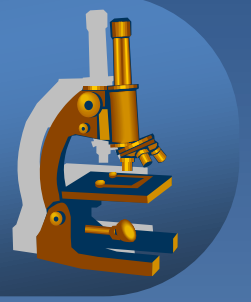
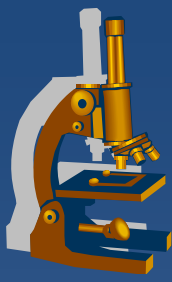
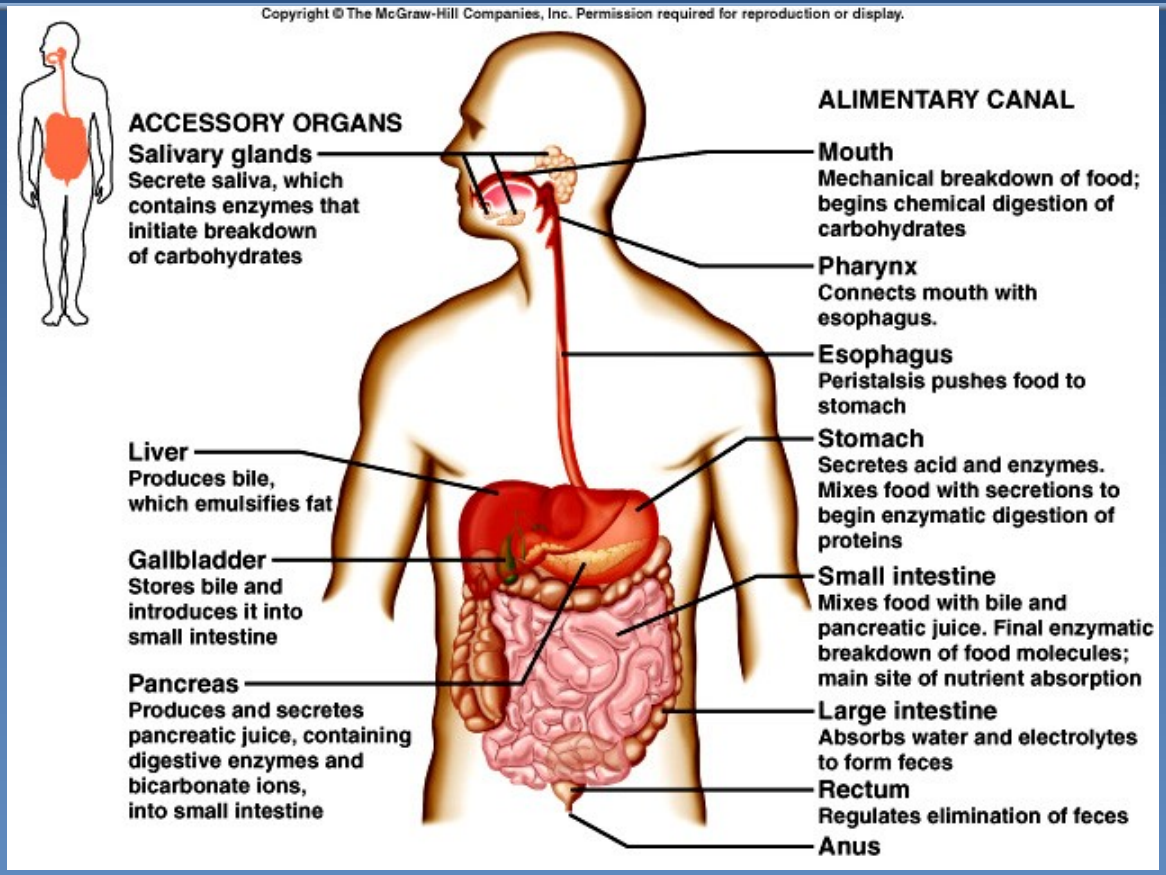
Systematic pathology practice



GIT PATHOLOGY

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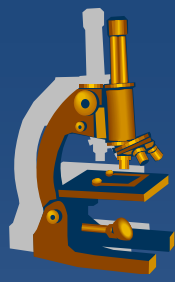
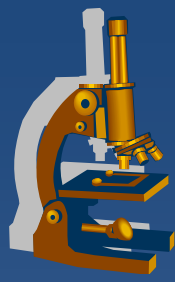
ACCESSORY ORGANS
Salivary glands
Secrete saliva, which contains enzymes that initiate breakdown of carbohydrates
Liver
Produces bile, which emulsifies fat
Gallbladder
Stores bile and introduces it into small intestine
Pancreas
Produces and secretes pancreatic juice, containing digestive enzymes and bicarbonate ions, into small intestine
ALIMENTARY CANAL
Mouth
Mechanical breakdown of food; begins chemical digestion of carbohydrates
Pharynx
Connects mouth with esophagus.
Esophagus
Peristalsis pushes food to stomach
Stomach
Secretes acid and enzymes. Mixes food with secretions to begin enzymatic digestion of proteins
Small intestine
Mixes food with bile and pancreatic juice. Final enzymatic breakdown of food molecules; main site of nutrient absorption
Large intestine
Absorbs water and electrolytes to form feces
Rectum
Regulates elimination of feces
Anus



ORAL CAVITY

Congenital disorders: hare-lip and cleft palate



- incidence 1 : 950 newborns
- lateral cleft – isolated or complete
  - ⇨ ***fusion defect*** **of the first branchial arch –maxilar process with fronto-nasal lateral process**

  genetic x acquired (environmental)
  unilateral x bilateral

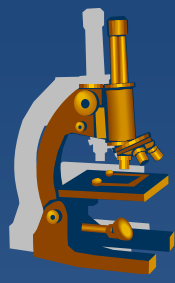
  - ⇨***cheiloschisis (upper lip) – complete/incomplete***
  - ⇨***gnathoschisis (jaw)***
  - ⇨***palatoschisis (hard palate)***
  - ⇨***uranoschisis (soft palate)***
  - ⇨***staphyloschisis (uvula)***

- medial, oblique, transverse cleft (rare)

Cheilognathopalatoschisis

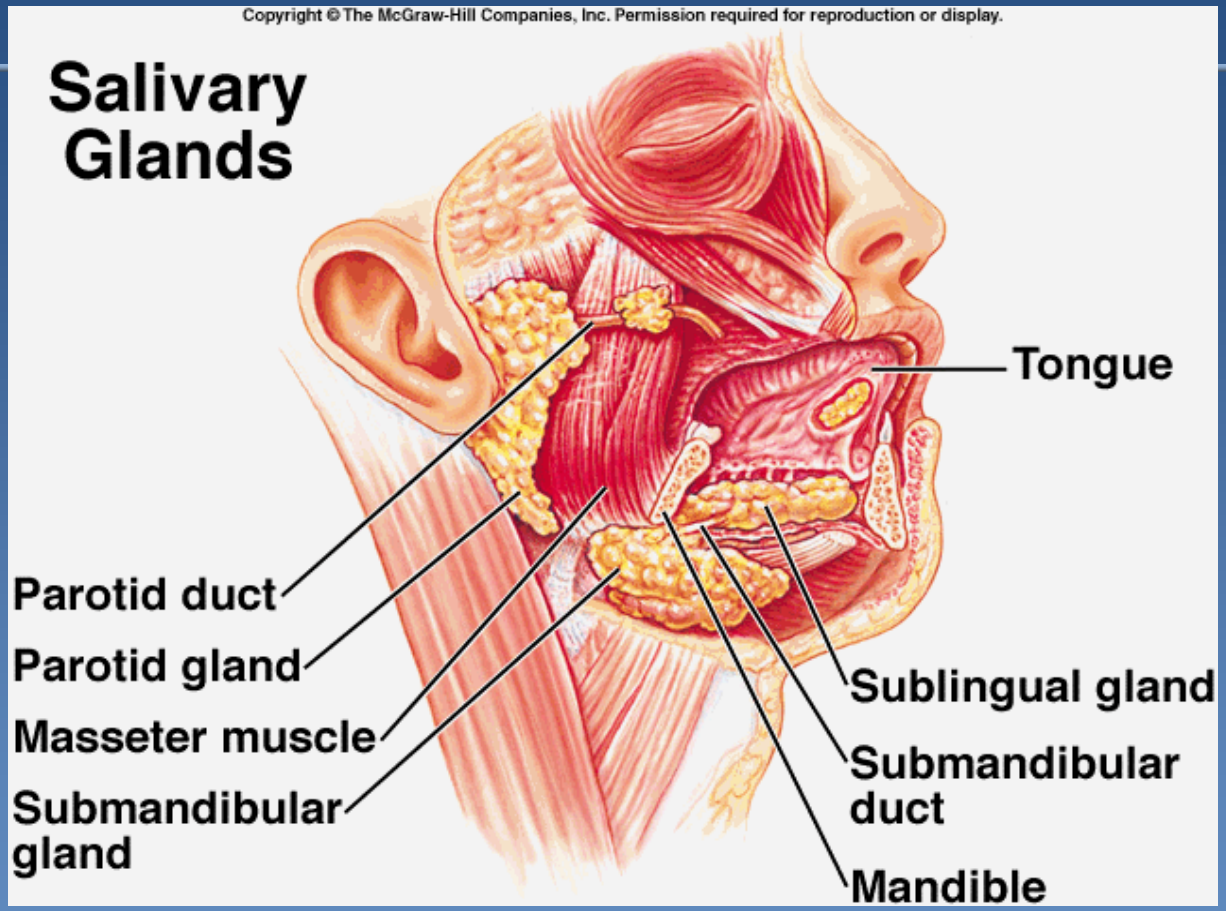
copy

Salivary glands

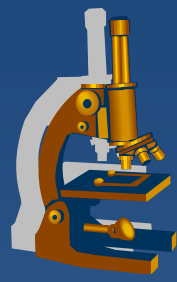


- 3 pairs of large major salivary glands, numerous small ones
- serous / mucinous
- secretory units → glandular ducts
- double cell layer – external myoepithelia
- tumors mostly in the parotid gland, in adults usually epithelial tumors

Salivary Glands

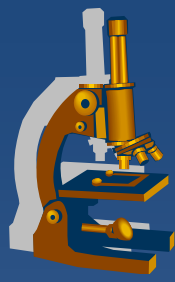


Salivary gland tumors



- parotid
  - ⇨ ***cca 75%, mostly benign (70-85%)***
- submandibular
  - ⇨ ***40% malignant***
- minor salivary glands
  - ⇨ ***50% malignant***
- sublingual
  - ⇨ ***mostly malignant***

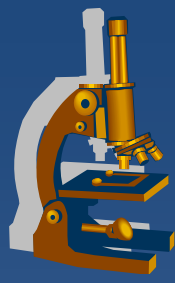
Histologic types



Selected types

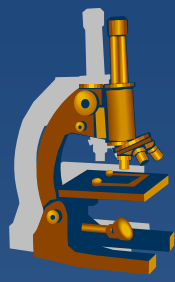
- pleomorphic adenoma (benign mixed tumor)
- adenolymphoma (Warthin tumor)
- oncocytoma
- mucoepidermoid carcinoma
- adenoid cystic carcinoma
- malignant mixed tumor

Pleomorphic adenoma (mixed tumor of salivary glands)



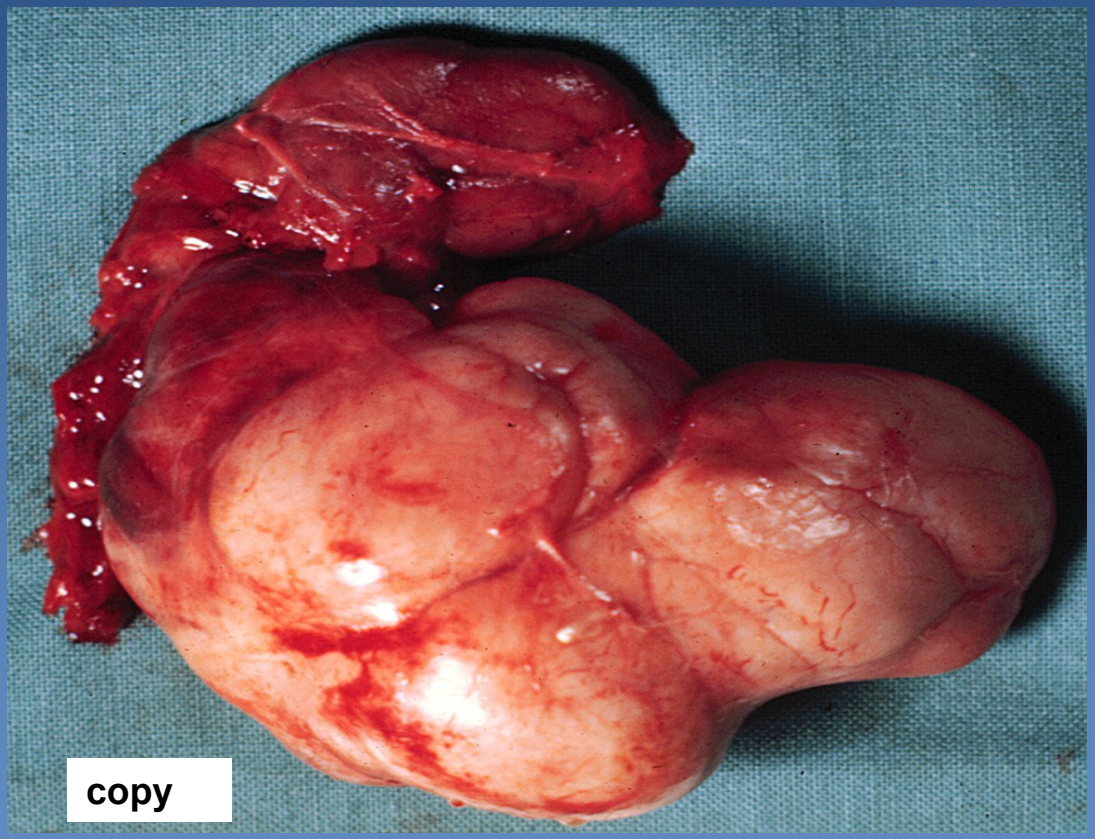
- former name „myxochondroepithelioma“
- benign epithelial tumor
- 80% in the parotid gland, most common parotid tu
- any age, mostly middle-late adult age
- slow-growing firm mass
- well-demarcated, but capsule incomplete
- frequent recurrences after incomplete resection
- low risk of malignant transformation (4%), in long duration, recurrences

