- Polyps of the GI tract

- Tumours of the lower Gastrointestinal Tract (LGIT)

15.08.2018

Objectives

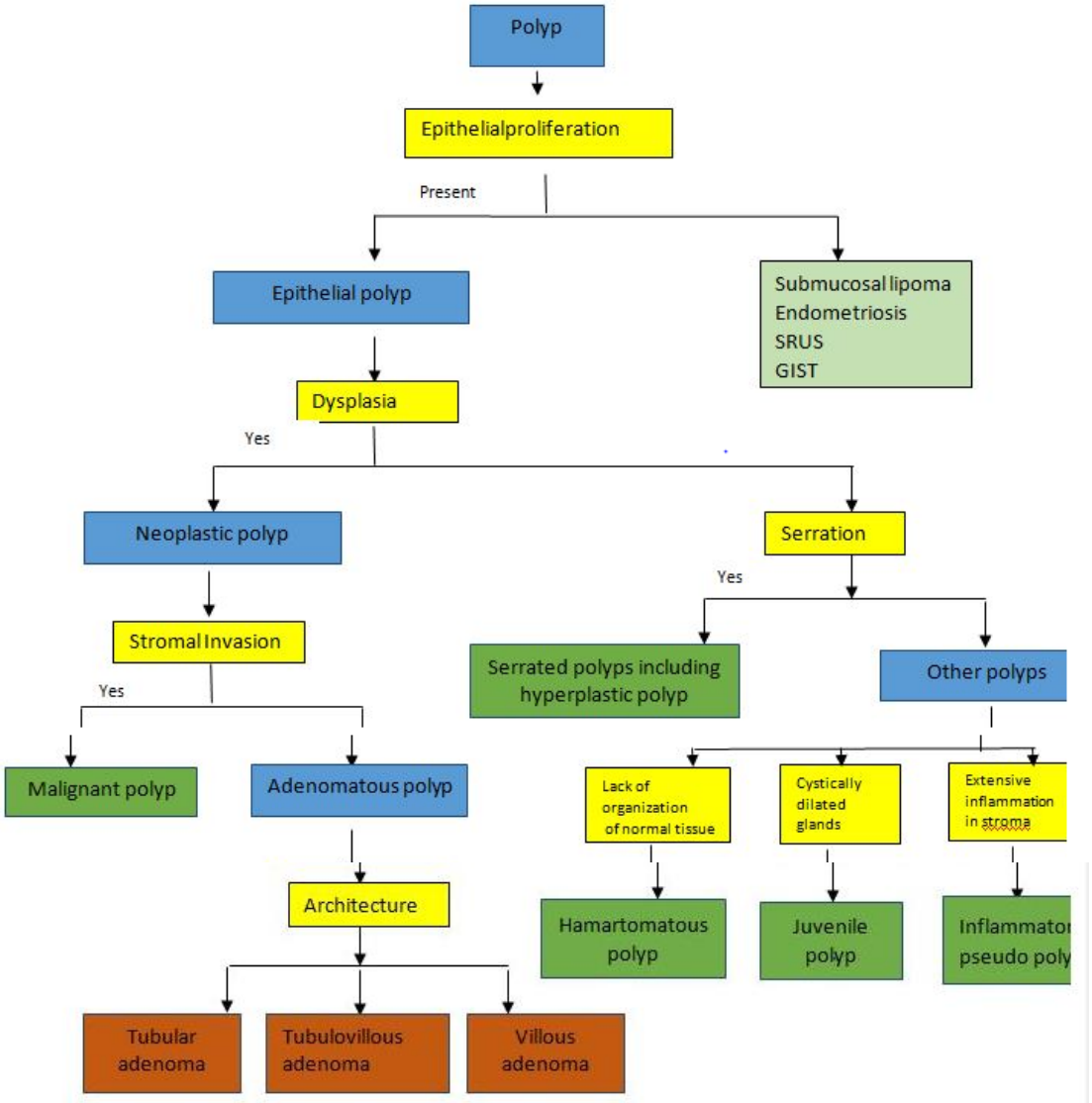
At the end of this lecture, you should be able to

- List , classify and briefly describe different types of polyps in the GIT
- List the different types of tumours of the LGIT

briefly describe

- Adenomas
- Adenocarcinomas
- Neuroendocrine neoplasms of the GIT
- GI lymphomas
- Gastrointestinal Stromal Tumours (GISTs)

Polyps of the GI tract - Classification



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Polyps of the intestine

- Elevations of the mucosa
- With / without a stalk

Neoplastic

Adenoma

Carcinoma

Lymphoma

GIST

Neuroendocrine tumours

Others

Non-neoplastic

Inflammatory polyps

Hyperplastic polyps

Hamartomaous polyps

Inflammatory polyps

Inflammatory polyps in IBD

Polyps in Solitary Rectal Ulcer Syndrome (SRUS)

Hamartomatous polyps

- Sporadic or
- Associated with various syndromes

Peutz-Jeghers syndrome

Juvenile polyposis

Cowden syndrome

Cronchite -Canada syndrome

Tuberous sclerosis

Adenomatous polyps

- Sporadic or

- Associated with syndromes

  FAP - Classic FAP

  - Attenuated FAP

  Gardner syndrome

  Turcot syndrome

  Hereditary Non polyposis Colorectal Cancer (HNPCC) /Lynch syndrome

Hyperplastic polyps

- Common epithelial proliferations
- No malignant potential

- Significance:
  - Must be differentiated from “sessile serrated adenomas” that have malignant potential

  - Similar epithelial changes can occur adjacent to other lesions - Tumours/ inflammatory lesions

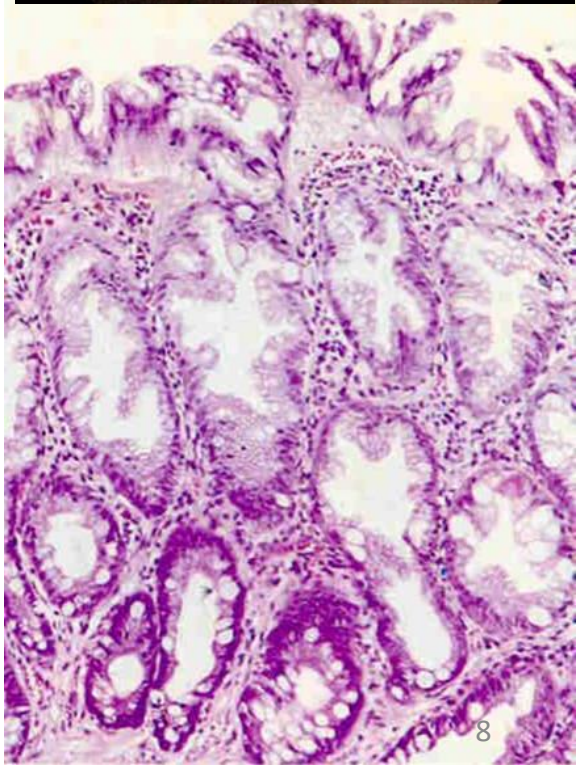
Hyperplastic polyps

Macroscopy

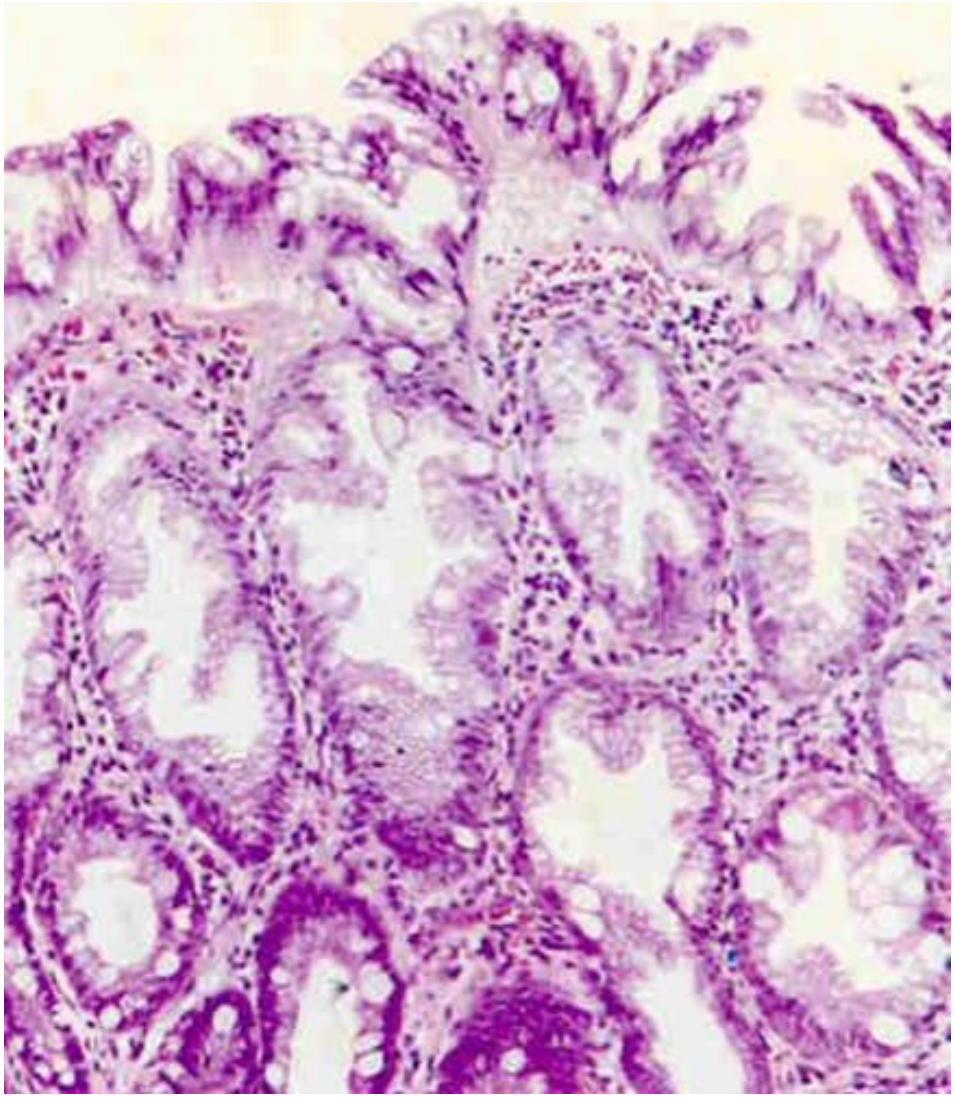
- Common in recto-sigmoid region
- Usually <5 mm and multiple
- Hemispheric, smooth, protrusions on tops of mucosal folds

Microscopy

- irregular, elongated glands with intraluminal infoldings / serrations
- non-dysplastic epithelial lining with differentiation into mature goblet or absorptive cells

