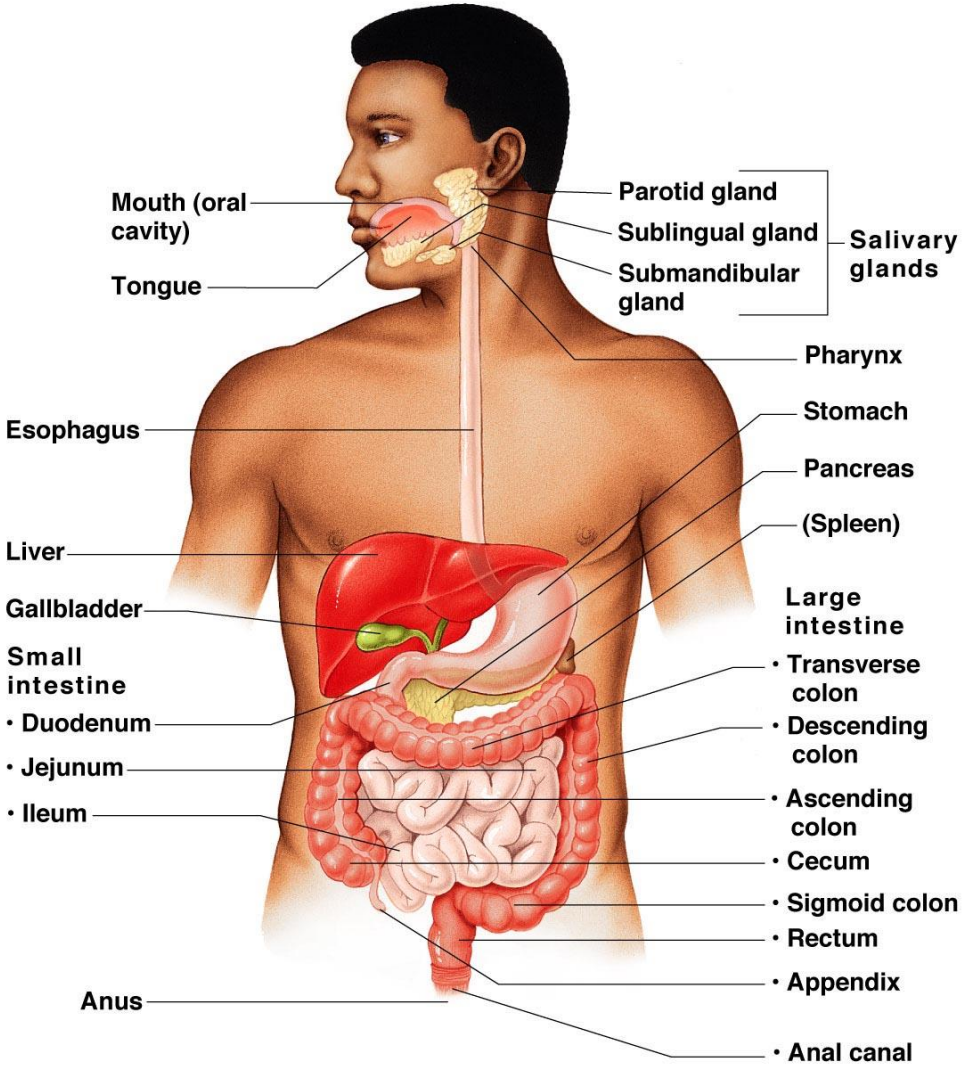
PATHOLOGY OF GI TUMORS

DR. SARITA
Prof. & Head
Dept. of Pathology,
GGSMC, Faridkot

Gastrointestinal Disorders



TUMOURS OF OESOPHAGUS

BENIGN TUMOURS

1. EPITHELIAL

SSE- Papilloma

Columnar– Adenoma

2. **STROMAL**

Fibroma

Neurofibroma

Haemangioma.

MALIGNANT TUMOURS

1. Carcinoma

Sq. cell carcinoma

Adenocarcinoma

2. Sarcoma (very rare)

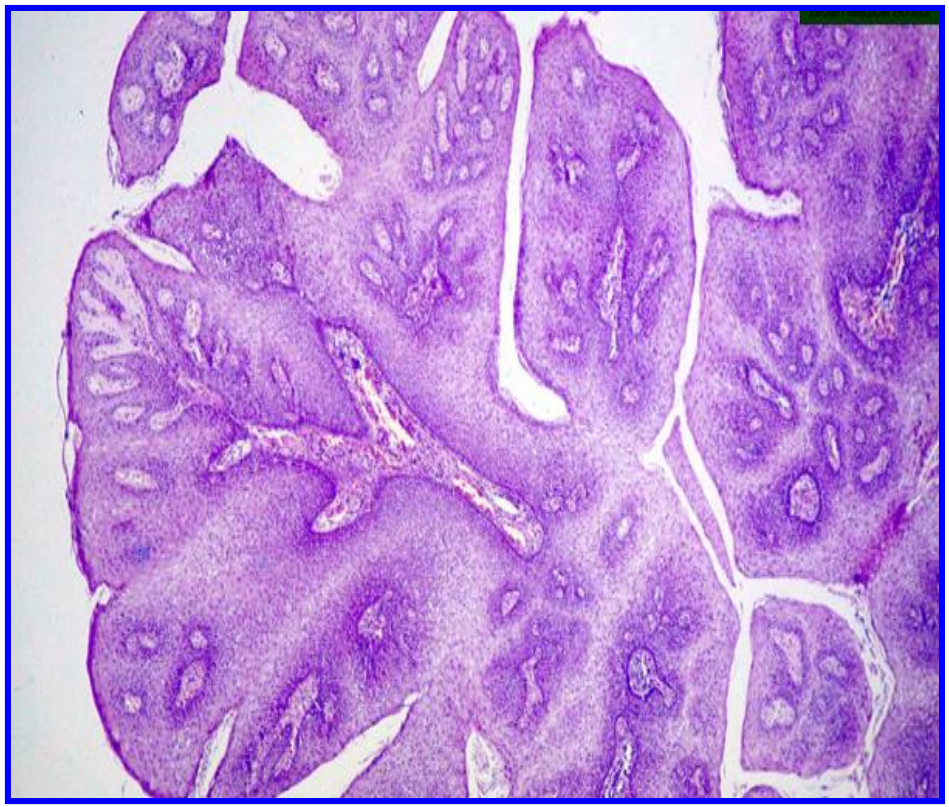
Leiomyosarcoma

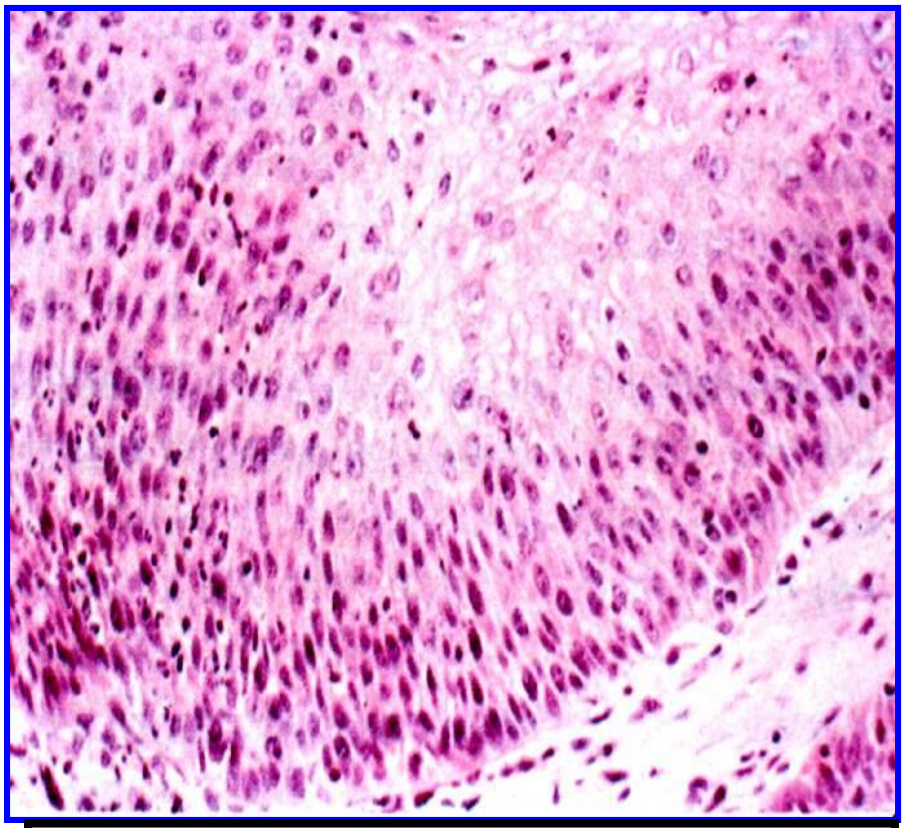
Fibro sarcoma

Benign neoplasms & tumor-like lesions

- Esophageal benign neoplasms are mostly of mesenchymal origin (non-epithelial): leiomyomas, lipomas, hemangiomas, neurofibromas.
- **Two distinctive lesions:**
  - **Fibrovascular polyp**
  - **Squamous papilloma**

Squamous papilloma





Low magnification: fronds of thickened squamous epithelium supported by connective tissue cores

Some have HPV-related cytologic changes or evidence of HPV DNA by in-situ hybridization methods

If squamous papilloma identified, respiratory tract should be examined for HPV-related papillomatosis (especially children)

Malignant neoplasms of esophagus- An overview

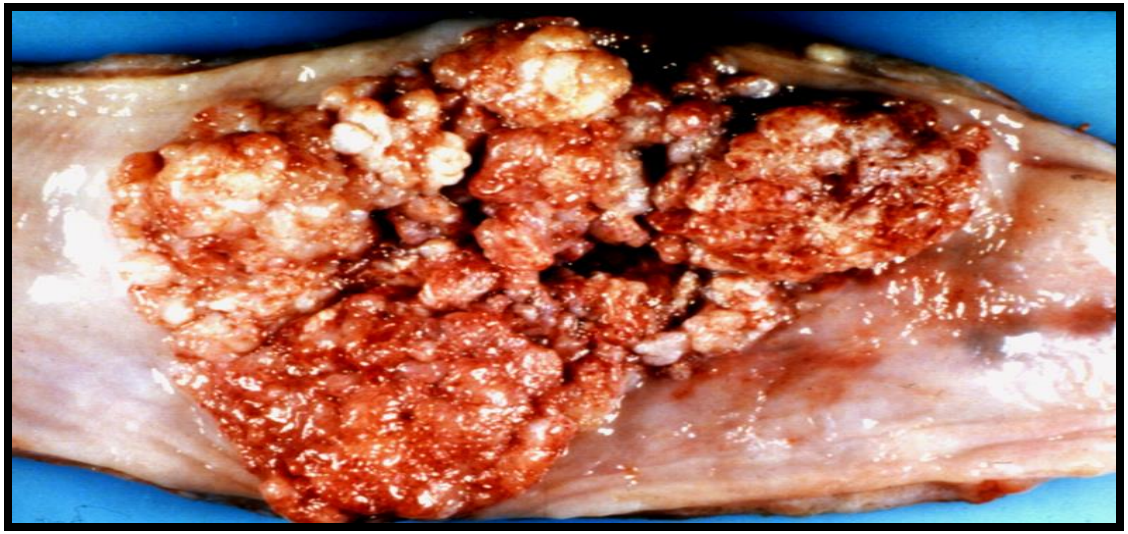
- Malignant tumors of esophagus comprise 6% of all gastrointestinal cancers.
- Problem: often asymptomatic until late, when they are deeply invasive or already metastatic

- Worldwide: **90% squamous / 10% adenocarcinoma.**

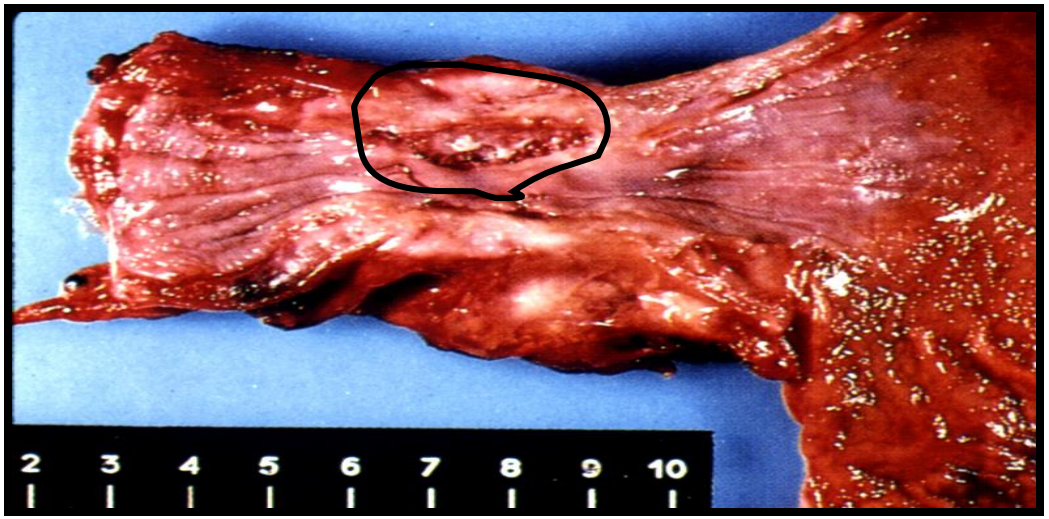
- Incidence of adenocarcinoma rising steadily since 1970, almost always arising in Barrett esophagus.

Squamous Carcinoma	Descriptor	Adenocarcinoma
M:F = 4:1; high incidence Iran, China, Puerto Rico (environmental initiators)	Epidemiology	M:F = 7:1; >95% from Barrett metaplasia; <5% from submucosal glands
Initiators: environmental carcinogens; promoters: nutritional deficiencies (vitamins A, B1, B2, B6, trace metals)	Pathogenesis	**Barrett dysplasia:** early mutation or overexpression of p53; amplfication cERB-B2, cyclin D, cyclin E
Ethanol, tobacco, achalasia, chronic esophagitis, Plummer-Vinson syndrome	Clinical Risk Factors	**chronic reflux esophagitis** tobacco, obesity
20% upper third 50% middle third 30% lower third	Anatomic Distribution	>95% lower third
5 yr. survival: 5-10% --75% 5 yr. survival if T1 lesion --25% 5 yr. survival for all cases subjected to surgery	Prognosis	**5 yr. survival: 25%** >80% 5 yr. survival with esophagectomy for T1 lesion

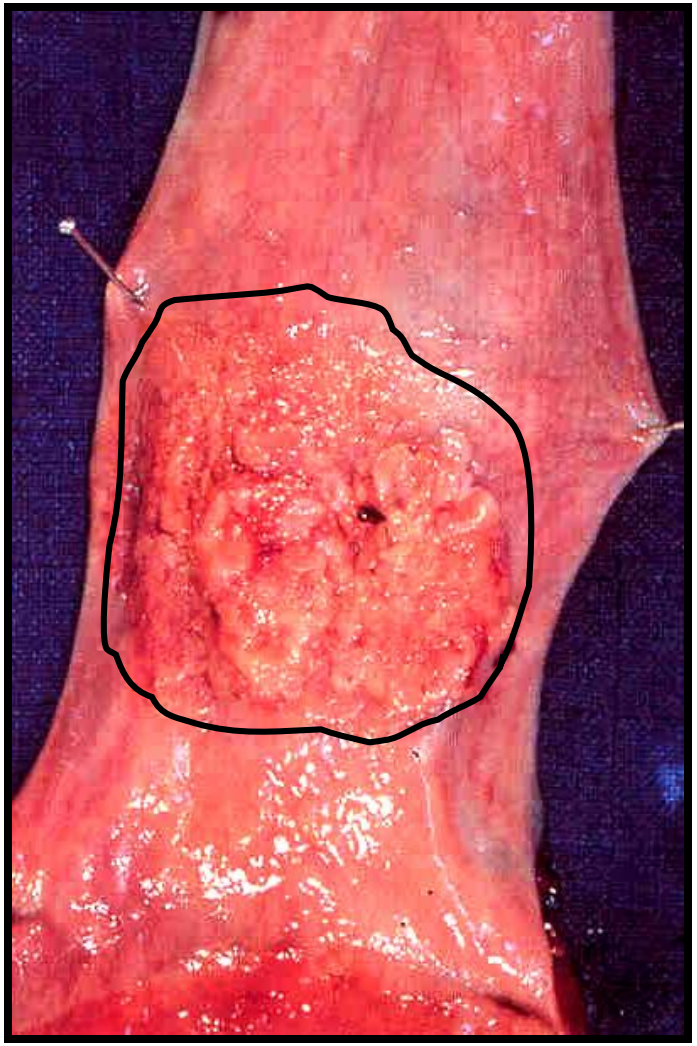
Squamous CA: gross pathology



Exophytic polypoid (obstructing lesion)



