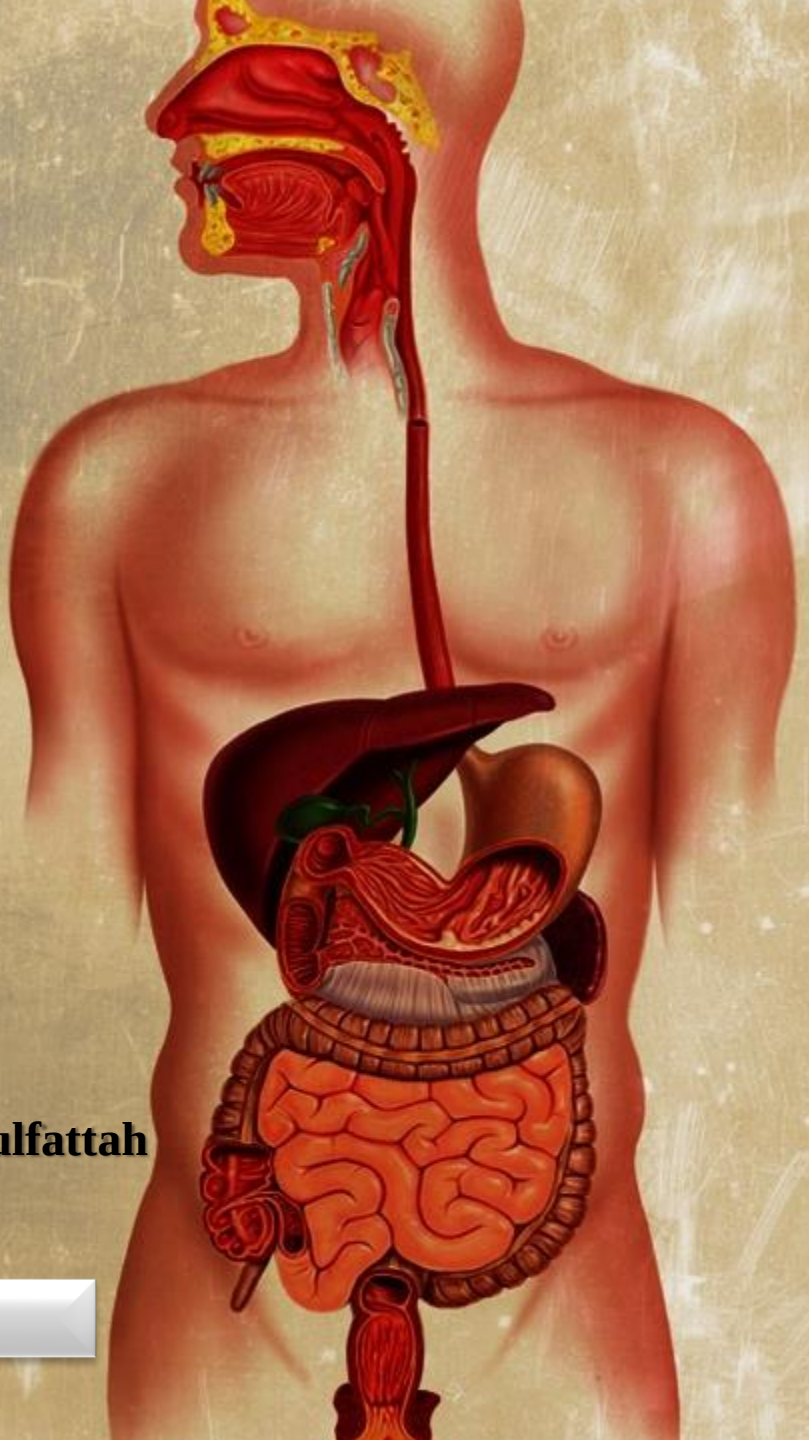
Lecture 6 & 7:

Colonic tumor and polyps



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Objectives

Upon completion of this lecture the students will

1. **Know common types of intestinal polyps**
2. **Differentiate between the neoplastic and non-neoplastic polyps**
3. **Know the clinical presentation of left and right sided colon cancer, and the environmental factors that increase its risk**
4. **Understand the pathogenesis of colon cancer**
5. **Discribe the Pathological features of colon cancer**

