

Gastrointestinal Malignancies

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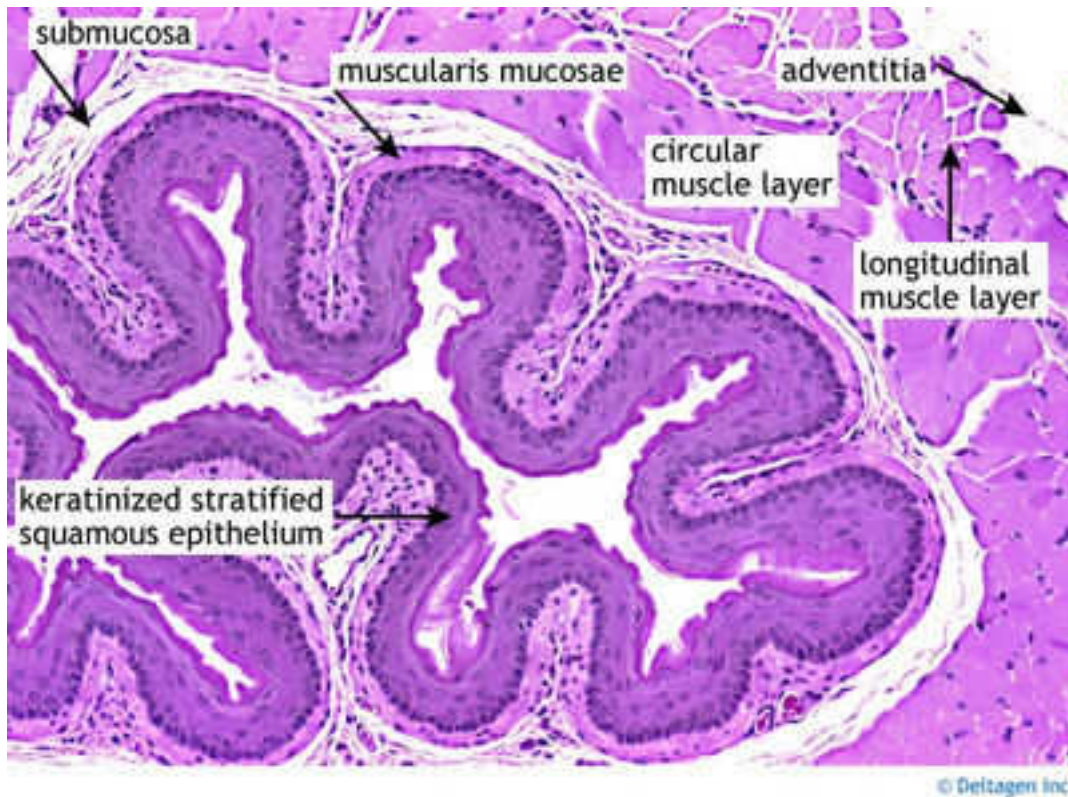
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Anatomical Pathology Discipline

Esophagus – normal anatomy

- Hollow tube
- 23-25cm long in adults
- Extends from pharynx to level of T11-T12.
- Has upper (level of cricopharyngeus muscle) lower esophageal sphincters (level of esophagogastric junction).
- Function is to conduct food and fluids from pharynx to stomach.

Esophagus – normal anatomy

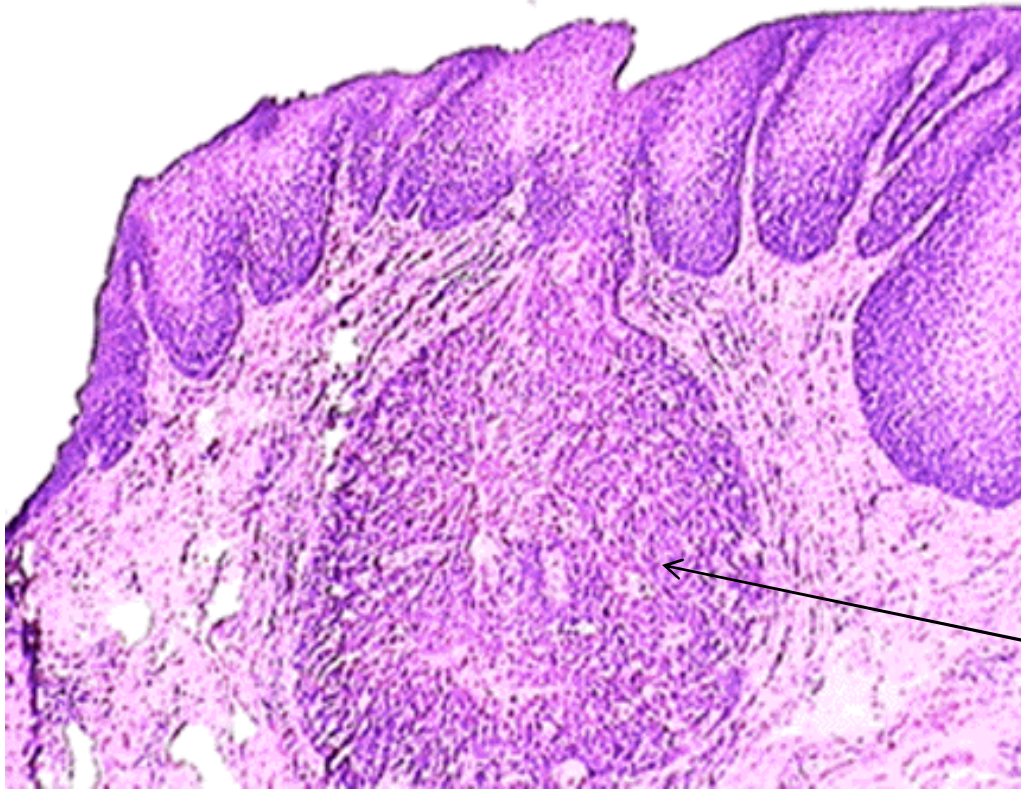


- Mucosa - non-keratinising stratified squamous epithelium
- Submucosa – loose connective tissue, lymphatic vessels, lymphoid follicles, leucocytes
- No serosal layer.
- Muscularis propria contains striated muscle fibres

Esophagus – Benign Tumors

- Most benign tumors mesenchymal in origin and lie within esophageal wall.
- Most are smooth muscle tumors – leiomyomas.
- Fibromas, lipomas, hemangiomas, neurofibromas and lymphangiomas can also arise.
- Mucosal polyps
- Squamous papillomas.
- Inflammatory polyp – may resemble malignant lesion (inflammatory pseudotumor).

Esophagus – Malignant Tumors



- 90% of esophageal tumors worldwide are SCC.
- Incidence varies from country to country
- Diet and environmental factors have significant role.

Malignant squamous cell invading submucosa

Ref: Robins Pathological Basis of Diseases, 6th Ed.

Esophageal Tumors – Risk Factors for SCC

Table 18-1. FACTORS ASSOCIATED WITH THE DEVELOPMENT OF SQUAMOUS CELL CARCINOMA OF THE ESOPHAGUS

Dietary

Deficiency of vitamins (A, C, riboflavin, thiamine, pyridoxine)
Deficiency of trace metals (zinc, molybdenum)
Fungal contamination of foodstuffs
High content of nitrites/nitrosamines
Betel chewing

Lifestyle

Alcohol consumption
Tobacco use
Urban environment

Esophageal Disorders

Long-standing esophagitis
Achalasia
Plummer-Vinson syndrome

Genetic Predisposition

Long-standing celiac disease
Ectodermal dysplasia, epidermolysis bullosa
Tylosis palmaris et plantaris
Racial disposition

Ref: Robins Pathological Basis of Diseases, 6th Ed.

Esophagus – Malignant Tumors Morphology



Figure 18-8

Large ulcerated squamous cell carcinoma of the esophagus.



Figure 18-9

Squamous cell carcinoma of the esophagus. Low-power microscopic view showing invasion into the submucosa.

Ref: Robins Pathological Basis of Diseases, 6th Ed.

Esophageal SCC

- Metastasis occur locally and into adjacent structures.
- Metastasis into mediastinum as well.