Pleomorphic adenoma

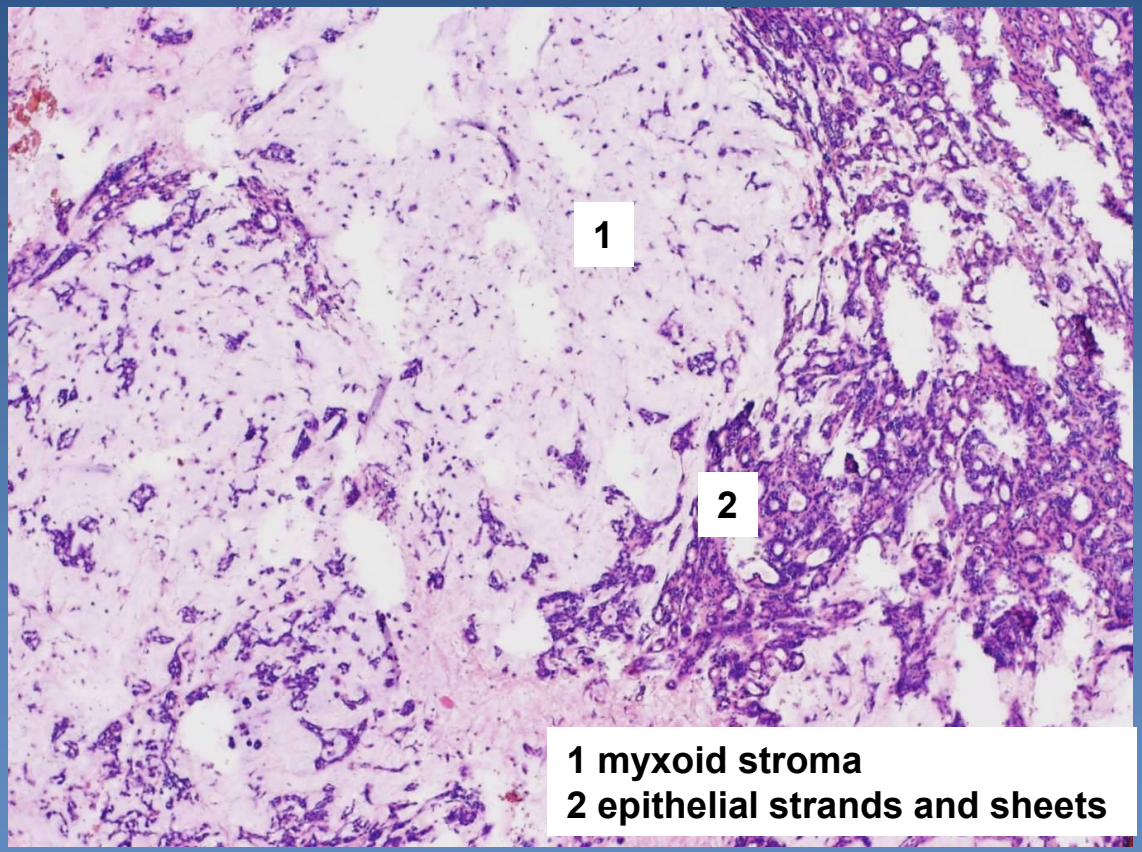


- micro:
  - ⇨ *histologic diversity*
  - ⇨ *ductal and myoepithelial tumor cells*
  - ⇨ *epithelial elements in strands or sheets*
  - ⇨ *myxoid to chondroid stroma produced by myoepithelia*
  - ⇨ *often penetrates the capsule → protuberances*

Pleomorphic adenoma

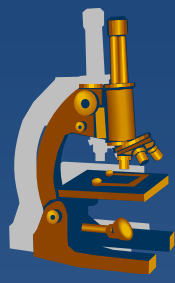


Pleomorphic adenoma



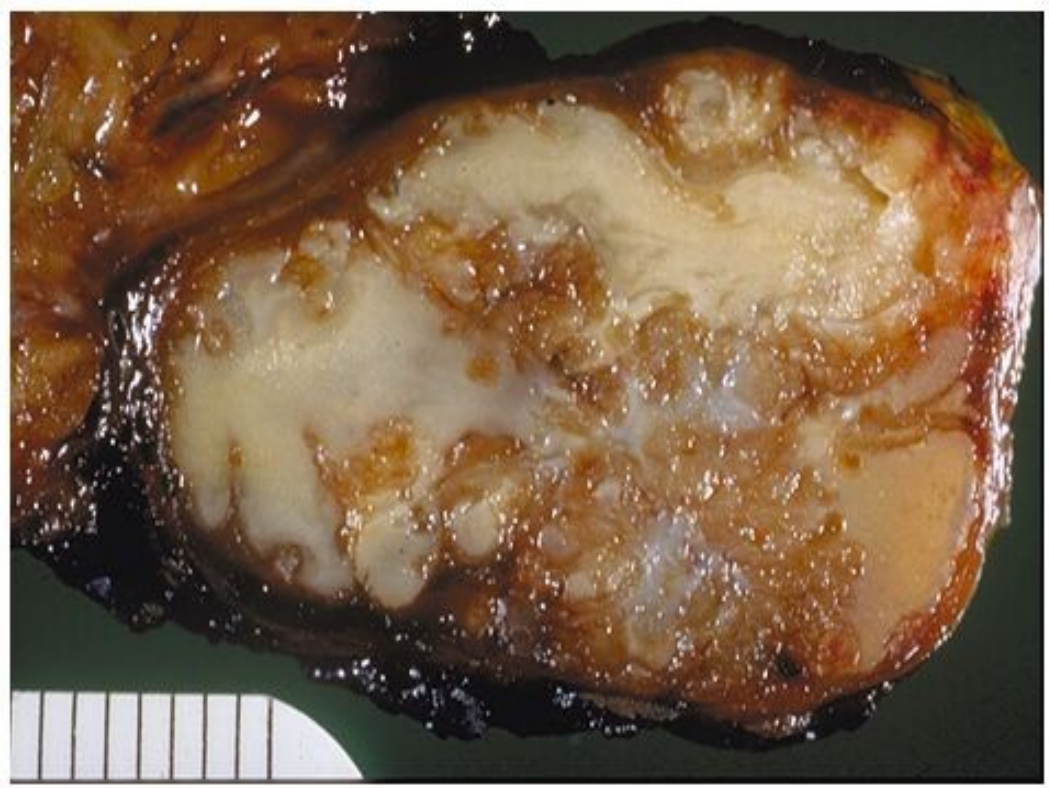
1 myxoid stroma
2 epithelial strands and sheets

Warthin's tumor (cystadenolymphoma)

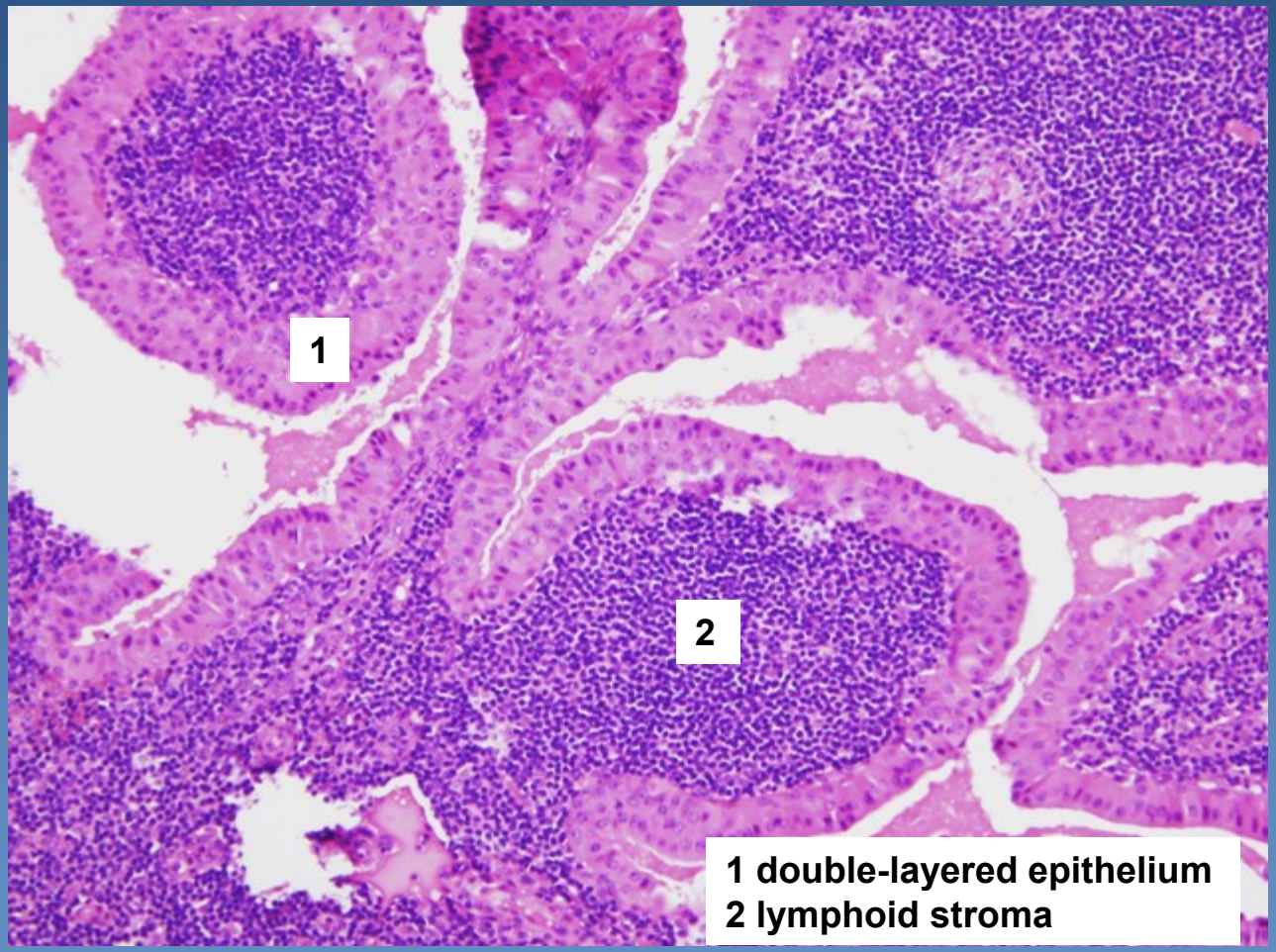


- 5-10% of total salivary gland tumors, benign
- M> F, 6th-7th decade
- lower pole of the parotid gland
- low recurrence rate, malignant transformation (ca, malignant lymphoma) highly uncommon
- risk factors:
  - ***smoking (8x), radiation, EBV***
- origin? (heterotopic salivary tissue in a LN; reactive epithelial proliferation + lymphocytic infiltration)
- histology:
  - ***cystic or cleftlike spaces with double-layered epithelial lining, dense lymphoid stroma (usually + germinal centers)***

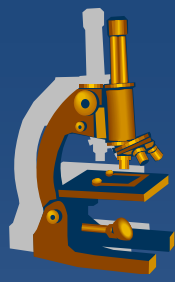
Warthin's tumor (cystadenolymphoma)



Warthin's tumor (cystadenolymphoma)

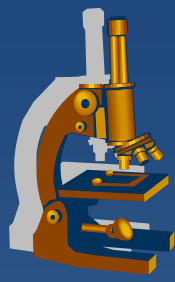


Tonsillitis chronica



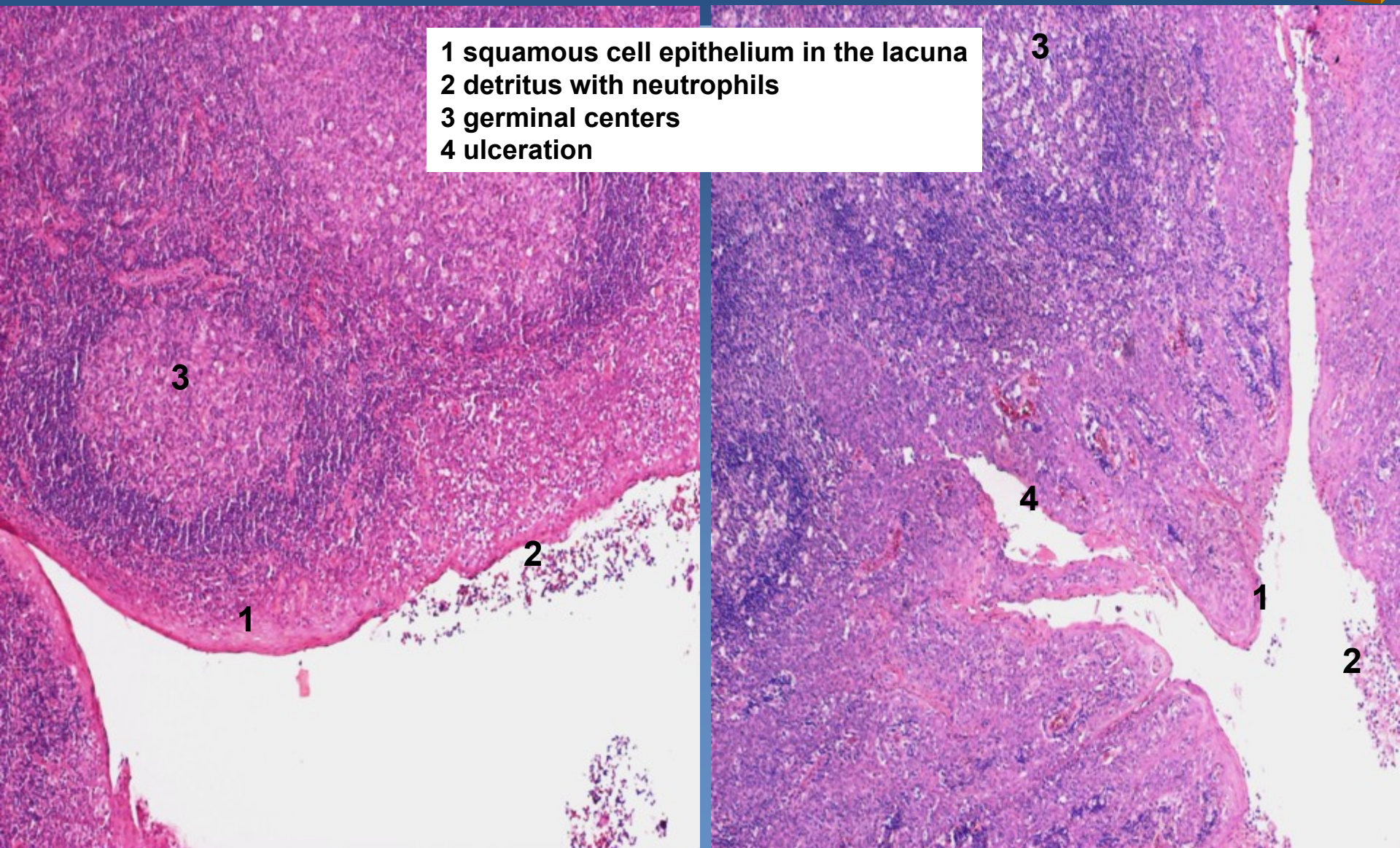
- recurrent chronic inflammation
- acute exacerbations - enlarged, red, swollen painful tonsils
- gross:
  - ⇨ ***mostly purulent exudate with necrotic epithelial cells and bacteria in crypts forming semi-firm foul-smelling debris***
  - ⇨ ***pseudomembranous tonsillitis (diff. dg. x EBV)***

Tonsillitis chronica

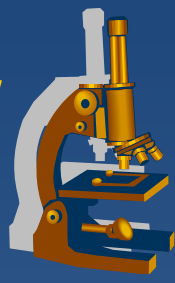


- complications: local, distant
  - ⇨ ***phlegmonous acute tonsillitis (necrosis and ulceration, penetration of bacteria into the interstitium → inflammation may progress into retrotonsillar stroma)***
  - ⇨ ***abscessi (tonsillar, peritonsillar, retropharyngeal) + spread***
  - ⇨ ***distant – rheumatic fever, glomerulonephritis***
- micro:
  - ⇨ ***reactive hyperplasia of lymphoid tissue, lacunae filled with neutrophils, debris and bacteria, local fibrotisation***