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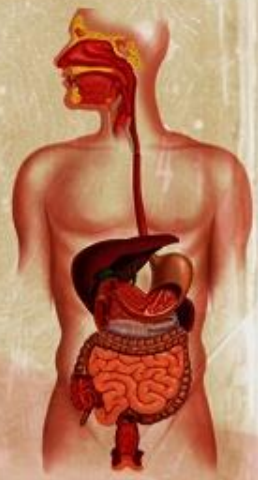


Helpful definitions:

1- Polyp: any mass that protruding from mucous membrane

2- Carcinoid tumor : tumor that leads to increase releasing some hormones mostly in GIT and lungs

3- Carcinoma : cancer developed from epithelial cells of any organ

(Polyps)

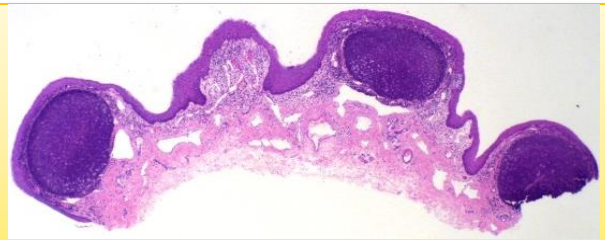
1- Non-neoplastic polyps

Hyperplastic polyps :Asymtomatic ‹50% rectosigmoid, Sawtooth surface, Star shaped crypts lined by differentiated goblet or absorptive cells, Composed of well-formed glands. *Most common type in adult and no polyposis syndromes.

Hamartomatous polyps: 1-Juvenile polyps 2-Peutz-Jeghers polyps

Inflammatory polyps: longstanding IBD (chronic ulcerative colitis), Represent an exuberant reparative response to longstanding mucosal injury called pseudopolyps

Lymphoid polyps:
Normal polyps



-Hamartomatous polyps:

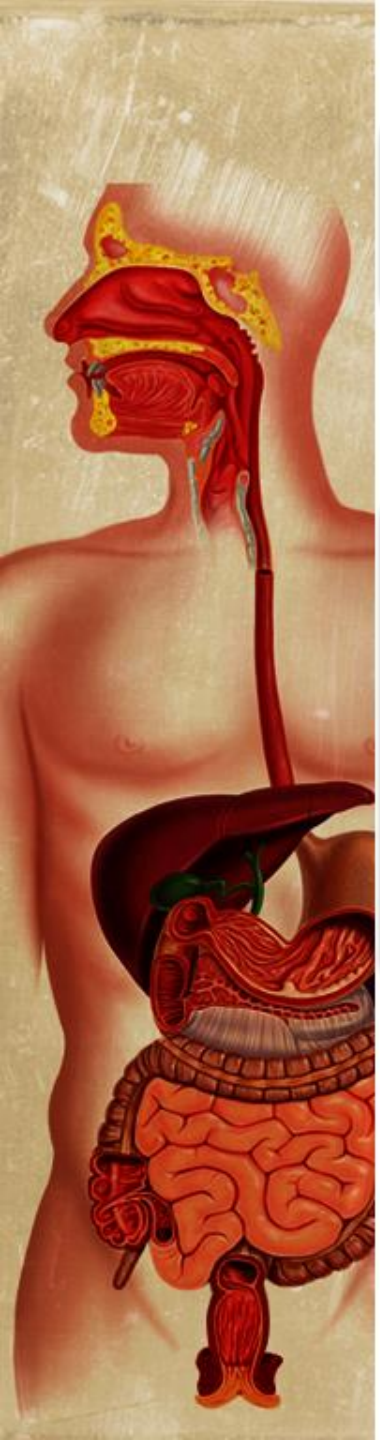
1-Juvenile Polyps

-Developmental malformations affecting the glands and lamina propria
-Commonly occur in children under 5 years old in the rectum.
-In adult called retention polyp.