Ulcerated stricture (dysphagia)



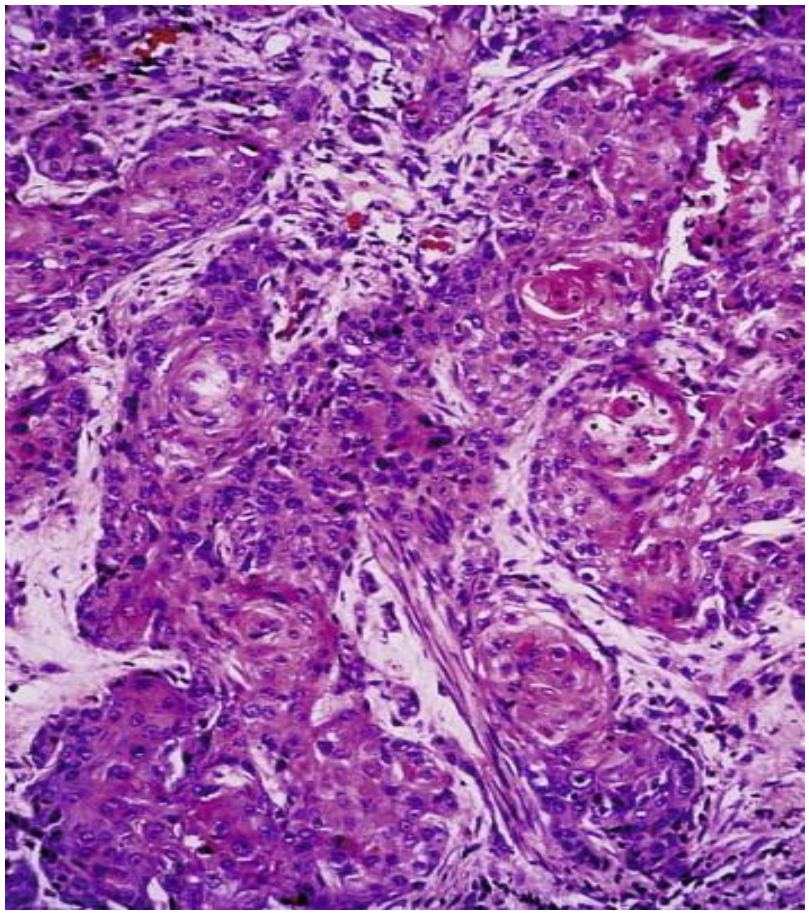
Early, superficial T1 lesion, good prognosis

SQUAMOUS CELL CA- HISTOLOGY

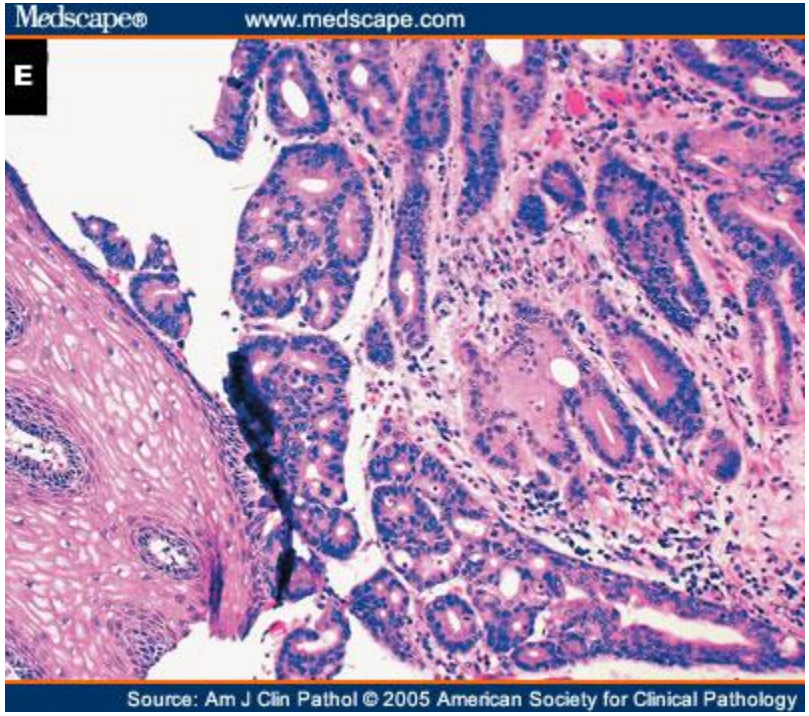
Grade 1 well differentiated

Grade 11 **moderately differentiated**

Grade 111 poorly differentiated



M/E—Adenocarcinoma.



Site – lower 1/3rd (from Barrett's)

Majority of carcinomas are **mucin** producing adeno carcinoma of **gastric type or intestinal type**

Spread of esophageal carcinoma

1.LOCAL SPREAD

Most imp- both transverse and longitudinal……..

longitudinal — Stomach below,

Hypo pharynx above.

Trachea– tracheo esophageal fistula

transverse — Larynx--- hoarseness

Mediastinum, lungs, Trachea, bronchi,

pleura, aorta, etc.

2.LYMPHATIC SPREAD

Submucosal lymphatics ---- multiple satellite nodules

Cervical Lymphadenopathy

Paraoesophageal **Lymphadenopathy.**

Tracheobronchial Lymphadenopathy.

. Sub diaphragmatic **Lymphadenopathy.**

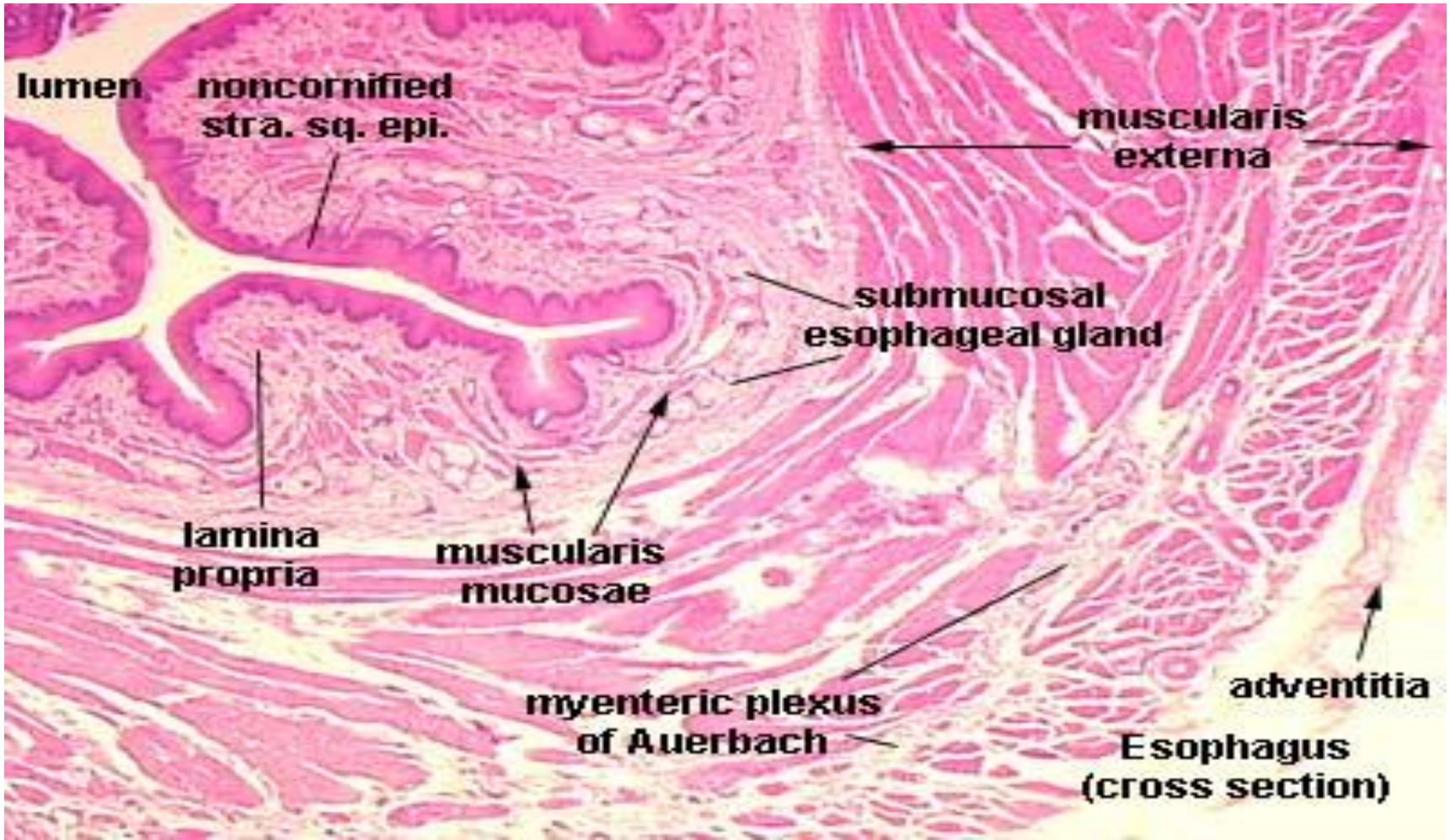
3.HAEMATOGENOUS SPREAD--- rare, can involve lung, liver etc.

Esophagus

- The specimen received are:
- Mucosal biopsies
- Resection specimen (partial or total esophagectomy)

INTERPRETATION OF THE ESOPHAGEAL BIOPSY

1. Is the esophageal biopsy is normal or abnormal?



APPROACH TO INTERPRETATION OF NEOPLASTIC LESIONS

- What is the tumour type and differentiation?
- Does the biopsy include normal esophageal mucosa?
- Is there any overlying squamous dysplasia , glandular dysplasia or Barrett's metaplasia?
- Is it possible to comment on the submucosal invasion in the biopsy specimen?
- Extent of invasion in resection specimen (Layers involved)
- Presence or absence of LVE (Lympho-vascular emboli)
- Lymph node status
- Distant spread

PATHOLOGY OF STOMACH

Four anatomical regions

- Cardia
- Fundus
- Body
- Antrum

Highly vascular mucosa

Majority of gastric lesions are in antrum and cardia.

Fundus and body spared- rich blood supply.

Tumours of Stomach

Non neoplastic(Polyps)

Hyper plastic polyp

Inflammatory polyp

Hamartomatous polyp

Neoplastic tumours

Benign

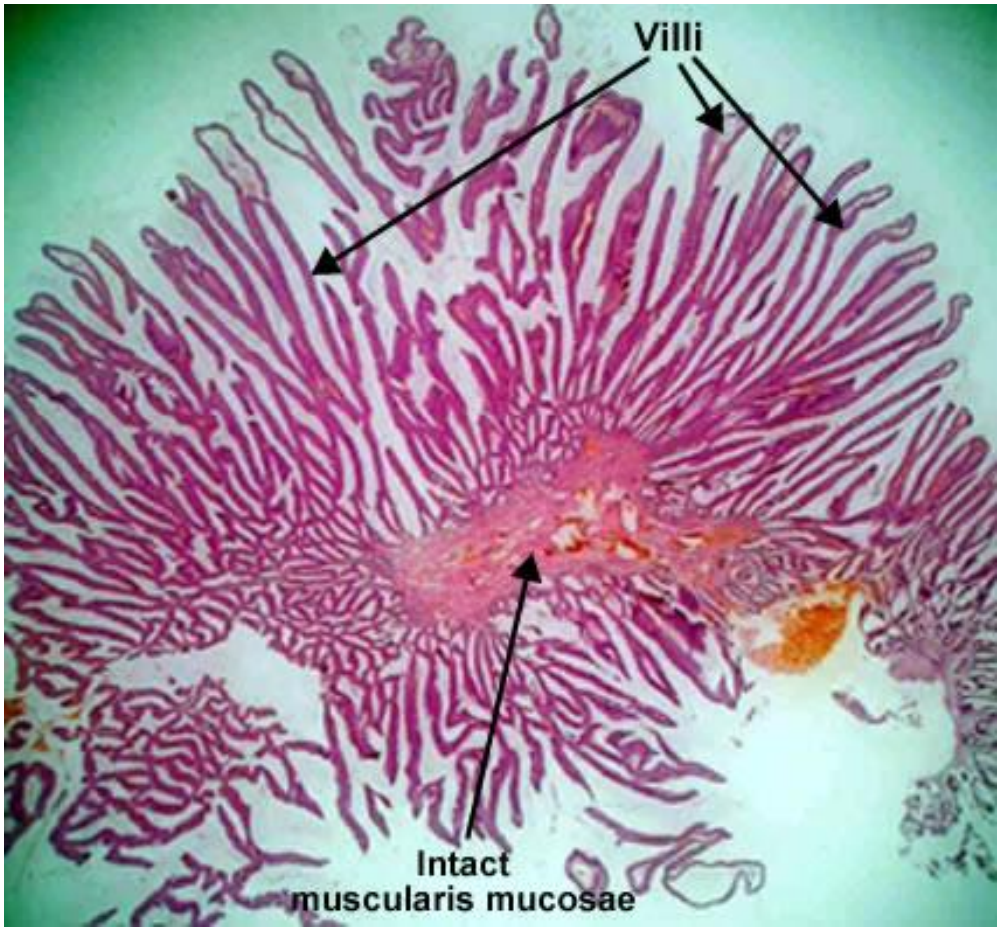
Malignant

ADENOMA….Stomach

- Rare in Stomach.
- Pyloric Antrum.
- **M/E**-DYSPLASTIC CELLS within gastric glands.
- **By definition all gastric adenomas have epithelial dysplasia.**
- Gastric adenoma being removed endoscopically.
- **Solitary.**
- < 2cm. in dia.
- Commonly located in the antrum.

Adenoma….Stomach

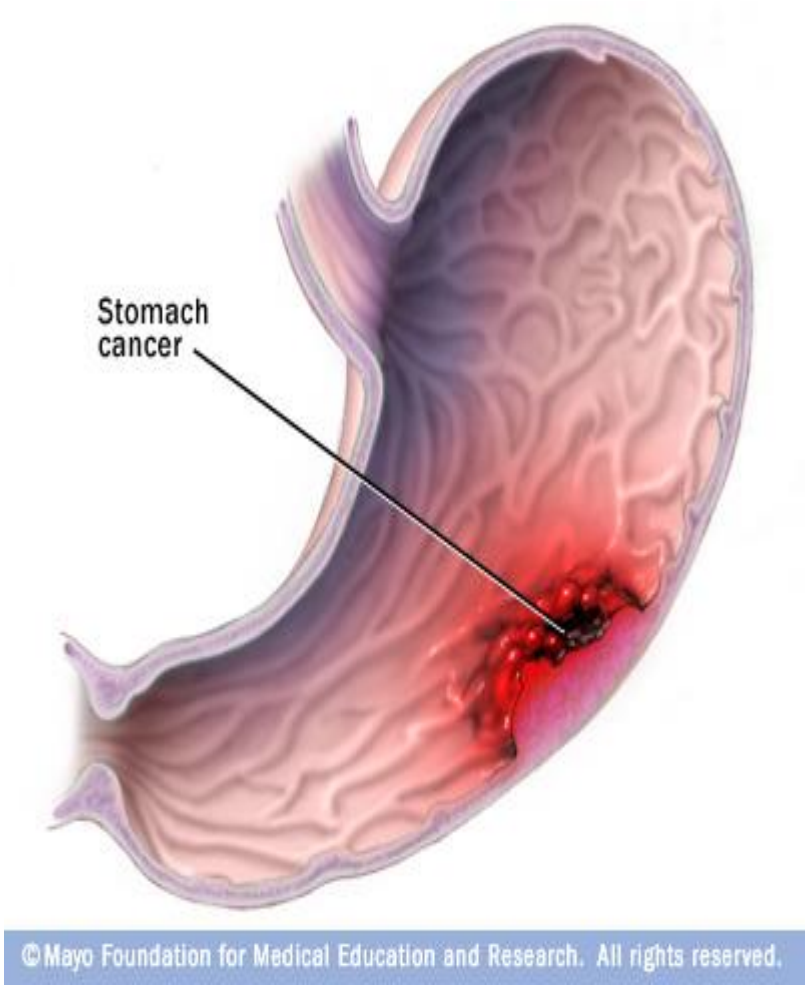
Villous gastric adenoma (non-pedunculated)



CARCINOMA STOMACH

- > 90% of malignancies of stomach- **Adenoca. stomach.**
- Leading cause of death in parts where its incidence is high.
- SITES-**PYLORIC CANAL**

  BODY,CARDIA OR FUNDUS.