Tumor Location	Metastasis Pattern
Upper Third	Cervical pattern
Middle Third	Mediastinal nodes, parathraceal, tracheobroncial nodes
Lower Third	Gastric and celiac groups of nodes

Clinical Presentation – Esophageal Tumors

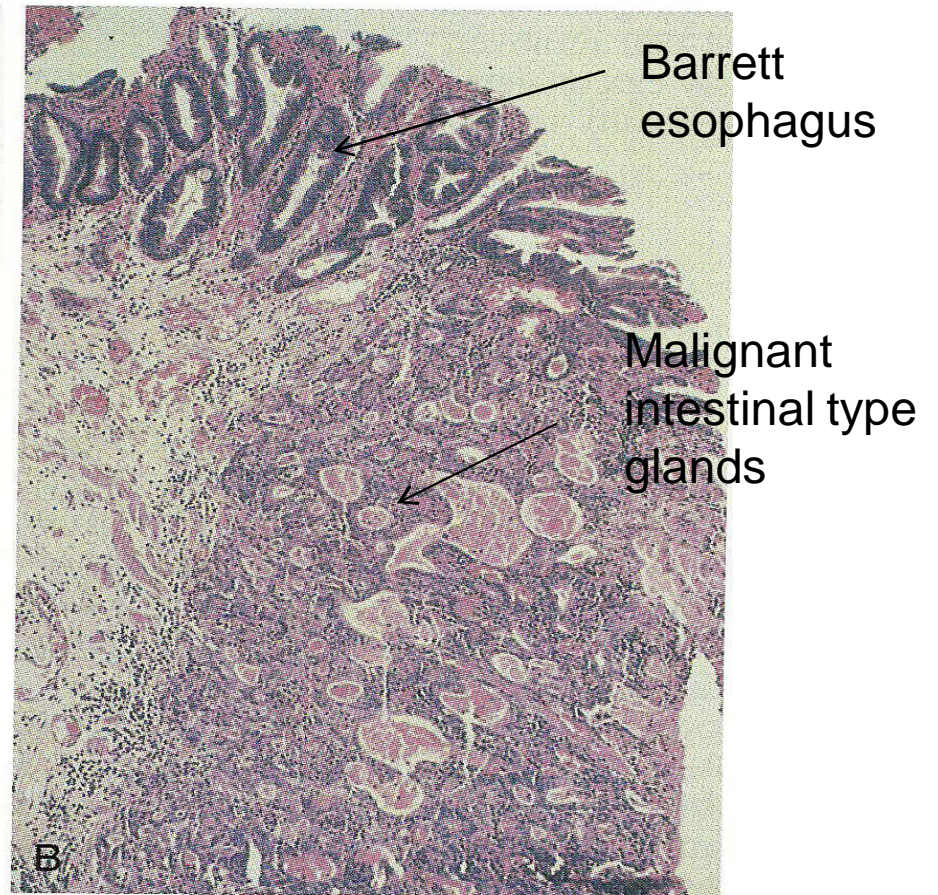
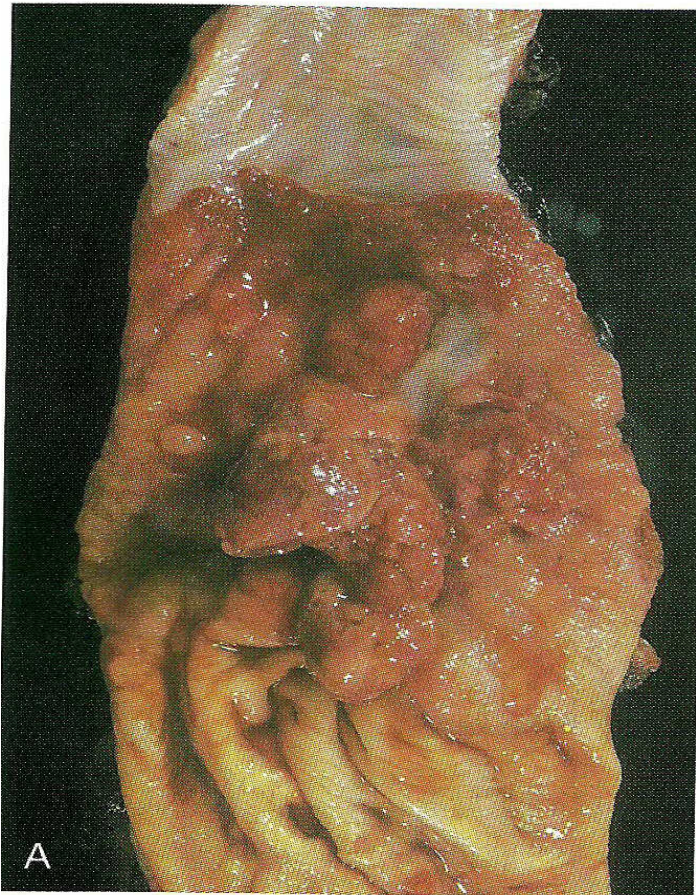
- Insidious so usually late presentation
- Dysphagia – fluids then to solids. Patients adjust their diet so late presentation.
- Weight loss.
- Hemorrhage into mediastinum is late presentation.
- Prognosis – 75% five year survival rate in superficial tumors. 25% in advanced cases.
- Lymph node metastasis reduces 5 year survival rates.

Adenocarcinoma of Esophagus

- Occur lower third of esophagus
- Barrett esophagus is a risk factor.
- Chronic injury to mucosa with resultant mutation in P53 is proposed as a cause.
- Other mutations also occur thus disruption in cell cycle.

- Morphology
 - Distal esophagus and may invade gastric cardia
 - Microscopic shows mucin-producing glandular tumors showing intestinal type features

Adenocarcinoma - Esophagus



Ref: Robins Pathological Basis of Diseases, 6th Ed.

Clinical Features

- Over 40 years of age. PNG may be younger.
- Progressive dysphagia and weight loss.
- Five year survival rate is 80% if identified early and treated where invasion limited to mucosa and submucosa.
- Late diagnosis, five year survival rate is less than 30%.

Stomach Malignancies

Normal anatomy

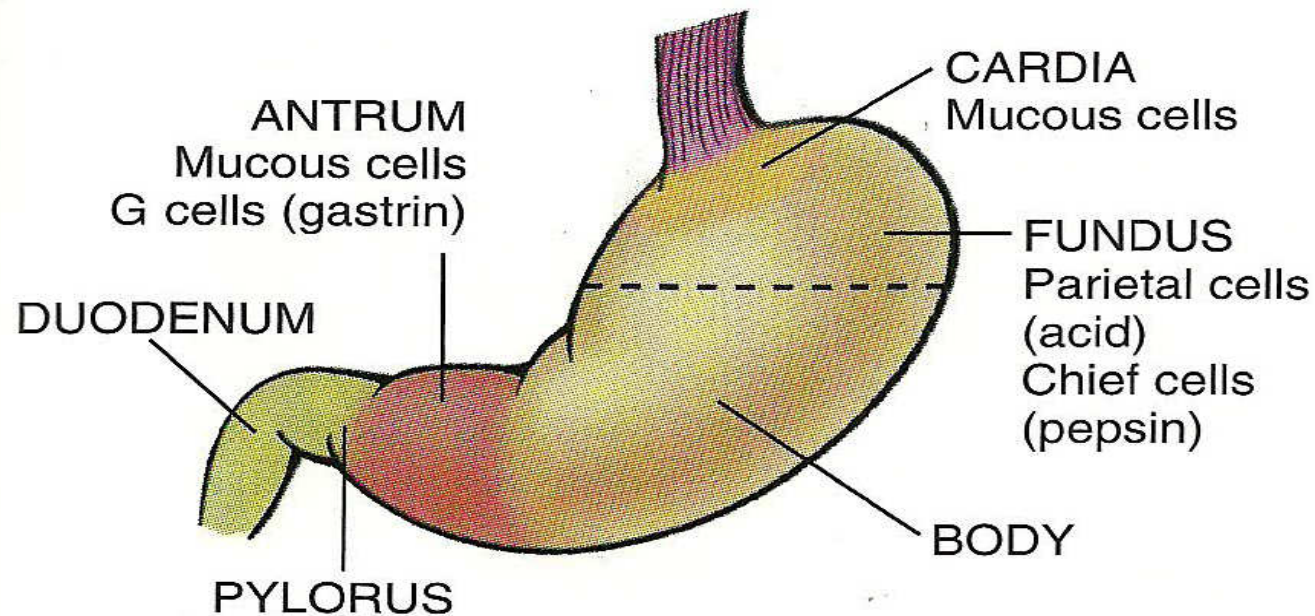


Figure 18-11

Anatomy of the stomach.

Ref: Robins Pathological Basis of Diseases, 6th Ed.

Benign Tumors - Stomach

- Polyps – rare. Incidental finding on endoscopy or autopsy.
- Polyps can occur as single or multiple lesions.
- Adenomas – has dysplastic epithelium and has potential to become malignant.
- Adenomas occur without a stalk (sessile) or with a stalk (pendunculated).
- Adenomas occur in 20% stomach resected for carcinomas.
- Adenomas affect more males than females with a ratio of 2:1.
- Endoscopy is mandatory for diagnosis.



Gastric Carcinoma

- Most common cancer of the stomach – 90-95% of cases.
- Others – lymphomas (4%), carcinoids (3%), stomal cell tumors (2%).
- Occur worldwide.
- Multiple risk factors identified.