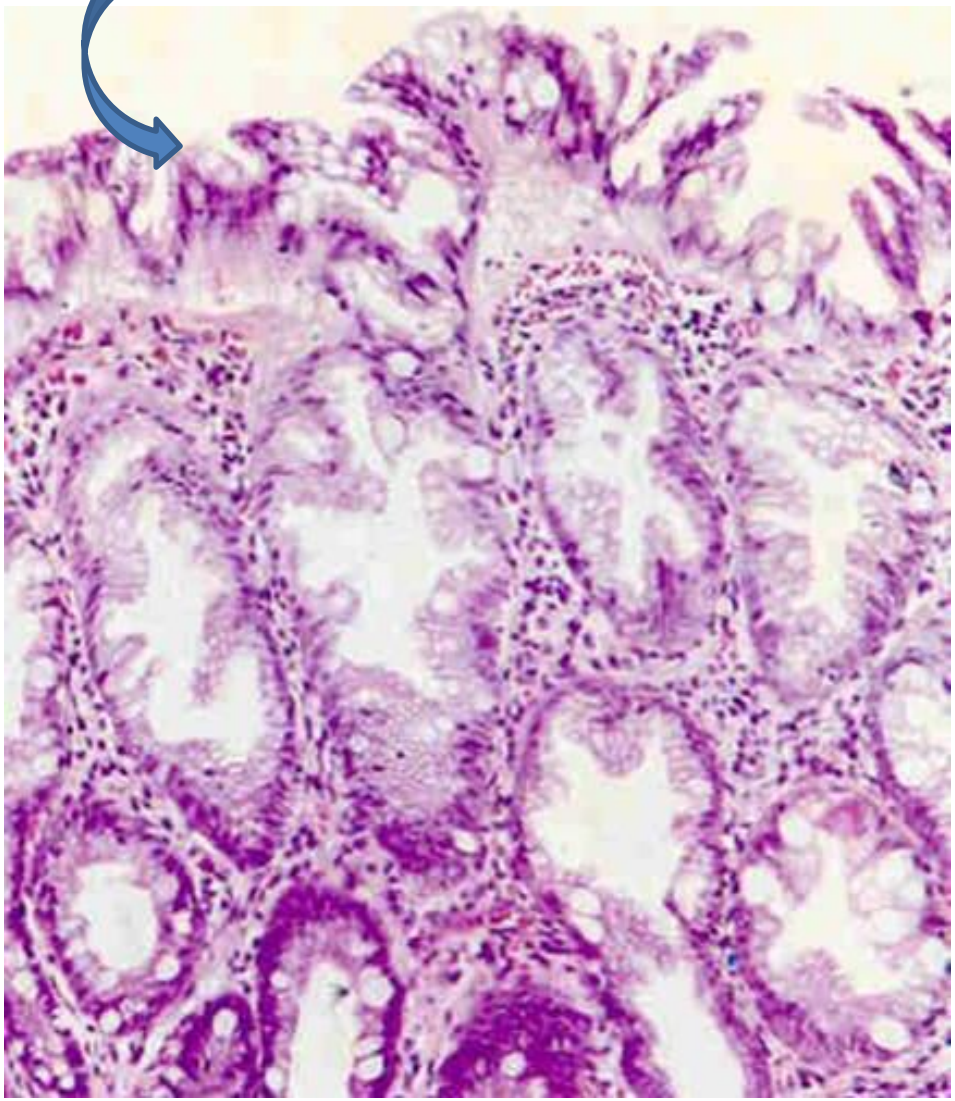


Hyperplastic polyp

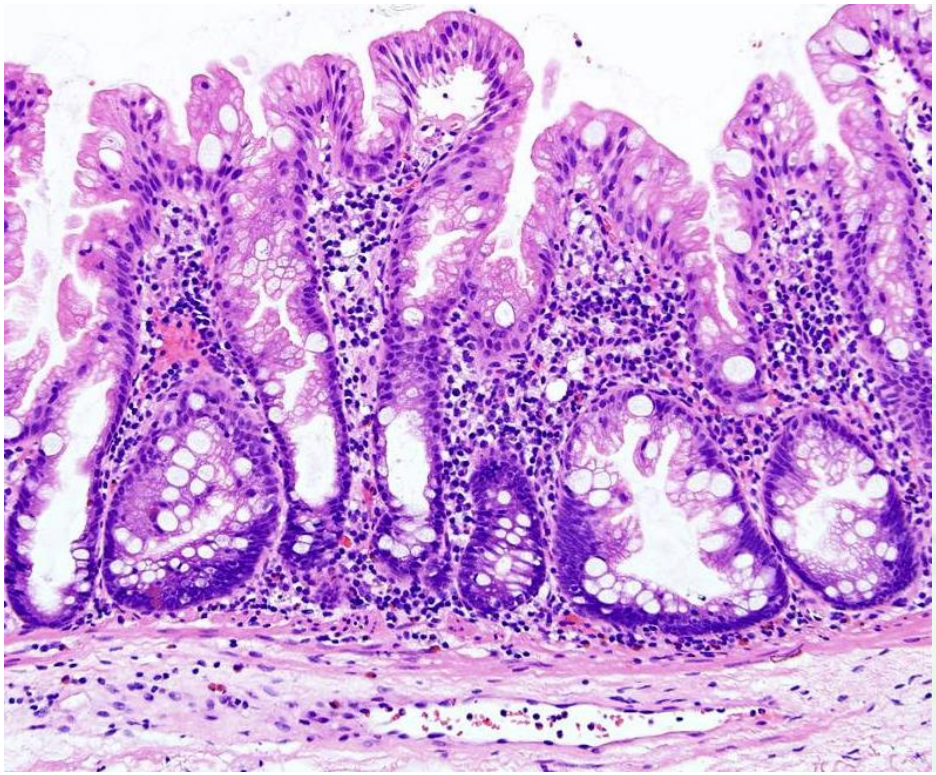


Hyperplastic polyp

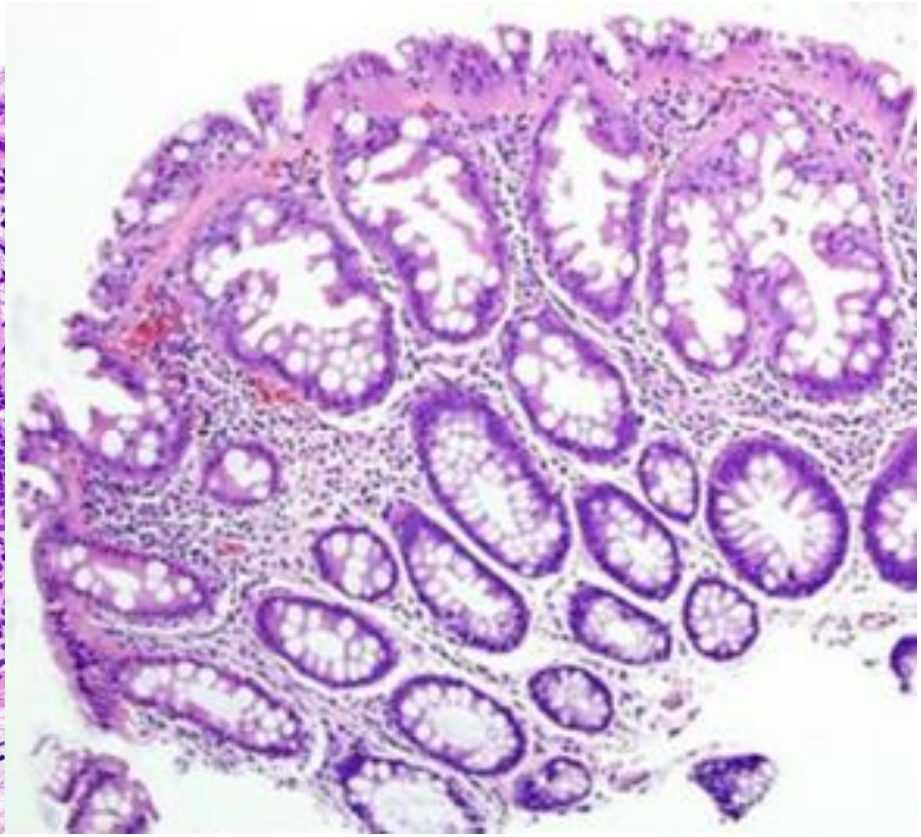
Normal crypts



Hyperplastic crypts – **Serrated appearance**



Sessile serrated adenoma



Hyperplastic polyp

Juvenile polyps

- Focal malformation of the mucosal epithelium and the lamina propria
- Majority in < 5 years of age
- Commonly in Rectum

  minority in stomach and small intestine
- Sporadic - Usually solitary

  Syndromic - Juvenile polyposis (3-100 polyps)

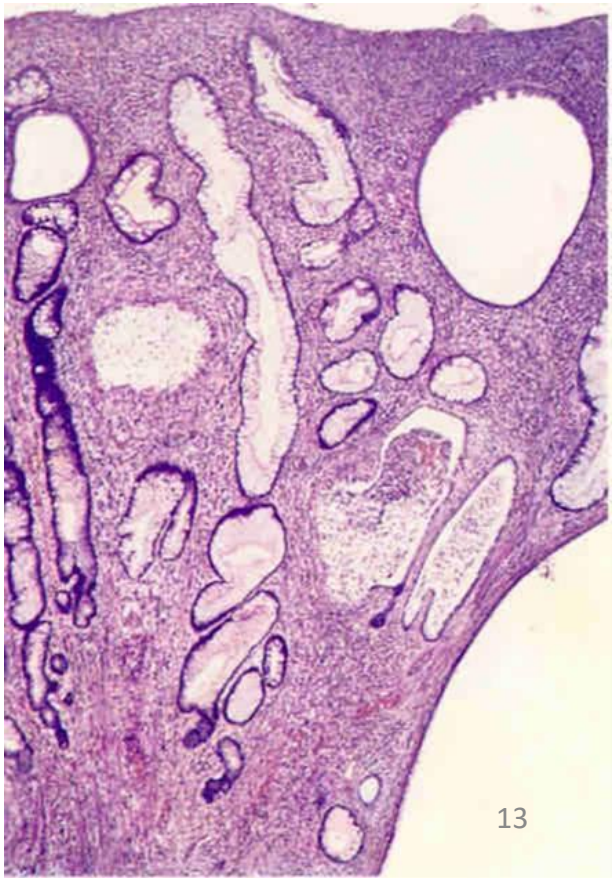
  Increased risk of colonic adenocarcinoma

  - Morphology is similar-

Juvenile polyps

Macroscopy

- Most < 3 cm
- Pedunculated, rounded, smooth lobulated surface
- Cut surface shows cystic spaces



Microscopy

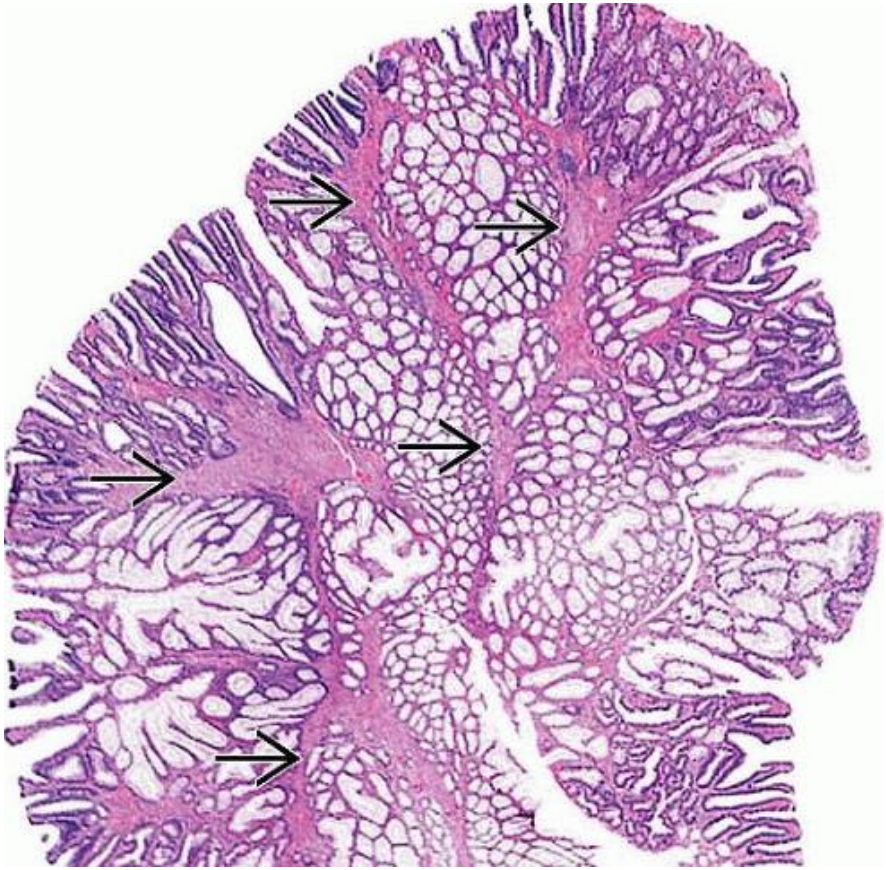
- Cystically dilated glands lined by a flattened epithelium
- Lamina propria expanded by mixed inflammation
- Surface may be ulcerated