CLASSIFICATION CA. STOMACH

MOST USEFUL CLASSIFICATION-

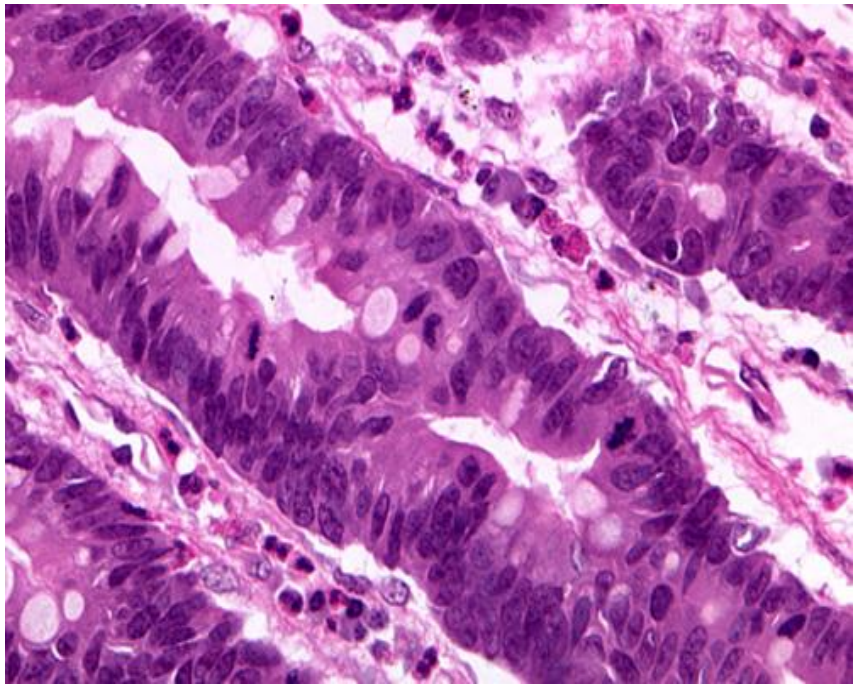
LAUREN'S CLASSIFICATION- 2 TYPES

1.INTESTINAL GASTRIC CA.

Tumour with intestinal morphology …..Form **polypoidal** growths.

Usually arises from intestinal metaplasia.

Composed of **glandular** structure.



Adenocarcinoma stomach

2.DIFFUSE GASTRIC CARCINOMA

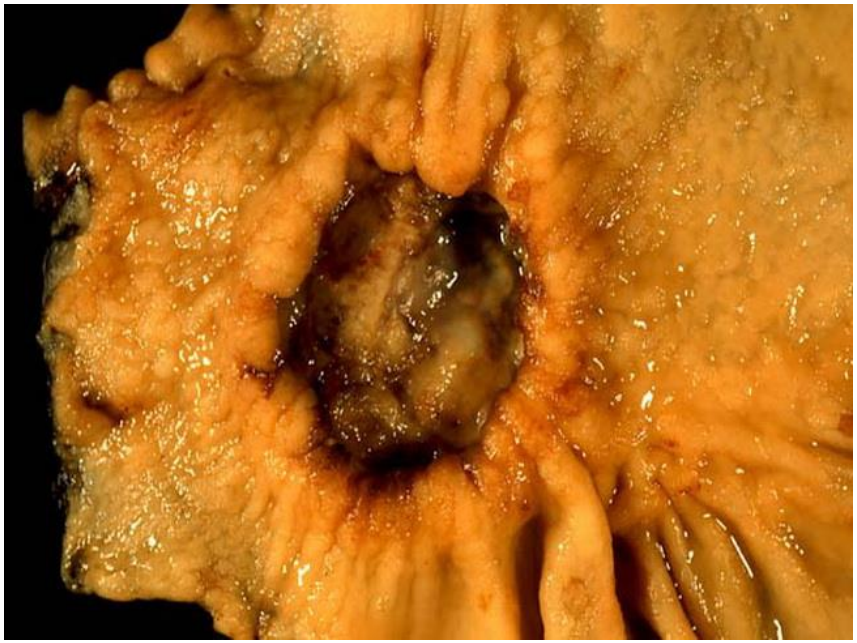
Infiltrates deeply into stomach without forming obvious polypoidal mass but **spreading within the wall.**

Composed of mucin secreting **signet ring cells.**

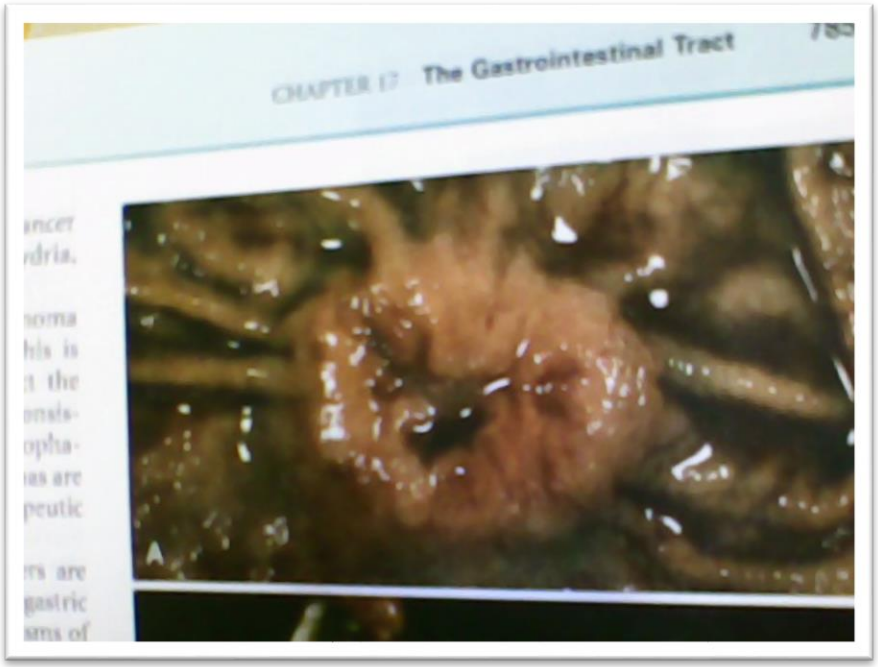
POOR PROGNOSIS.

Ca. Stomach

Ulcerative type



Polypoidal type



LINITIS PLASTICA…Leather bottle

Stomach….Scirrhous-type adenocarcinoma

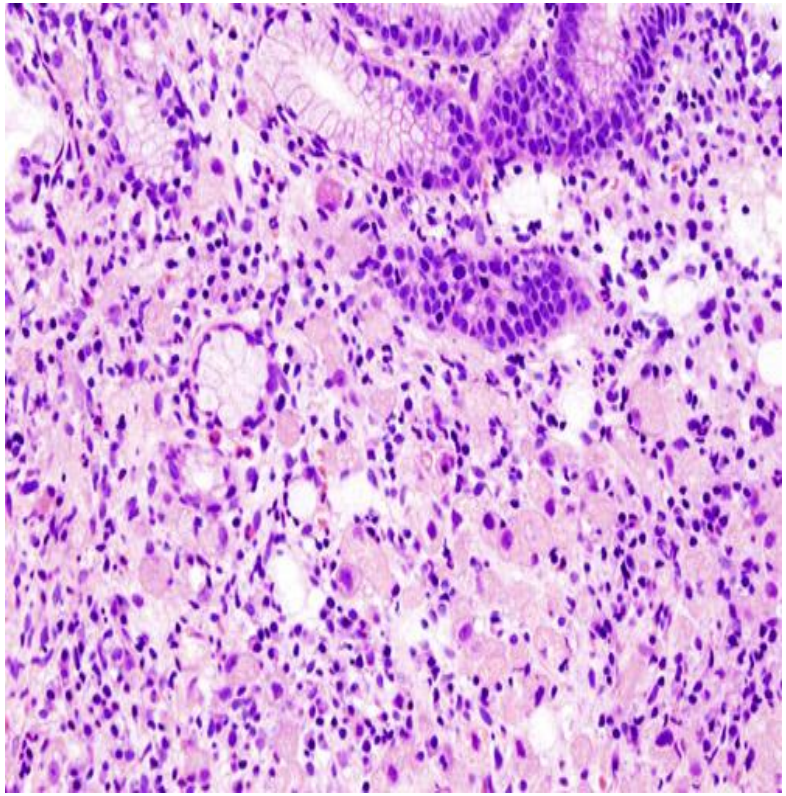
- Stomach wall is thickened due to desmoplasia.
- Lumen of the stomach is reduced.

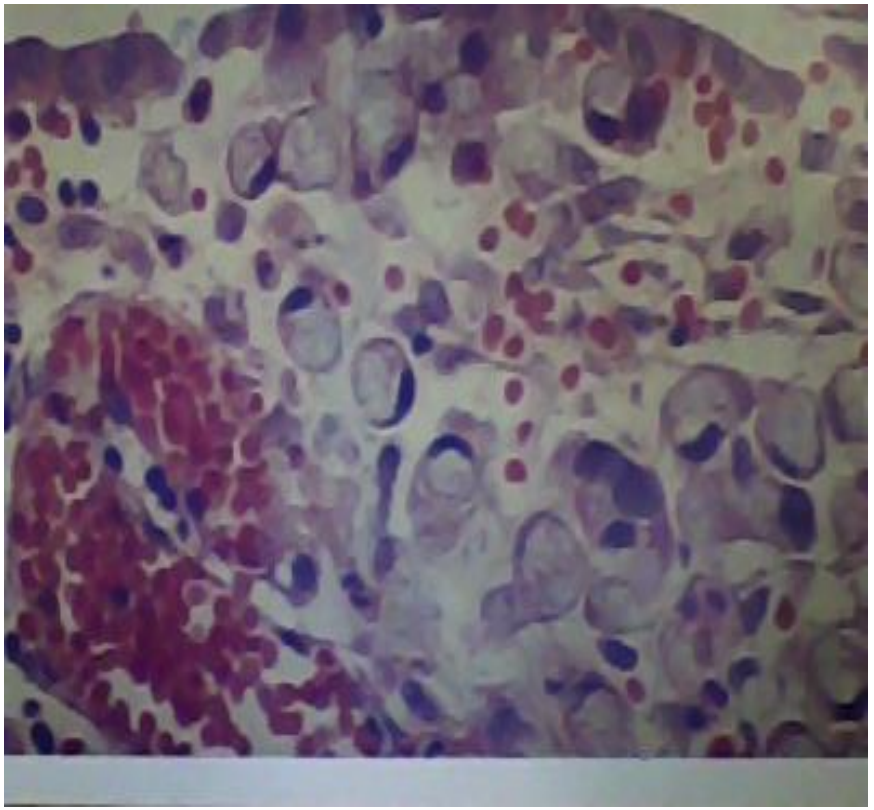
M/E

SIGNET RING CELLS.

- **But due to excessive desmoplasia….cancer may be difficult to find.**

Morphology…..Ca.Stomach…..M/E





Signet ring type Gastric adenocarcinoma

SPREAD….Ca. Stomach

1.DIRECT-

Local extension into mucosa, submucosa, -muscularis & serosa.
TRANSCOELOMIC DISSEMINATION …e.g. OVARIES ……
KRUKENBERG TUMOUR.

OTHER ORGANS-OMENTUM,PANCREAS ,LIVER, CBD ,SPLEEN, DIAPHRAGM, T. COLON etc.

2. LYMPHATIC-TO REGIONAL LYMPH NODES.

- SUPRACLAVICULAR L. NODES.
- **VIRCHOW'S SIGN.**

- COMMON IN **SCHIRROUS TYPE GASTRIC CARCINOMA.**

- **3. HAEMATOLOGICAL SPREAD-**
- **Common in poorly differentiated carcinoma.**

  Liver, lungs, brain ,kidney, bones

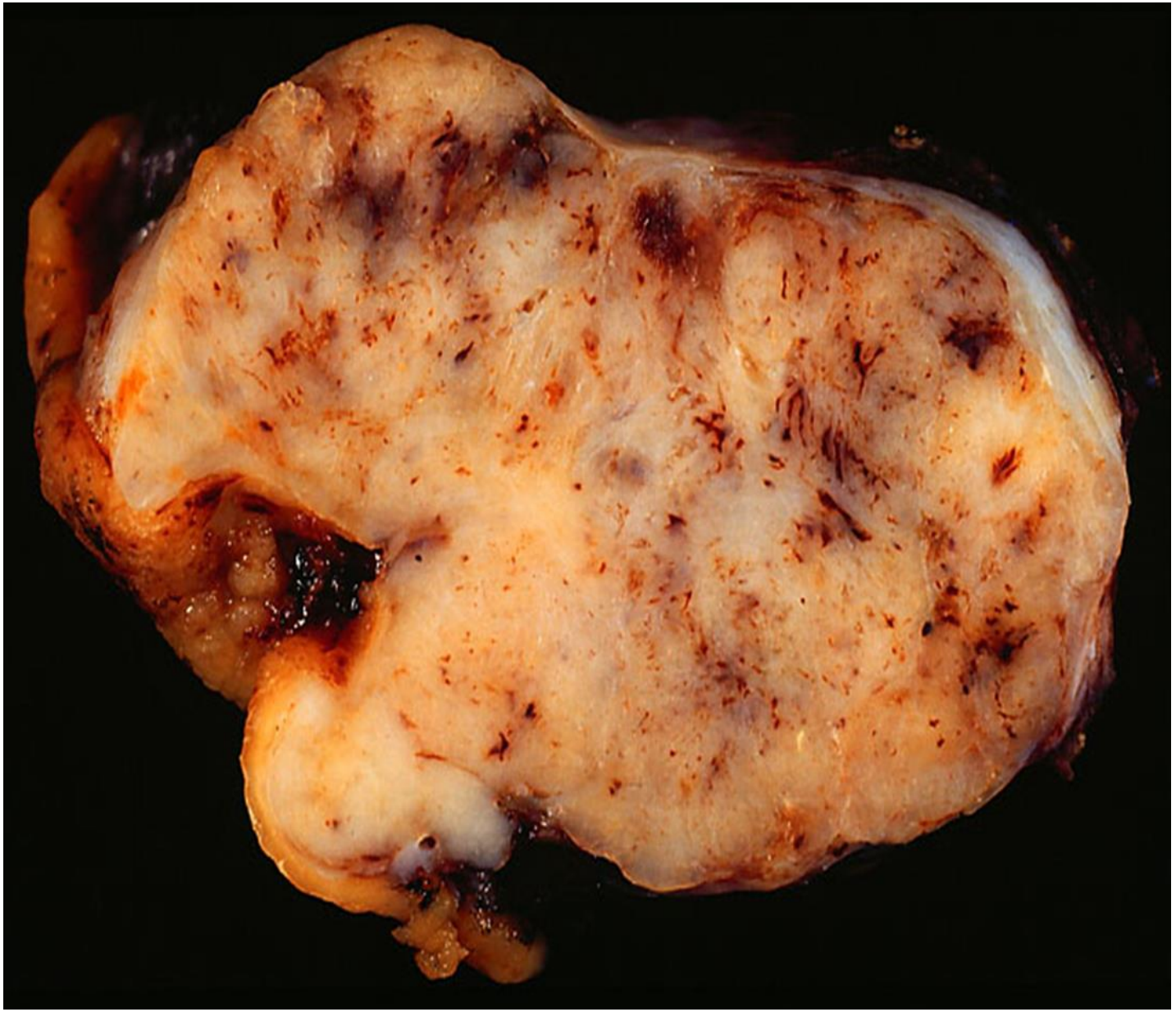
  Adrenal , subcutaneous tissue.