Risk Factors for stomach

CA

Table 18-4. FACTORS ASSOCIATED WITH INCREASED INCIDENCE OF GASTRIC CARCINOMA

Environmental

Diet

- Nitrites derived from nitrates (water, preserved food)
- Smoked and salted foods, pickled vegetables
- Lack of fresh fruit and vegetables

Low socioeconomic status

Cigarette smoking

Host Factors

Chronic gastritis

- Hypochlorhydria: favors colonization with *Helicobacter pylori*
- Intestinal metaplasia is a precursor lesion

Infection by *H. pylori*

- Present in most cases of intestinal-type carcinoma

Partial gastrectomy

- Favors reflux of bilious, alkaline intestinal fluid

Gastric adenomas

- 40% harbor cancer at time of diagnosis
- 30% have adjacent cancer at time of diagnosis

Barrett esophagus

- Increased risk of gastroesophageal junction tumors

Genetic

Slightly increased risk with blood group A

Family history of gastric cancer

Hereditary nonpolyposis colon cancer syndrome

Stomach CA - Morphology

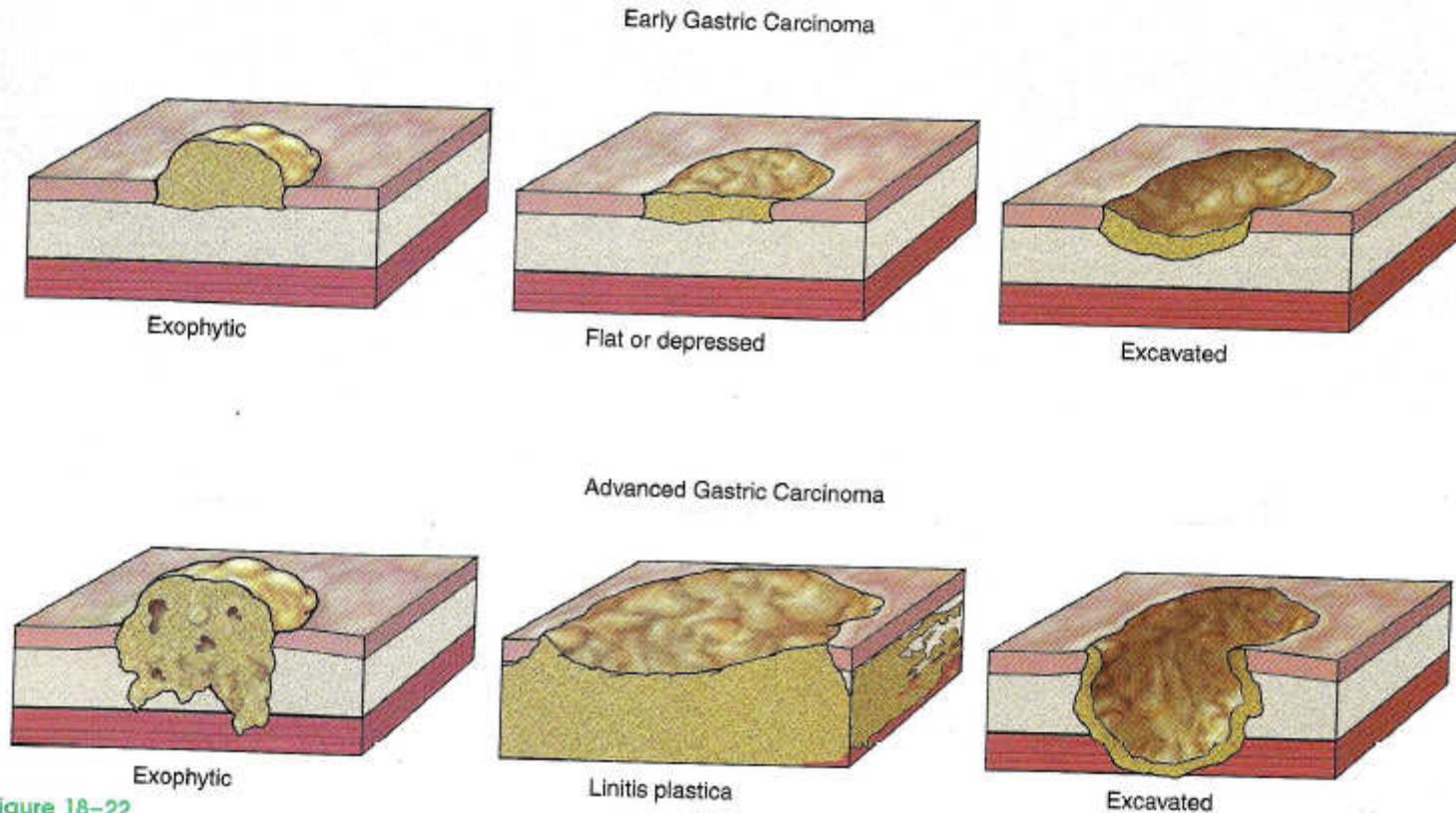


Figure 18-22

Diagram of growth patterns and spread of gastric carcinoma. In early gastric carcinoma, tumor is confined to the mucosa and submucosa and may exhibit an exophytic, flat or depressed, or excavated conformation. Advanced gastric carcinoma extends into the muscularis propria and beyond. Linitis plastica is an extreme form of flat or depressed advanced gastric carcinoma.

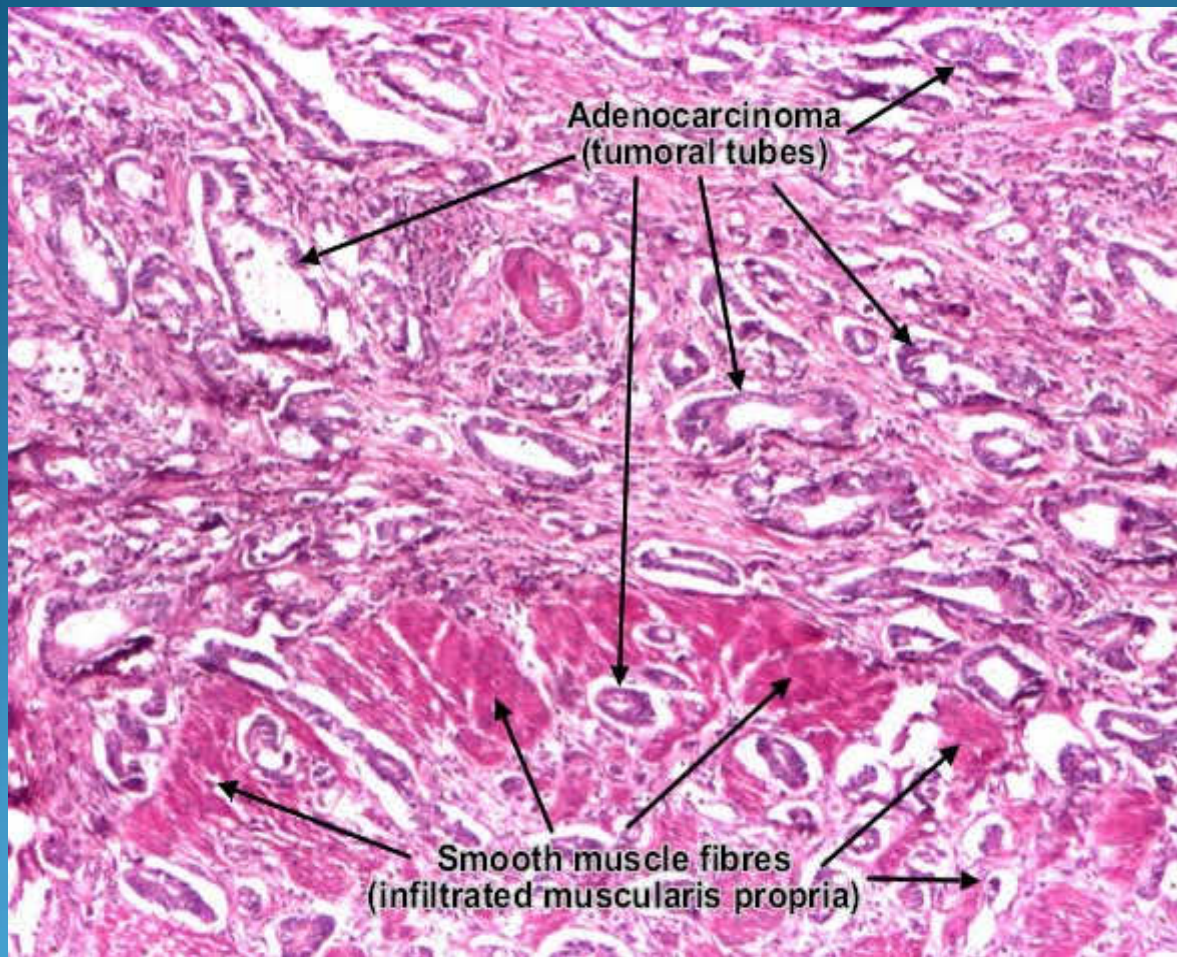
Stomach CA – anatomical Sites

Anatomical Site	Occurrence Rate
Pylorous & antrum	50-60%
Cardia	25%
Body & Fundus	Remainder