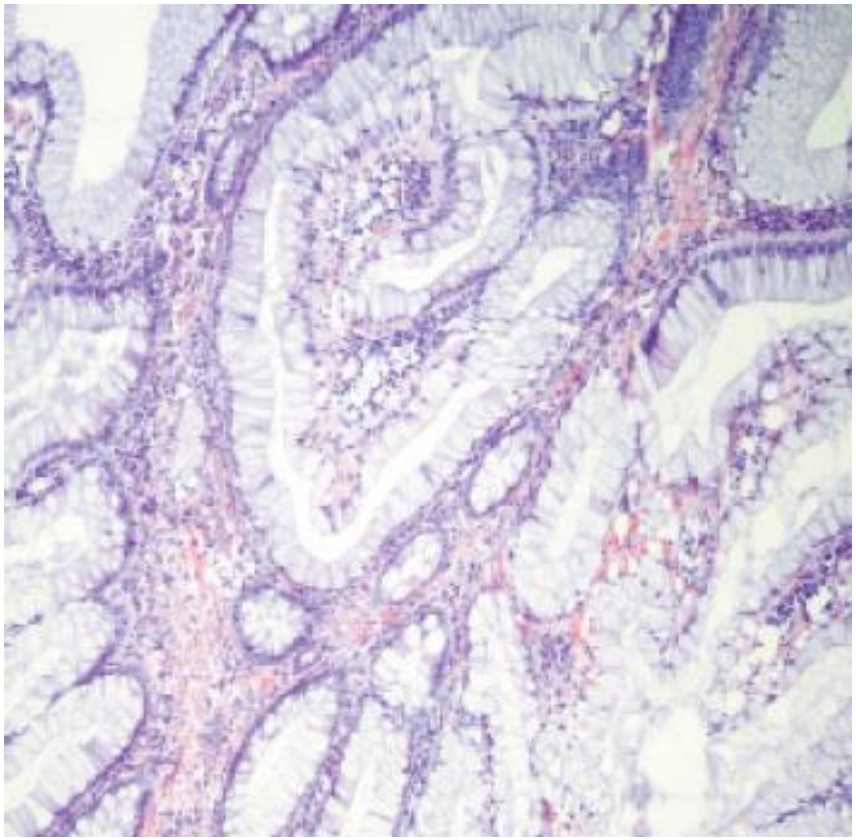
Polyps in Peutz-Jeghar Syndrome (PJS)

- Autosomal dominant
- Majority in children
- Polyps are common in SI, may occur in stomach and colon

Macroscopy: Large, pedunculated, lobulated polyps

Polyps in PJS - **Microscopy**





- **Branching network of connective tissue** with well developed smooth muscles and lamina propria extends into the polyp

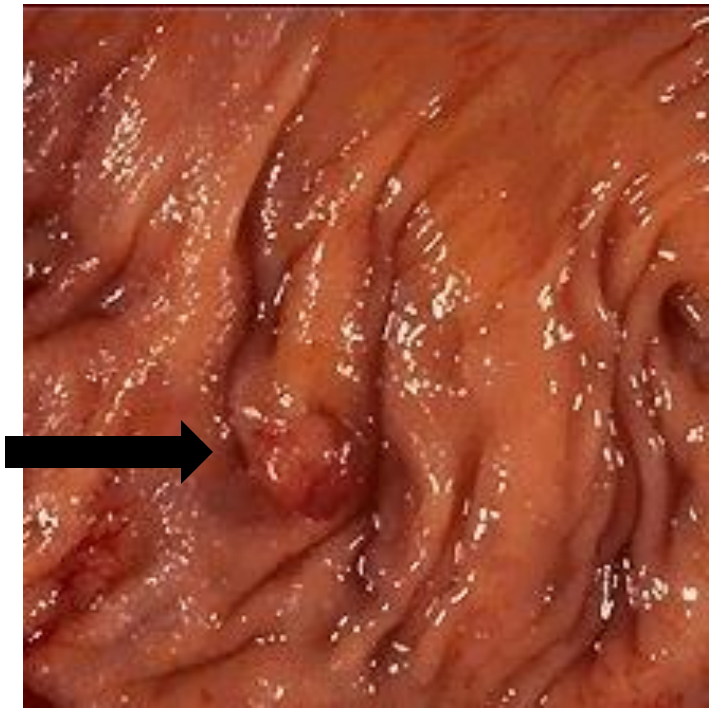
-Glands lined by non-dysplastic epithelium

Adenomatous polyps

Intraepithelial benign neoplasms

> 90% in the colon

also in stomach and SI

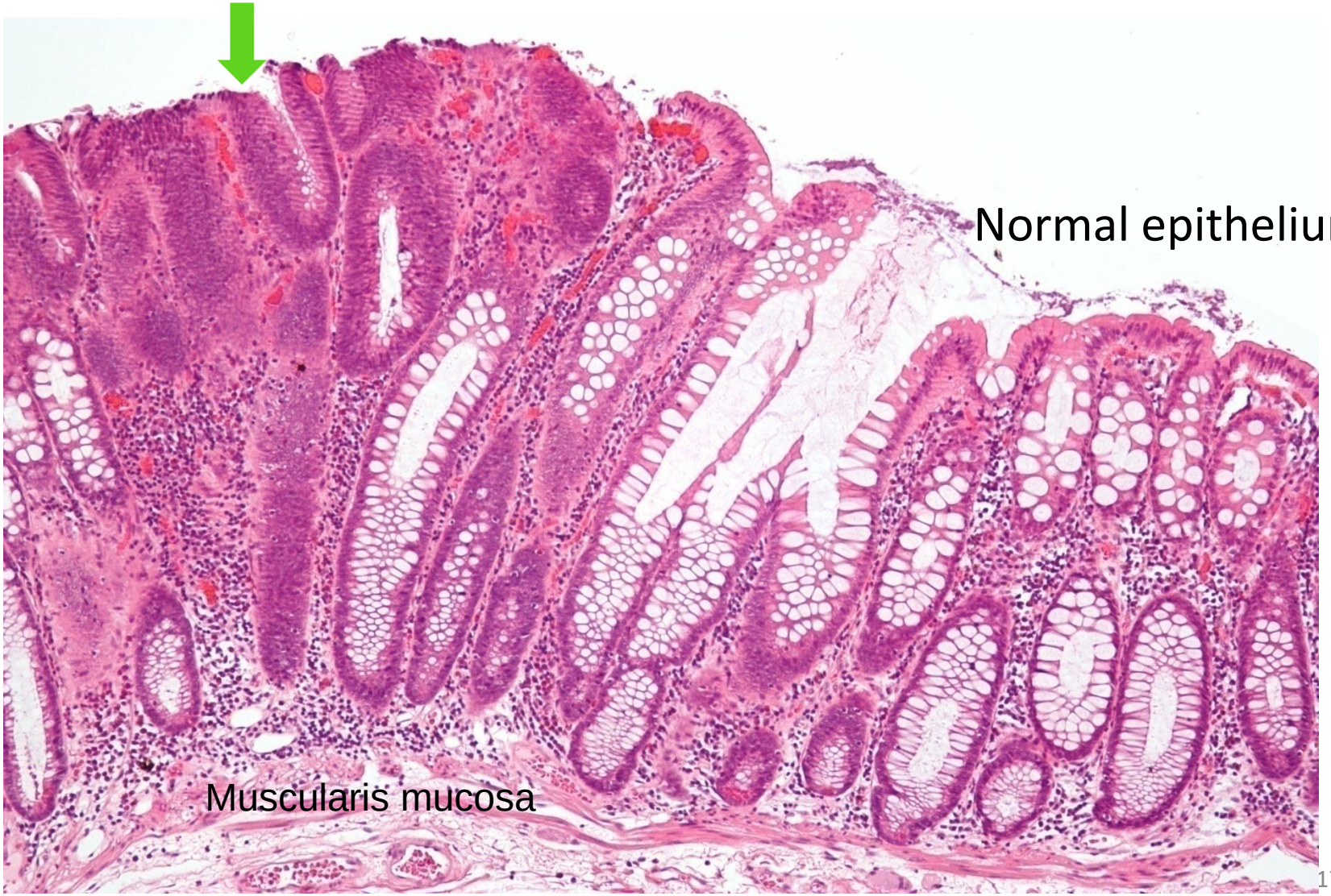


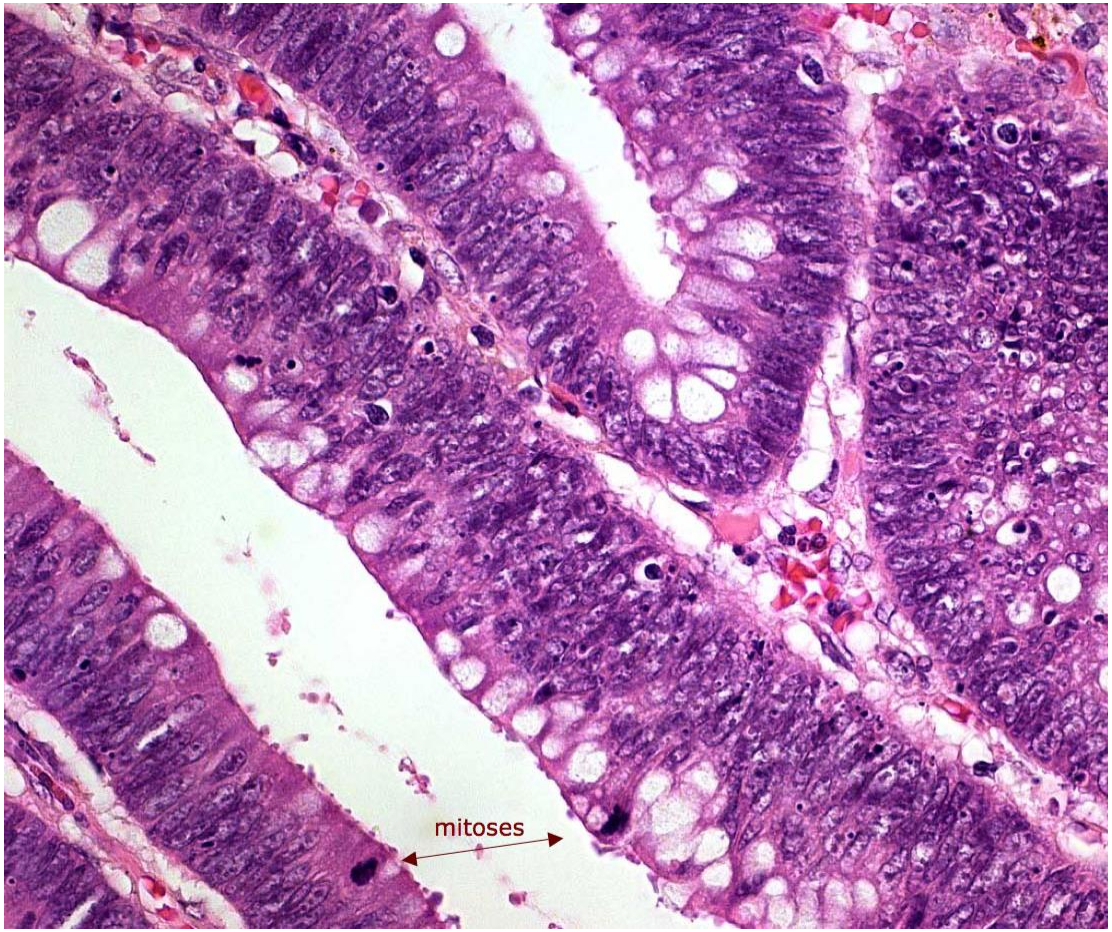
Macroscopy

- Single / multiple lesions
- Sessile /pedunculated
- Range from 0.3 to several cm
- Velvety surface