Tonsilla palatina
chronic purulent inflammation

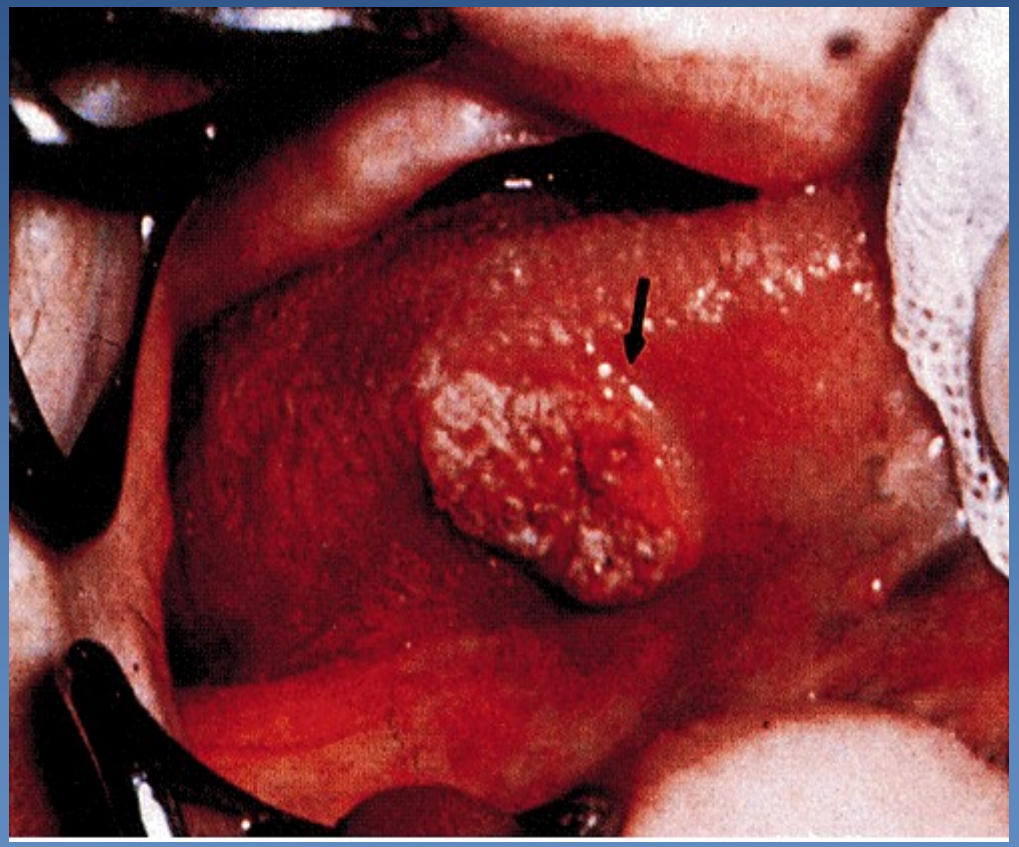


Precanceroses and tumors of the oral cavity



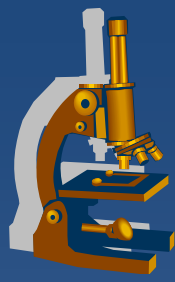
- mostly epithelial, less commonly mesenchymal lesions
- sequence
  - ⇨ ***normal tissue – hyperplasia – dysplasia – CIS – invasive carcinoma***
- risk factors
  - ⇨ ***smoking, alcohol, their combination; irradiation, HPV, betel, other chronic irritation***

Squamous cell carcinoma



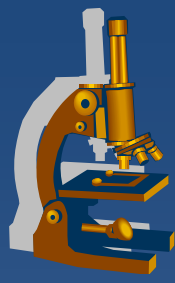
elevated/ulcerated firm lesion

Esophageal diverticula



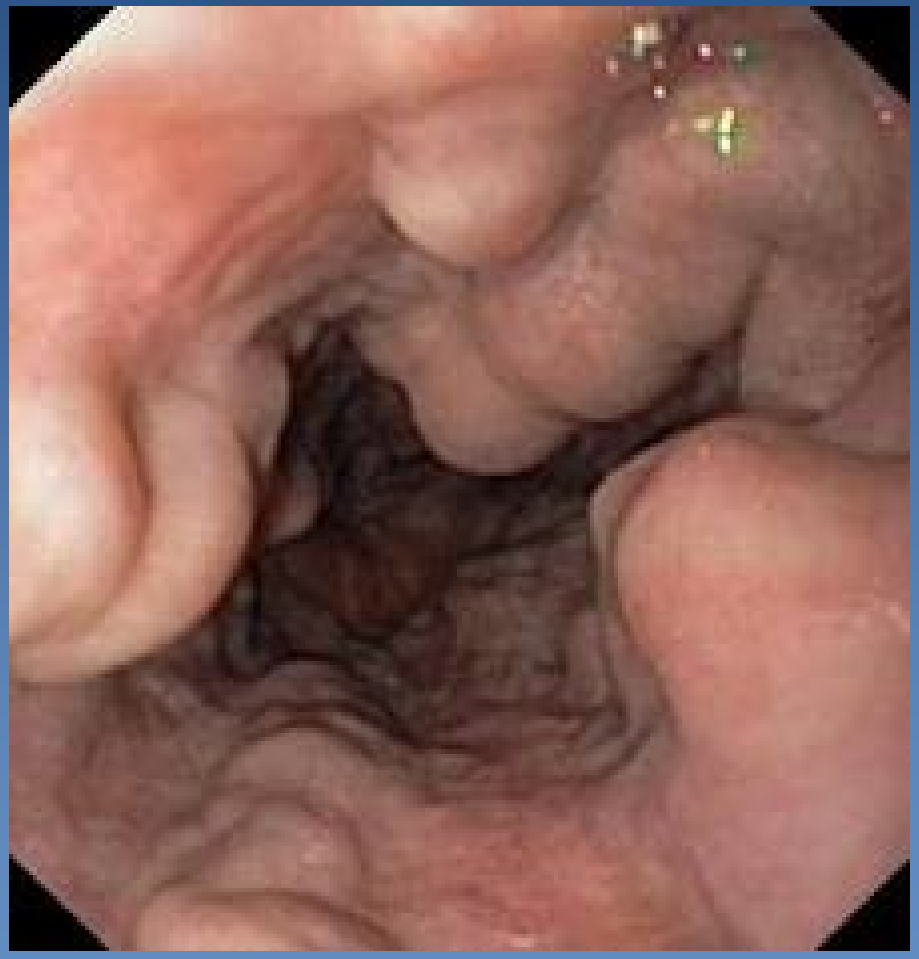
- **diverticulum** – an acquired outpouching of the esophageal wall involving all the layers of the wall (true diverticulum)
- Zenker‘s diverticulum (pharyngoesophageal) - ***most common type, located on the posterior wall in the pharyngoesophageal junction, weakening of m. constrictor pharyngis, developed by pulsion (forcible distension of the esophagus)*** → pulsion diverticulum
- Midthoracic diverticulum - ***in the mid-chest; developed by traction (external forces pulling on the wall - inflammation with scarring e.g.)*** → traction diverticulum
- Epiphrenic diverticula - ***above the diaphragm***
- Signs: ***dysphagia, regurgitation, foetor ex ore***
- Complications: ***putrid inflammation, ulceration, perfortion into mediastinum***

Esophageal varices



- congested and dilated submucosal veins in the distal third of the esophagus
- in portal hypertension
- porto-caval anastomoses
- complications - ***rupture with massive hemorrhage into the lumen, haematemesis, haemorrhagic shock***

Esophageal varices
- endoscopy



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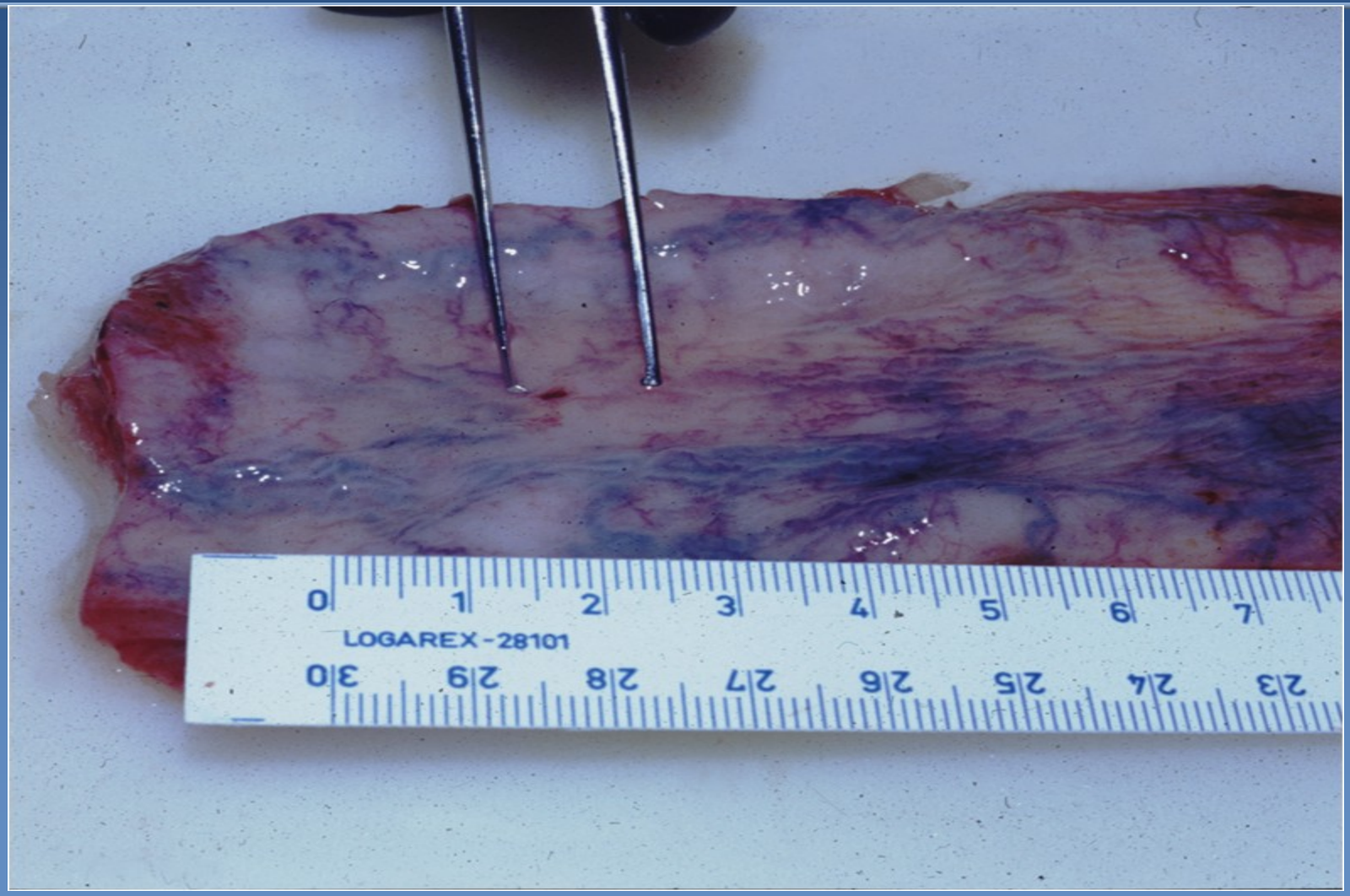
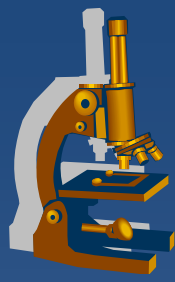
Esophageal varices
gross

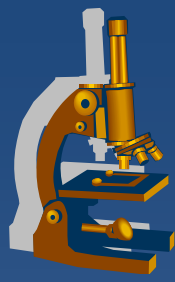


Mycotic oesophagitis



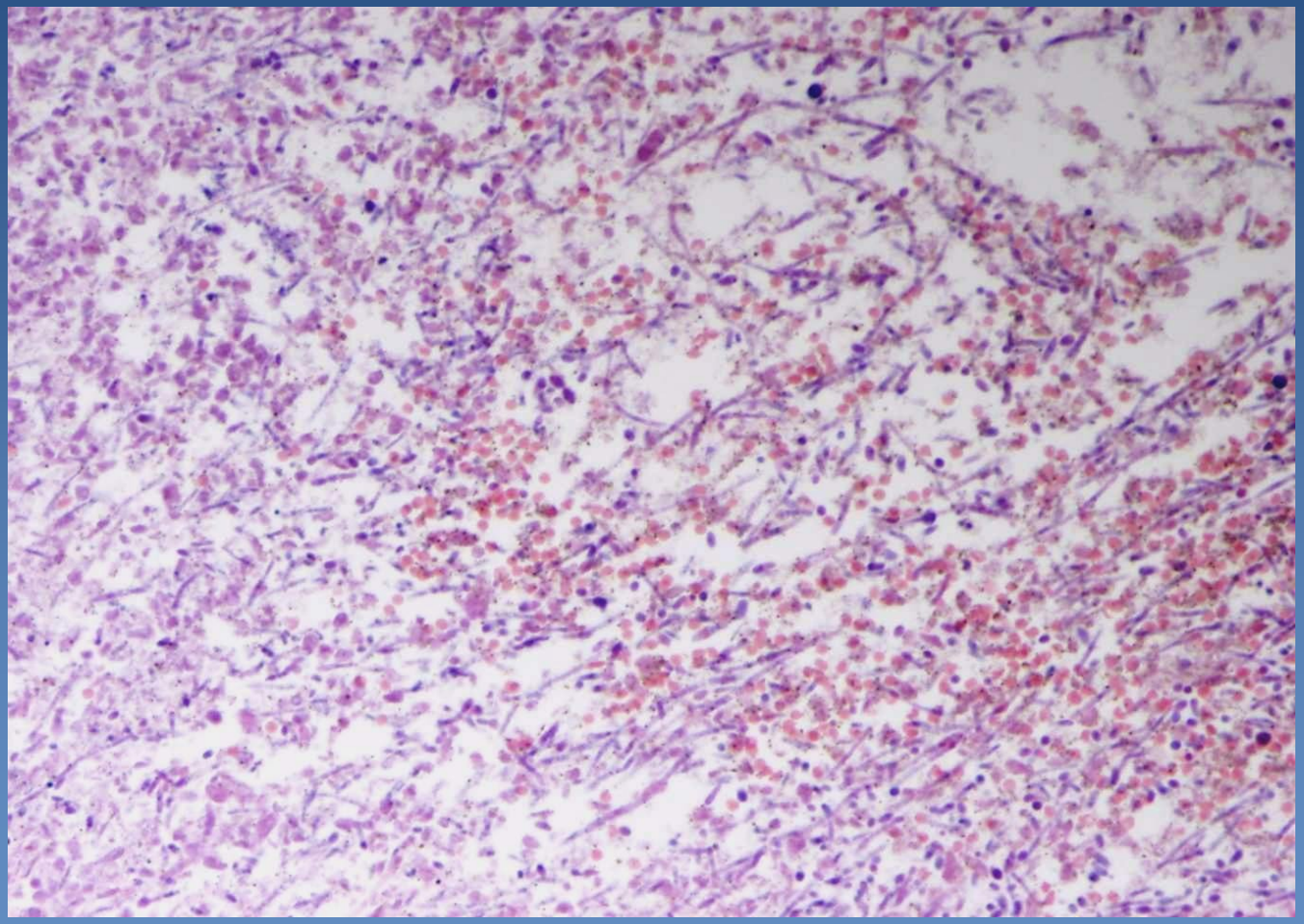
- candida, aspergillus, mucor, cryptococcus
- superficial form ***low-level immunodeficiency, patients on broad-spectrum ATB or corticosteroids therapy, diabetics, pregnancy…***
- generalised form + secondary deep mycotic infections ***– high-grade immunodeficiency - AIDS, neoplasia (haemathologic), immunosuppression, debilitated patients***