- Lesser curvature – 40%
- Greater curvature – 12%

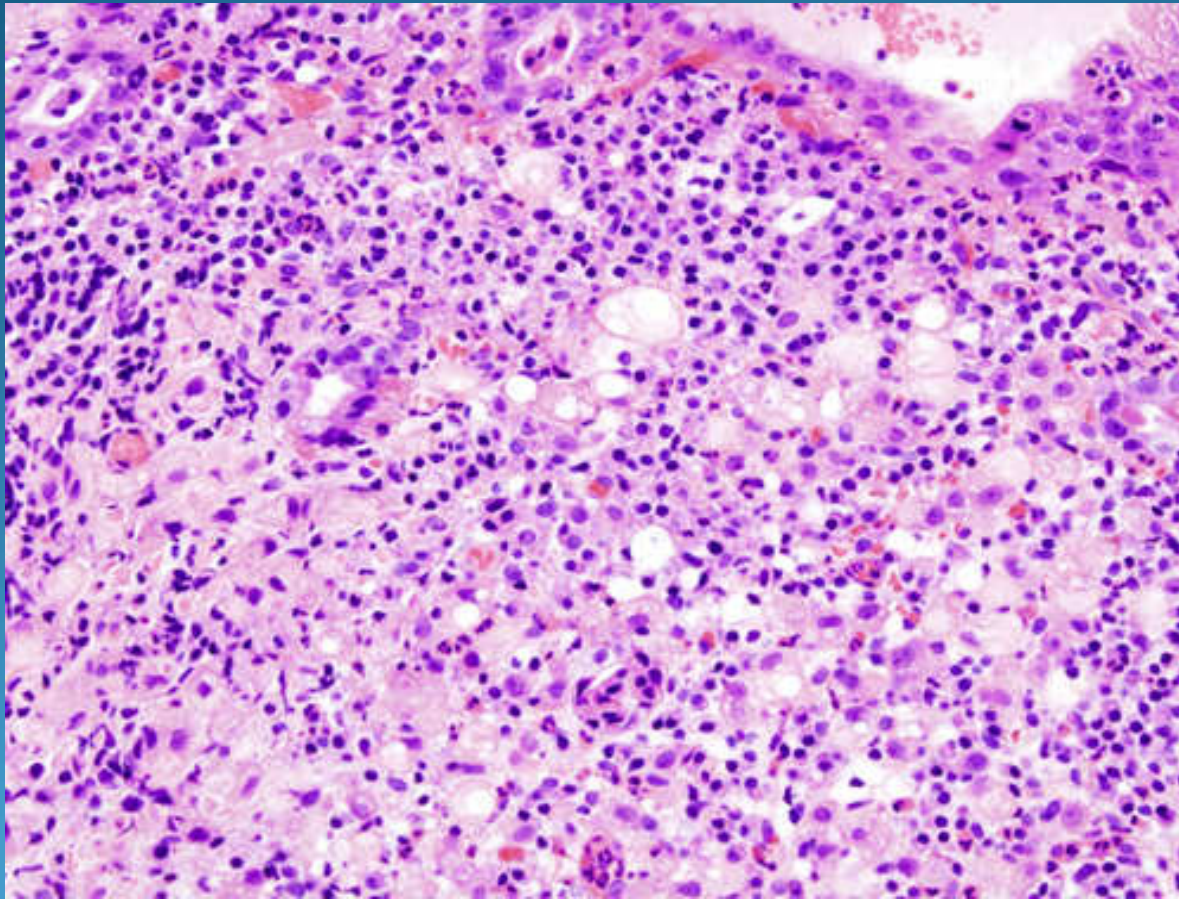
• **Most common site therefore is : lesser curvature at the antropyloric region.**

Microscopic features



- Two general histological types.
- Intestinal variant shows glands with mucin

Microscopic features



- Signet-ring variant shows gastric type mucous cells.
- Mucin formation pushes nucleus to side – signet ring appearance



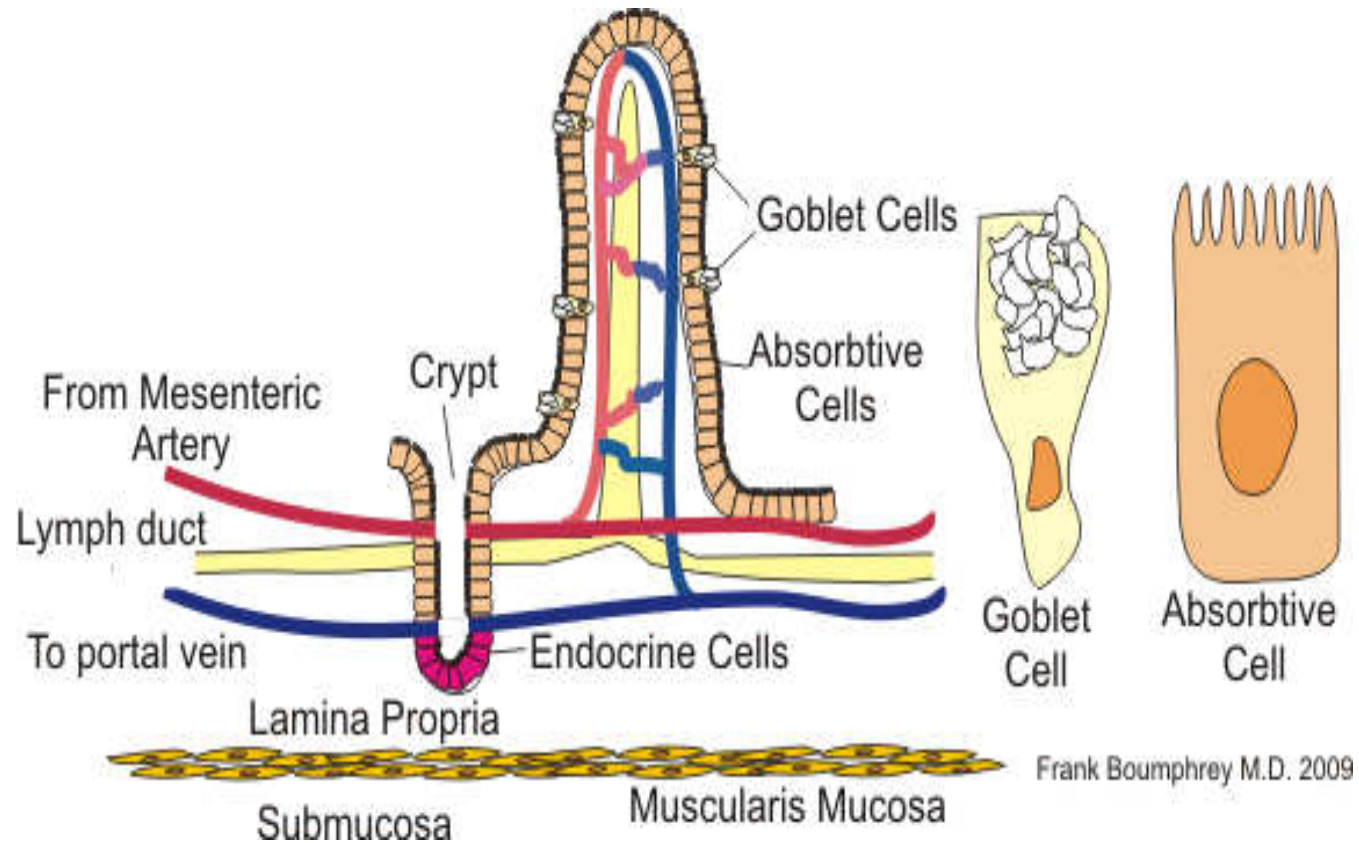
Ref: www.wikipedia.org

Stomach Carcinoma – Clinical Features

- Insidious onset – weight loss, dysphagia, anaemia, altered bowel habits, haemorrhage.
- Metastasis to regional structures and supraclavicular node (Virchows node) can be a early sign.
- Krukenburg tumor – metastasis to ovaries.
- Prognosis – 90-95% 5 year survival rate if detected early. Late diagnosis carries 15% 5 year survival rate.
- Detection by screening programs? Expensive.
- Secondaries to stomach – leukemia, lymphoma, malignant melanoma common.