Adenomatous polyps

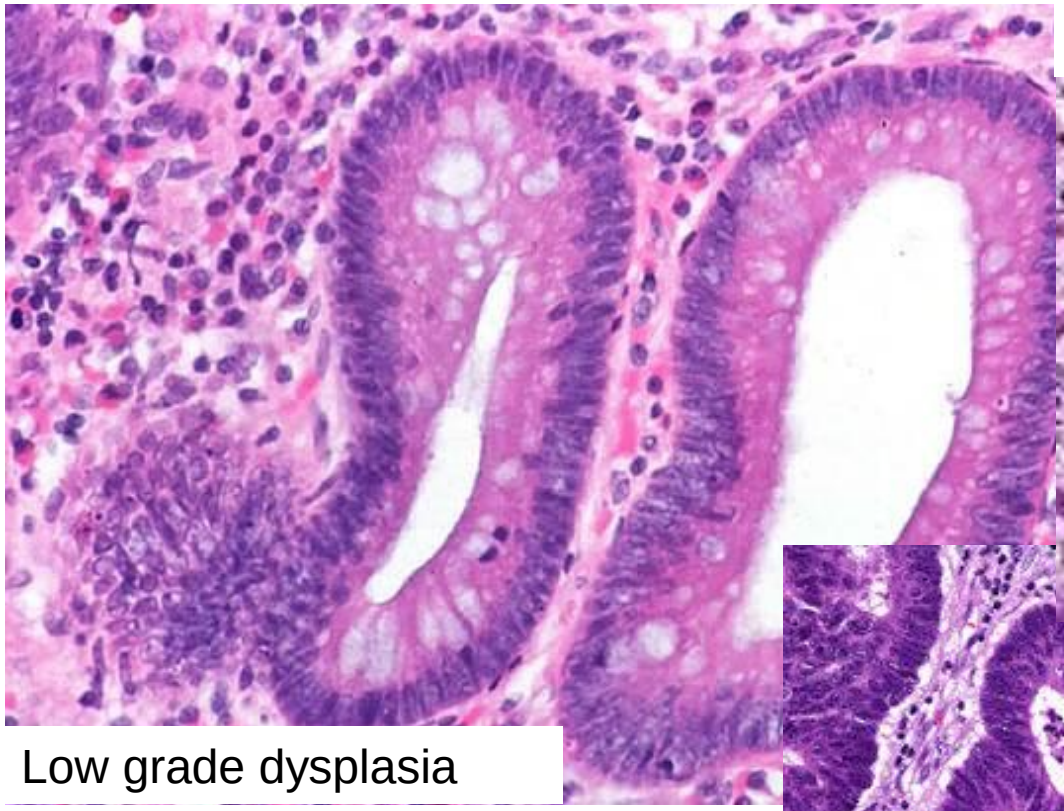
Glands lined by dysplastic epithelium





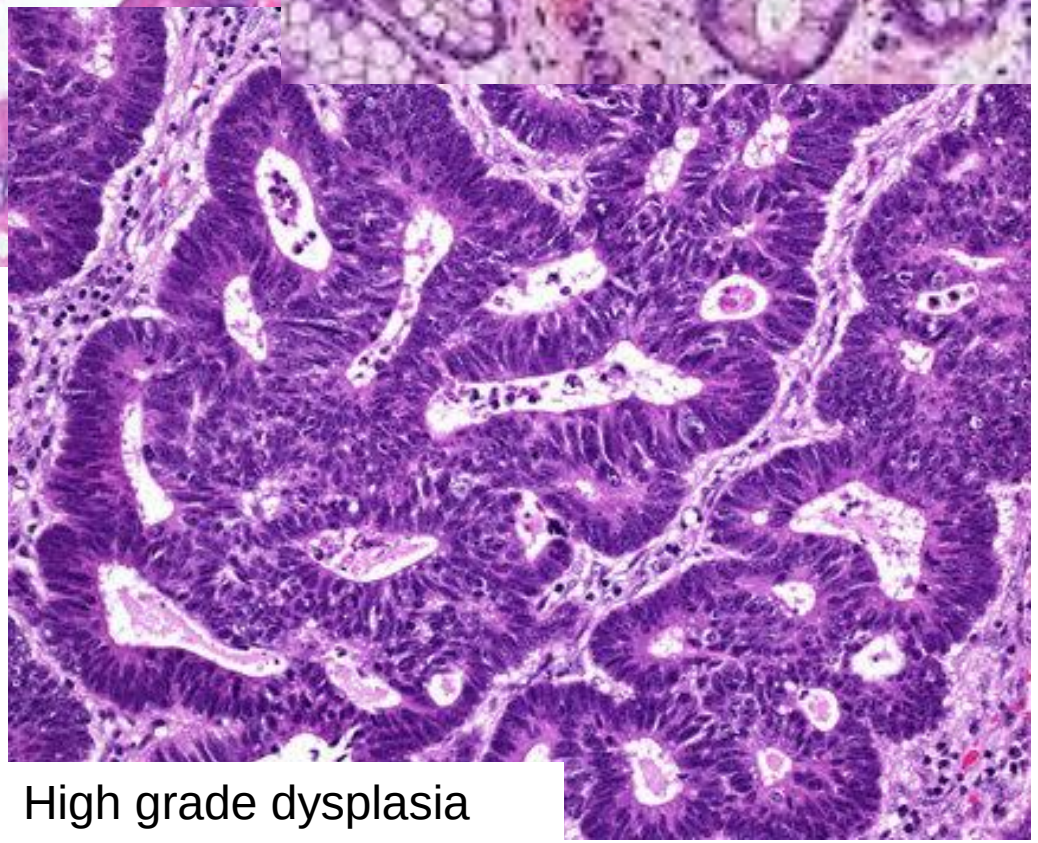
- **Dysplastic epithelium** shows cellular stratification, elongated, hyperchromatic and crowded nuclei and mitoses

- Often have large nucleoli and eosinophilic cytoplasm and reduced number of goblet cells



Low grade dysplasia

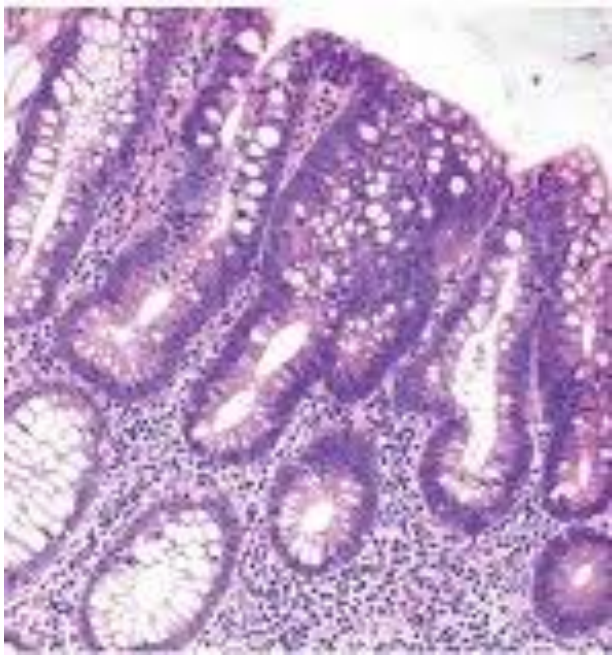
Normal appearing mucosa



High grade dysplasia

Adenomatous polyps

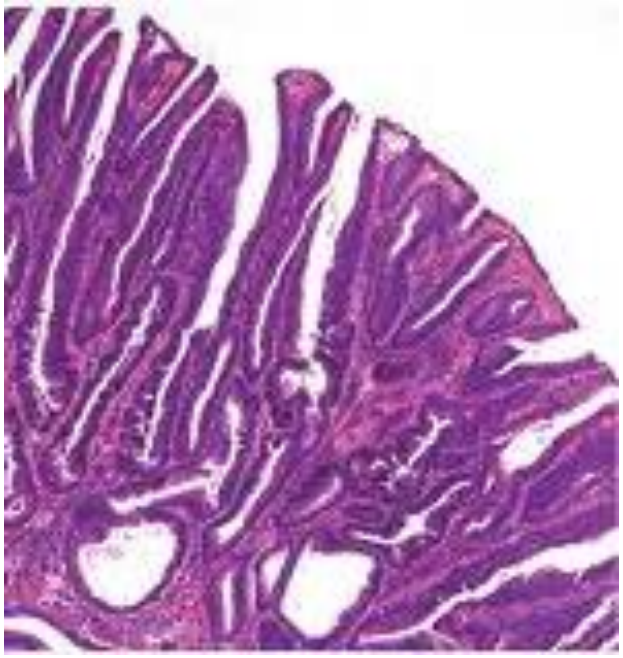
Based on the epithelial architecture,



Tubular adenoma

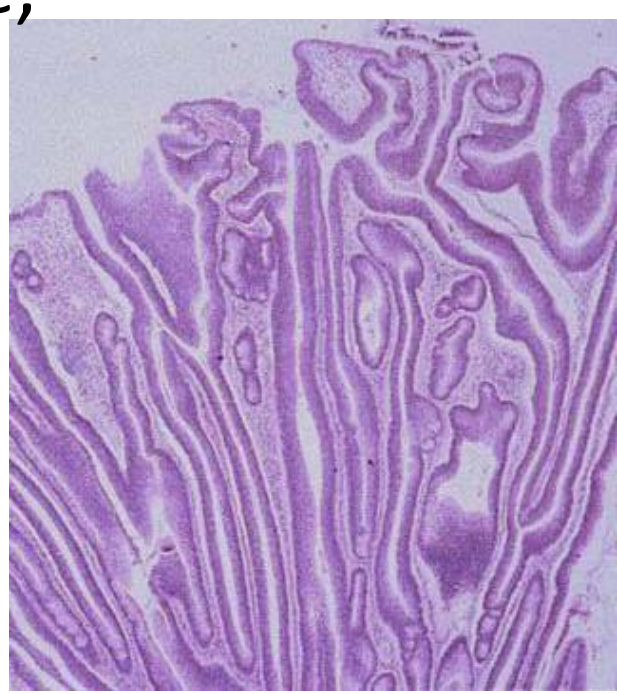
Commonest type

> 75% tubular architecture



Tubulovillous adenoma

25-50% villous architecture



Villous adenoma

> 50% villous architecture

Adenomatous polyposis syndromes

- **FAP** – Familial Adenomatous Polyposis
- **HNPCC** / Lynch syndrome

FAP syndrome

Autosomal dominant

Caused by mutations of the *APC* gene

Develop adenomas early in life

At least 100 adenomatous polyps

- 100% risk of carcinoma, often before 30 years
- Spectrum of clinical manifestations

  Classic FAP

  Attenuated FAP

  Gardner syndrome

  Turcot syndrome

Classic FAP syndrome

- Minimum - 100 adenomas
- Majority - tubular adenomas occasionally villous adenomas

Cancer prevention

Screening and prophylactic colectomy in siblings and first degree relatives at risk

HNPCC/Lynch Syndrome

- Cancers occur in GIT (right colon) and

  other sites : endometrium, stomach, ovary, ureters, brain, hepatobiliary tract, skin

- Caused by inherited mutation in **mismatch repair genes**, commonest – *MSH2* and *MLH1*

- Mismatch repair gene defects result in **microsatellite instability**

Adenomatous polyps
- Malignant risk -

- Correlate with

  Number of adenomas

  Size of the adenoma

  Degree of dysplasia

- When does an adenoma become a carcinoma?