SISTER MARY JOSEPH NODULE-PERIUMBILICAL

SUBCUTANEOUS NODULE

GIST

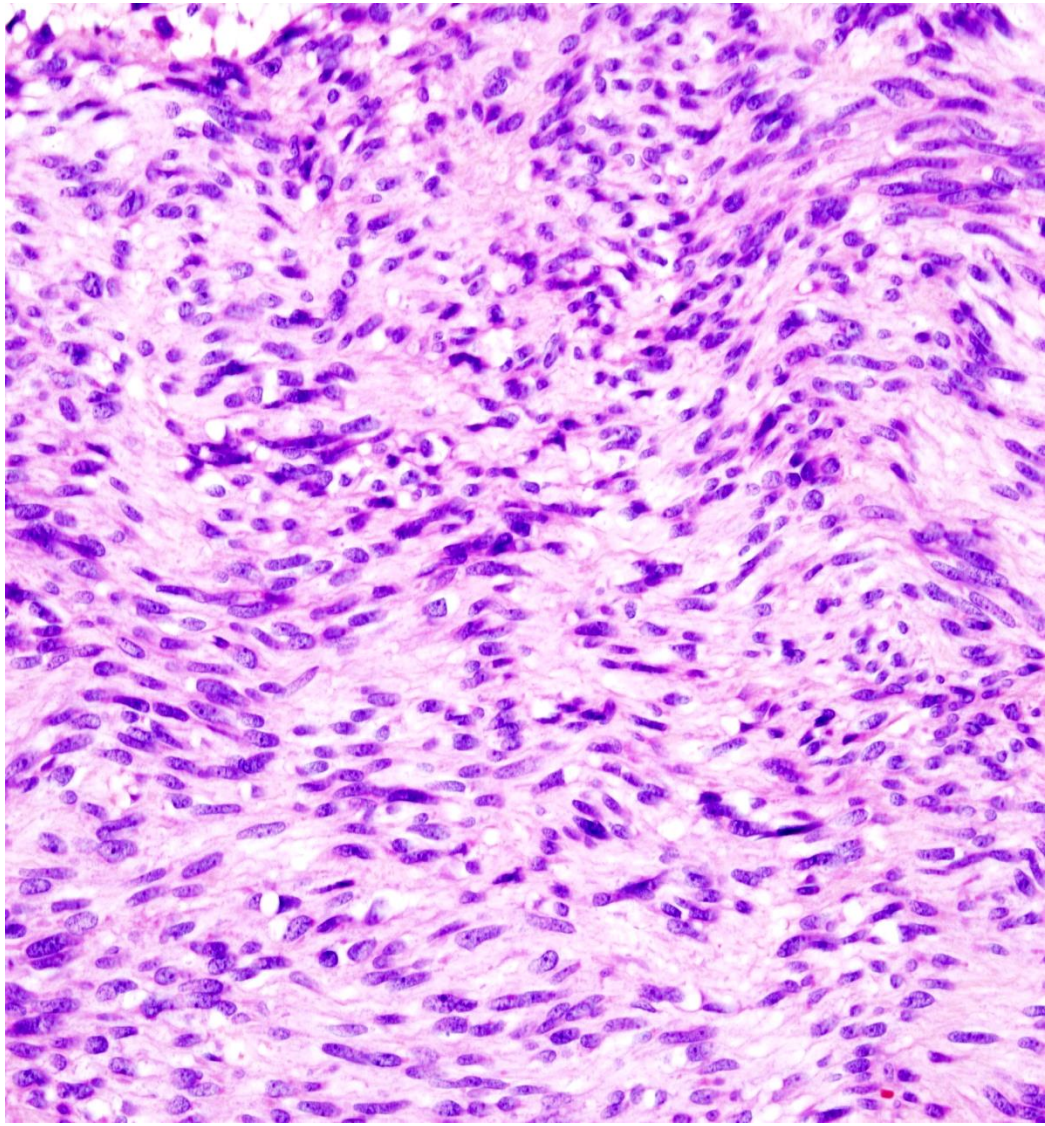
- MC mesenchymal neoplasm of GIT
- Origin
  - Interstitial cells of Cajal (ICC)
    - Pacemaker cells
    - Present in myenteric plexus
    - Coordinate gut peristalsis
  - CD34+ stem cells which differentiate towards ICC phenotype
- 95% are +ve for c-KIT (CD 117)
- 35% of c-KIT negative GISTs are +ve for PDGFR-α mutation
- c-KIT & PDGFR-α mutation – alternative oncogenic mechanisms
- 70% +ve for CD 34



Cut surface is solid and shows foci of hemorrhage

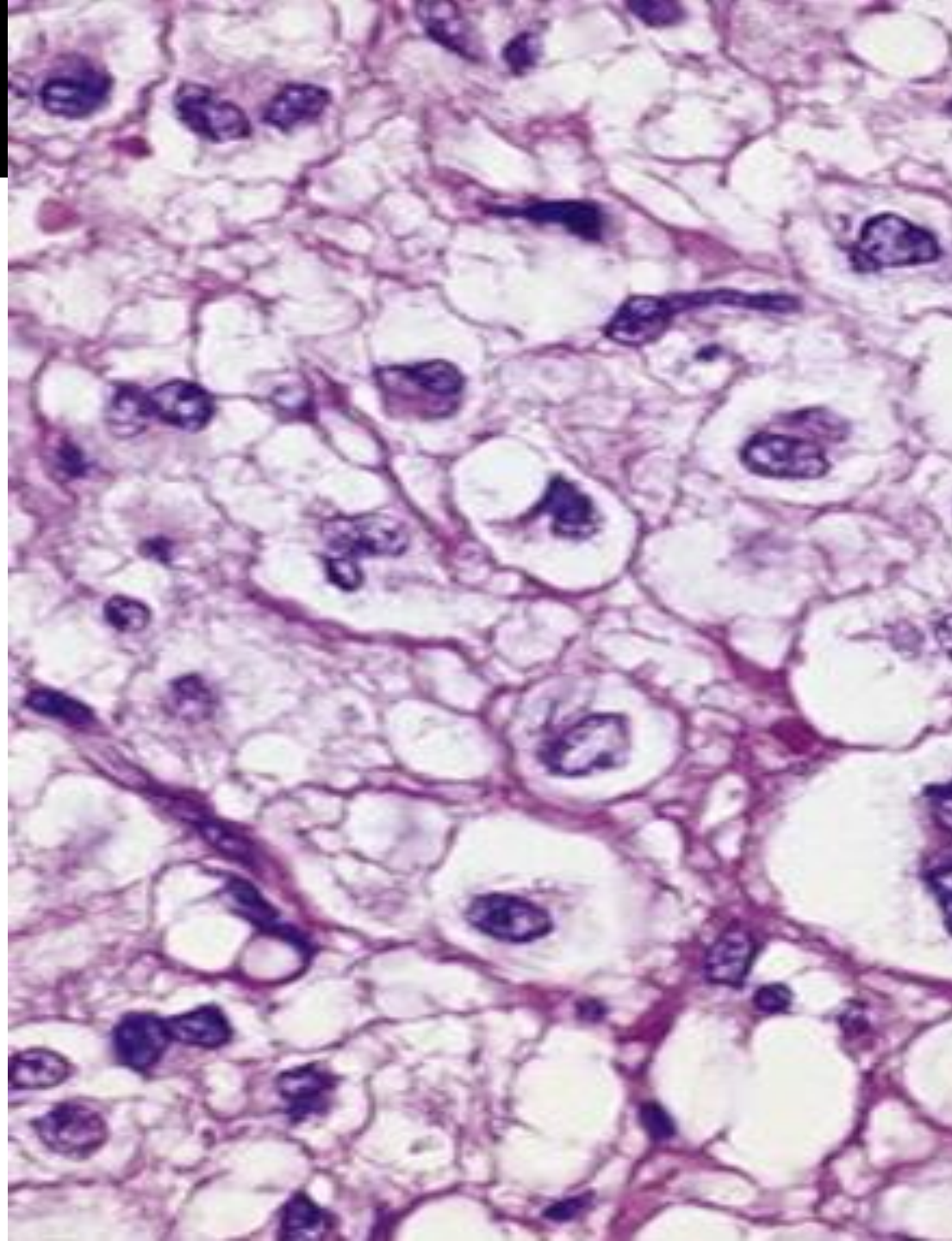
Spindle Cell GIST

- **Oval uniform blunt-ended nuclei with abundant eosinophilic slightly fibrillary cytoplasm**
- Pattern:
  - Cellular sheets
  - Fascicles with whorled or Palisaded patterns
- Cells are separated by hyalinized or calcified stroma
- Large areas of liquefactive necrosis are seen



Epithelioid GISTs

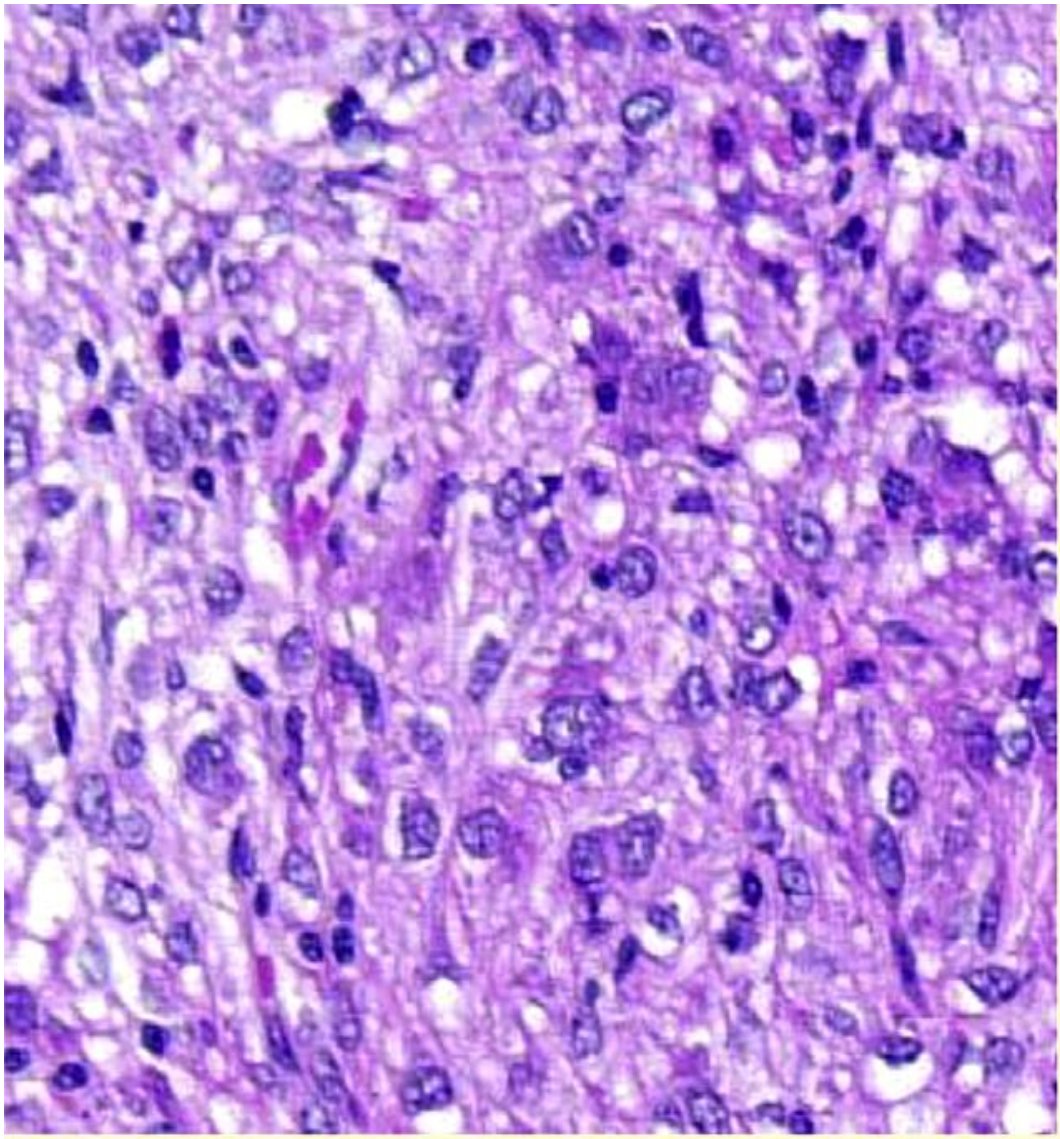
- Most occur in the fundus of the stomach
- **Rounded cells with abundant prominent cleared cytoplasm & well defined cell borders**
- The tumour cells are arranged in sheets , rather than fascicles



Mixed type

- Admixture of spindled and epithelioid tumours cells or an intermediate cell type is observed.

- The epithelioid and mixed cell types are significantly more often found in gastric GIST.

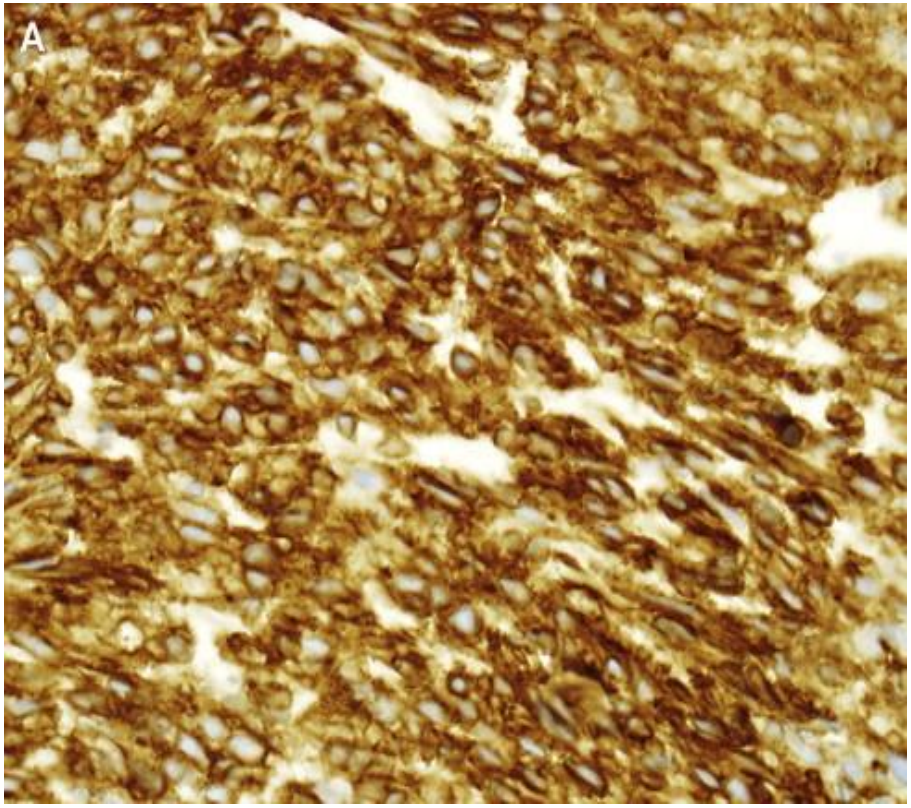


Immunohistochemistry

Markers used include-

- CD34
- KIT
- DOG1
- PDGFR-alpha
- SDHB
- SMA and h-caldesmon
- S100, CD56 and NSE
- Desmin

Strong membranous CD117 staining

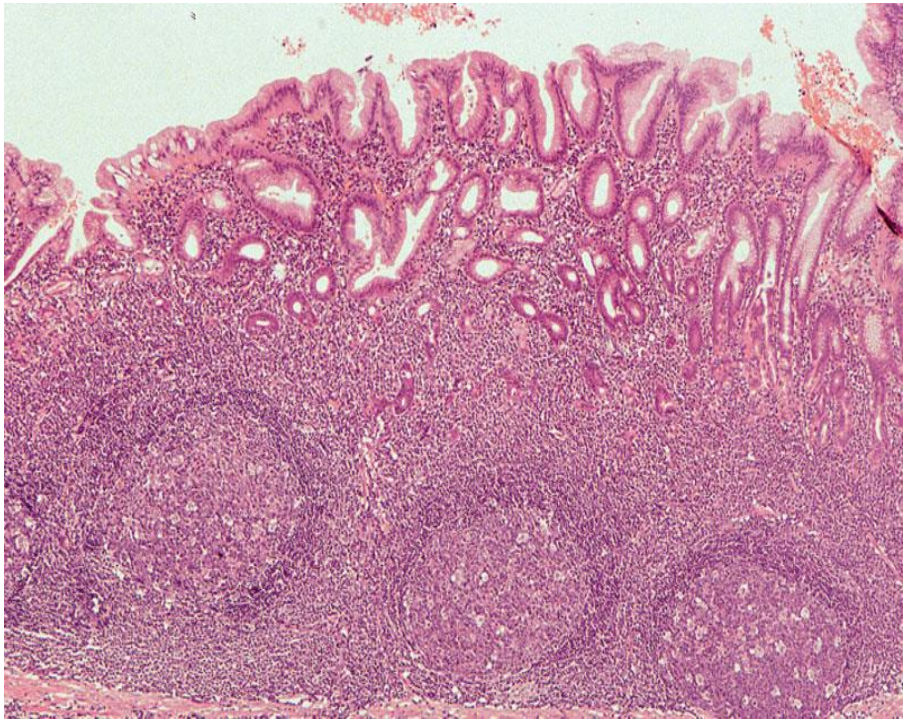


MALTOMAS

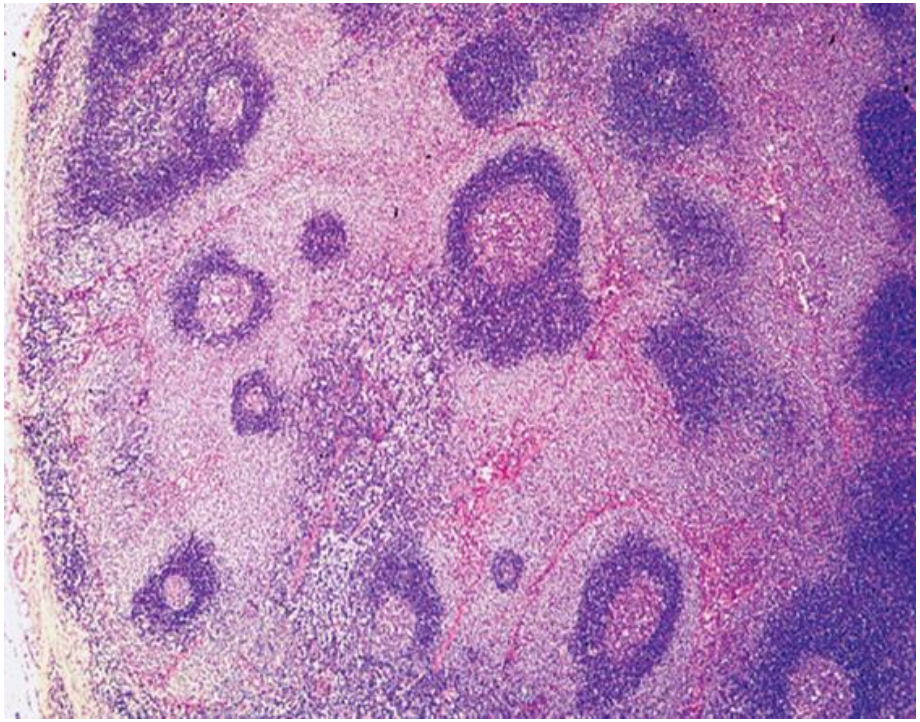
- Nearly 5% of all gastric malignancies are primary lymphomas**…..m/c is extranodal marginal zone B-cell Lymphoma**