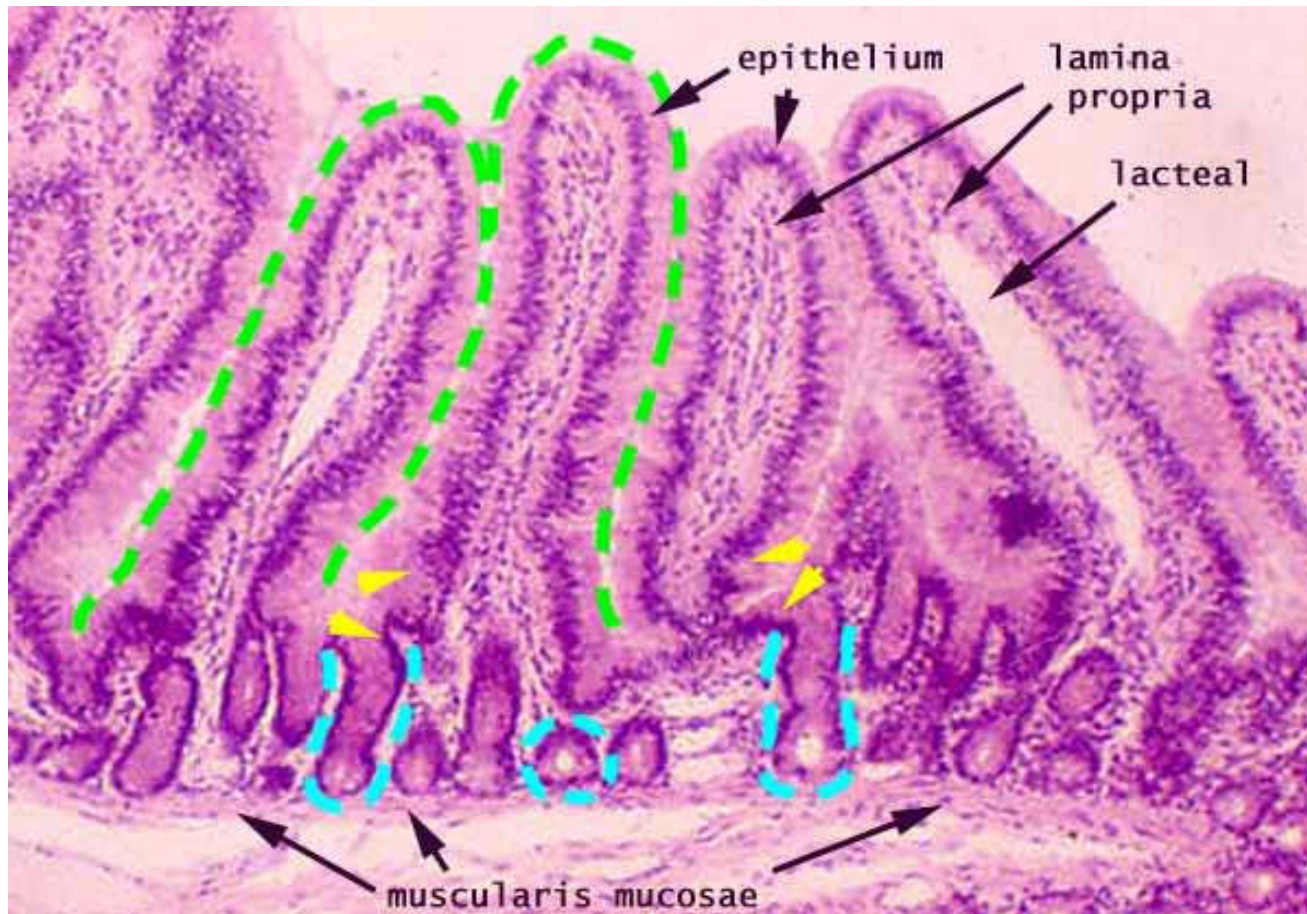
Small & Large Intestinal Tumors

Normal Anatomy Review



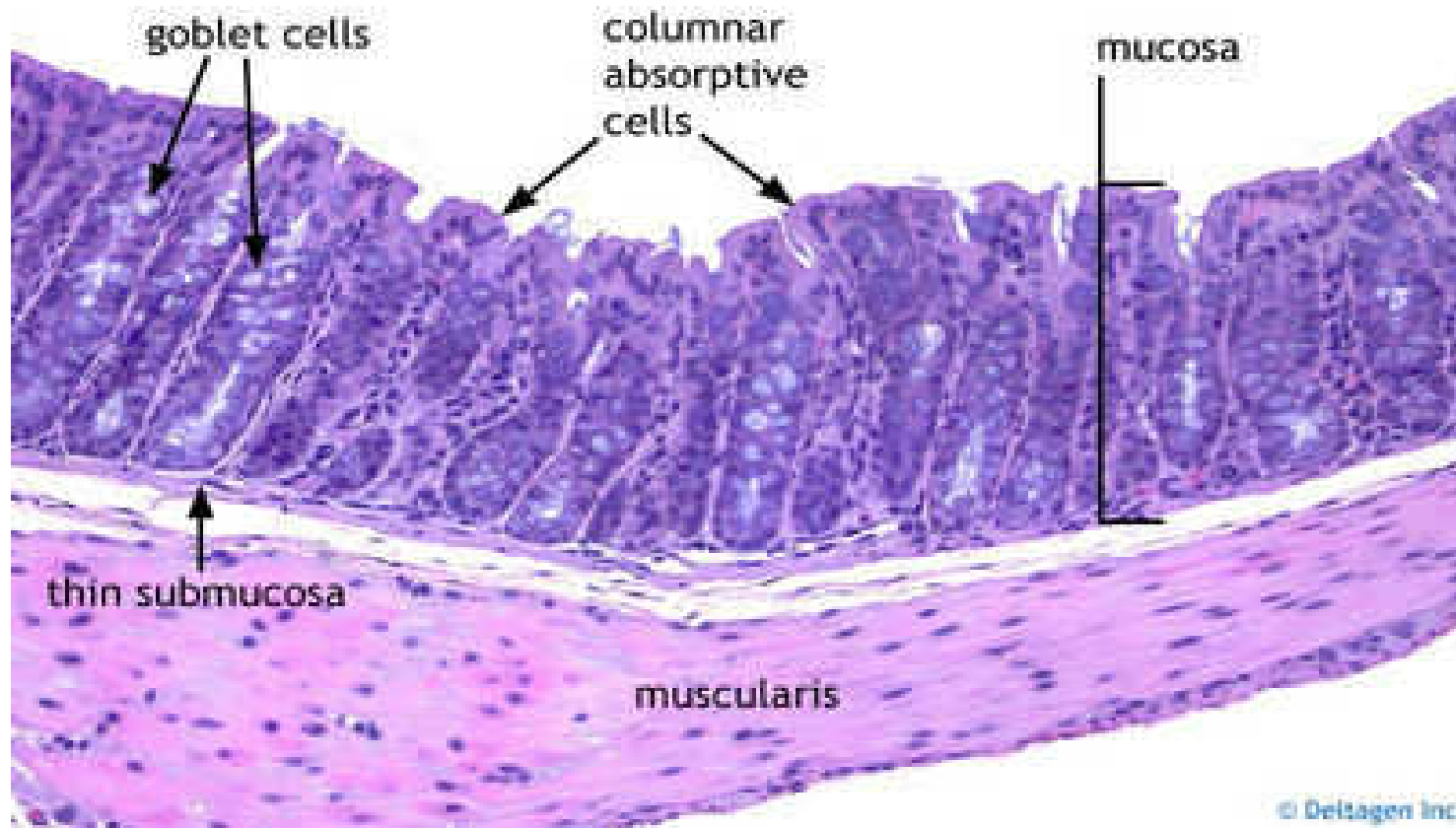
Ref: www.wikipedia.org

Small Intestine Normal Histology



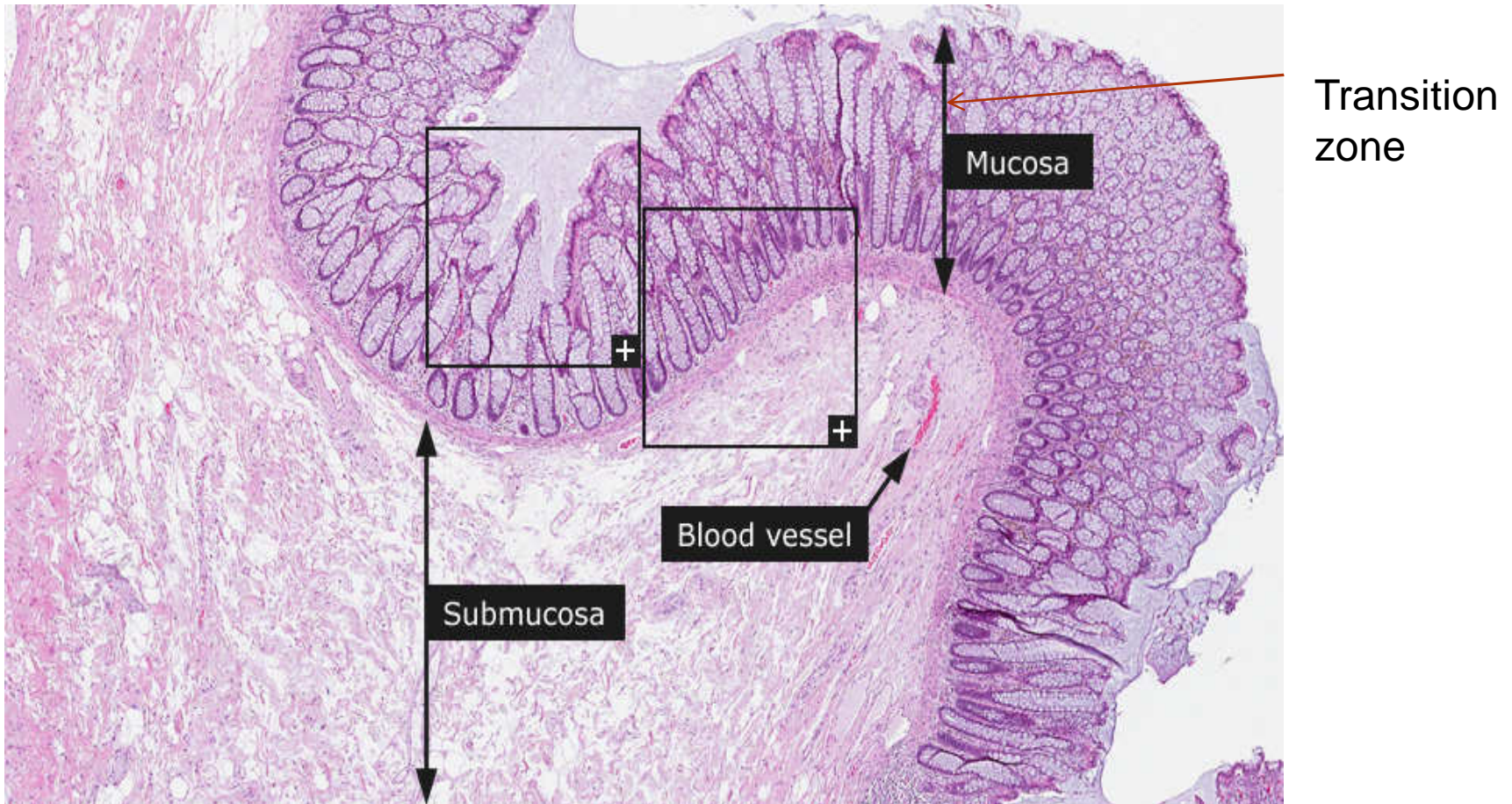
Ref: www.wikipedia.org

Large Intestine Normal Histology



Ref: www.histology-world.com

Colon – Rectum Transition



Small Intestinal Tumors

Table 18–11. TUMORS OF THE SMALL INTESTINE AND COLON

Non-neoplastic (Benign) Polyps

- Hyperplastic polyps
- Hamartomatous polyps
 - Juvenile polyps
 - Peutz-Jeghers polyps
- Inflammatory polyps
- Lymphoid polyps

Neoplastic Epithelial Lesions

- Benign