  - When the dysplastic glands invade muscularis mucosa

Adenoma carcinoma sequence

- Molecular events lead to colonic adenocarcinoma are heterogenous and include genetic and epigenetic factors

- Two distinct genetic pathways

  APC/ β-catenin pathway

  Microsatellite instability pathway

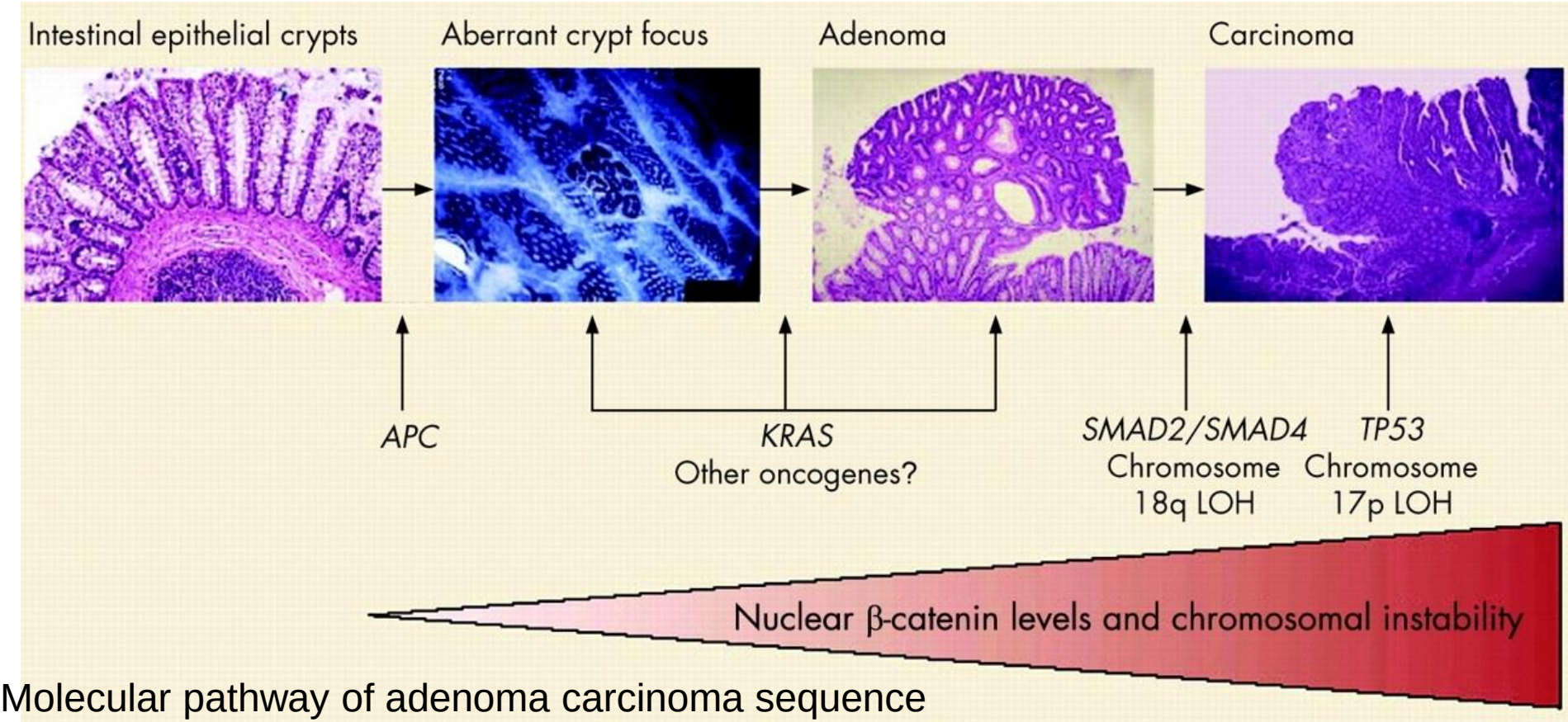
  } **Read**

- Both involve stepwise accumulation of multiple mutations

Colorectal carcinogenesis

- Well described genetic alterations ultimately leads to colorectal carcinoma

  “The adenoma - carcinoma sequence”



Molecular pathway of adenoma carcinoma sequence

- Read – Adenoma carcinoma sequence

Tumours - Lower GIT (SI/LI)

Epithelial tumours

- Adenoma
- Carcinoma

  Adenocarcinoma

  Mucinous adenocarcinoma
  Signet-ring cell carcinoma
  Small cell carcinoma
  Squamous cell carcinoma
  Adenosquamous carcinoma
  Medullary carcinoma
  Undifferentiated carcinoma

- Neuroendocrine neoplasms

Tumours - Lower GIT (SI/LI)

- **Non-epithelial tumours**

  Lipoma

  Leiomyoma

  Gastrointestinal stromal tumour (GIST)

  Leiomyosarcoma

  Angiosarcoma

  Kaposi sarcoma

  Malignant melanoma

  Malignant lymphomas

- **Secondary tumours**

- Tfhe ollowing three slides show WHO classification of tumours of the colon and rectum, small intestine and appendix
- Types of polyps are als

WHO histological classification of tumours of the colon and rectum[1]

Epithelial tumours

Adenoma
- Tubular
- Villous
- Tubulovillous
- Serrated

Intraepithelial neoplasia[2] (dysplasia)
associated with chronic inflammatory diseases
- Low-grade glandular intraepithelial neoplasia
- High-grade glandular intraepithelial neoplasia

Carcinoma
- Adenocarcinoma
- Mucinous adenocarcinoma
- Signet-ring cell carcinoma
- Small cell carcinoma
- Squamous cell carcinoma
- Adenosquamous carcinoma
- Medullary carcinoma
- Undifferentiated carcinoma

Carcinoid (well differentiated endocrine neoplasm)
- EC-cell, serotonin-producing neoplasm
- L-cell, glucagon-like peptide and PP/PYY producing tumour
- Others

Mixed carcinoid-adenocarcinoma
Others

Non-epithelial tumours

Lipoma
Leiomyoma
Gastrointestinal stromal tumour
Leiomyosarcoma
Angiosarcoma
Kaposi sarcoma
Malignant melanoma
Others

Malignant lymphomas
- Marginal zone B-cell lymphoma of MALT Type
- Mantle cell lymphoma
- Diffuse large B-cell lymphoma
- Burkitt lymphoma
- Burkitt-like /atypical Burkitt-lymphoma
- Others

Secondary tumours

WHO histological classification of tumours of the small intestine[1]

Epithelial tumours

Adenoma
- Tubular
- Villous
- Tubulovillous

Intraepithelial neoplasia[2] (dysplasia)
associated with chronic inflammatory diseases
- Low-grade glandular intraepithelial neoplasia
- High-grade glandular intraepithelial neoplasia

Carcinoma
- Adenocarcinoma
- Mucinous adenocarcinoma
- Signet-ring cell carcinoma
- Small cell carcinoma
- Squamous cell carcinoma
- Adenosquamous carcinoma
- Medullary carcinoma
- Undifferentiated carcinoma

Carcinoid (well differentiated endocrine neoplasm)
- Gastrin cell tumour, functioning (gastrinoma) or non-functioning
- Somatostatin cell tumour
- EC-cell, serotonin-producing neoplasm
- L-cell, glucagon-like peptide and PP/PYY producing tumour

Mixed carcinoid-adenocarcinoma
Gangliocytic paraganglioma
Others

Non-epithelial tumours

Lipoma
Leiomyoma
Gastrointestinal stromal tumour
Leiomyosarcoma
Angiosarcoma
Kaposi sarcoma
Others

Malignant lymphomas

Immunoproliferative small intestinal disease (includes α-heavy chain disease)
Western type B-cell lymphoma of MALT
Mantle cell lymphoma
Diffuse large B-cell lymphoma
Burkitt lymphoma
Burkitt-like /atypical Burkitt-lymphoma
T-cell lymphoma
- enteropathy associated
- unspecified

Others

Secondary tumours

WHO histological classification of tumours of the appendix[1]

Epithelial tumours

Adenoma
- Tubular
- Villous
- Tubulovillous
- Serrated

Carcinoma
- Adenocarcinoma
- Mucinous adenocarcinoma
- Signet-ring cell carcinoma
- Small cell carcinoma
- Undifferentiated carcinoma

Carcinoid (well differentiated endocrine neoplasm)
- EC-cell, serotonin-producing neoplasm
- L-cell, glucagon-like peptide and PP/PYY producing tumour
- Others

Tubular carcinoid

Goblet cell carcinoid (mucinous carcinoid)

Mixed carcinoid-adenocarcinoma

Others

Non-epithelial tumours

Neuroma
Lipoma
Leiomyoma
Gastrointestinal stromal tumour
Leiomyosarcoma
Kaposi sarcoma
Others

Malignant lymphoma

Secondary tumours

Tumours - SI

- Length - ¾ of the GIT
- But harbour only 3-6% of GIT tumours

Benign tumours

Adenomas - most around the ampulla of Vater

Malignant tumours

Adenocarcinoma

- Majority in the duodenum

- Most are sporadic

Colorectal adenocarcinoma

- 98% are adenocarcinomas
- Commonest precursor lesion – Adenoma
- 60-79 yrs

  < 20 %occur before 50 years and usually with

  - Polyposis syndrome

  - Ulcerative colitis
- Distribution
  - Recto-sigmoid colon (55%)
  - Caecum/ascending colon (22%)
  - Transverse colon (11%)
  - Descending colon (6 %)

Macroscopy

Proximal colon

- Polypoidal , exophytic /plaque like
- Obstruction unlikely

↓

Late presentation

Distal colon

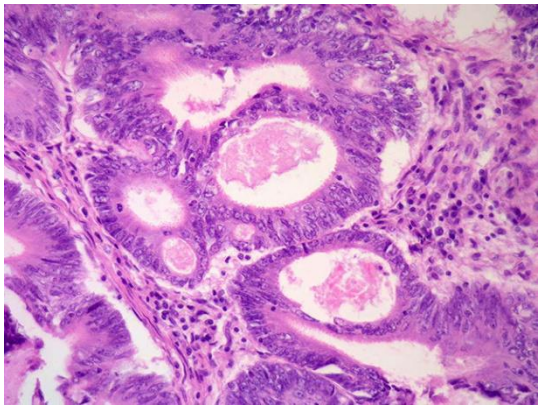
- Ulcerated with elevated margins
- Annular ,encircling tumours
- Encircles the bowel wall
- Narrow lumen
- Dilated proximal bowel