Extranodal marginal zone B-cell lymphoma usually arises at sites of chronic inflammation

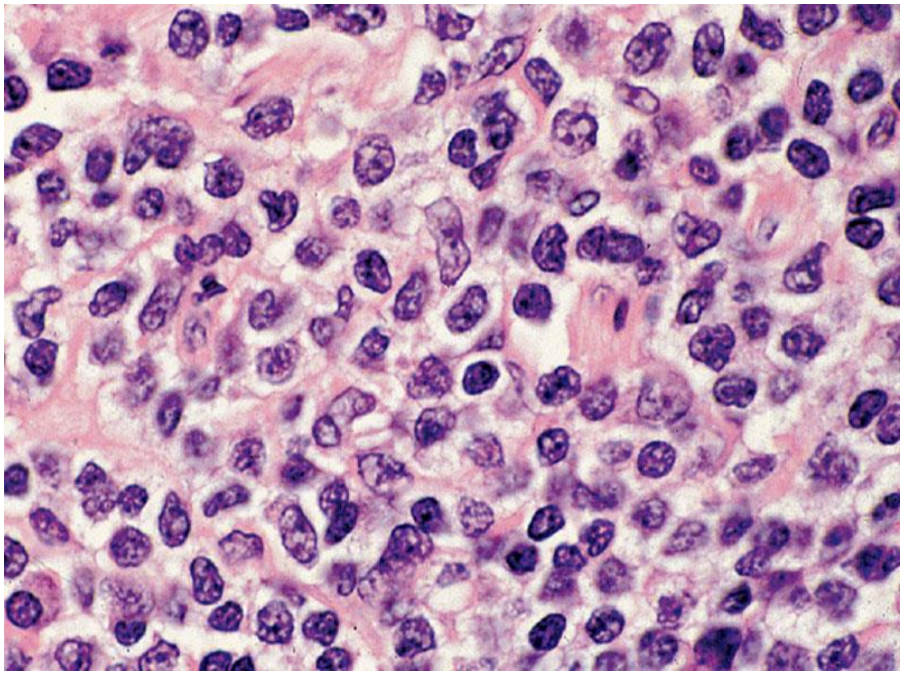
- In stomach, MALT is induced as a result of chronic gastritis (**H. pylori infection is the m/c inducer in stomach.)**



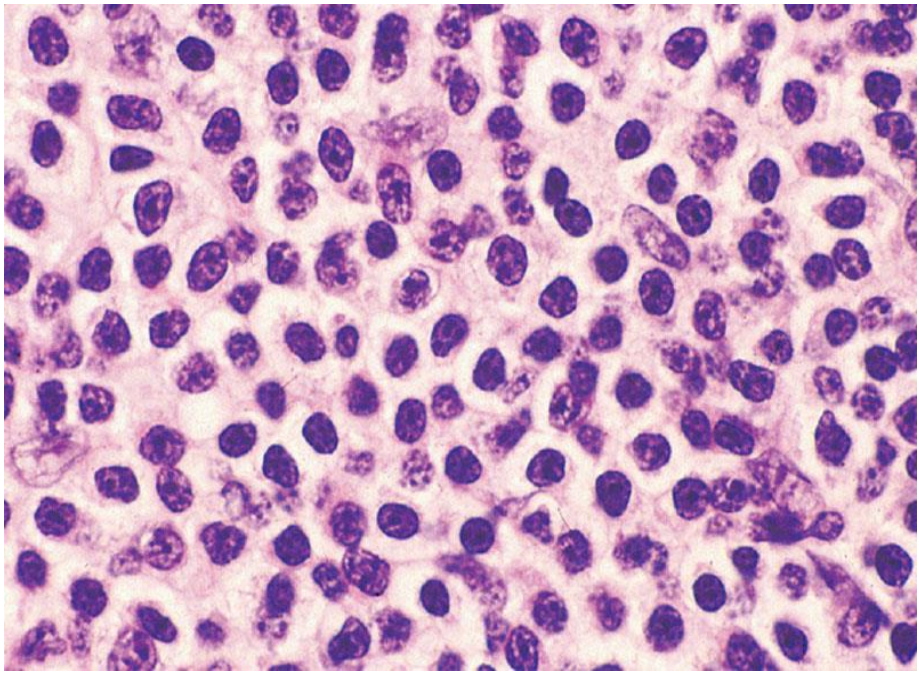
The tumour cells surround reactive follicles and infiltrate the mucosa. The follicles have a typical starry-sky appearance.



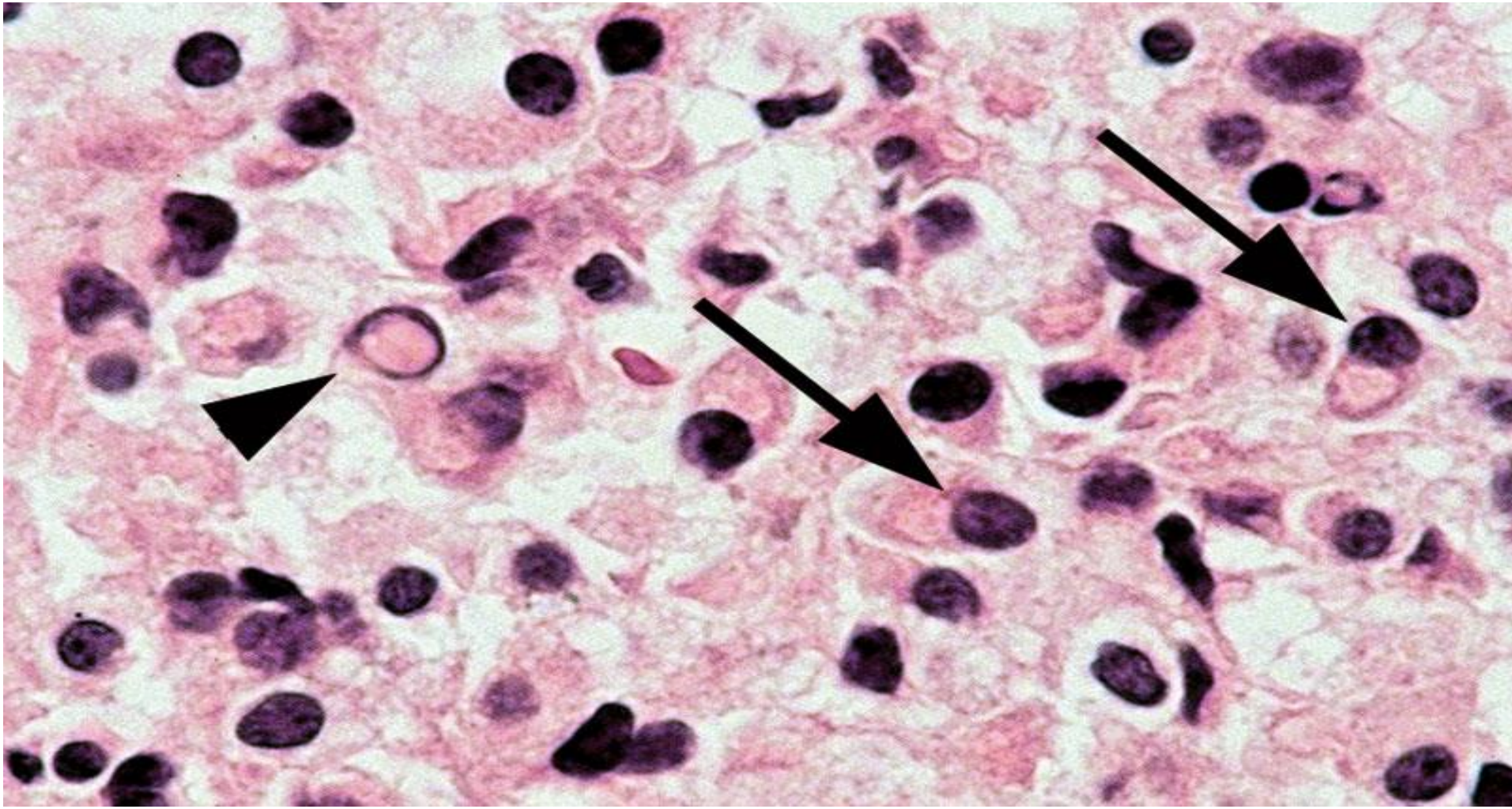
Gastric lymph node involved by MALT lymphoma. The tumour cells infiltrate the marginal zones and spread into the interfollicular areas.



Neoplastic marginal zone B-cells with nuclei resembling those of centrocytes, but with more abundant cytoplasm



The cells of this MALT lymphoma have abundant pale staining cytoplasm leading to a monocytoid appearance



Plasma-cell differentiation (arrows) and
Dutcher bodies (arrowhead)

MALTOMAS

- Immunophenotypically neoplastic cells express pan B cell markers, CD19, CD20, CD22, CD79a,PAX5
- Immunoglobulins show clonal rearrangement , high loads of somatic hypermutation
- MALT lymphomas have recurrent translocations
- m/c is t(11;18), (q21;q21)

APPROACH TO INTERPRETATION OF MALIGNANCIES Of STOMACH

Procedures

- Endoscopic Resection
- Gastrectomy (Partial or Complete)
- Tumor site:
- Fundus: Anterior wall, posterior wall
- Body and antrum:
- Anterior wall
- Posterior wall
- Lesser curvature
- Greater curvature

APPROACH TO INTERPRETATION OF MALIGNANCIES Of STOMACH

Histologic Type

- Adenocarcinoma, intestinal type
- Adenocarcinoma, diffuse type
- Papillary adenocarcinoma
- Tubular adenocarcinoma
- Mucinous adenocarcinoma (greater than 50% mucinous)
- Signet-ring cell carcinoma (greater than 50% signet-ring cells)
- Other (specify): Carcinoma, not otherwise specified

APPROACH TO INTERPRETATION OF MALIGNANCIES Of STOMACH

- **Microscopic Extent of Tumor**
- High-grade dysplasia/carcinoma in situ
- Tumor invades lamina propria
- Tumor invades muscularis mucosae
- Tumor invades submucosa
- Tumor invades muscularis propria
- Tumor invades subserosal connective tissue
- Tumor penetrates serosa (visceral peritoneum)
- Tumor directly invades adjacent structures (specify):
- Tumor penetrates to the surface of the visceral peritoneum (serosa) AND directly invades adjacent structures (specify: _____)
- Margins (select all that apply)

APPROACH TO INTERPRETATION OF MALIGNANCIES Of STOMACH

- Lymph node status
- Perineural invasion
- Local versus distant spread
- Ancillary findings
- IHC

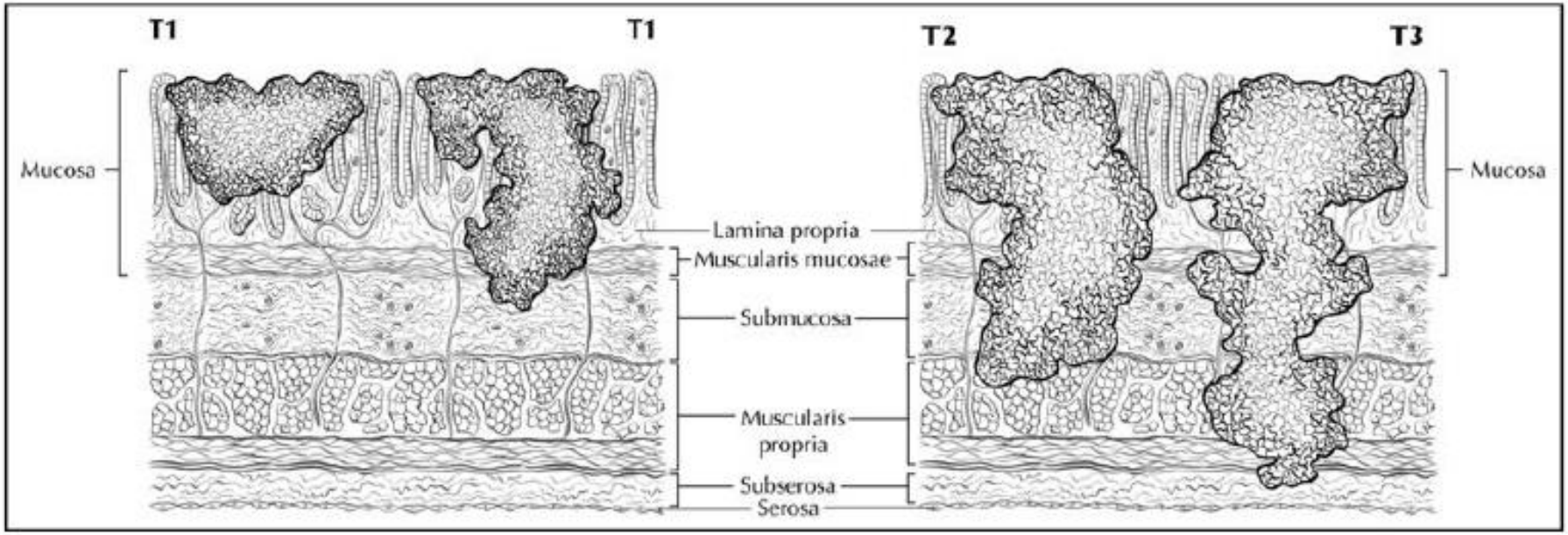
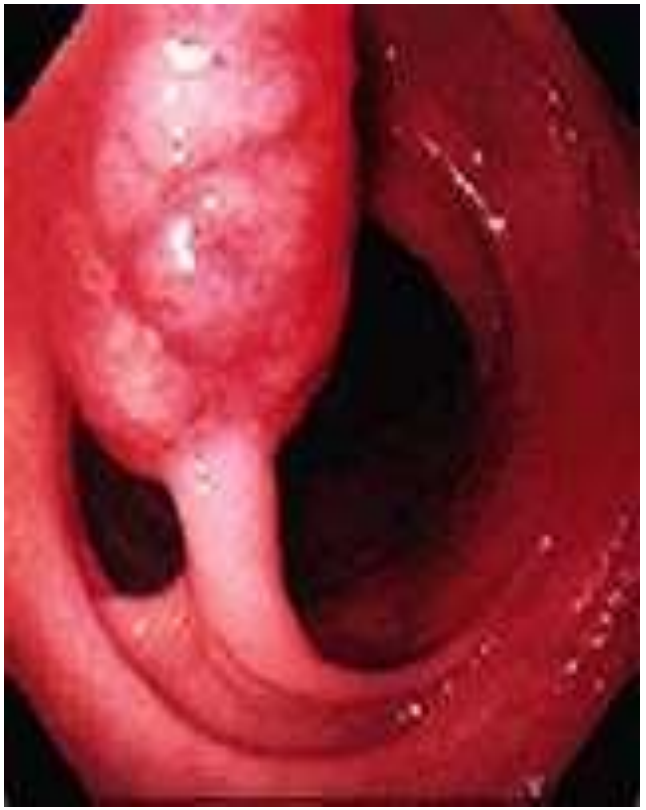


Figure 2. Definitions of T1, T2, and T3. Tumor invading the lamina propria is classified as T1a (left side or T1 illustration), whereas tumor invading the submucosa is classified as T1b (right side). T2 tumor invades the muscularis propria. T3 tumor invades the subserosal adipose tissue. Modified from: Greene FL, Compton CC, Fritz AG, et al, eds. *AJCC Cancer Staging Atlas*. New

Tumors and polyps of Colon

- A mass protruding from m/m into the lumen-polyp.
- More common in colon but can also occur in esophagus, stomach & S .I.