Mycotic oesophagitis

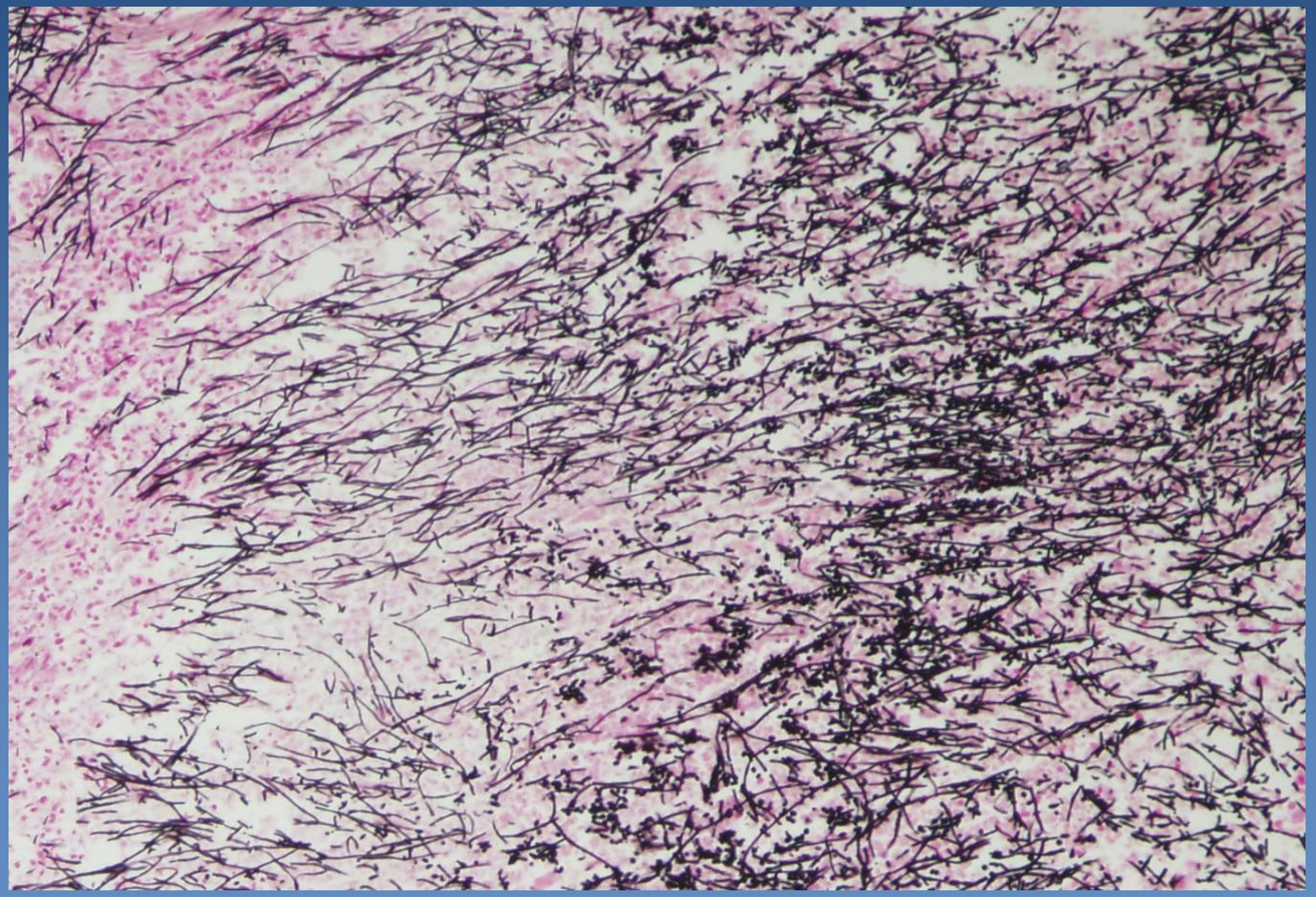


- gross:
  - ⇨ ***white to gray pseudomembranes with hemorrhagic bases after removal***
- micro:
  - ⇨ ***necrotic mucosa with mixed inflammatory infiltrate, numerous fungal organisms (pseudo/hyphae, yeasts)***
- special impregnation/staining for detection of the fungi (Groccott, PAS, Giemsa)

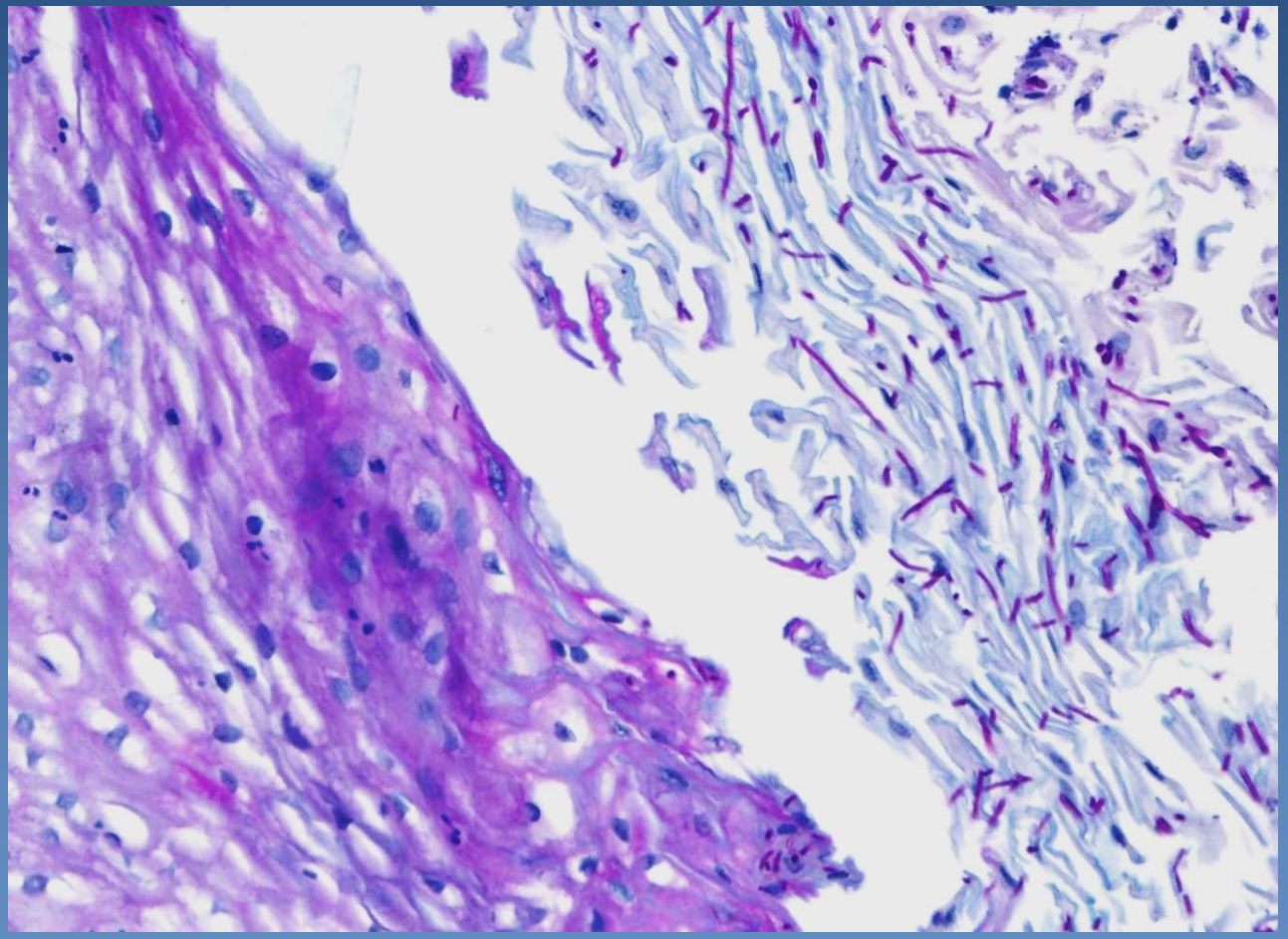
Mycotic oesophagitis



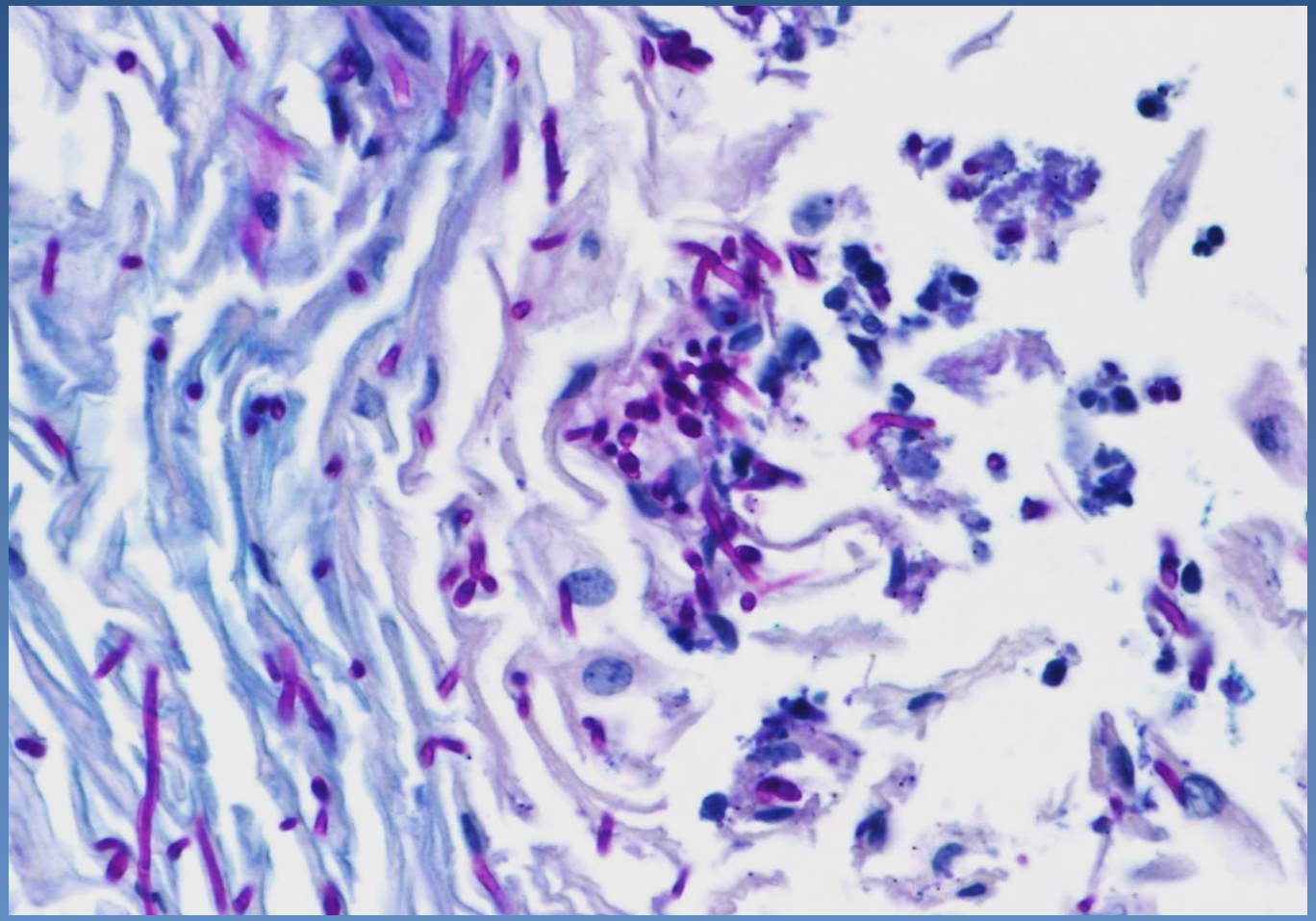
Mycotic oesophagitis
(Groccott silver impregnation)



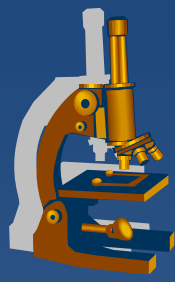
Mycotic oesophagitis - detail
(PAS staining)



Mycotic oesophagitis - detail
(PAS staining)