↓

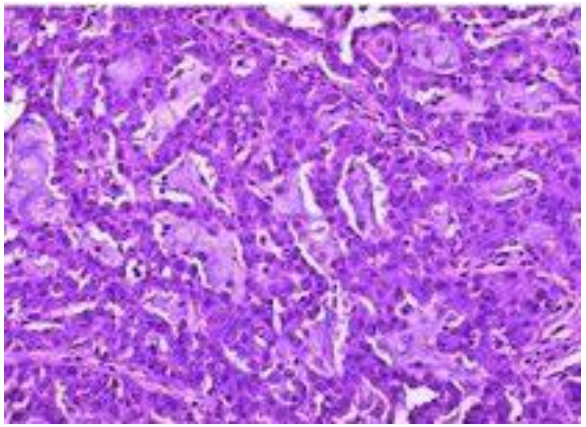
Early presentation with obstruction

Colorectal adenocarcinoma - Microscopy

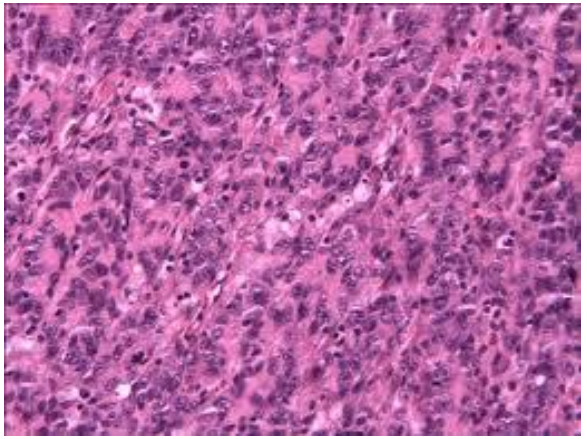
- Similar in right and left colon



Well differentiated Adenocarcinoma
Note
– well formed glands



Moderately differentiated Adenocarcinoma
- Vague gland formation

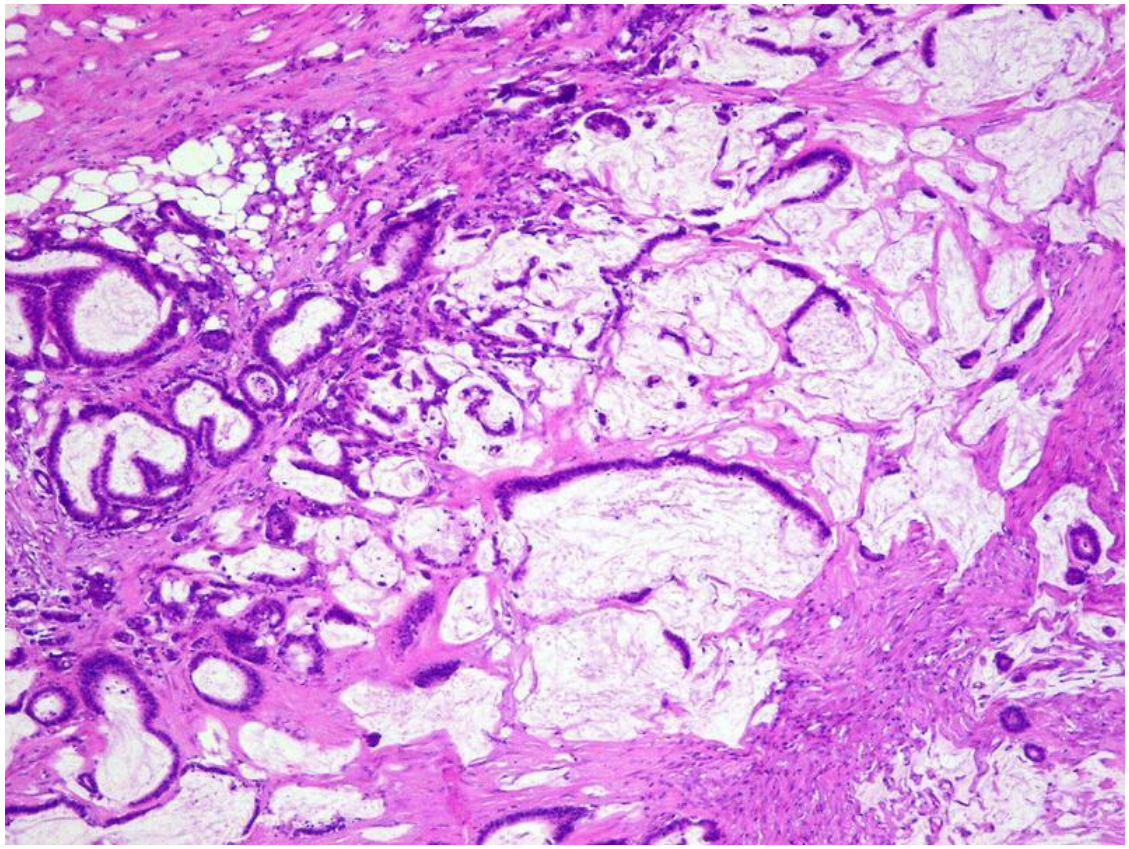


Poorly differentiated adenocarcinoma

Colorectal carcinoma - Microscopy

- May produce mucin – Mucinous adenocarcinoma

  - Intracellular /extracellular mucin



Tumour spread

- Direct extension
- Metastasis - Lymphatics and blood vessels

  Regional LNs , Liver ,lungs, bone

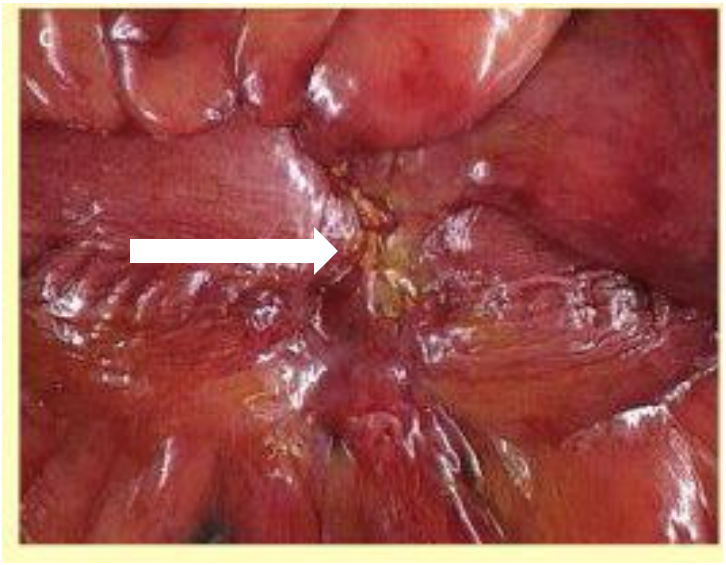
Prognosis

- Single most important prognostic indicator is the extent of the tumour at the time of diagnosis /**stage**
- Staging systems

  TNM staging(Tumour Nodes Metastasis)

  Duke staging

Colorectal adenocarcinoma



- Gradually penetrates the bowel wall and infiltrate into the sub serosa
- When the serosa is involved

  - puckering of the serosal surface (arrow)

TNM staging

Primary Tumor	Regional Lymph Nodes	Distant Metastasis
T0 No Primary Tumor	N0 No Regional LN	M0 No Metastasis
Tis CA in situ	N1 Metastasis in 1-3 pericolic nodes	M1 Distant Metastasis
T1 Invasion into submucosa	N2 Metastasis into 4 or more pericolic nodes	
T2 Invasion into muscularis propria	N3 Metastasis into any nodes along the course of named vascular trunks	
T3 Invasion into serosa		
T4 Invasion into adjacent structures		

Dukes staging

- Dukes A - Invade the **bowel wall** but does not involve the pericolic fat / serosa

- Dukes B - Infiltrate through the bowel wall into the **pericolic fat and serosa**

- Dukes C - Involvement of the **lymph nodes**

Neuroendocrine neoplasms

- <2% of colorectal malignancies
- About 50% of SI malignant tumours
- Derived from neuroendocrine cells located throughout the GIT at the base of the crypts
- Generate bioactive compounds, peptide and non-peptide hormones
- All have a **malignant potential -** Low / high

Neuroendocrine neoplasms

- Appendix is the commonest site
- Followed by SI (primarily ileum), rectum, stomach, and colon

Neuroendocrine neoplasms

- New classification (WHO 2010)

  Neuro Endocrine Tumour - Grade 1 (**NET G1)**

  Neuro Endocrine Tumour - Grade 2 (**NET G2)**

  Neuroendocrine carcinoma (**NEC**)

  Mixed adenoneuroendocrine carcinoma (**MANEC**)

Classification systems

WHO 1980	WHO 2000	WHO 2010
Carcinoid	Well differentiated endocrine tumour	NET G1 (Carcinoid)
	Well differentiated endocrne carcinoma	NET G2
	Poorly differentiated endocrine carcinoma/ small cell carcinoma	NEC (large cell or small cell)
	Mixed exocrine endocrine carcinoma	Mixed adenoneuroendocrine carcinoma

Neuroendocrine neoplsms Definitions

- NET

  Well differentiated neuroendocrine neoplasm composed of tumour cells resembling the normal gut endocrine cells

- NEC

  Poorly differentiated , high grade malignant neoplasm

Neuroendocrine neoplasms-Reporting

- Minimum requirements

  Exact site and size

  Distance from the resection margins
- Microscopy

  Mitoses/10HPF

  Ki67 index (Proliferative activity)
- Assessment of endocrine function

  (upon special clinical response)

