **early symptoms** of obstruction. [because it is constricting]



- **Right-sided carcinomas :**

1. Tend to grow as polypoid Masses [resembling a polyp]
2. fungating [resembling a fungus]masses.
3. obstruction is uncommon.
4. Mucinous adenocarcinoma secret abundant mucin that may dissect through cleavage planes in the wall.



Signs and symptoms

- If located closer to the anus:

- I. change in bowel habit
- II. feeling of incomplete defecation
- III. PerRectal bleeding

- Right-sided lesions :

are more likely to **bleed** and result in **iron deficiency anemia**

- Left-sided tumors:

are usually detected later and could present with **bowel obstruction**.

A tumor that is large enough to fill the entire lumen of the bowel may
cause bowel obstruction

- Serum levels of carcinoembryonic antigen (CEA) :
 - related to tumor size and extent of spread.
 - They are helpful for detecting **RECURRENCE** of tumor after resection.

ONLY RECURRENCE

Malignant Tumors of the Small Intestine

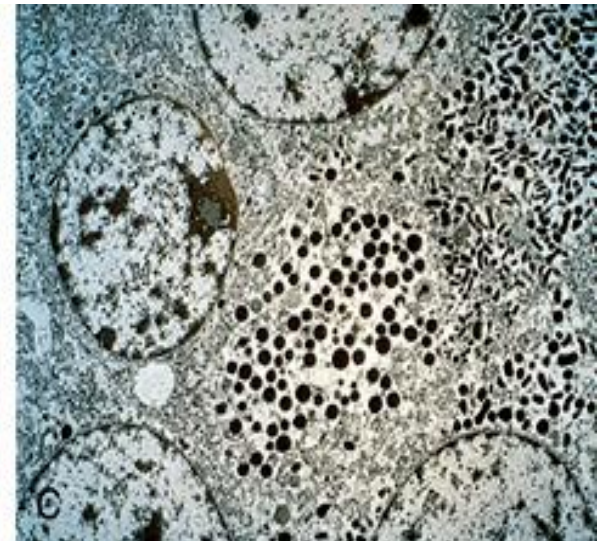
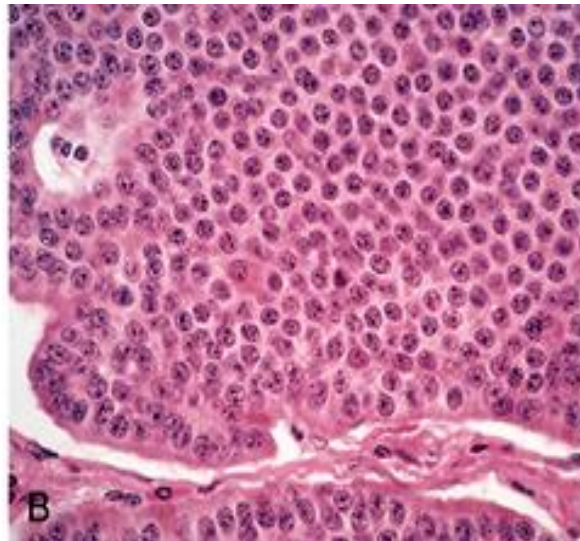
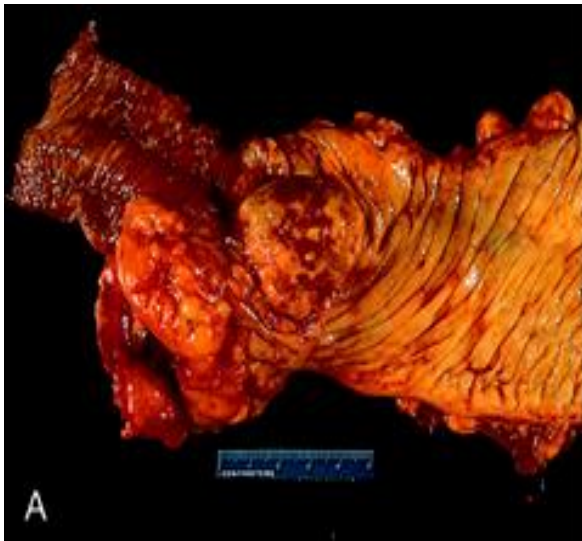
Malignant Small Intestinal Neoplasms

- In descending order of frequency:
- carcinoid,
- adenocarcinomas,
- Lymphomas
- leiomyosarcomas.

Small Intestinal Neoplasms

Carcinoid Tumors

- Neoplasms arising from endocrine cells found along the length of GIT mucosa.
- 60 to 80% appendix and terminal ileum: 10 to 20% rectum.
- **Ultrastructural features: neurosecretory electron dense bodies in the cytoplasm**



Small Intestinal Neoplasms

Carcinoid Tumor

Clinical features

- Asymptomatic
- May cause obstruction, intussusception or bleeding.
- May elaborate hormones: Zollinger-Ellison, Cushing's carcinoid or other syndromes.
- 5 years survival rate is 90%, small bowel Carcinoid with liver metastasis the 5 years survival rate is better than 50%

Intussusception: medical condition in which a part of the intestine has [invaginated](#) into another section of intestine

Small Intestinal Neoplasms

Carcinoid tumor

Carcinoid syndrome

- 1% of carcinoid tumor & in 20% of those of widespread metastasis
- Paroxysmal 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.

Small Intestinal Neoplasms

Lymphoma

- 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;
- the ileocecal region is a favored site for Burkitt's lymphoma.