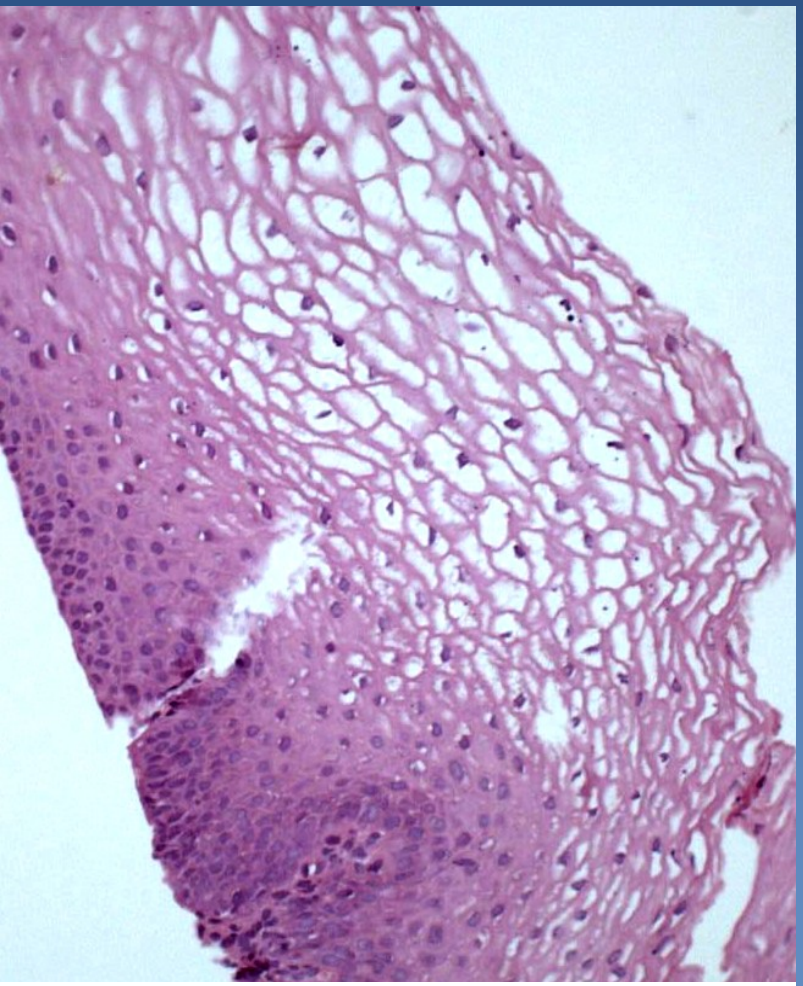


Reflux oesophagitis

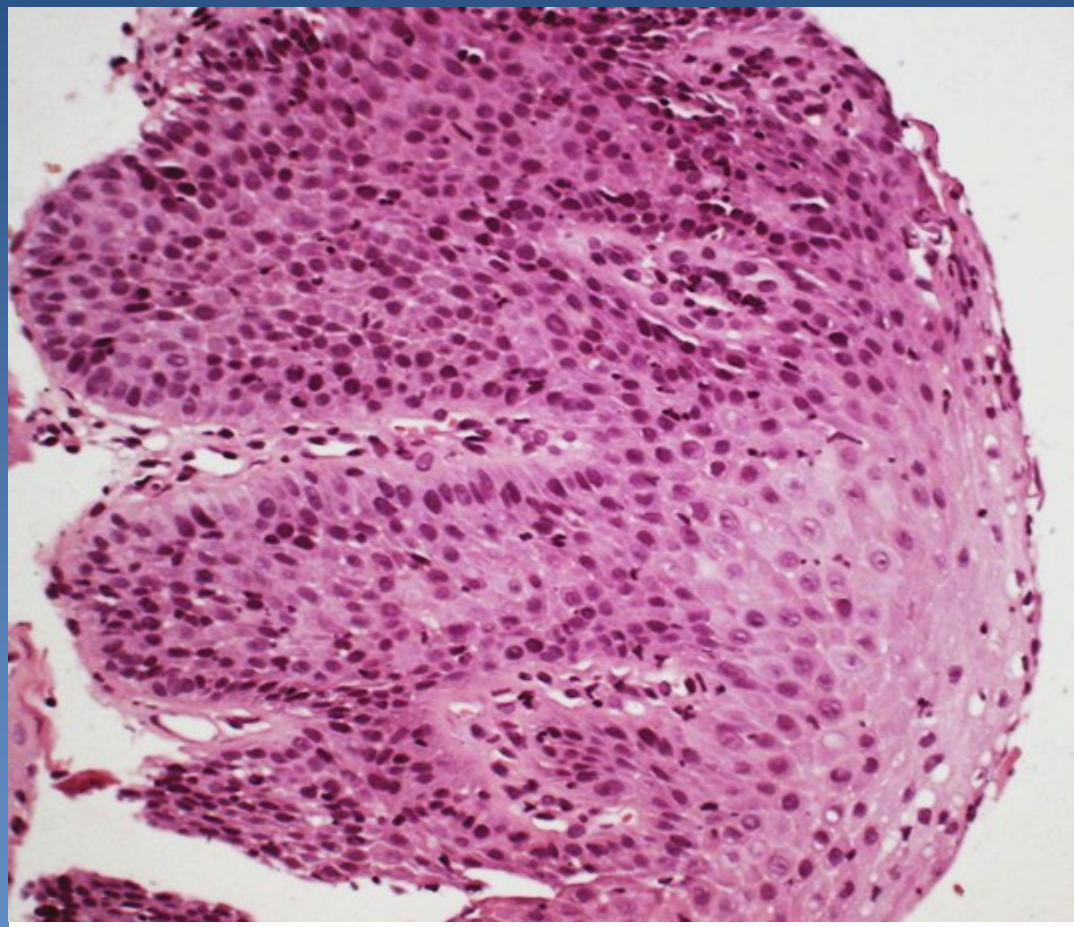


- chemically caused inflammation in gastro-oesophageal reflux disease (sq. epithelium sensitive to acids)
- signs x pathology – low correlation
  - ***heartburn, dysphagia***
- gross:
  - ***mucosal hyperemia, epithelial erosions, ulcerations, scarring, stenosis***
- micro:
  - ***3 reactive alterations of the squamous cell epithelium: basal zone hyperplasia, elongation of lamina propria papillae, inflammatory infiltrate with eosinophils.***
- complication: Barrett‘s oesopagus (predisposition to maligancy)!

Reflux oesophagitis

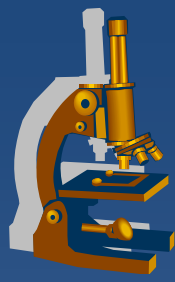


Regular oesophageal epithelium



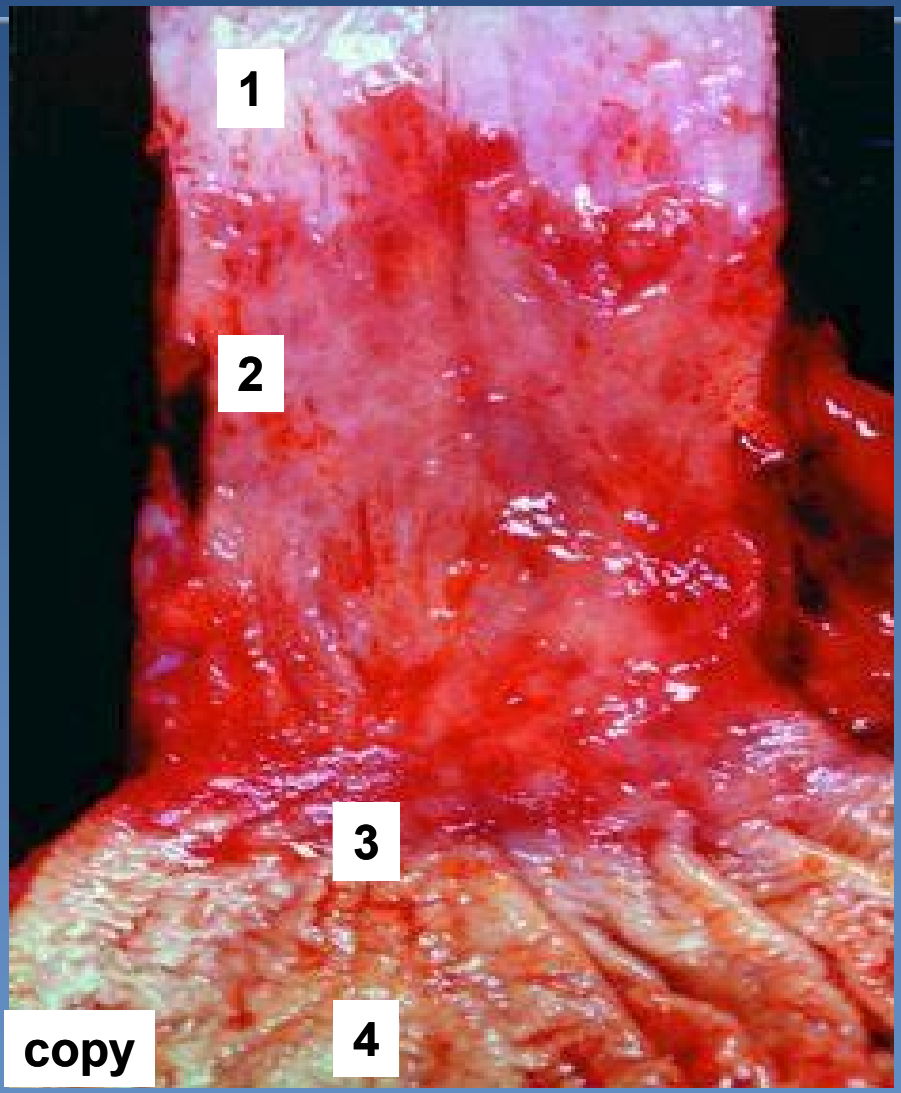
Reflux oesophagitis: basal zone hyperplasia (>20%), elongation of lamina propria papillae (into the superficial 1/3)

Barrett's oesophagus



- complication of reflux oesophagitis
- risk for the development of adenocarcinoma!
- replacement of the normal squamous cell epithelium by columnar epithelium with goblet cells (= intestinal metaplasia) → risk of dysplasia
- → oesophageal adenocarcinoma (so-called Barrett's carcinoma)