2-Peutz-Jehgers syndrome

-Rare, autosomal dominant
-mucosal and cutaneous pigmentation around the lips, oral mucosa, face and genitalia, present with red blood in stool .
-Polyps tend to be large and pedunculated.
- Increased risk of developing carcinoma of the pancreas, breast, lung, ovary and uterus

- Juvenile polyposis: Autosomal dominant or nonhereditary.
- Cronkhite-Canada syndrome:
Nonhereditary polyposis syndrome
Polyps plus ectodermal abnormalities of the nails



2-Neoplastic Polyps (Adenomas)

Occur mainly in large bowel, Spordic and familial, Vary from small pedunculated to large sessile, Epithelium proliferation and **dysplysia**

1-Tubular adenoma:
- The most common of all neoplastic polyps.
-75 % occur in the distal colon and rectum and most common site is sigmoid colon.

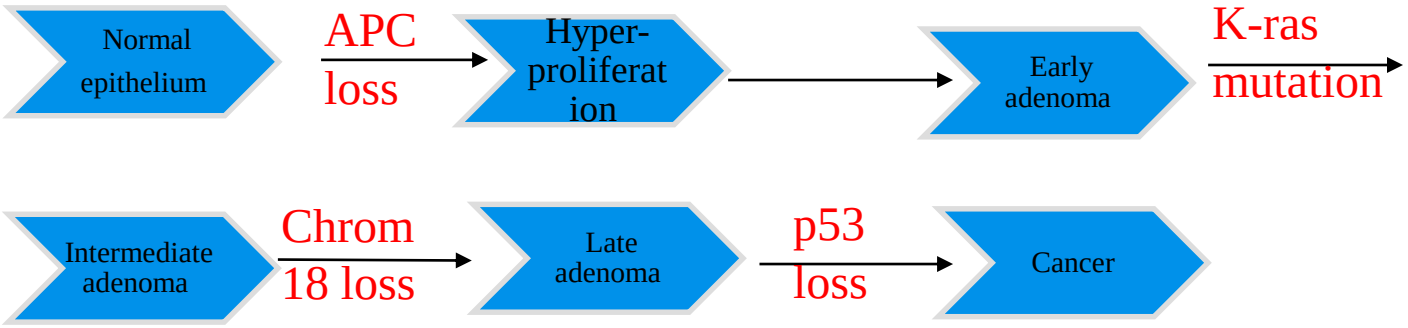
2-Villous Adenoma:
- Age 60-65
- Present with rectal bleeding or anemia, large ones may secrete copious amounts of mucoid material rich in protein and potassium.
- Produce hypokalemia and hypoalbuminemia.
- Located in rectosigmoid area.
- Largest and most ominous مشؤوم of epithelial polyps

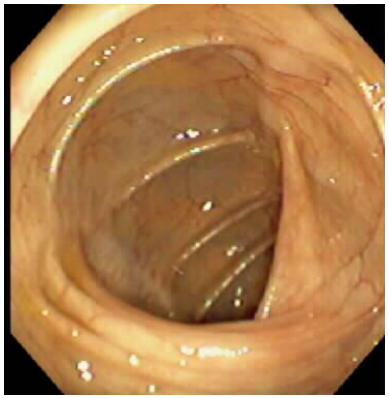
3-Tubulovillous adenoma:
Intermmediate in size, degree of dysplasia and malignant potential between tubular and villous adenomas.

The probability of a neoplastic polyp to become carcinoma is depends on:

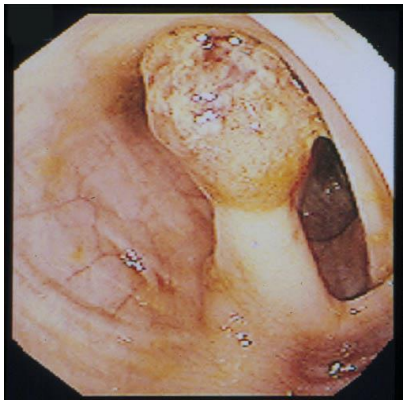
1. The size of the polyp.
2. The relative proportion of its villous features.
3. The presence of significant cytologic atypia (dysplasia) in the neoplastic cells.
4. Multiple polyps.