 - Adenoma*
- Malignant
 - Adenocarcinoma*
 - Carcinoid tumor
 - Anal zone carcinoma

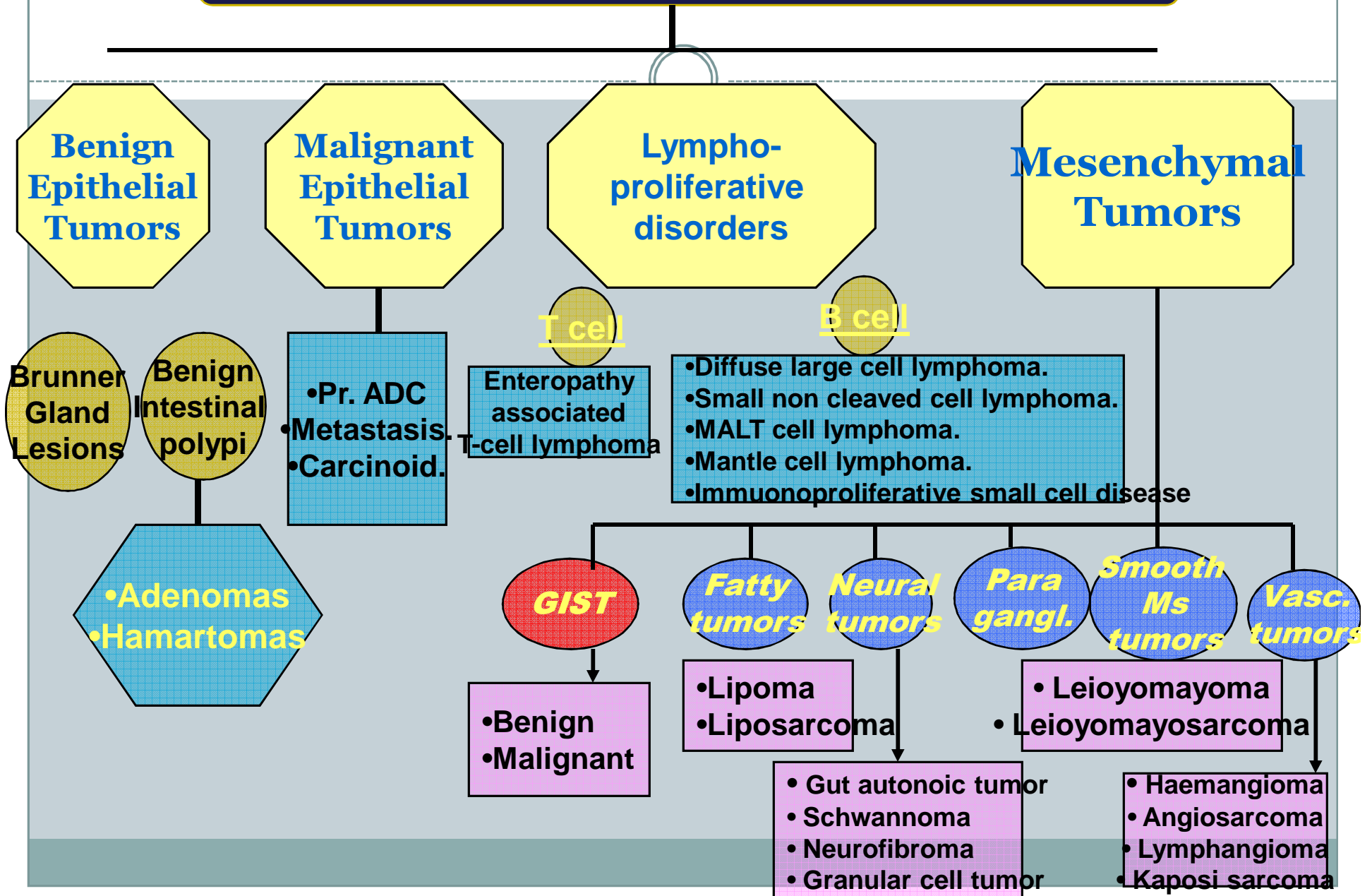
Mesenchymal Lesions

- Gastrointestinal stromal tumors (gradation from benign to malignant)
- Other benign lesions
 - Lipoma
 - Neuroma
 - Angioma
 - Kaposi sarcoma

Lymphoma

Ref: Robins Pathological Basis of Diseases, 6th Ed.

SMALL INTESTINE TUMORS



BENIGN:

- ★ **GI stromal tumors (GIST) (45%)**
- ★ **Adenomas (20-40%)**
- ★ **Lipomas (16%)**
- ★ **Hemangiomas (13%)**
- ★ **Lymphangioma (5%)**
- ★ **Neuroma (1%)**
- ★ **S.intestinal polyps**

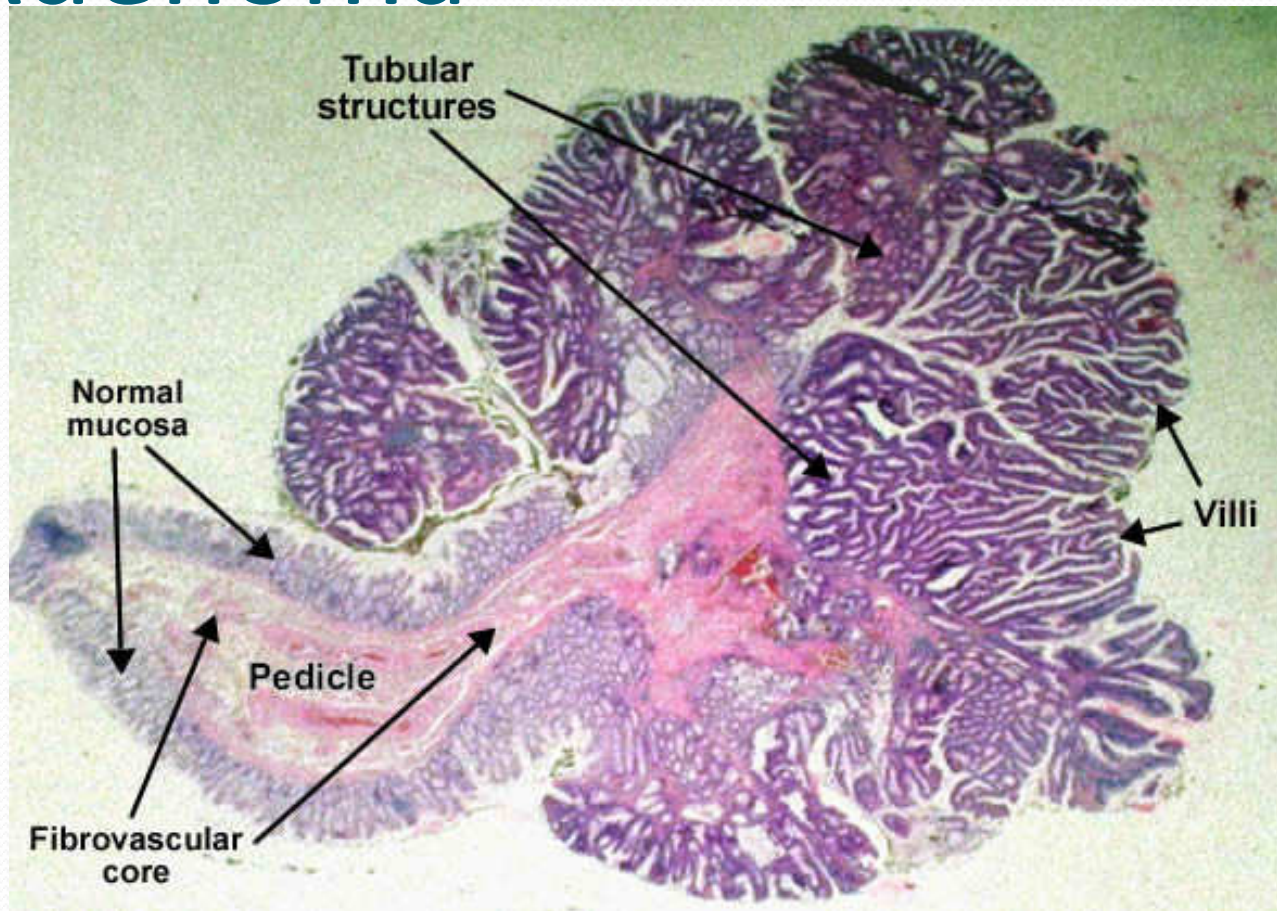
MALIGNANT:

- ★ **Carcinoids (47%)**
- ★ **Adenocarcinomas (25%)**
- ★ **Lymphomas (16%)**
- ★ **Sarcomas or GIST (1%)**
- ★ **Metastasis (1%)**

Small Intestinal Tumors - Benign

- Adenomas are the common tumors.
- 25% of benign tumors of the GIT.
- Occur commonly at ampulla of Vater.
- Age onset – 30-60 years of age.
- Familial polyposis coli is a recognised risk factor.

Adenoma

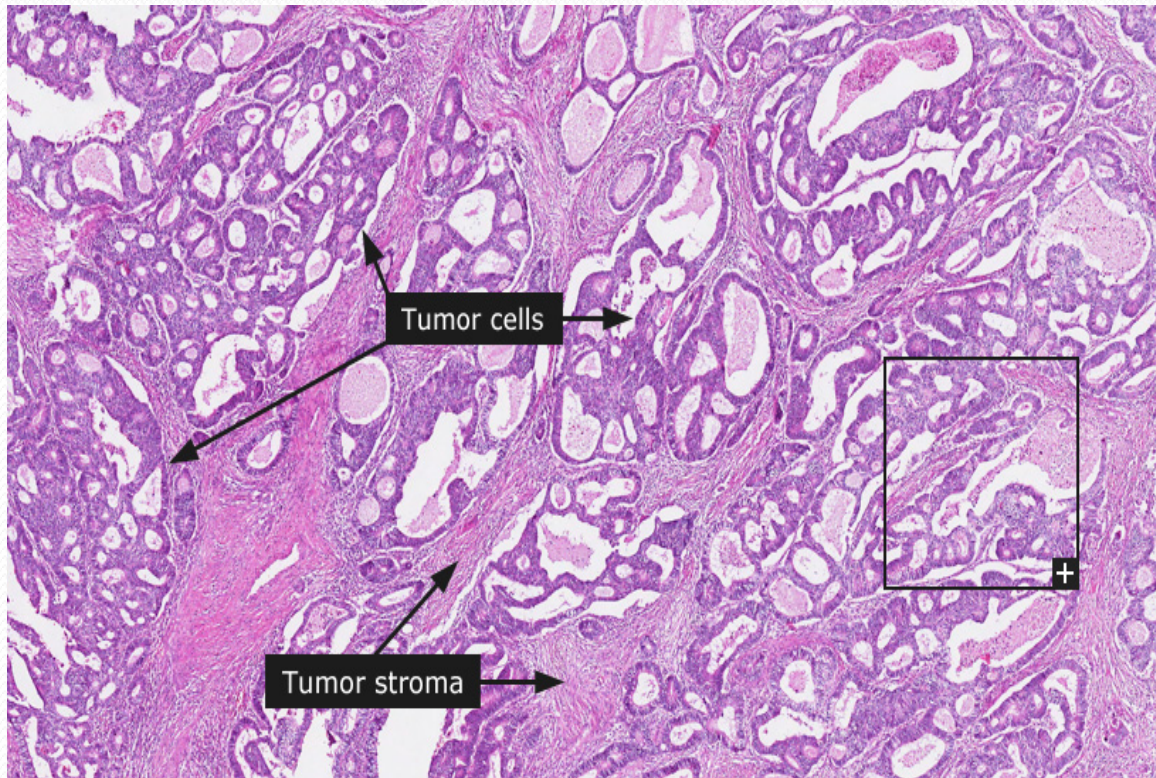


Ref: www.mdblogger.com

Malignant Tumors Of Small Intestine- Adenocarcinoma

- AdenoCa – majority of malignant tumors
 - Age onset – 40-70.
 - Clinically present with obstructive jaundice, anaemia, weight loss and signs of bowel obstruction.
 - Most tumors penetrate bowel wall at time of diagnosis.
 - Metastasis to regional lymph node, mesentry, live and lung.
 - Five year survival rates of 70% if early diagnosis and en bloc excision.

Adenocarcinoma



- Tall columnar cells with mucin infiltrating muscle wall

Ref: www.proteinatlas.com

Large intestinal tumors – Benign lesions

- Large intestinal tumors – tumors of the colon & rectum.
 - Non-neoplastic polyps
 - Sporadic
 - Age onset – over 60 years.
 - Adenomas
 - Common over 60 years of age but can occur before 40 years of age.
 - Cancer rare in tubular adenomas
 - Cancer high in sessile villous adenomas.
 - Familial syndromes
 - Familial polyposis syndromes are autosomal dominant disorders.
 - Propensity to develop into malignant lesions



Colorectal Carcinoma

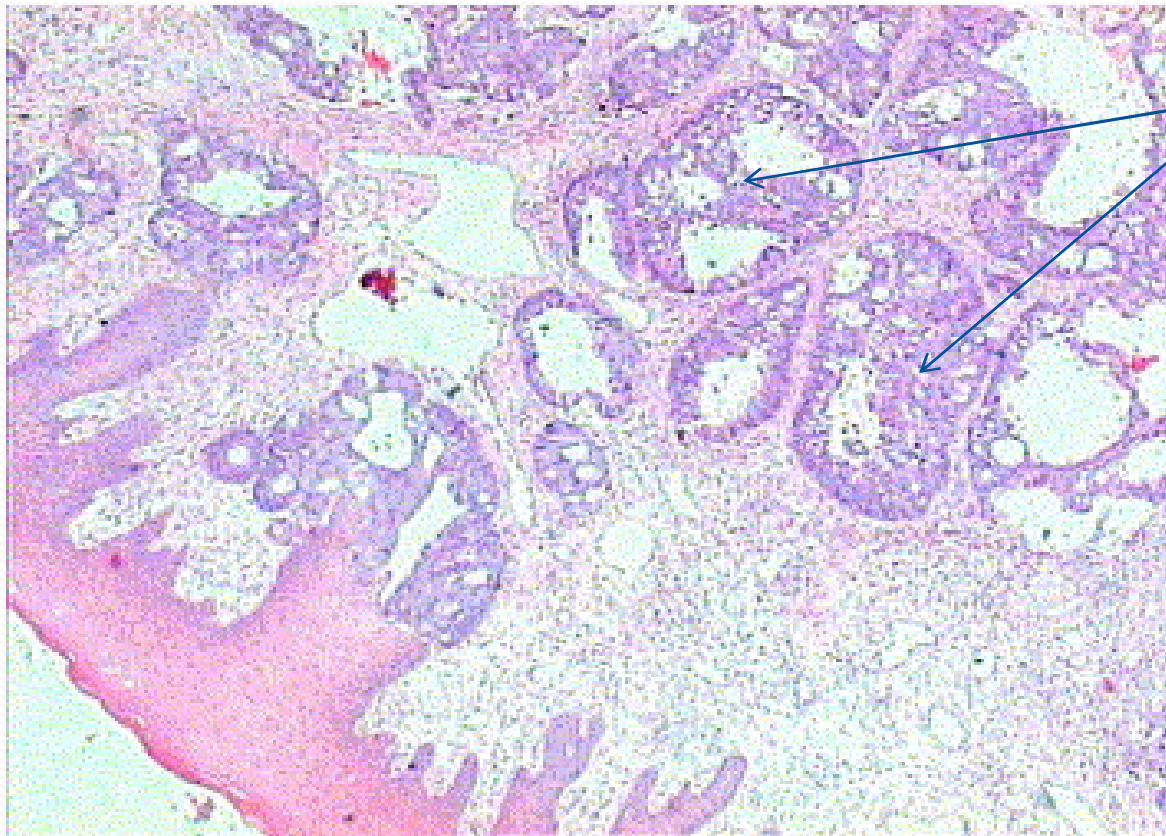
- Colorectal carcinoma
 - 98% of all cancers in large intestines are adenocarcinomas
 - Age onset – 60-79 years of age.
 - Worldwide distribution.
 - Risk factors – diet (low fibre, high red meat intake)
 - Clinical presentation – insidious onset. Anaemia common (signs of anaemia), PR bleeding.
 - Metastasis – direct extension into nearby structures. By lymphatic and blood to lung and liver common.
 - Colorectal metastasis – regional lymph nodes, liver, lungs and bones and other sites.
 - Five year survival rate – depends on Astler-Coller Classification (histological).