Barrett's oesophagus



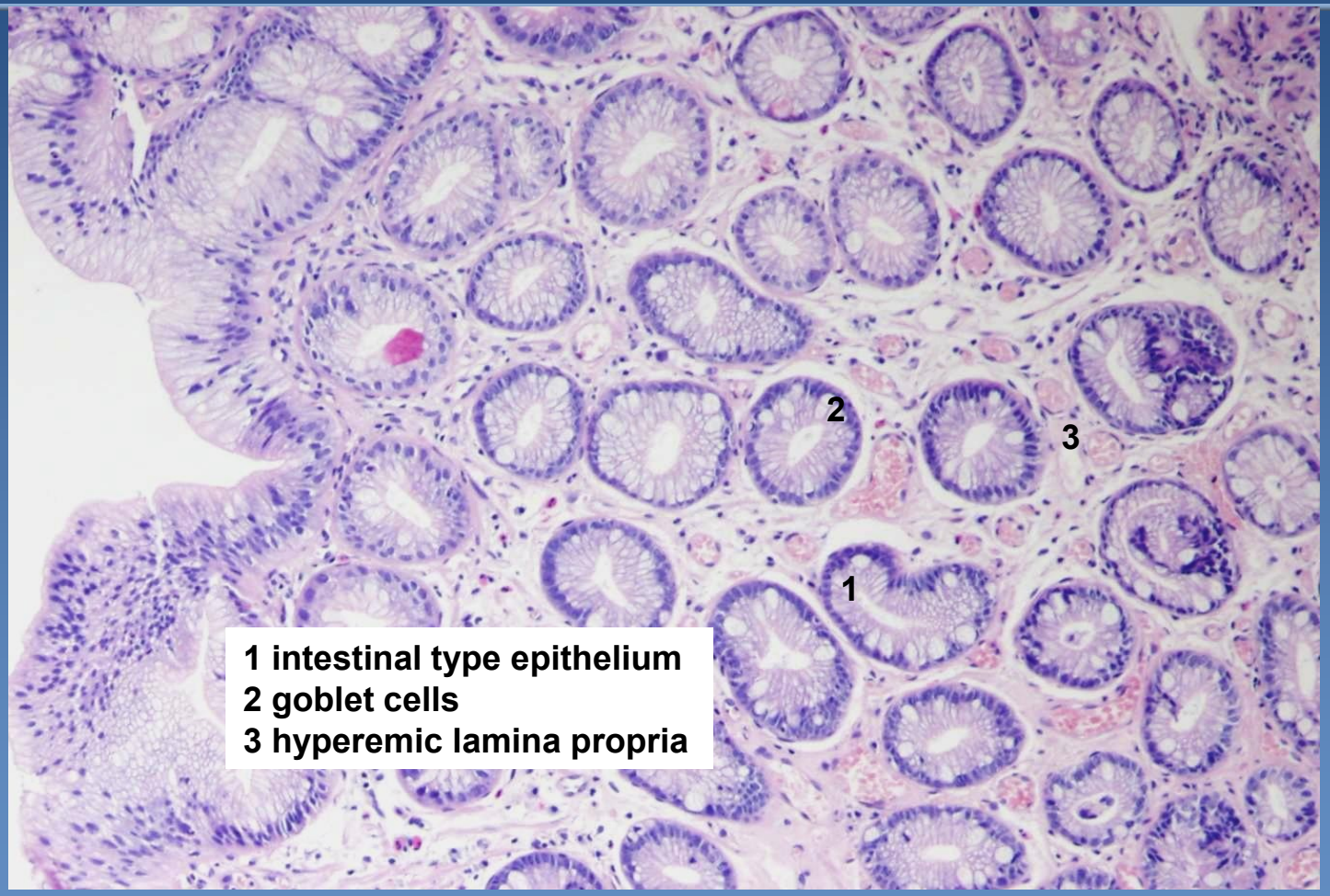
1 regular oesophageal mucosa

2 metaplasia

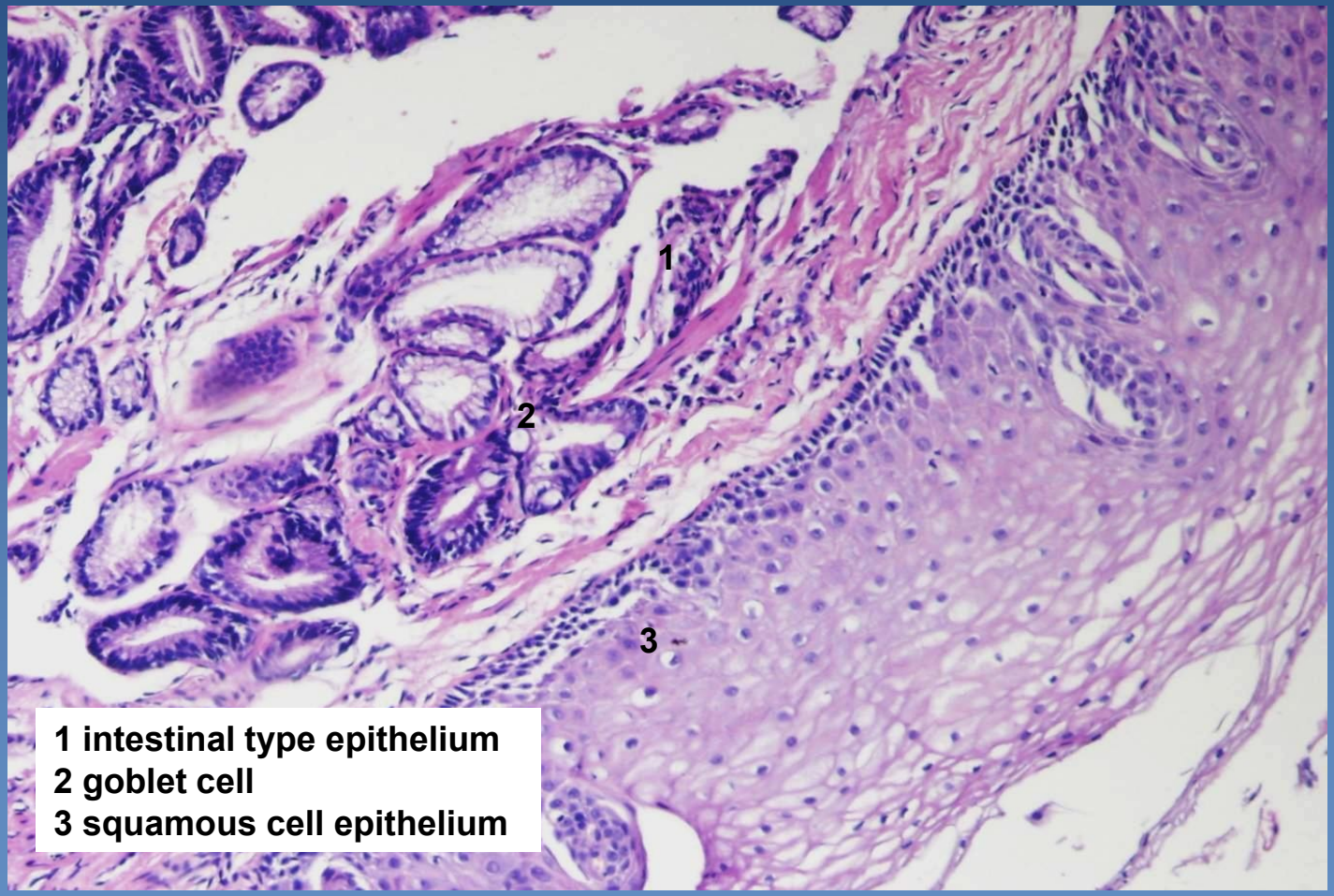
3 gastro-oesophageal junction

4 cardia

Barrett's oesophagus

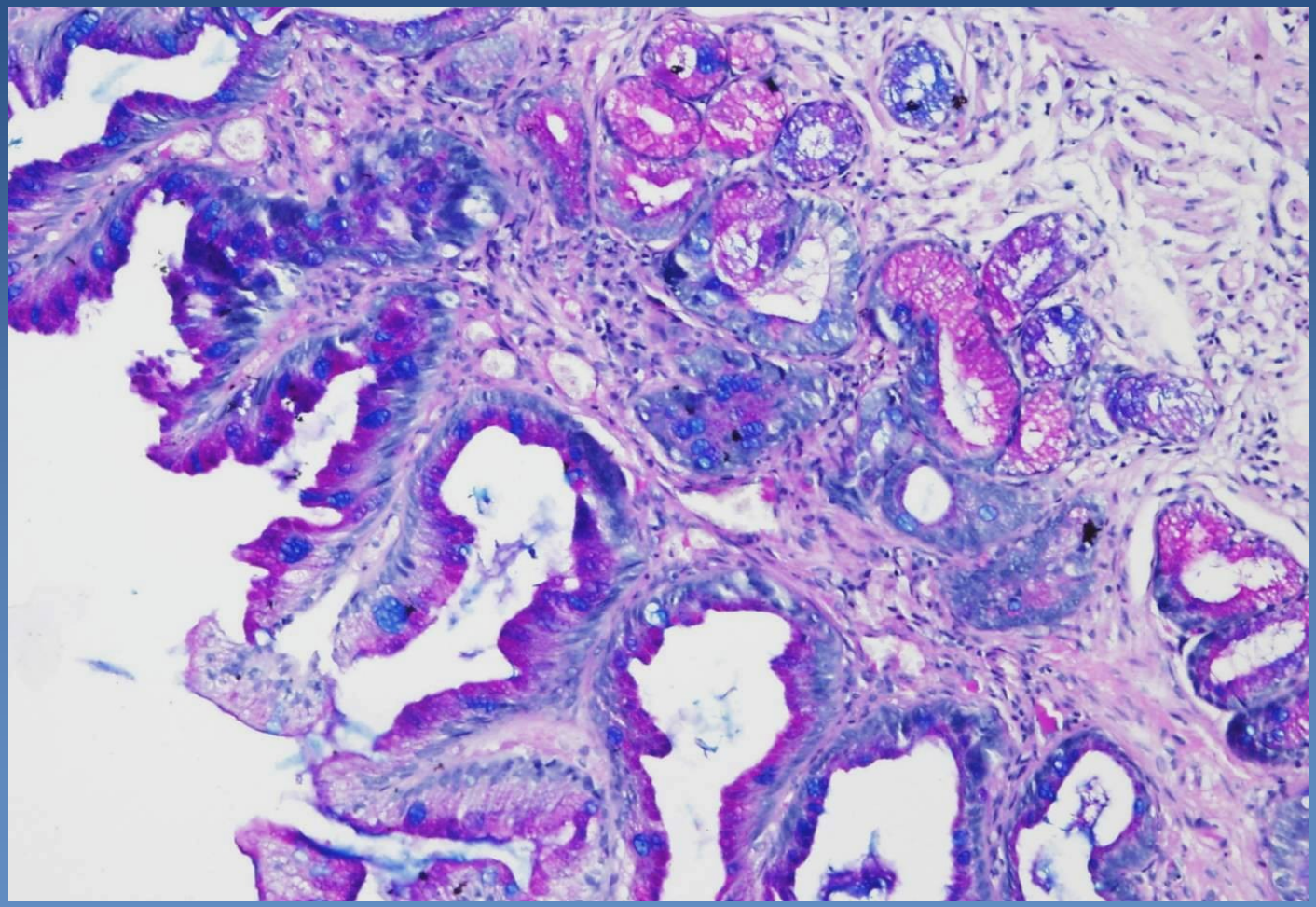


Barrett's oesophagus

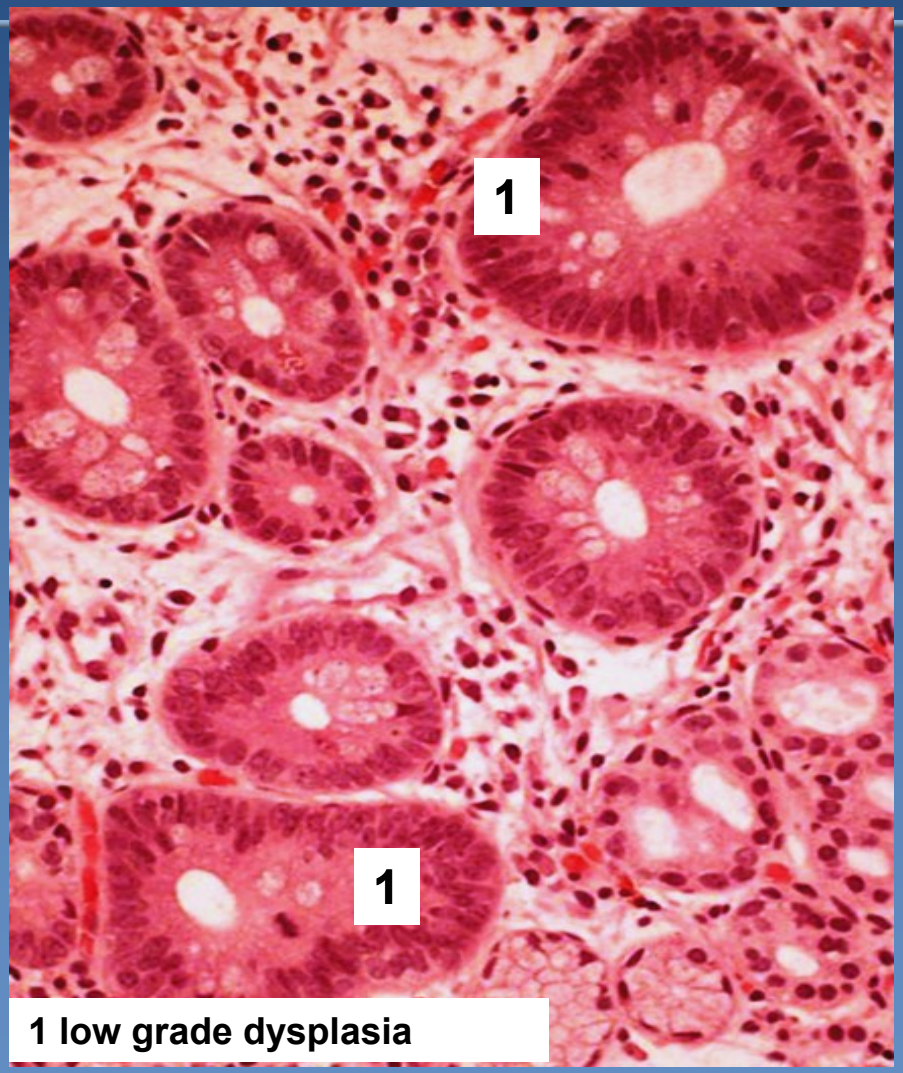


Barrett's oesophagus

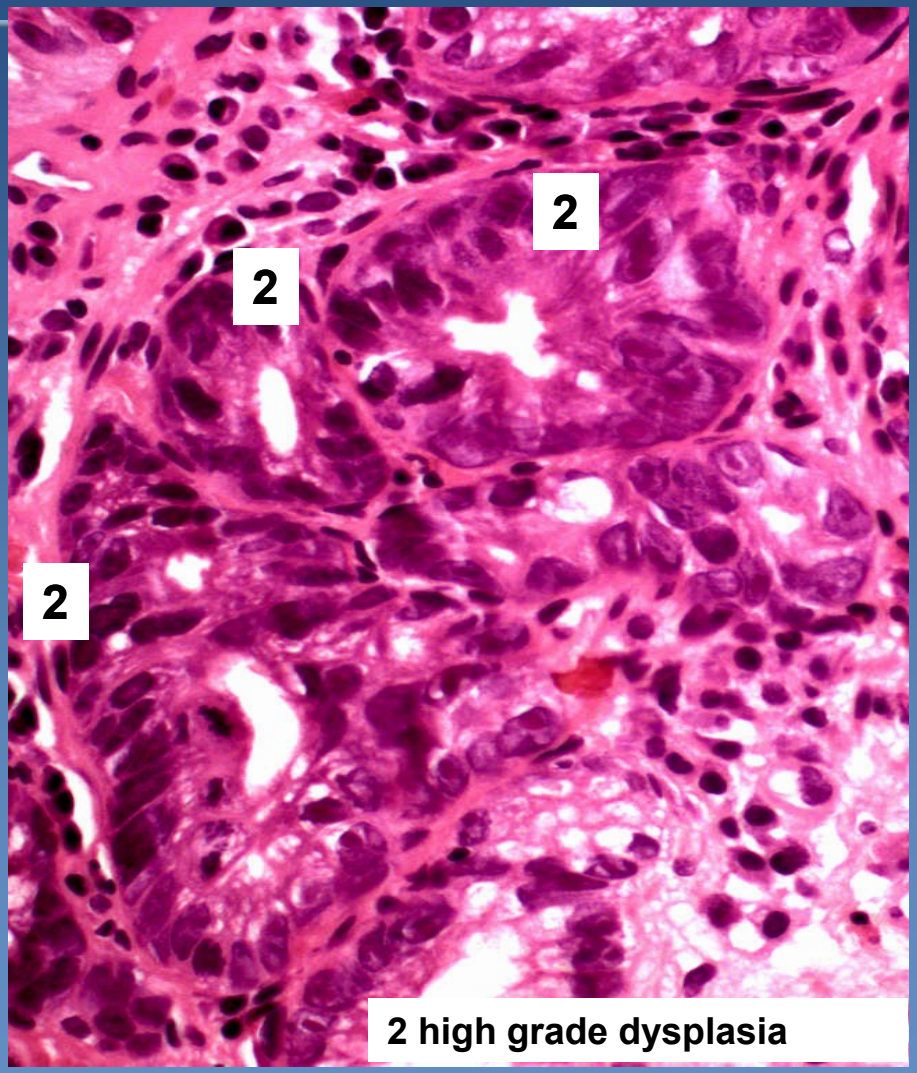
PAS ALC staining – blue goblet cells



Barrett's oesophagus
- dysplastic epithelium

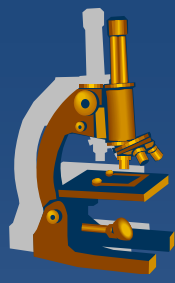


1 low grade dysplasia



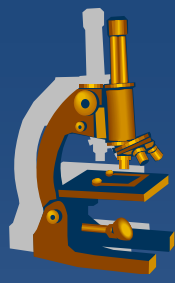
2 high grade dysplasia

Squamous cell carcinoma of the oesophagus



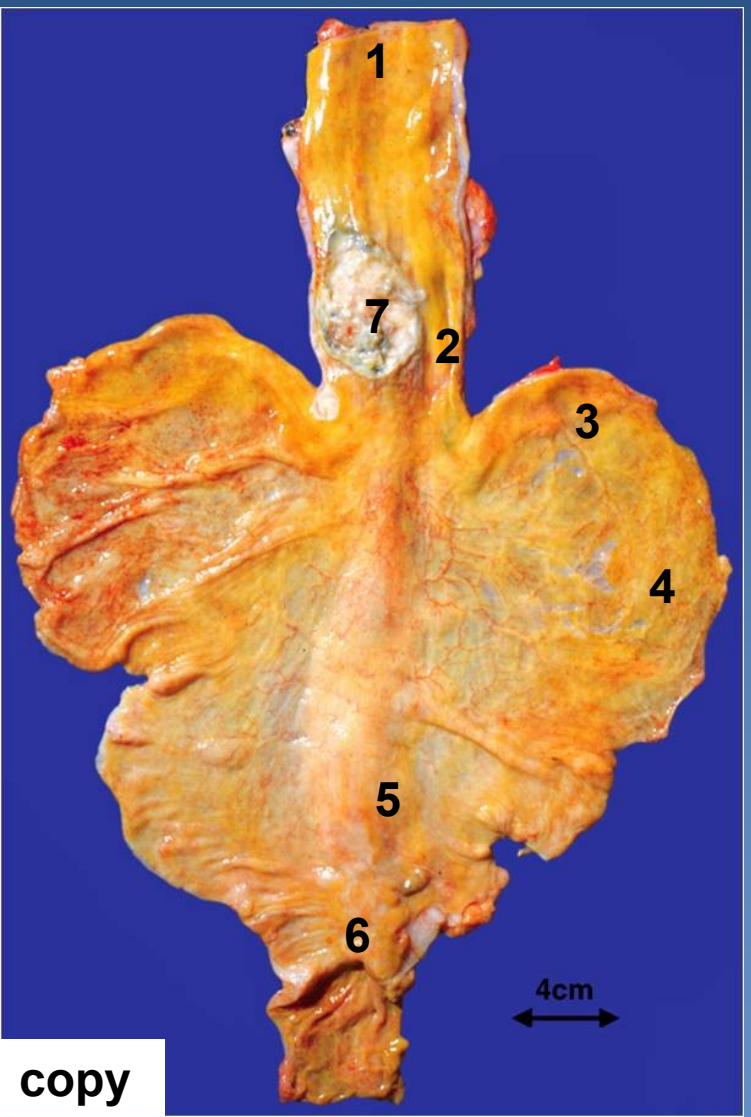
- usually in the mid-third of the esophagus
- M>F, >45 yrs of age
- Risk factors:
  - ⇨***carcinogenic substances in food (aflatoxin, nitrosamines), tobacco, alcohol, HPV, very hot beverages, chronic inflammation***
- Symptoms:
  - ⇨***dysfagia, weight loss, cachexia***