The pathway

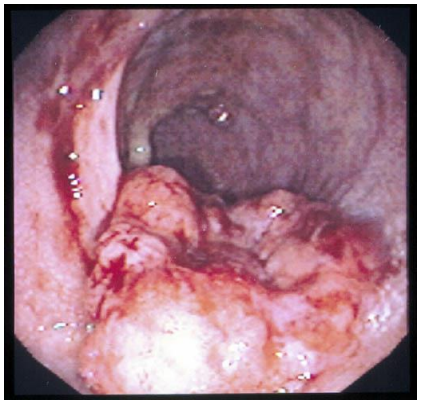




Normal



adenoma

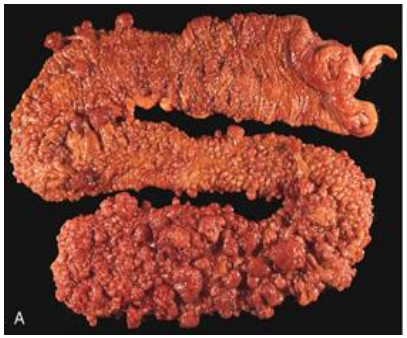


carcinoma

(Large intestine malignant tumors)

Familial Polyposis Syndromes:

Patients have genetic tendencies to develop neoplastic polyps



Familial polyposis coli (FPC)

- Genetic defect of Adenomatous polyposis coli (*APC*) on the long arm of chromosome 5 /(5q21).
- Multiple or (Innumerable) neoplastic polyps in the colon (500 to 2500)
- Polyps are also found elsewhere in alimentary tract
- The risk of colorectal cancer is 100% by midlife.

Gardener's syndrome

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

Turcot syndrome

Polyposis coli, glioma and fibromatosis

fibromatosis not confused with neurofibromatosis 'schwanoma'

Adenocarcinoma

Adenocarcinoma of the colon is the most common malignancy of the GI tract , 98% of all cancers in the large intestine.

-Predisposing factors:

IBD, adenomas , polyposis syndrome.

Diet :

Low fibres diet, High fat content, Alcohol, ↓ intake of Vit A, C & E.

-Carcinogenesis of colon adenocarcinoma:

Two pathogenetically distinct pathways, both as a result of accumulation of multiple mutations:

1- The APC/B-catenin pathway (85 %)

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

APC , K-ras, p53 (Only these mutations you should know it)

2- The DNA mismatch repair genes pathway:

10% to 15% of sporadic cases.

There is accumulation of mutations (as in the *APC/B-catenin schema)*

DNA mismatch repair genes (**MSH2, MSH6, MLH1**, PMS1, AND PMS2) give rise to the *Hereditary non polyposis colon carcinoma (HNPCC)*

*studies showing that some NSAIDs cause polyp regression in FAP patients in whom the rectum was left in place after colectomy.

*FAP: Hereditary mutation of the *APC* gene is the cause of familial adenomatous polyposis (FAP)

Colorectal Carcinoma

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

Left-sided carcinomas: patient present with rectal bleeding

Right-sided carcinomas patient present with Iron deficiency anemia

Intestinal tumor markers:

1- Carcinoembryonic antigen (CEA):can be raised also with ulcerative colitis, pancreatitis, cirrhosis, COPD, Crohn's disease and in smokers.
2- Carbohydrate antigen (CA19-9): can be raised also with colon cancer and pancreatic cancer, esophageal cancer and hepatocellular carcinoma.
***CEA & CA19-9 :** Useful to assess disease recurrence (late stage).
3-Duke classification is used for staging.

*prognostic factors : depth invasion and presence or absence of lymph node metastases .

(small intestine malignant tumors)

In descending order of frequency:
carcinoid, adenocarcinomas, lymphomas and leiomyosarcomas.

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.

Ultrastructral features:
neurosecretory electron dense bodies in the cytoplasm.

Clinical features:

✓ Asymptomatic
✓ May cause obstruction, intussusception or bleeding.
✓ May elaborate hormones: Zollinger-Ellison, Cushing's carcinoid .

Carcinoid syndrome

✓ 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.

Lymphomas:

- ✓ low-grade lymphomas arising in mucosal-associated lymphoid tissue (MALT) lymphoma
- ✓ high-grade non-Hodgkin's lymphomas of B cell type.

#Those two occur in any part of the intestine

- ✓ Burkitt's lymphoma occurs in the ileocecal

Summary from Robbins

SUMMARY

Colonic Polyps, Adenomas, and Adenocarcinomas

- *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 hyperplastic 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*.