Large Intestinal Tumors

- Lymphomas
 - Common site for lymphoma. 4% of all GIT malignancies are lymphomas.
 - Risk factors – H.pylori infection causing gastritis, HIV infection, patients undergoing immunosuppressive therapy and patients with sprue (long standing malabsorption syndrome).
 - Clinical features: insidious onset and present with weakness and weight loss.
 - Early diagnosis improves outcome – up to 85% (10 year survival rate).
- Mesenchymal tumors
 - Lipomas are common and can occur anywhere along the GIT.
 - Asymptomatic.
 - PR bleeding common

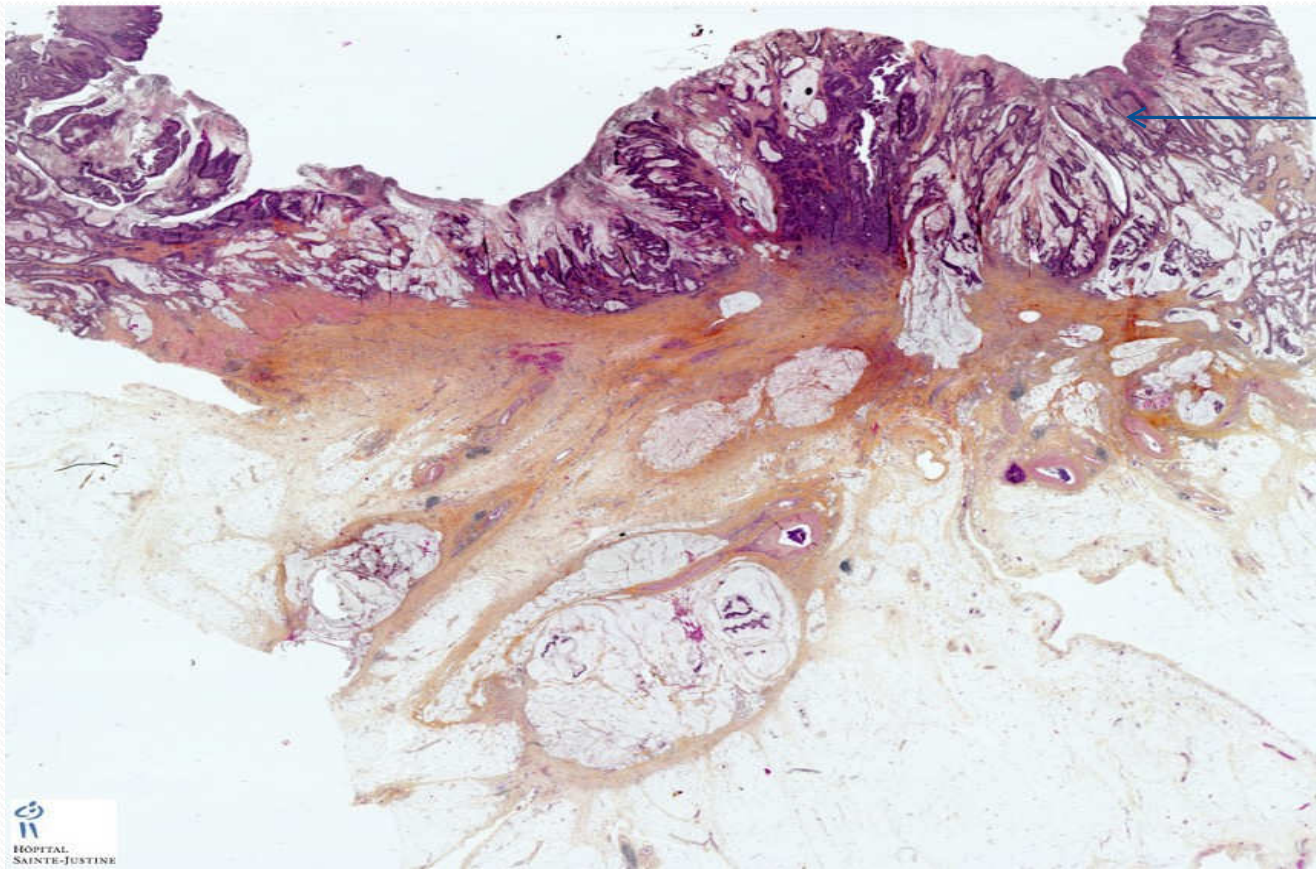
Adenocarcinoma Large Intestine



Tumor Cells

Ref: www.sciencedirect.com

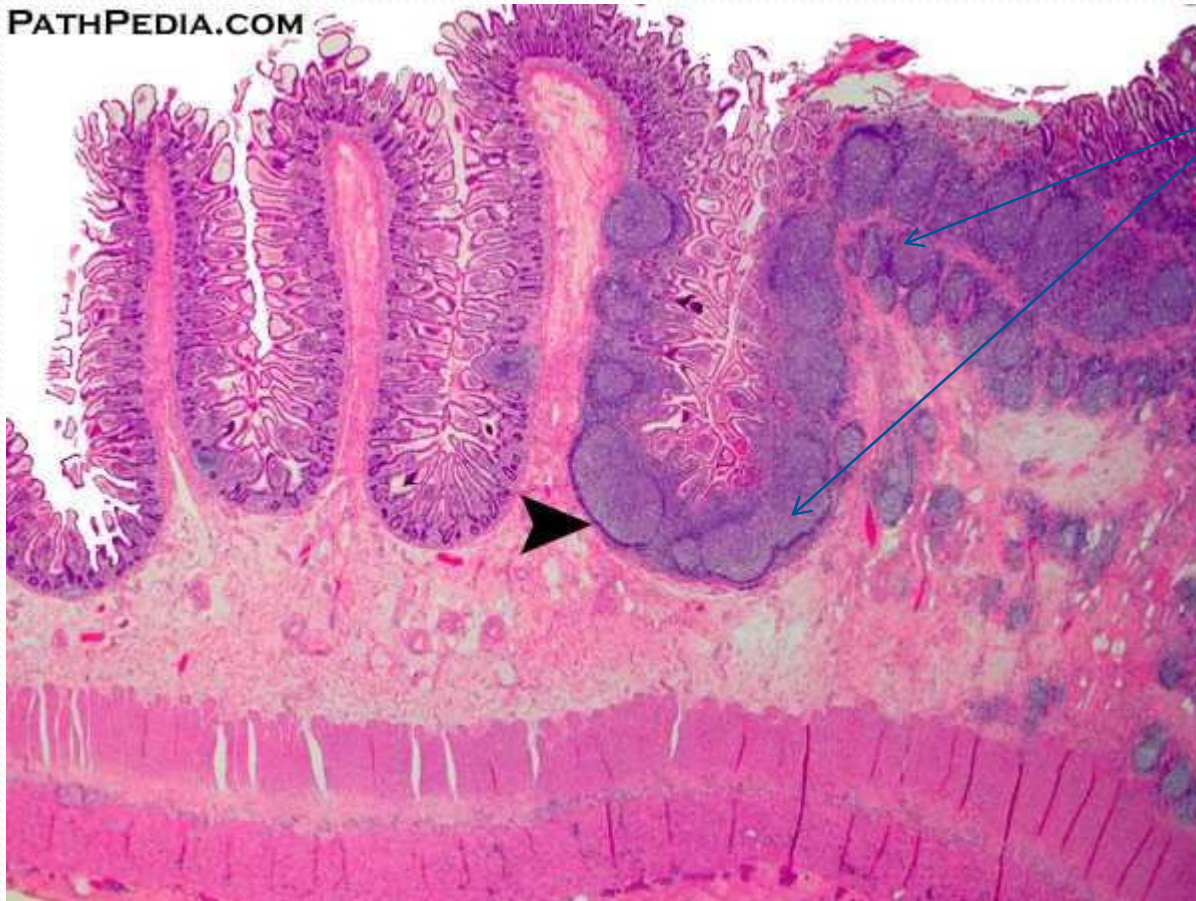
Colon Adenocarcinoma



Normal
epithelium
distorted.

Lymphoma Intestine

PATHPEDIA.COM



Malignant
Lymphoid Follicles

Appendix & Peritoneum

- Appendix
- Mucocele & pseudomyxoma peritonei
 - Carcinoid is common form of tumor.
 - Distant spread is rare.
 - Discovered as incidental findings.
 - Mucocele & Pseudomyxoma peritonei.
 - Present with signs of acute appendicitis, bowel obstruction.
 - Discovered on surgery for bowel obstruction or acute appendicitis.
- Peritoneum Tumors
 - Primary – mesotheliomas
 - Secondary – metastasis from distant primary location. Common form observed.

Laboratory Investigation

- FBC – anaemia
- UEC – electrolyte abnormalities if bowel obstruction.
- Specific tests – tumor markers where appropriate.
Non-specific and used as screening tools.
- **Definitive diagnosis is by histology.**
- Role of screening – endoscopy & genetic counseling?



End

References:

Robins Pathological Basis of Diseases, 6th Ed. Read chapter on The Gastrointestinal Tract (chapter 18).

Seminar Notes will be available on this website:

www.pathologyatmhs.wordpress.com