Squamous cell carcinoma of the oesophagus

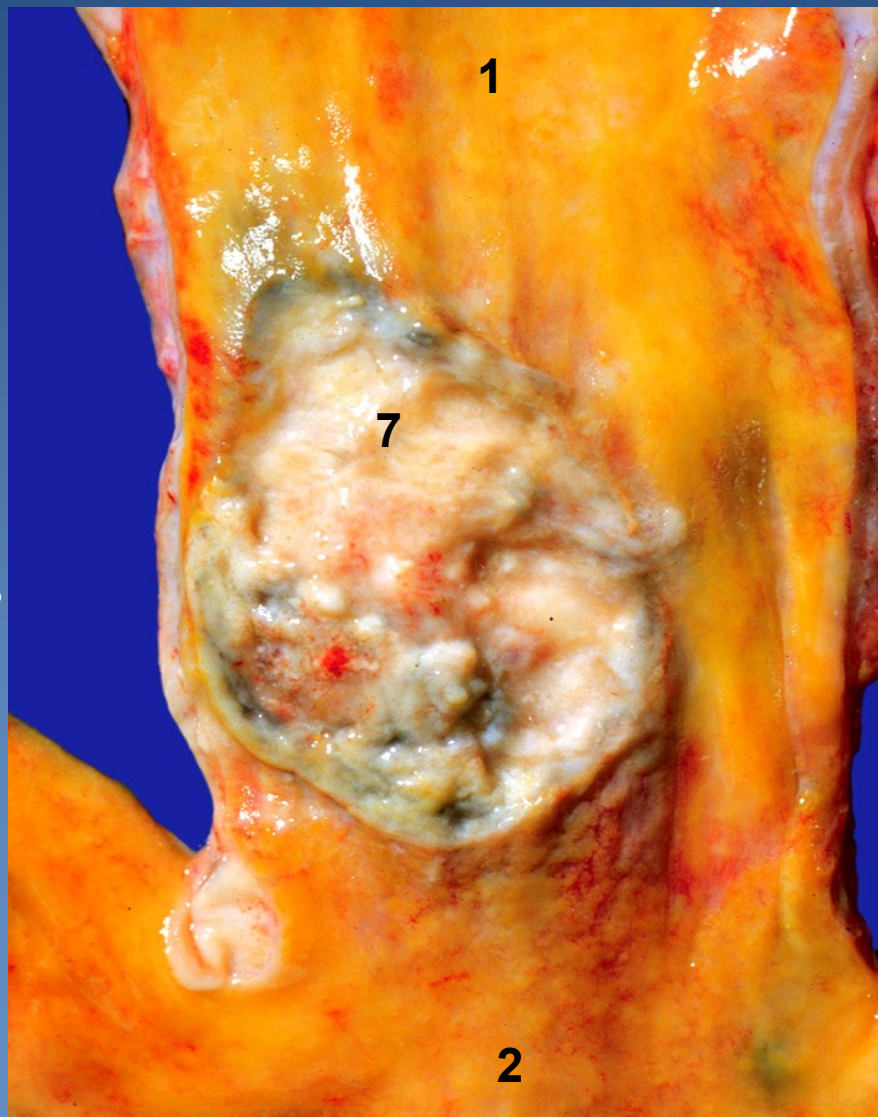


- gross:
  - ⇨ ***polypoid exophytic mass, ulcerative or diffuse infiltrative neoplasm***
- bad prognosis:
  - ⇨ ***tendency to spread through submucosal lymph vessels → distant satellite tumor foci***

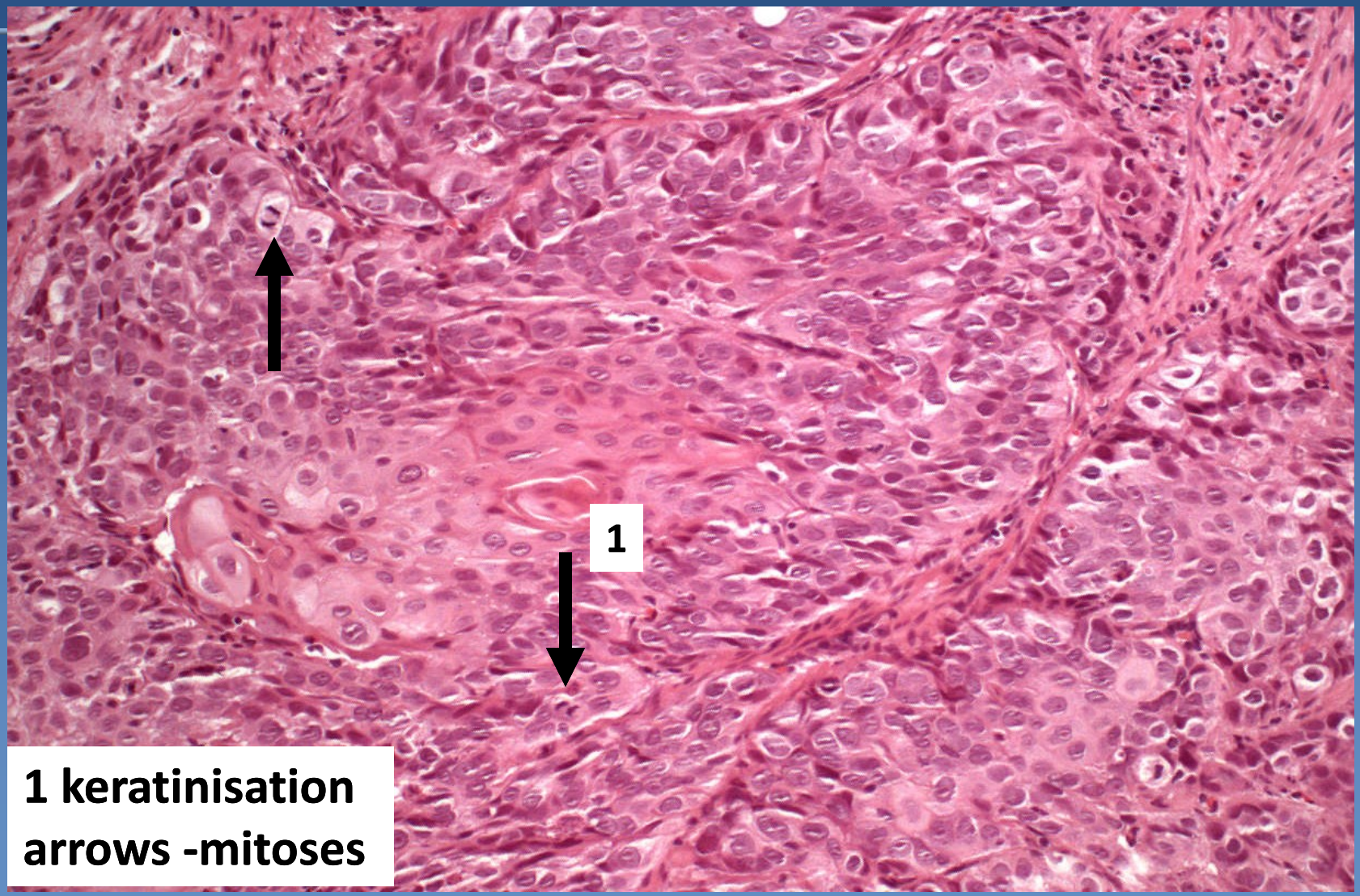
Squamous cell carcinoma of the oesophagus



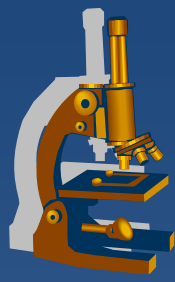
1 esophagus
2 cardia
3 fundus
4 body
5 antrum
6 pylorus
7 tumor



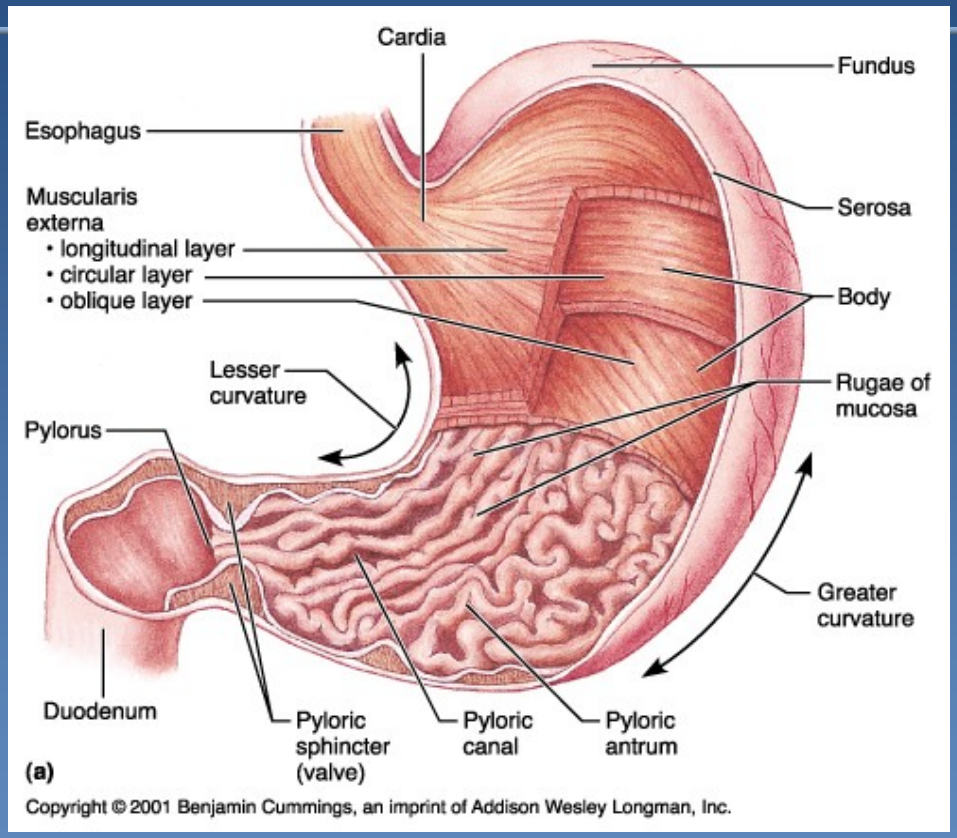
Squamous cell carcinoma of the oesophagus

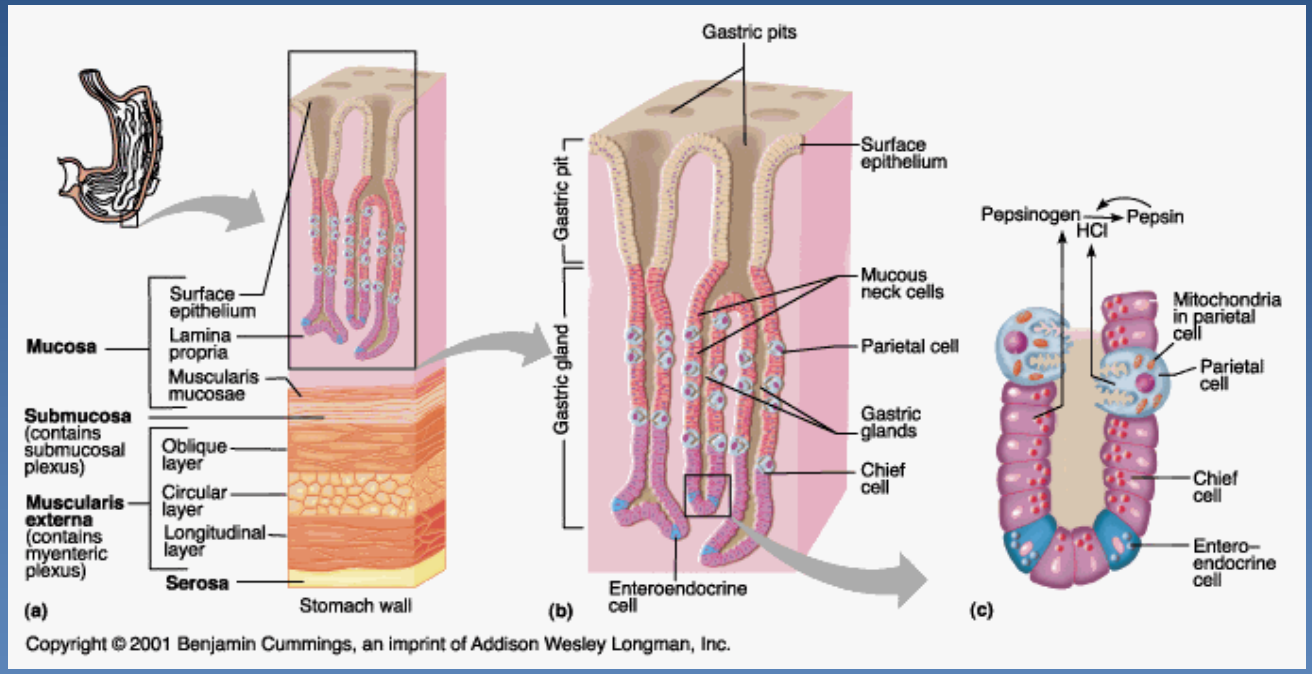


1 keratinisation
arrows -mitoses

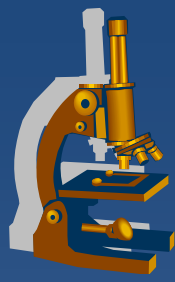


STOMACH





Gastritis

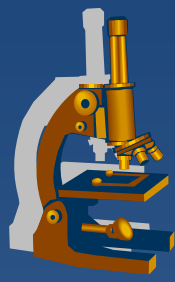


- two general types:
  - ⇨ ***acute*** *- acute mucosal inflammatory process of a transient nature, causes: salt, spices, alcohol, NSAIDs, stress, infection*
    - ***gross:***

      hyperemic, oedematous mucosa with erosions, haemorrhage
    - ***micro:***

      hyperemia, oedema, neutrophilic (foveolar) inflammatory infiltrate, erosions

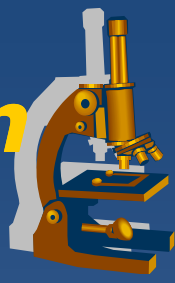
Gastritis



⇨***chronic*** ***- chronic inflammatory changes leading to mucosal atrophy and epithelial metaplasia***

- ***usually associated with Helicobacter pylori***
- ***micro evaluation:***
  - *inflammatory infiltrate in lamina propria mucosae - lymfoplasmocytic (grade of chronicity) + neutrophils (grade of activity)*
  - *presence of HP (+/-) and quantitative analysis*
  - *presence of atrophy, intestinal metaplasia (complete, incomplete) and possible dysplasia*

Clinical-pathological classification of chronic gastritis



1) Chronic non-atrophic gastritis (superficial) („B“)

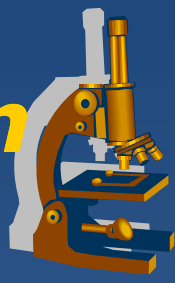
2) Chronic atrophic gastritis

I. Autoimmune gastritis („A“)

II. Chronic multifocal atrophic gastritis

3) Special forms (chemical - reactive, lymphocytic, eosinophilic, granulomatous)