  - 1. Sessile
- 2. Pedunculated Polyps
- 1.Non neoplastic
- 2.Neoplastic

NEOPLASTIC POLYP

1.Benign Polyps **ADENOMA**

TUBULAR

VILLOUS

TUBULOVILLOUS

2.Malignant Polyps

Adenocarcinoma

Leiomyosarcoma

Lymphoma

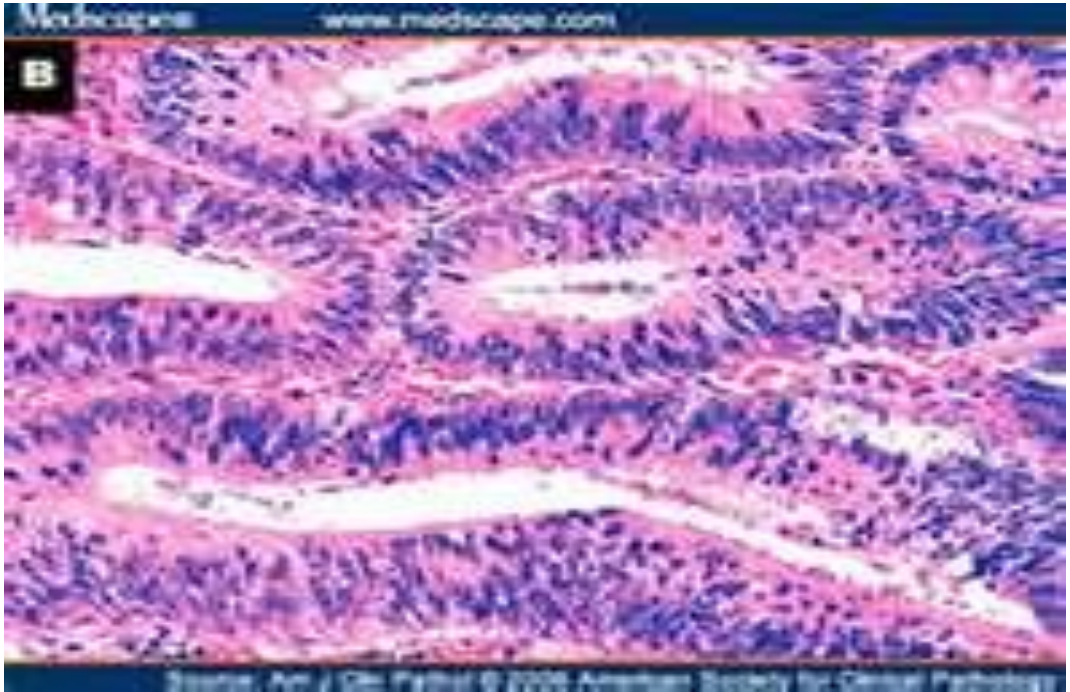
Neoplastic polyps

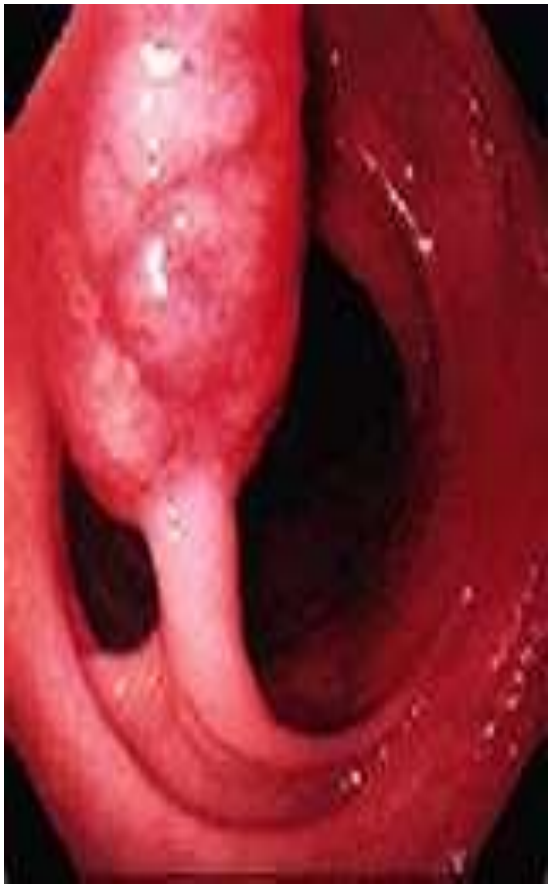
Adenomas

- **Benign neoplastic polyps.**
- **As a result of neoplastic epithelial proliferation overlying the muscularis mucosae.**
- **Colorectal adenomas are characterized by the presence of epithelial dysplasia.**
- **Are precursors of majority of the colorectal adenocarcinomas.**

Colonic Adenoma…..M/E and gross

- **Colorectal adenomas are characterized by the presence of epithelial dysplasia.**





Neoplastic polyps

3 subtypes……

1.Tubular Adenoma(tubular glands)

2.Villous Adenoma(villous projections)

3.Tubulovillous Adenoma.(mixture of the two.)

1.Tubular Adenoma

- **Most common neoplastic polyp.**
- **Singly / multiple (familial polyposis syndrome).**

Gross

- **Single or multiple.**
- **Sessile or pedunculated.**
- **<1cm or large.**
- **Malignant transformation…….upto 5%.**

M/E-Lining epithelium with decreased mucus secreting capacity.

- **Disordered epithelium with large hyperchromatic nuclei.**
- **Increased mitotic activity**
- **Variable degree of cytological atypia can be present**

2.Villous Adenoma

- Less common.
- Size can go upto 10 cm.
- Sessile.
- Malignant transformation….. 30%.

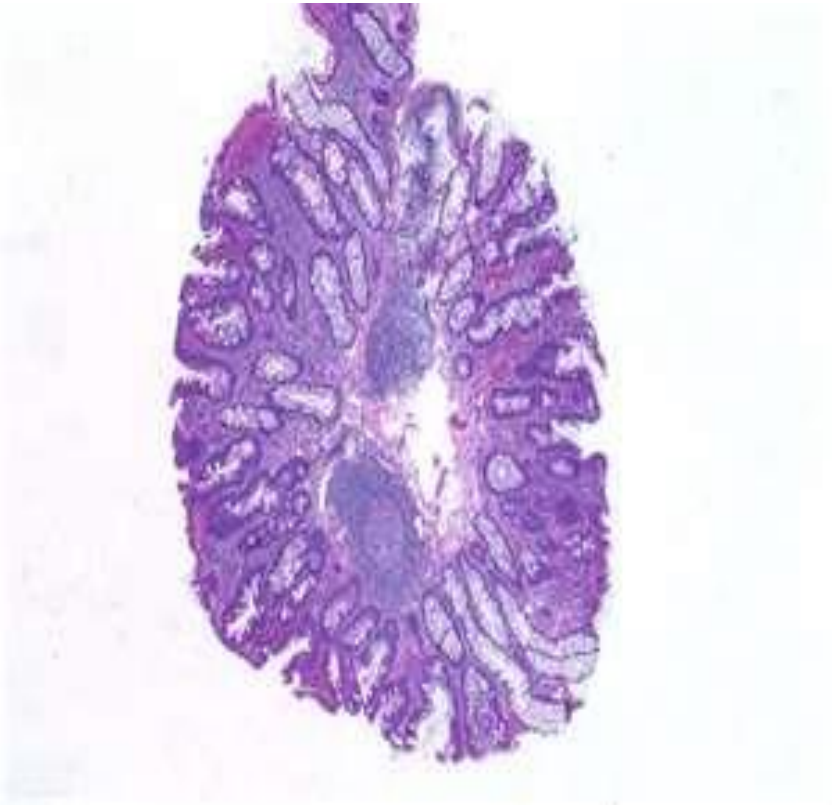
M/E

Many slender finger like villi arising from muscularis mucosae. Villi having fibrovascular core….covered by epithelial cells(benign to atypical cells).

3.Tubulovillous Adenoma…..Mixed pattern.

Neoplastic polyps

VILLOUS ADENOMA



Pedunculated Tubular Adenoma

FAMILIAL POLYPOSIS SYNDROMES

- Group of disorders with **multiple polyposis** of the colon.
- Have **familial** basis.
- **Autosomal dominant** inheritance pattern.
- Imp. conditions included in familial polyposis are…..

FAMILIAL POLYPOSIS SYNDROMES

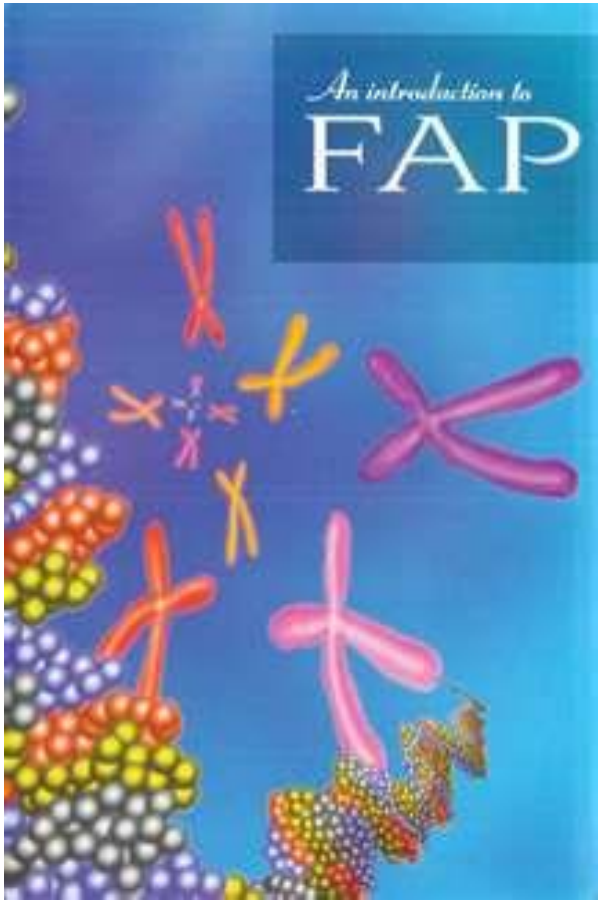
1.FAMILIAL POLYPOSIS COLI(FAP)

(Familial Adenomatous Polyposis.)

2.GARDNERS SYNDROME.

3.TURCOT SYNDROME.

4.JUVENILE POLYPOSIS SYNDROME.



FAMILIAL ADENOMATOUS POLYPOSIS(FAP)

- **Hereditary (Familial disease).**
- **Multiple polyps.(average -1000)**
- **Also called Adenomatosis or FAP.**

Precancerous. Malignant potential in FAP is very high – CA. develops in 100% of untreated cases over a period of several yrs.

- **D/D------MULTIPLE ADENOMAS COLON. (HERE THE NO. OF POLYPS < 100).** FAP is asso. with a variety of **extra-intestinal manifestations….**

Congenital hypertrophy of the retinal pigment epithelium. …..which is generally detected at birth.

This can serve as an **adjunct to early screening**

FAMILIAL ADENOMATOUS POLYPOSIS(FAP)

GROSS

500-2500 adenomas carpeting the colonic mucosal surface.(**At least 100 polyps are necessary for diagnosis of classic FAP**.)

M/E

Majority are **tubular adenomas**.

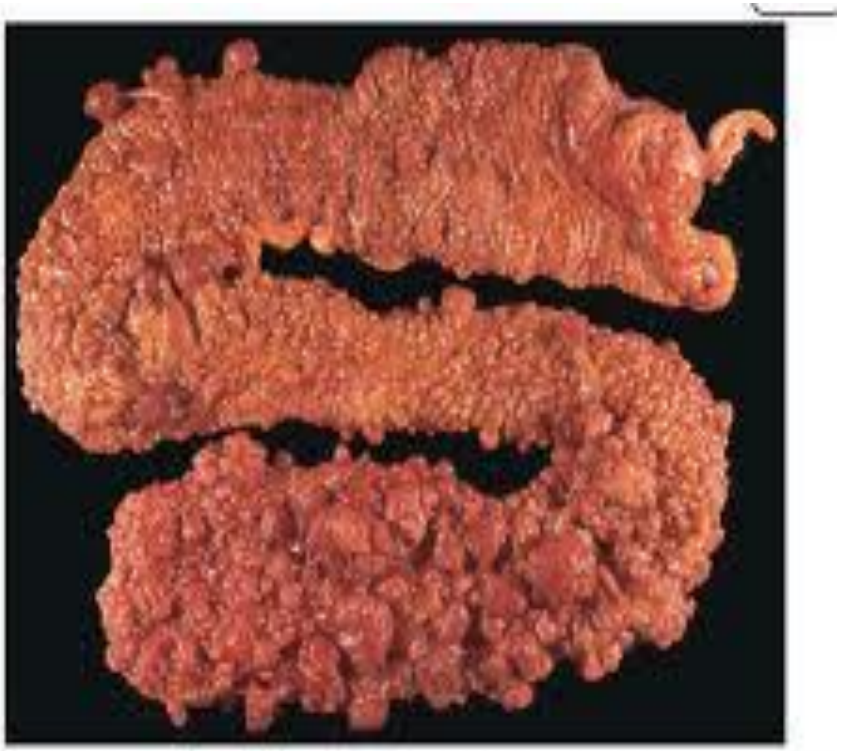


Figure 15-35 Familial adenomatous polyposis. The surface is carpeted by innumerable polypoid adenomas. (Courtesy of Dr. Tad Wieczorek, Brigham and Women's Hospital, Boston.)

PREVENTIVE MEASURES…in FAP

- EARLY DETECTION OF DISEASE IN SIBLINGS & FIRST DEGREE RELATIVES.

- PROPHYLACTIC COLECTOMY

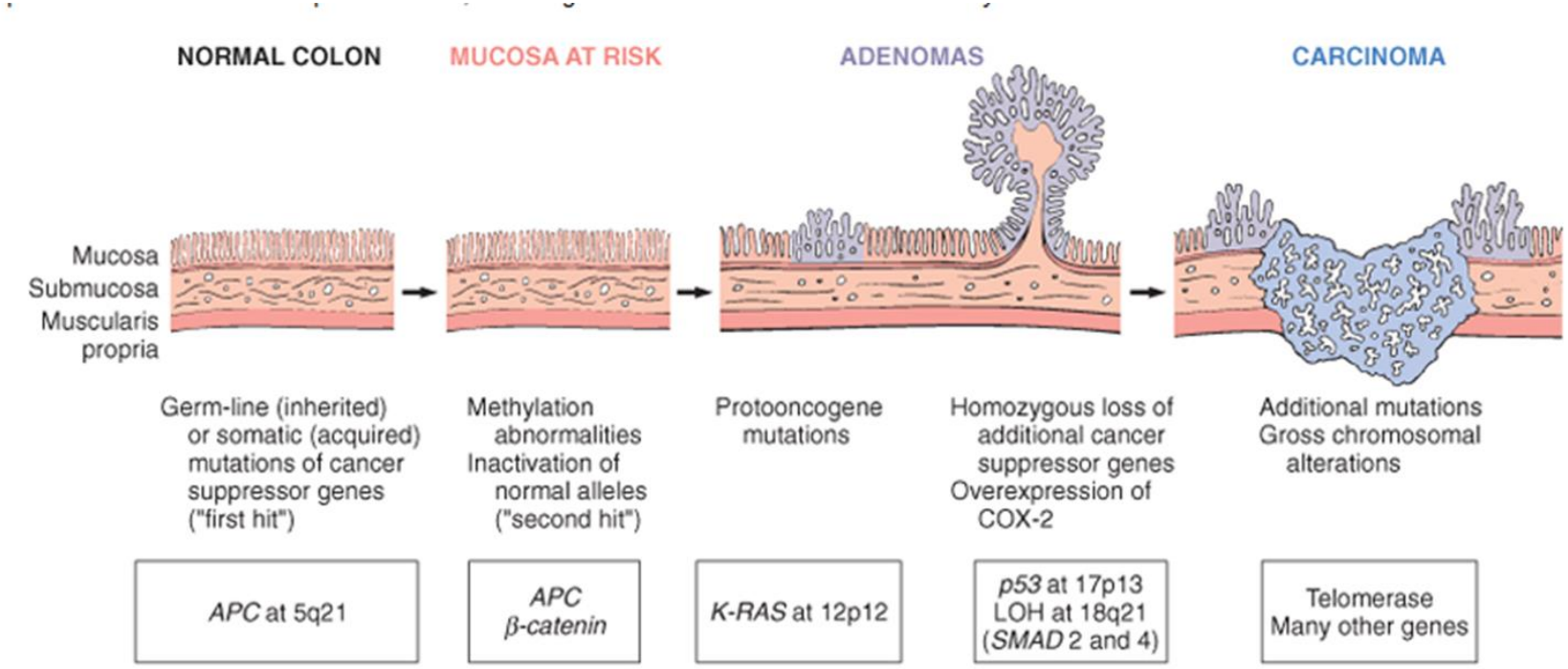
TABLE 19-9 -- Familial Adenomatous Polyposis and Variants