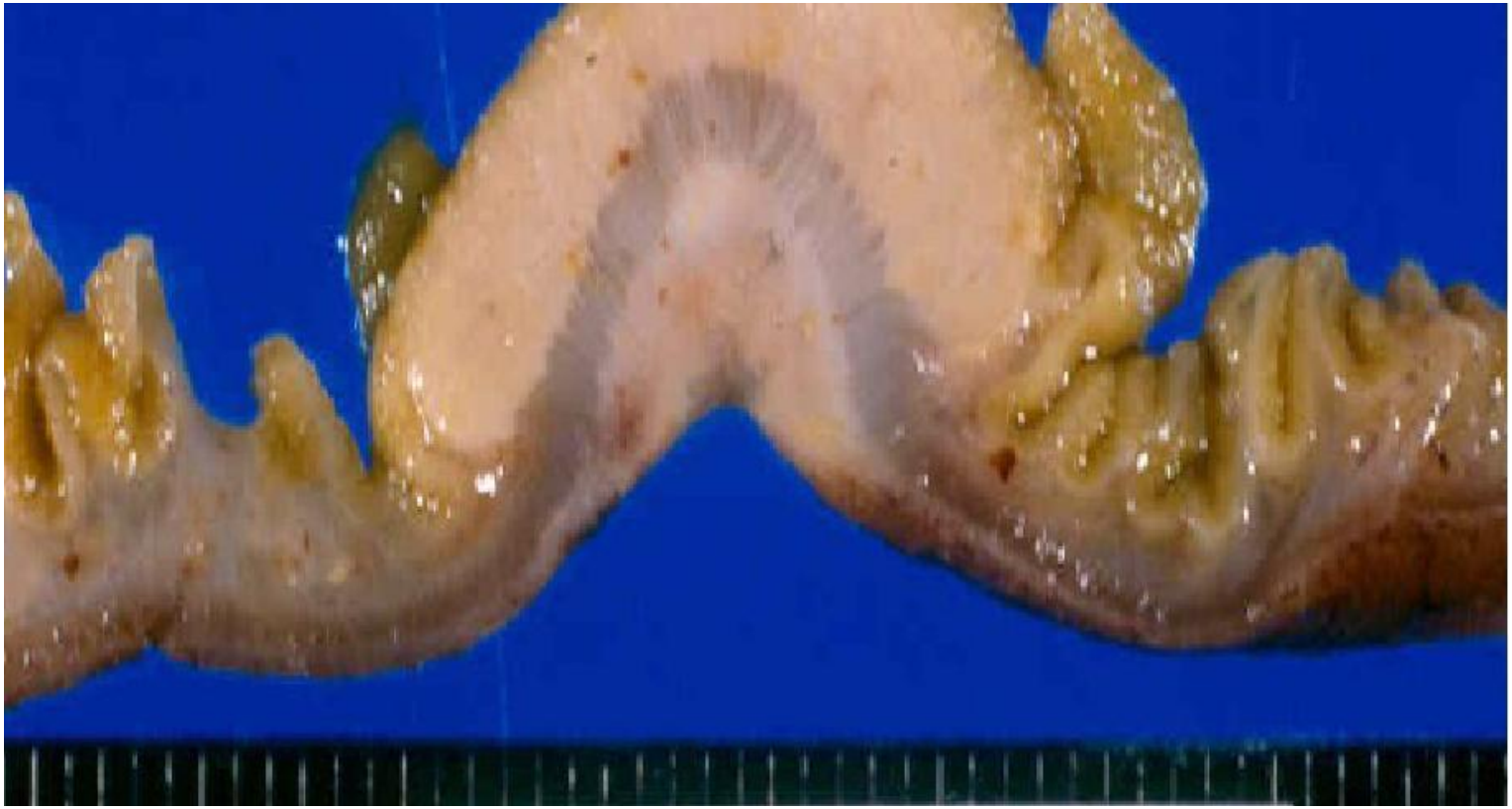
Neuroendocrine neoplasms -Diagnosis

- Classification
- Grade
- Stage (TNM)
- Cell type and functional activity

Neuroendocrine neoplasms

- **Grading** is performed on the basis of
  - morphological criteria
  - Proliferative activity
    mitotic count/ 50 high power fields or
    Ki67 index as a percentage of 500-2000 cells
- **Site specific staging**

Neuroendocrine tumour



NET of the ileum

Appendix -Neuroendocrine neoplasms

- Commonest tumour (50-77% of all neoplasms)
- Usually an incidental finding
- Majority - NET; NEC - Extremely rare

May produce serotonin ,substance P

Macroscopy

Solid bulbous swelling of the

Tip of the appendix

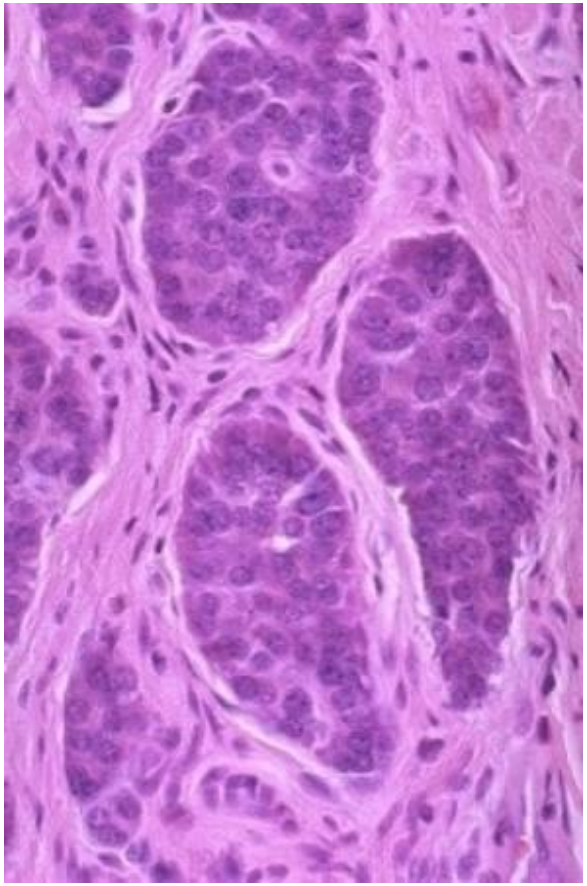
Cut surface

- solid yellow-tan in colour

Appendix – NE neoplasms

Microscopy (NET)

- Stromal desmoplasia
- Discrete islands , strands,
  of uniform tumour cells with
  scant, pink granular cytoplasm
  Round to oval stippled nucleus



- Carcinoid syndrome - **Read**

Tumours of the appendix

- Other tumours

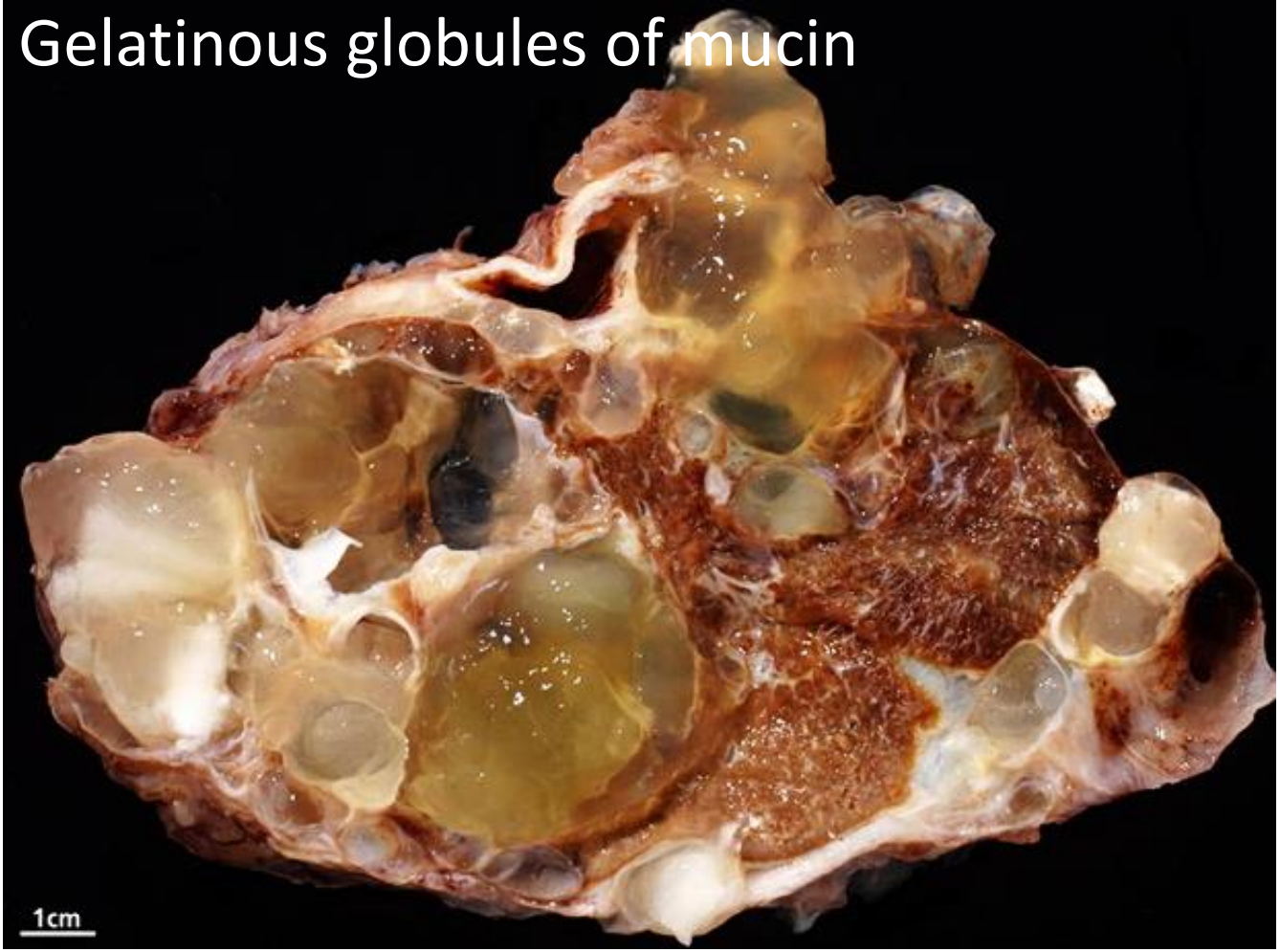
  Adenocarcinoma

    Low grade appendiceal mucinous neoplasms
    Mucinous adenocarcinoma

  Pseudomyxoma peritoneii

  Growth of neoplastic mucin secreting cells within the peritoneal cavity producing accumulation of mucin causing galatinous ascites

Gelatinous globules of mucin



GIT - Lymphomas

- Extra-nodal lymphoma can arise at any site

- Most common site – GIT, particularly stomach

- Common type of lymphomas
  1. Extra-nodal marginal zone B – cell lymphoma
     In the gut known as
     Mucosa Associated Lymphoid Tissue (MALT) / MALTomas
  2. **Diffuse large B-cell lymphoma**

Primary gastrointestinal lymphomas

- No evidence of liver, spleen, mediastinal LN or BM involvement at the time of diagnosis
- Regional LN may be involved
- Usually sporadic, but more frequently seen in

Chronic gastritis caused by *Helicobacter pylori*

Chronic sprue like syndromes

Congenital immunodeficiency states

Infection with HIV

Organ transplant with immunosuppression

Epstein – Barr –virus – positive B cell-lymphoproliferation

MALT lymphoma

- Arise anywhere in the GIT

  Stomach - 55-60% Small intestine - 25-30%

  Proximal colon - 10-15% Distal colon - upto 10%

  Appendix and oesophagus - Rarely involved

- Behavior- different from node based lymphomas
  - Early focal lesions are resectable
  - Relapse may be exclusively on the GIT
  - Different genotypic changes
  - Different immunoreactivity

GIT - Lymphoma

- **Macroscopy** - Variable

  Early lesions - Plaque like expansions of the mucosa and submucosa

  - Diffuse, infiltrating lesions
    - Full thickness mural thickening
    - Effacement of the mucosal folds
    - Focal ulceration

  or

  - Polypoid or fungating and ulcerating masses
  - May develop intestinal obstruction or perforation