Syndrome	Colorectal Polyps	Extracolonic Lesions	Genetics	Risk of Malignancy
Familial adenomatous polyposis	Adenomatous polyps (100s to 1000s)	Duodenal/periampullary adenomas, gastric fundic gland polyps, congenital hypertrophy of the retinal pigment epithelium	Autosomal dominant *APC* mutation	100% risk of colorectal carcinoma (mean age 35-40 years) 3% to 5% risk of duodenal/periampullary carcinoma
Gardner's syndrome	Adenomatous polyps (100s to 1000s)	Osteomas, epidermoid cysts, dental abnormalities, fibromas, desmoid tumors (especially mesenteric)	Autosomal dominant *APC* mutation	Same as above
Turcot's syndrome	Adenomatous polyps (100s to 1000s)	Central nervous system tumors (especially medulloblastoma)	Autosomal dominant *APC* mutation	Same as above
Attenuated familial adenomatous polyposis	<100 Adenomatous polyps	Similar to conventional familial adenomatous polyposis	Autosomal dominant *APC* mutation	80% risk of colorectal carcinoma (mean age, 50 years)
MYH-associated polyposis	Usually 15-100 adenomatous polyps	Uncertain	Autosomal recessive *MYH* mutations	High risk of colorectal carcinoma

Colorectal tumors- Carcinogenesis

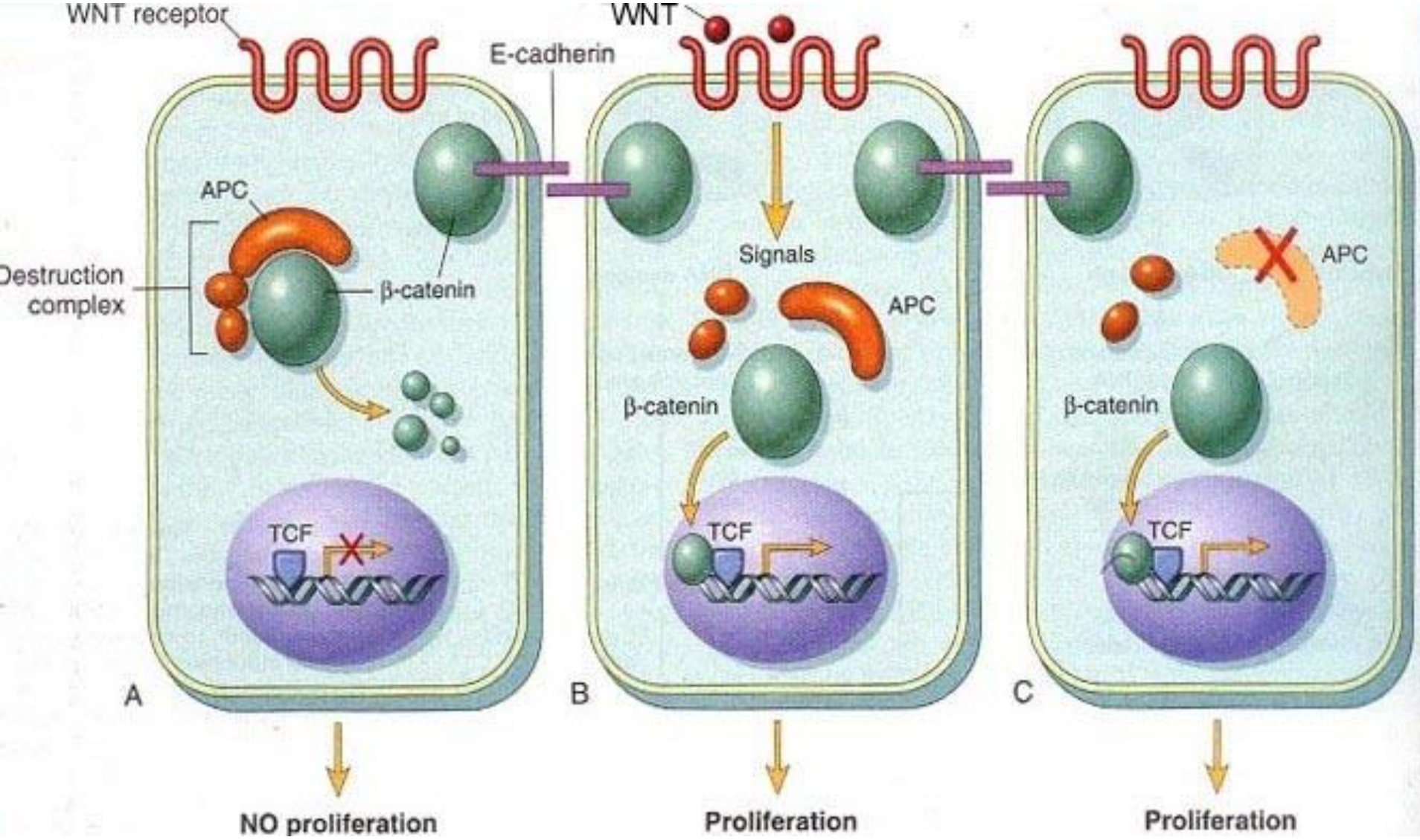
- Two distinct pathways
  - ***APC/ß-Catenin Pathway***
  - ***Microsatellite instability pathway***
- Both involve stepwise accumulation of multiple mutations
- Genes involved & mechanisms are different

APC/ß-Catenin Pathway
Adenoma →Carcinoma Sequence



APC/ß-Catenin Pathway
Loss of Adenomatous Polyposis Coli Gene

- 5q21
- Dual Function
  - Tumor Suppressor Gene- Inhibition of signal transduction
  - Gatekeeper Gene – regulates levels of ß-catenin (a member of cadherin based cell adhesive complex)
- 80% colorectal ca have APC mutation
- Half of tumors without APC mutations have ß-catenin mutations.
- Mutations in APC gene
  - Missense
  - Frameshift
  - Deletions
  - Location- 60% in upstream region of exon 15, the mutation cluster region


WNT receptor
WNT
E-cadherin
APC
Destruction complex
β-catenin
Signals
APC
β-catenin
APC
β-catenin
TCF
TCF
TCF
A
B
C
NO proliferation
Proliferation
Proliferation

Microsatellite Instability Pathway

- **Genetic lesions in DNA mismatch repair genes**
- **Present in 15% of sporadic cases and in HNPCC Syndrome**
- No clearly identifiable morphological correlates
- MSI-H Tumors

- **Germline mutations in any of 5 genes** involved in DNA repair responsible
  - hMSH 2 (2p22) responsible for 90% of cases
  - hMLH 1 (3p21)
  - hMSH 6 (2p21)
  - hPMS 1 (2q31-33)
  - hPMS 2 (7p22)

Microsatellite Instability Pathway

- **Distinct Features of Tumors**
  - Proximal colonic location
  - Mucinous histology
  - Infiltration by lymphocytes
  - More likely to be diploid
  - More likely to have a larger primary at diagnosis and node negative
  - Better long term prognosis

Microsatellite Instability Pathway

Loss of mismatch repair genes

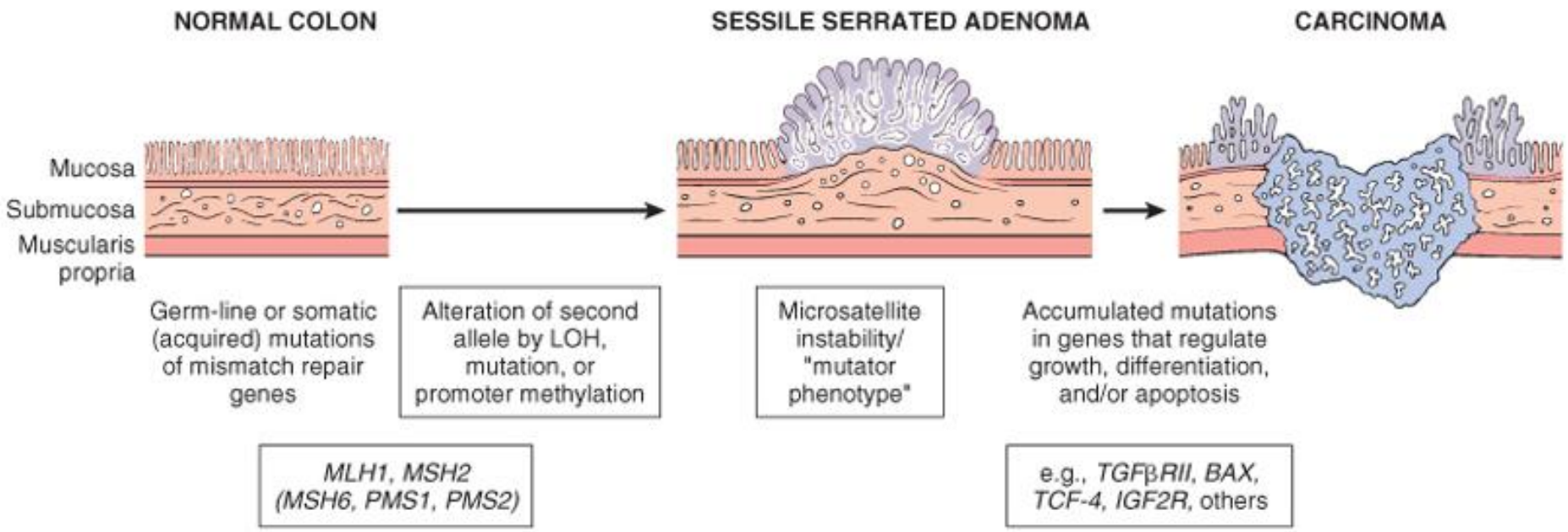
↓

Accumulation of mutations in growth regulating genes

↓

Colorectal carcinoma.

Microsatellite Instability Pathway



Microsatellite Instability Pathway

HNPCC(Lynch Syndrome)

- Autosomal Dominant Disorder
- 3% of all colorectal cancers

- One mutant DNA repair gene (first hit) is inherited
  - One allele is normal
  - Cells susceptible to somatic mutation in some organs (second hit)
  - This inactivates the normal allele (LOH)
  - Mutation rates are 1000 times higher than normal

Microsatellite Instability Pathway

HNPCC(Lynch Syndrome)

- Two types
  - **Lynch Type I** – Associated with large bowel tumors only
  - **Lynch type II** - Associated with tumors of endometrium, ovary, stomach, small bowel, renal pelvis etc.
- Few colonic polyps, hence the term non-polyposis
- Life time risk of colorectal carcinoma is 80%

Colorectal Carcinogenesis
Hamartomatous Polyposis Syndromes

- Rare, <1% colorectal cancers
- Adolescent and pediatric population affected

- Peutz Jeghers syndrome
  - Autosomal dominant
  - Multiple hamartomatous polyps throughout GIT
  - Melanotic mucosal and cutaneous pigmentation
  - Patients at increased risk of malignancies of pancreas, breast, lung, ovary and uterus.
  - Mutation of gene STK 11(LKB1) located on ch 19 which encodes a protein with serene/threonine kinase activity.

Colorectal Carcinogenesis
Hamartomatous Polyposis Syndromes

- **Juvenile polyposis syndrome**
  - Overlapping clinical feaures with PJS
  - Polyps confined to colon
  - Increased risk of adenoma and colorectal carcinoma
  - Germline mutations in PTEN & SMAD 4/ DPC 4 gene which encodes TGF-ß signaling intermediate.

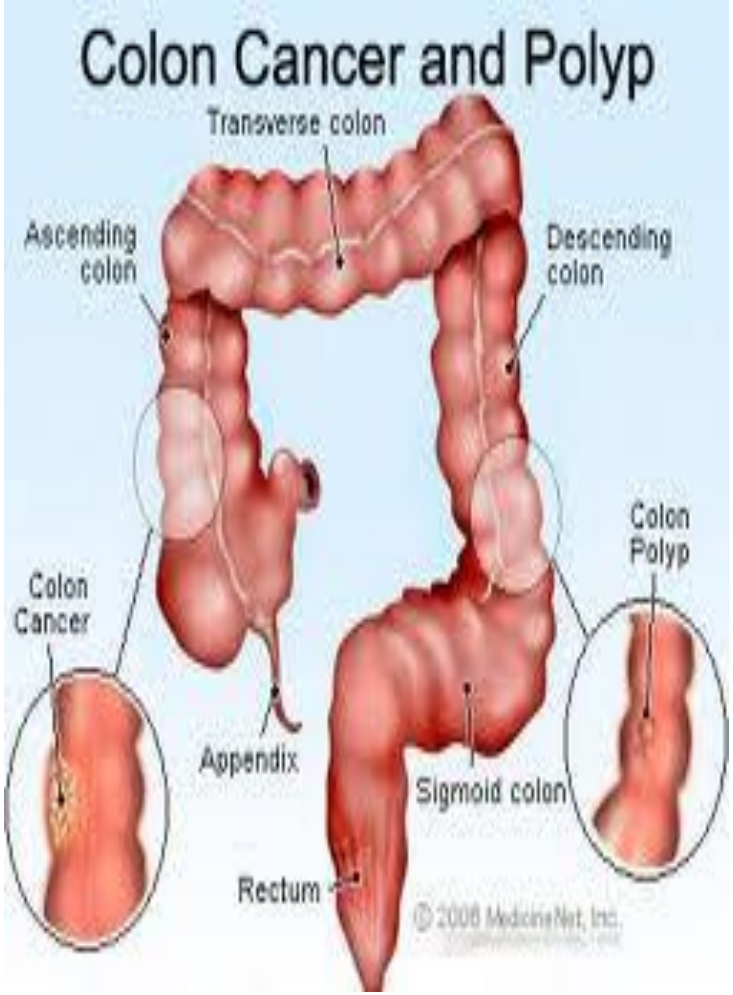
Colorectal Carcinoma

- **60% in rectum.**
- **Sigmoid colon, caecum, descending/ ascending colon.**

GROSS-

Right sided growth – --large ,soft, polypoidal mass projecting into the lumen.(liquid nature of the contents of ascending /Right sided colon.)

Left sided growth----napkin ring appearance i.e. they encircle the bowel wall with increased fibrosis forming an annular ring(solid contents of descending Colon permits spread of growth into the bowel wall).

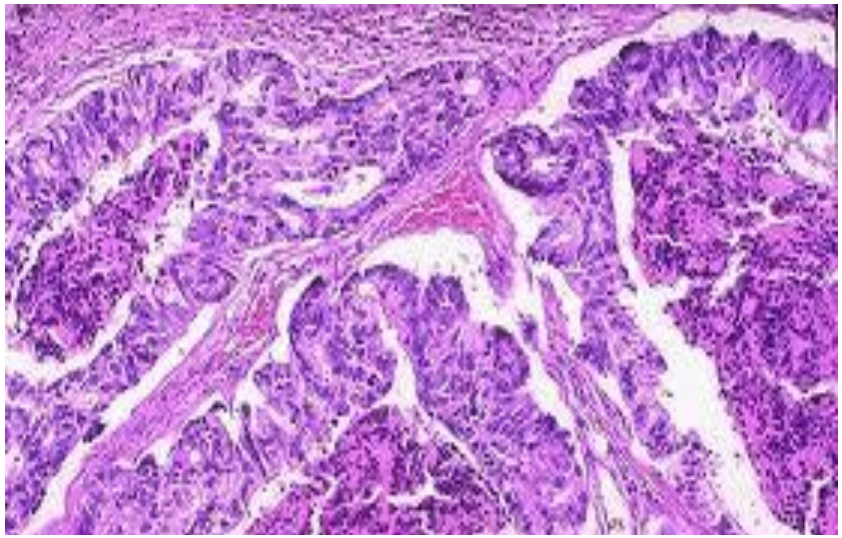


COLORECTAL CARCINOMA

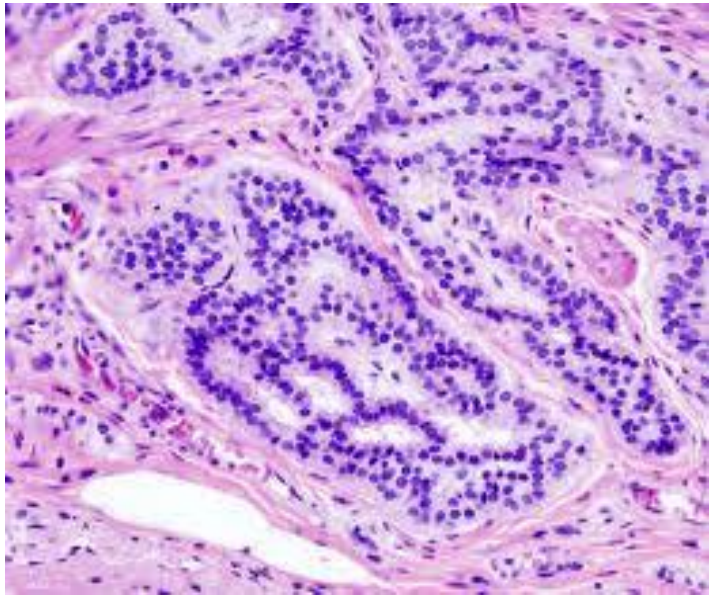
- **M/E** Some tumors may produce **abundant mucin** which dissects through the wall & helps in early metastasis…**poor prognosis.**
- Some may have **signet ring cells** **(like in Gastric Carcinoma)**

COLORECTAL CARCINOMA

Dysplastic Glands with desmoplasia



Anaplastic cells with desmoplasia



COLORECTAL CARCINOMA

Complications

- Obstruction.
- Haemorrhage.
- Perforation.
- Secondary infection.