GI Lymphoma - Macroscopy

Note: Thickened small intestinal wall

Cut surface – Homogenous , pale yellow-pink

- **Microscopy**

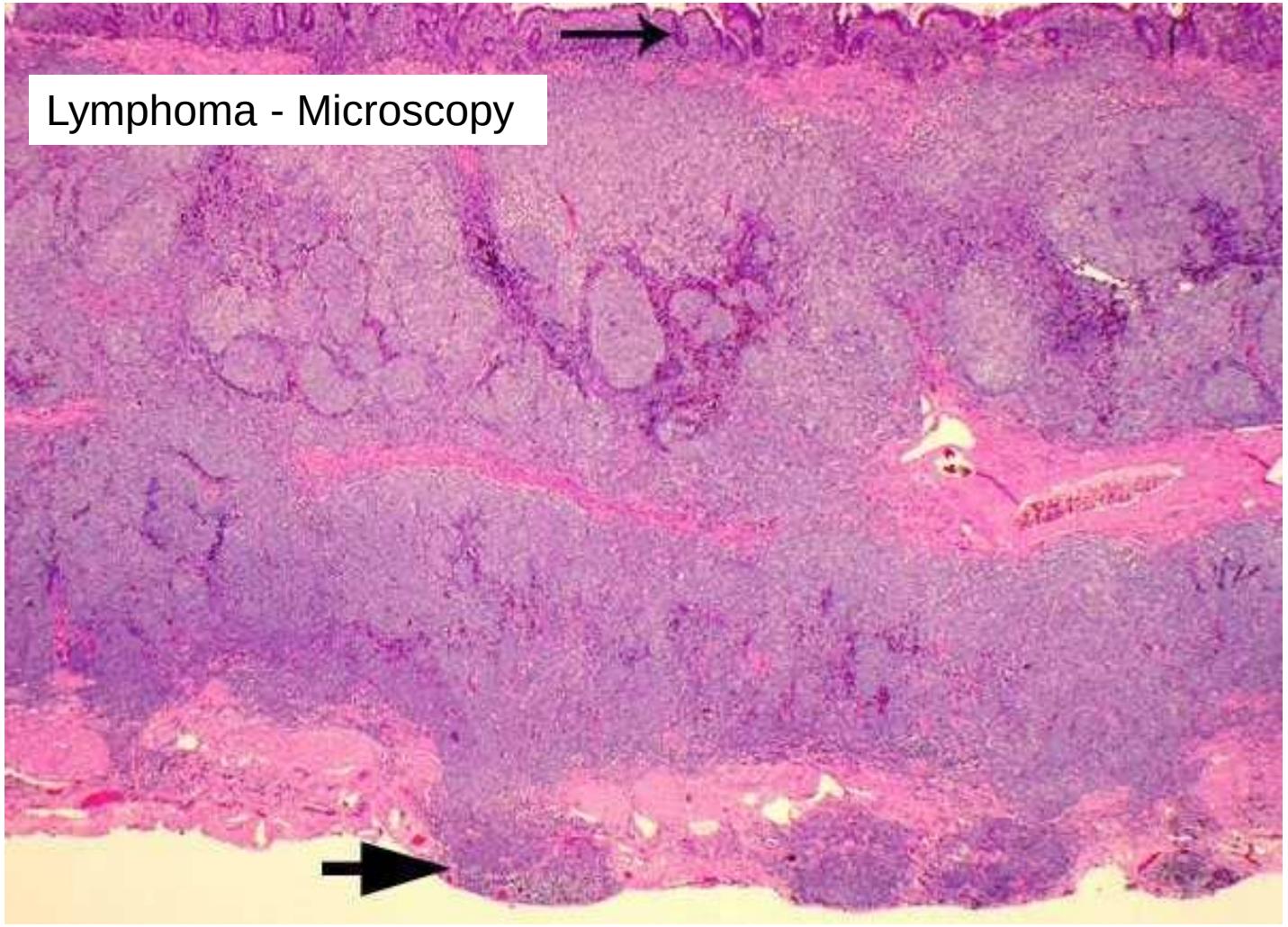
  Earliest lesions

  - Atypical lymphoid cells infiltrate the mucosa
  - Loss of normal glands
  - Massive expansion of the lymphoid tissue
  - **Lymphoepithelial lesions**

    Large numbers of atypical lymphoid cells infiltrate the superficial or glandular epithelium

  Late lesions

  Mucosa, submucosa and muscularis mucosa are replaced by a neoplastic lymphoid cells



Note: Diffuse infiltrate of malignant lymphoid cells involving the full thickness of the bowel wall

GI lymphomas - Prognosis

- Size of the tumour
- Histologic grade
- Depth of local invasion
- Extension into adjacent viscera

Gastrointestinal stromal tumours

- Mesenchymal neoplasms
- Cell of origin - interstitial cells of Cajal

  (pacemaker cells regulating autonomic motor activity)
- Involves stomach (60-70%) followed by

  Small intestine (20-30%)

  Colo-rectum and oesophagus (together < 10%)
  Oesophagus - Rare
- Other sites - Omentum , mesentery,

  retroperitoneum and pleura

- Most in adults
- In children, some related to *Carney triad*
- Around 60% - **stomach**
- Metastasize to liver, peritoneum, lungs and other sites

Pathogenesis

- Most show **mutations in *tyrosine kinase c-KIT* gene (**encodes a thyrosine kinase receptor CD117)

- Sensitive to the action of the tyrosine kinase inhibitor imatinib mesylate (Gleevac/Glivec)

Macroscopic and microscopic appearances are variable

(Need to think - Differential diagnosis)

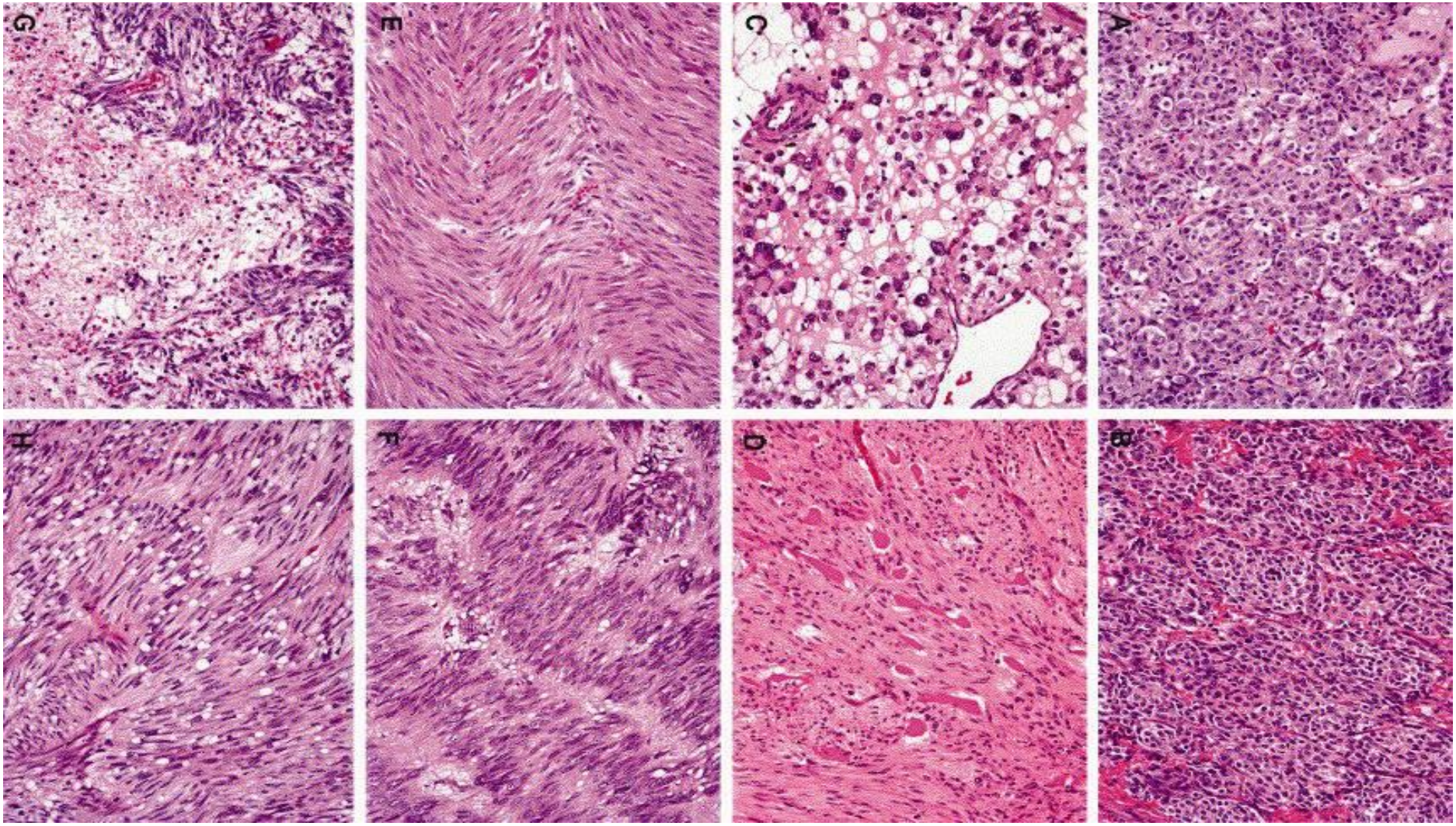
Macroscopy

- Usually well circumscribed, smooth, lobulated fleshy masses
- May be a polypoidal lesion in the mucosal surface or protrude towards the serosa

Microscopy

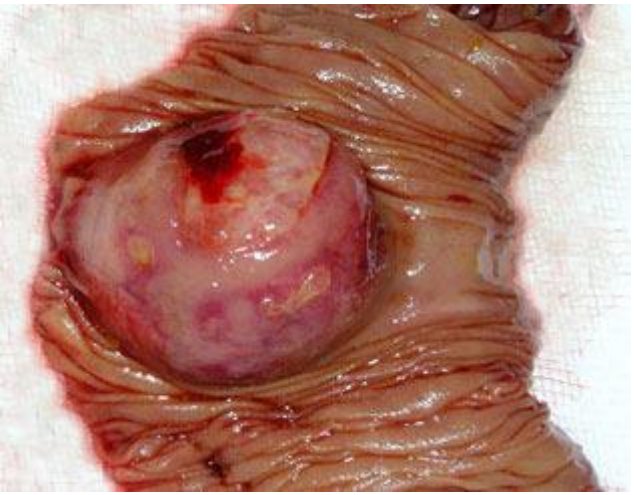
- Composed of spindle cells or epithelioid cells or a mixture of these cell types

GISTs - Microscopy

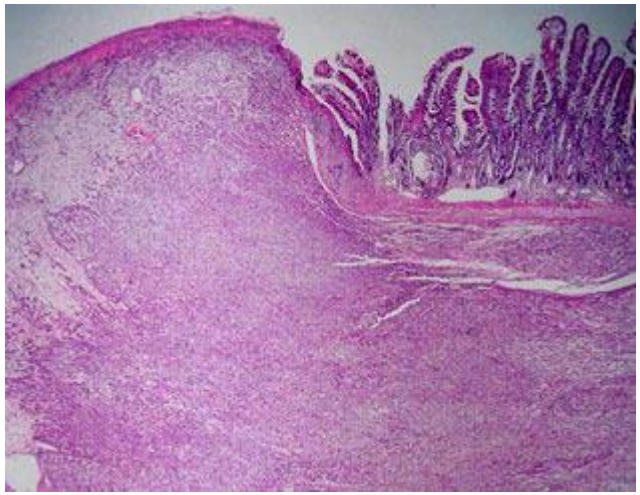


Histology - Variable

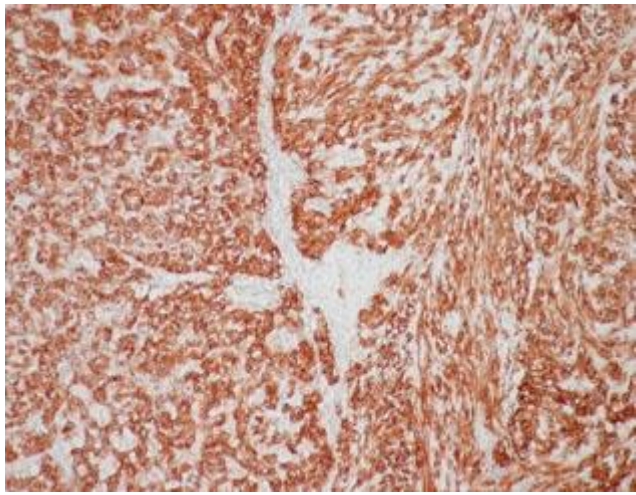
GISTs



Polypoidal lesion
With central ulceration



H&E



Positive c-kit/CD117

GISTs - Prognosis

- In children - often clinically malignant
- Histological assessment of malignancy is based on
  - Mitotic activity
  - Tumour size (< 5cm – usually benign)
  - Tumour site
- Risk categories
  - Low malignant potential
  - Uncertain malignant potential
  - High malignant potential

Summary

Now you should be able to

- List , classify and briefly describe different types of polyps in the GIT
- List the different types of tumours of the LGIT

briefly describe

- Adenomas
- Adenocarcinomas
- Neuroendocrine neoplasms of the GIT
- GI lymphomas
- Gastrointestinal Stromal Tumours (GISTs)