PROGNOSIS

1.Extent of bowel involvement.

2. Presence/ absence of metastases.

3.Histological grade of the tumor.

4.Location of the tumor.

But, the most imp. prognostic factor is……

The stage of the disease at the time of diagnosis.

Neuroendocrine tumors (NETs)

- Arise from neuroendocrine cells.
- Many are benign, while some are malignant.
- They most commonly occur in the intestine, where they are often called carcinoid tumors, but they are also found in the pancreas, lung and the rest of the body.
- Although there are many kinds of NETs, they are treated as a group of tissue because the cells of these neoplasms share common features, such as looking similar, having special secretory granules, and often producing biogenic amines and polypeptide hormones.

Classification of NETs

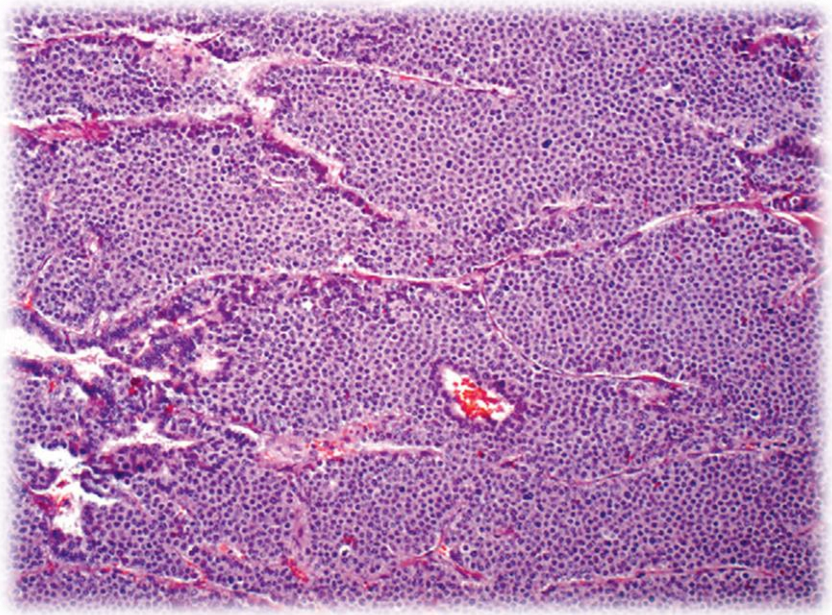
Nomenclature and classification for neuroendocrine tumors

Differentiation	Grade	Mitotic count*	Ki-67 index•	Traditional	ENETS, WHO
Well differentiated	Low grade (G1)	<2 per 10 HPF	≤2 percent	Carcinoid, islet cell, pancreatic (neuro)endocrine tumor	Neuroendocrine tumor, Grade 1
	Intermediate grade (G2)	2-20 per 10 HPF	3-20 percent	Carcinoid, atypical carcinoidΔ, islet cell, pancreatic (neuro)endocrine tumor	Neuroendocrine tumor, Grade 2
Poorly differentiated	High grade (G3)	>20 per 10 HPF	>20 percent	Small cell carcinoma	Neuroendocrine carcinoma, Grade 3, small cell
				Large cell neuroendocrine carcinoma	Neuroendocrine carcinoma, Grade 3, large cell

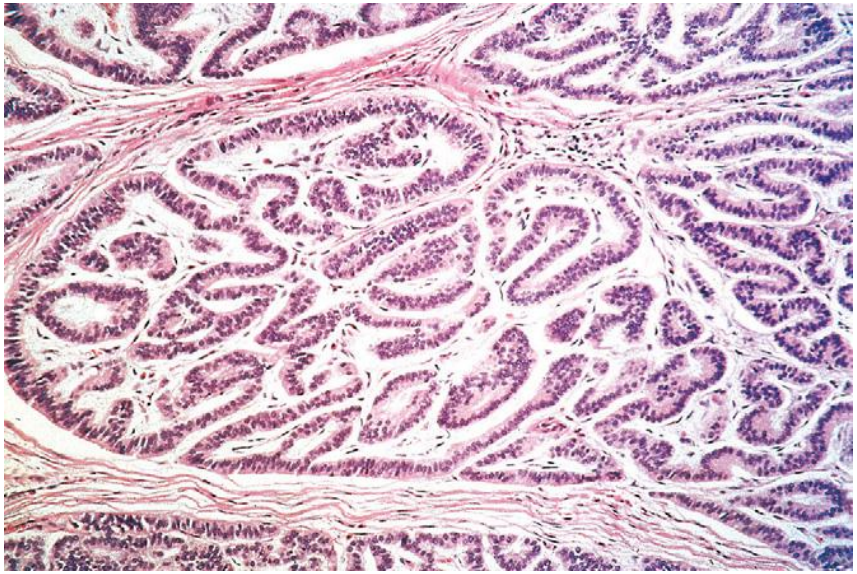
Morphological patterns in NENs

- Insular (nodular solid nests with peripheral invading cords)
- Trabecular (anastomosing trabeculae or ribbons)
- Glandular (tubules, rosettes)
- Poorly differentiated with no well-organized growth pattern

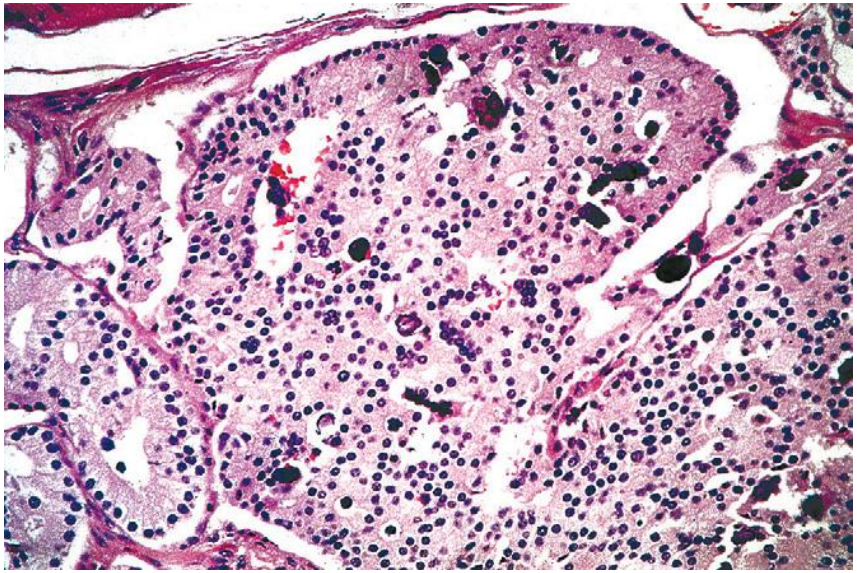
Type A (INSULAR OR NESTED GROWTH PATTERN



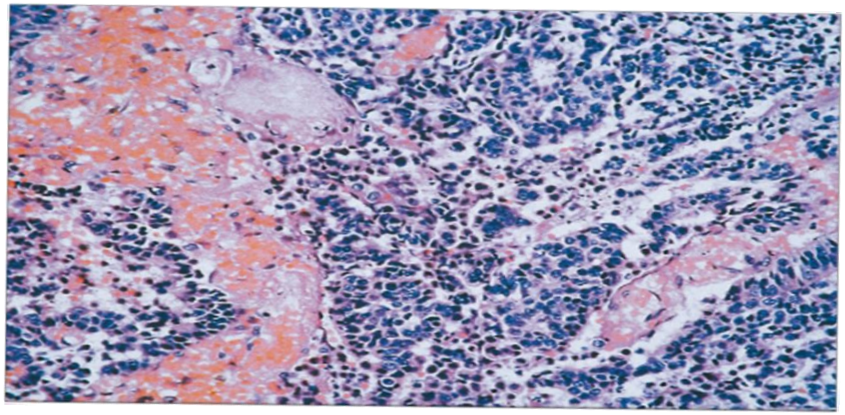
Type B TRABECULAR GROWTH PATTERN



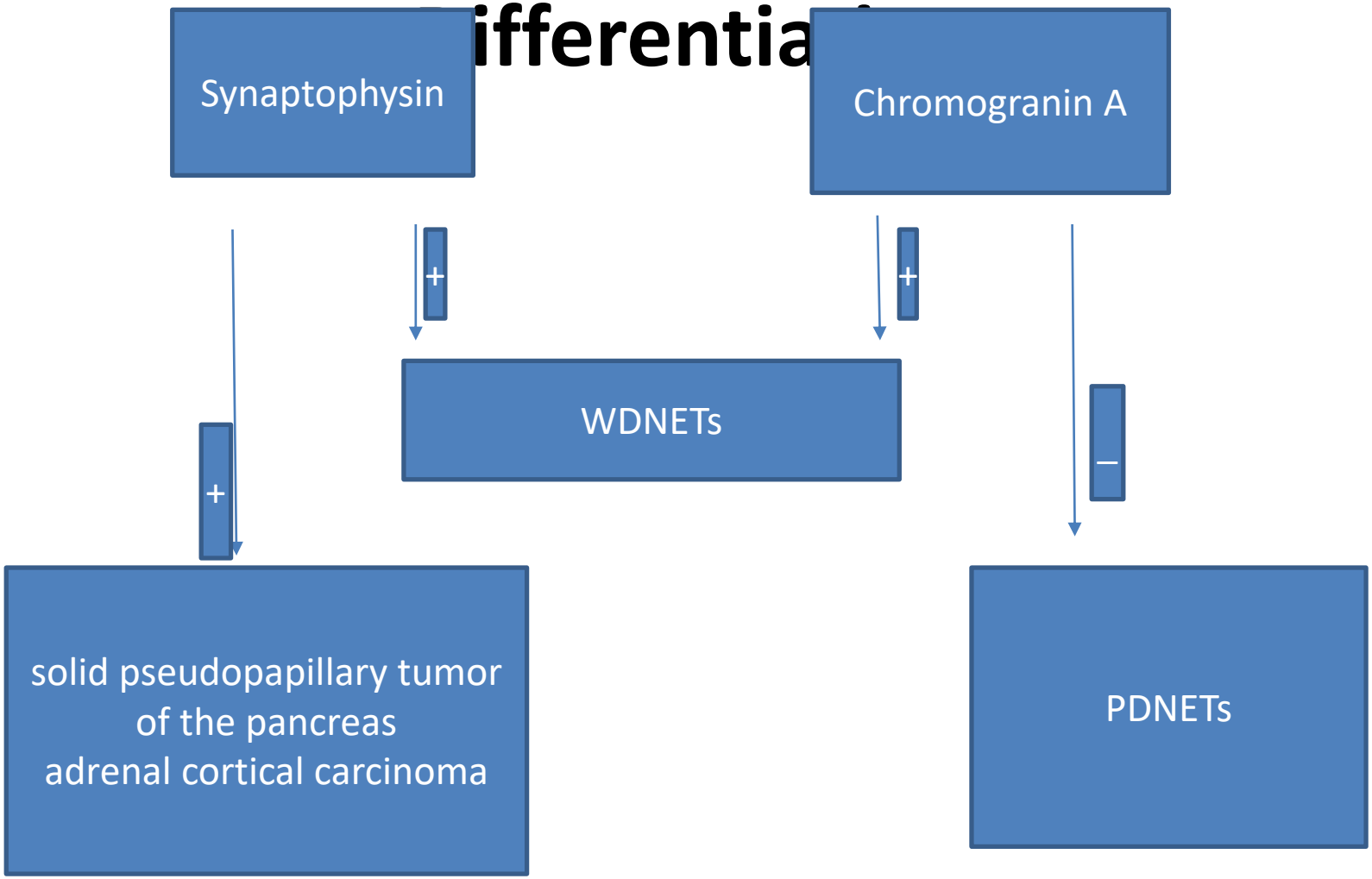
TYPE C (ACINAR GROWTH PATTERN)

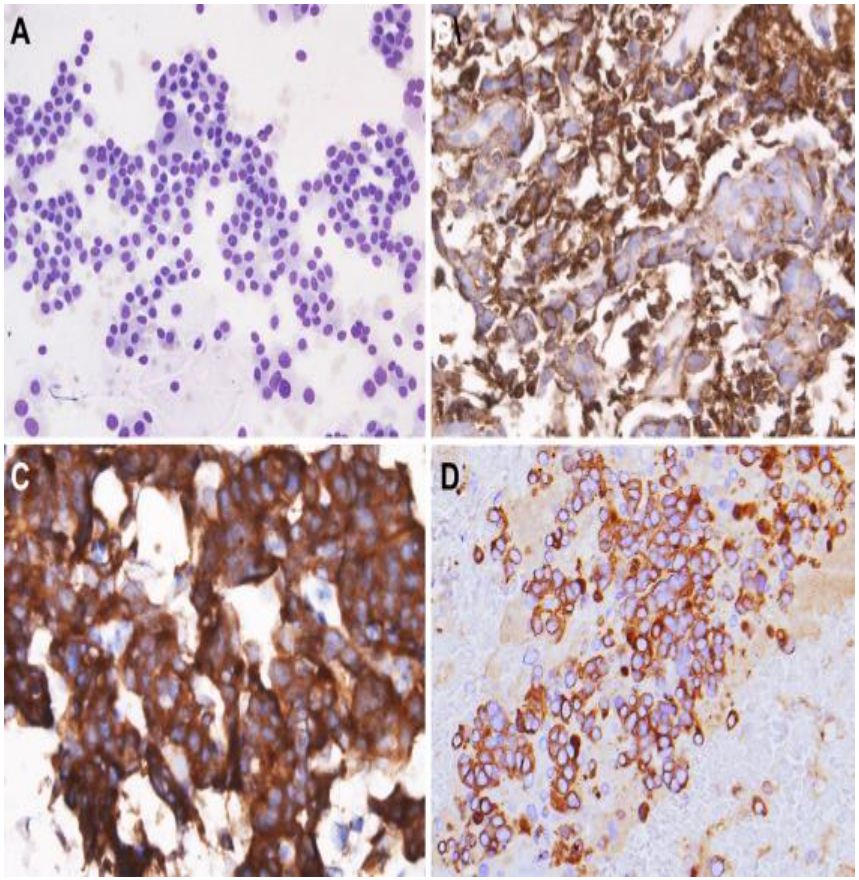


TYPE D (POORLY DIFFERENTIATED GROWTH PATTERN



Confirmation of Neuroendocrine differentia





Well-differentiated neuroendocrine tumor (A: Giemsa stain) with (B) chromogranin A, (C) synaptophysin, and (D) AE1/AE3 positivity.

SMALL AND LARGE INTESTINE

- ***Specimen received***
  Segmental resection specimens, partial or complete pancreatoduodenectomy, partial,or complete colectomy
- Submucosal biopsies
- ***Reporting of neoplastic lesions***
- Tumor site
- Tumor size
- Histologic type
- Histologic grade

REPORTING OF NEOPLASTIC LESIONS

- Microscopic tumor extension
- Margins
- Lympho-vascular invasion
- Regional lymph node status
- Local or Distant spread
- Ancillary studies:
- MSI
- IHC
- Comments

CLINICAL IMPLICATIONS

- **Early Diagnosis**
  - Non invasive detection of neoplasia
    - **Examination of stool, urine, gastric juice and plasma for detection of mutant oncogenes & tumor suppressor genes**
  - Detection more specific than conventional markers
  - **Expensive**
    - Not cost effective in routine detection
    - More useful in screening high risk cases of
      - HNPCC
      - Barrett's esophagus
  - **Analysis of nuclear DNA in stools to find gene sequences like APC, K-ras, p53 is helpful in colorectal cancer detection**
  - Amount of DNA ↑ in colorectal carcinoma

Early Diagnosis

Genetic Testing in Colorectal Cancers

FAP	APC truncating protein tested (preferred) If APC mutation found screen for mutation in family
HNPCC	MSI testing If +ve test for hMLH1 & hMSH2 genes If mutation found screen family for mutations
PJS, Juvenile Polyposis	Gene mutation analysis

Clinical Implications

Formulation of New Treatments

- Principle inhibition of protooncogenic products or replacement of inactivated tumor suppressor genes
  - **Reintroduction of p53, DCC, APC (using viral vectors) or knockout of mutated K-ras→ Growth arrest or reversion of colon cancer cell lines**

- Imantinib mesylate (STI 571/ Gleevac) (a tyrosine kinase inhibitor) used in GIST treatment →targeted therapeutic approach

THANKS