Clinical-pathological classification of chronic gastritis

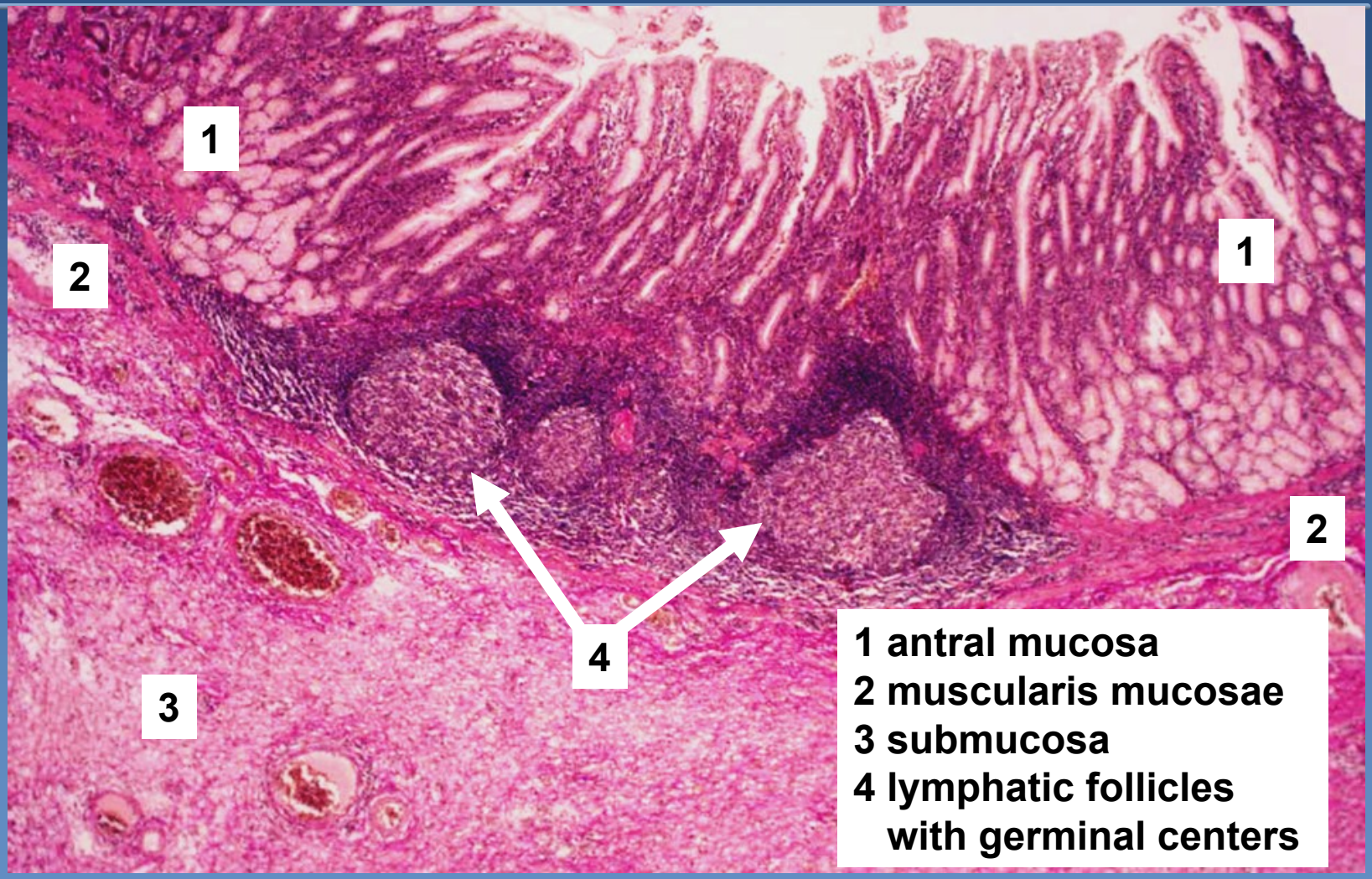


- **Chronic non-atrophic gastritis (superficial)**

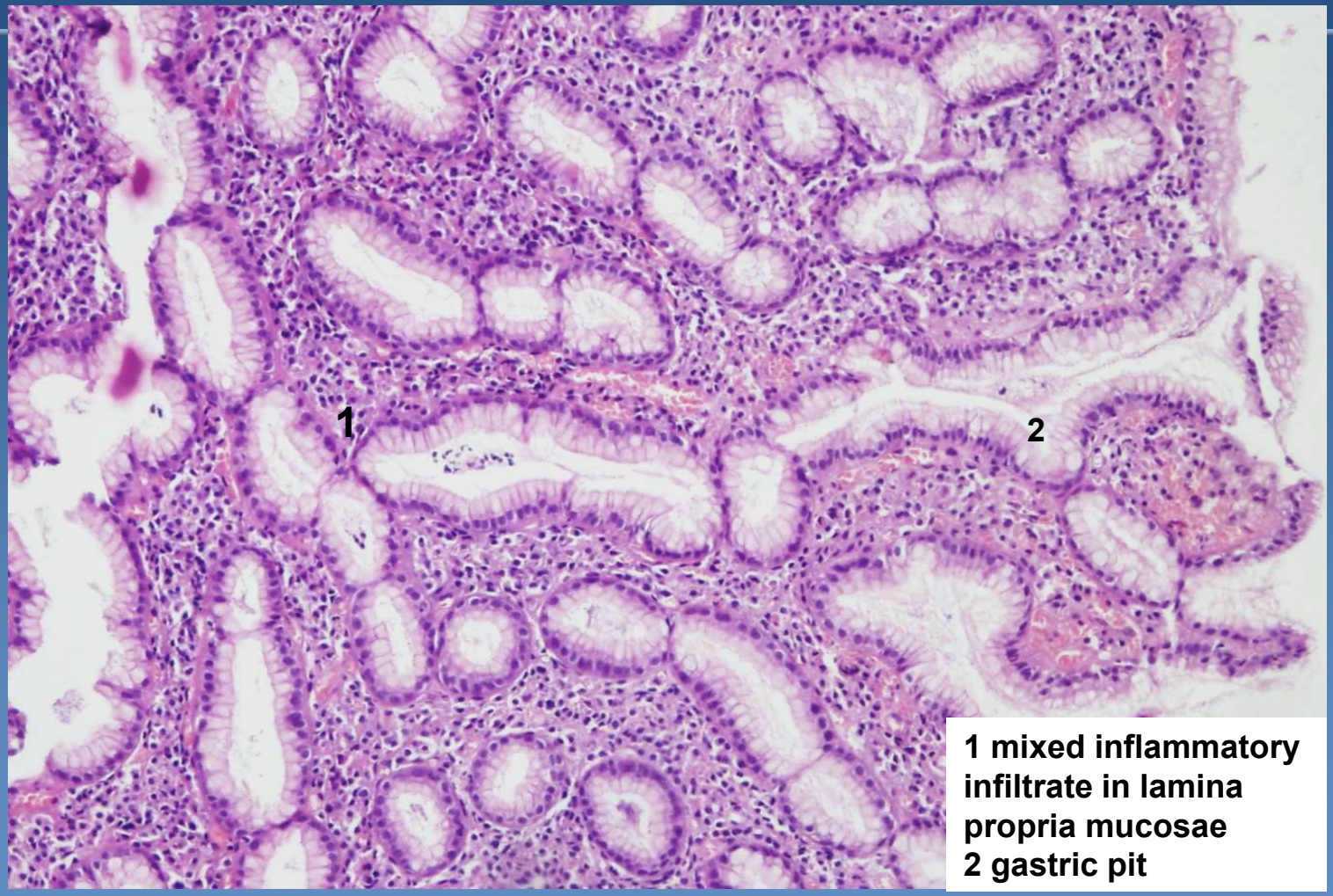
  ⇨ ***Helicobacter pylori***

  - ***gross:*** antrum and body mucosa
  - ***micro:*** superficial or deep inflammation, active chronic gastritis, lymphocyte and plasma cell response forming lymphatic follicles in the glandular area, final mucosal atrophy
  - ***higher risk of developing NHL***

Chronic non-atrophic gastritis - follicular

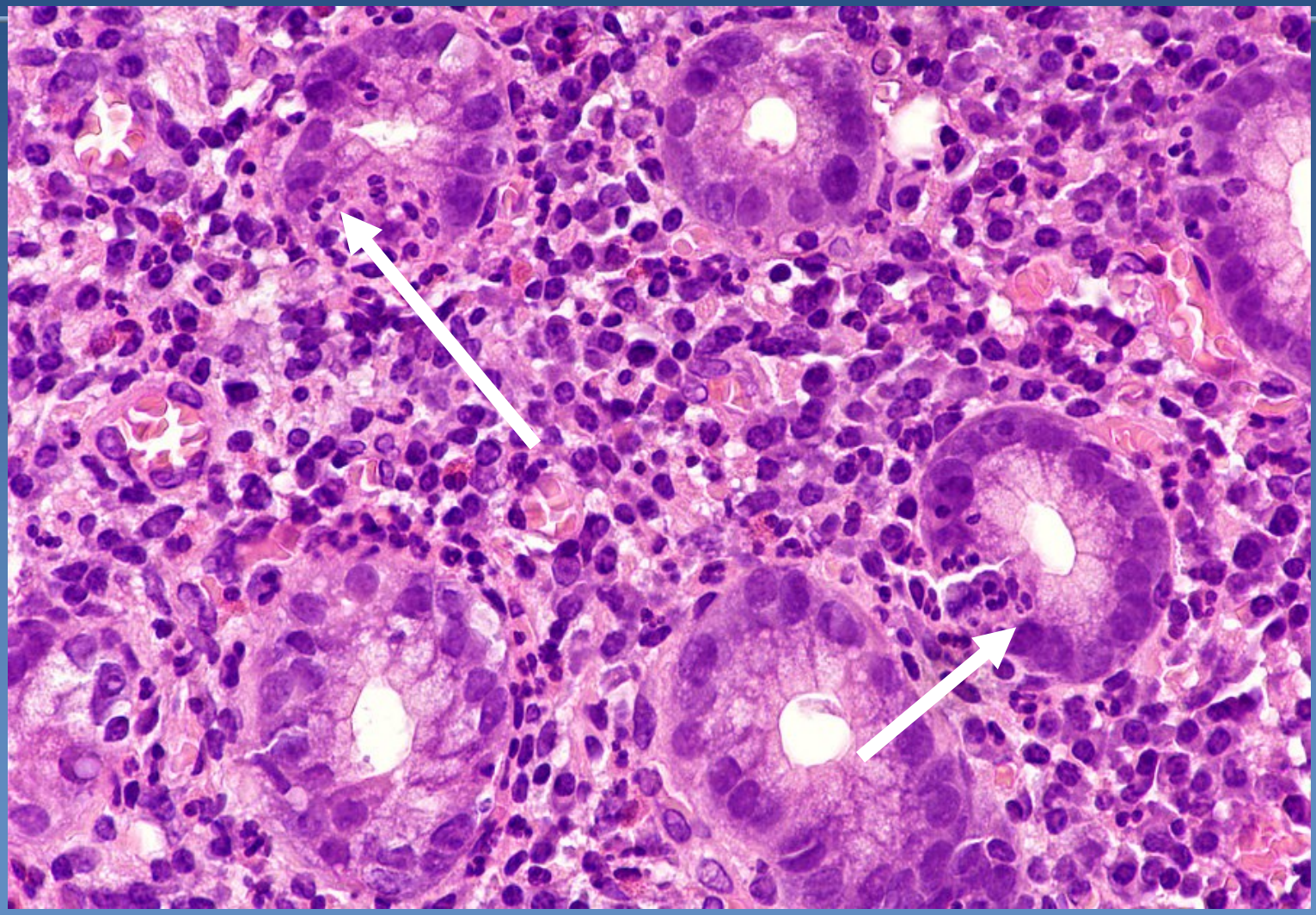


Chronic non-atrophic gastrits
- detail of the mucosa



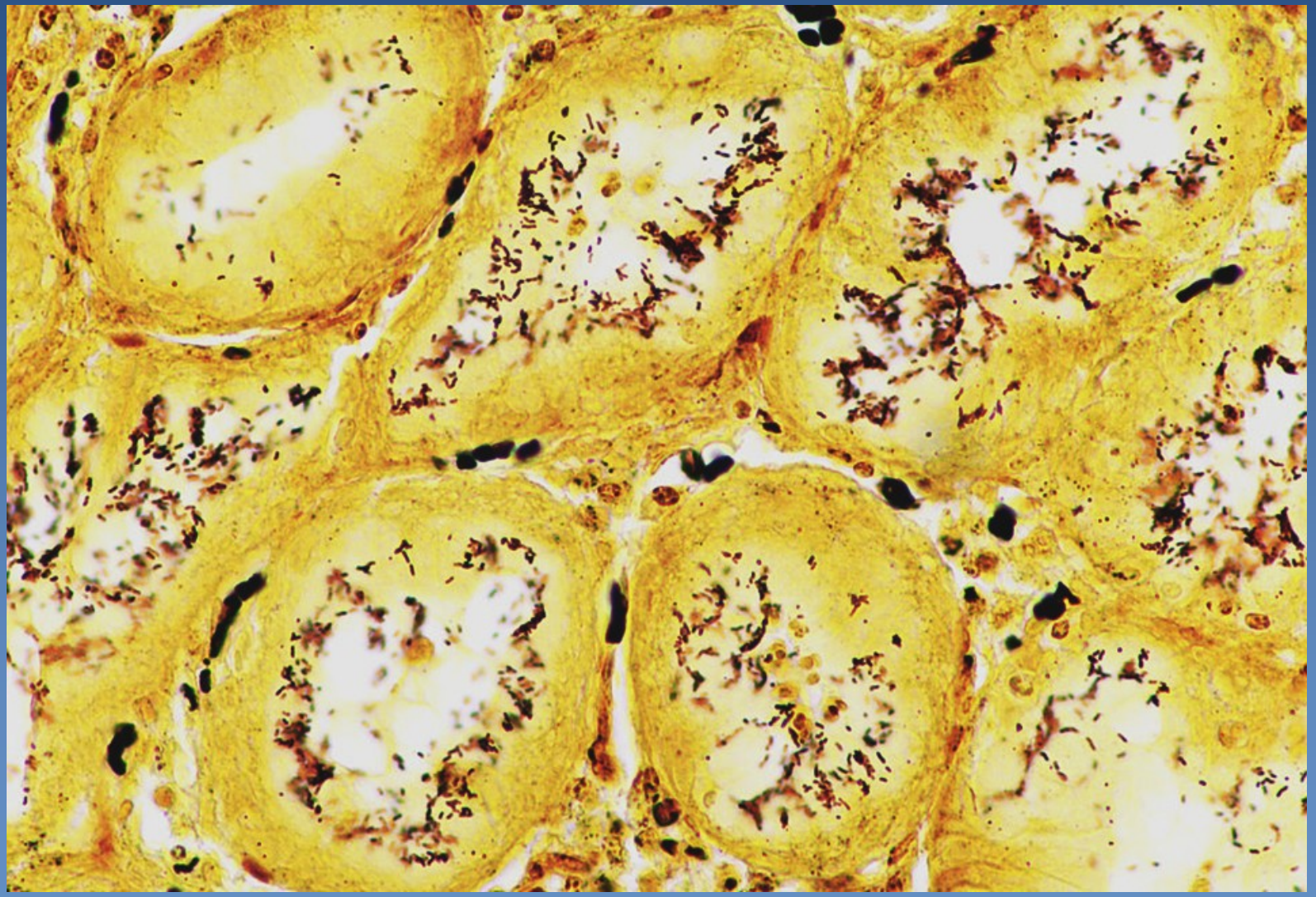
1 mixed inflammatory infiltrate in lamina propria mucosae
2 gastric pit

Chronic active gastritis
- grade of activity 2

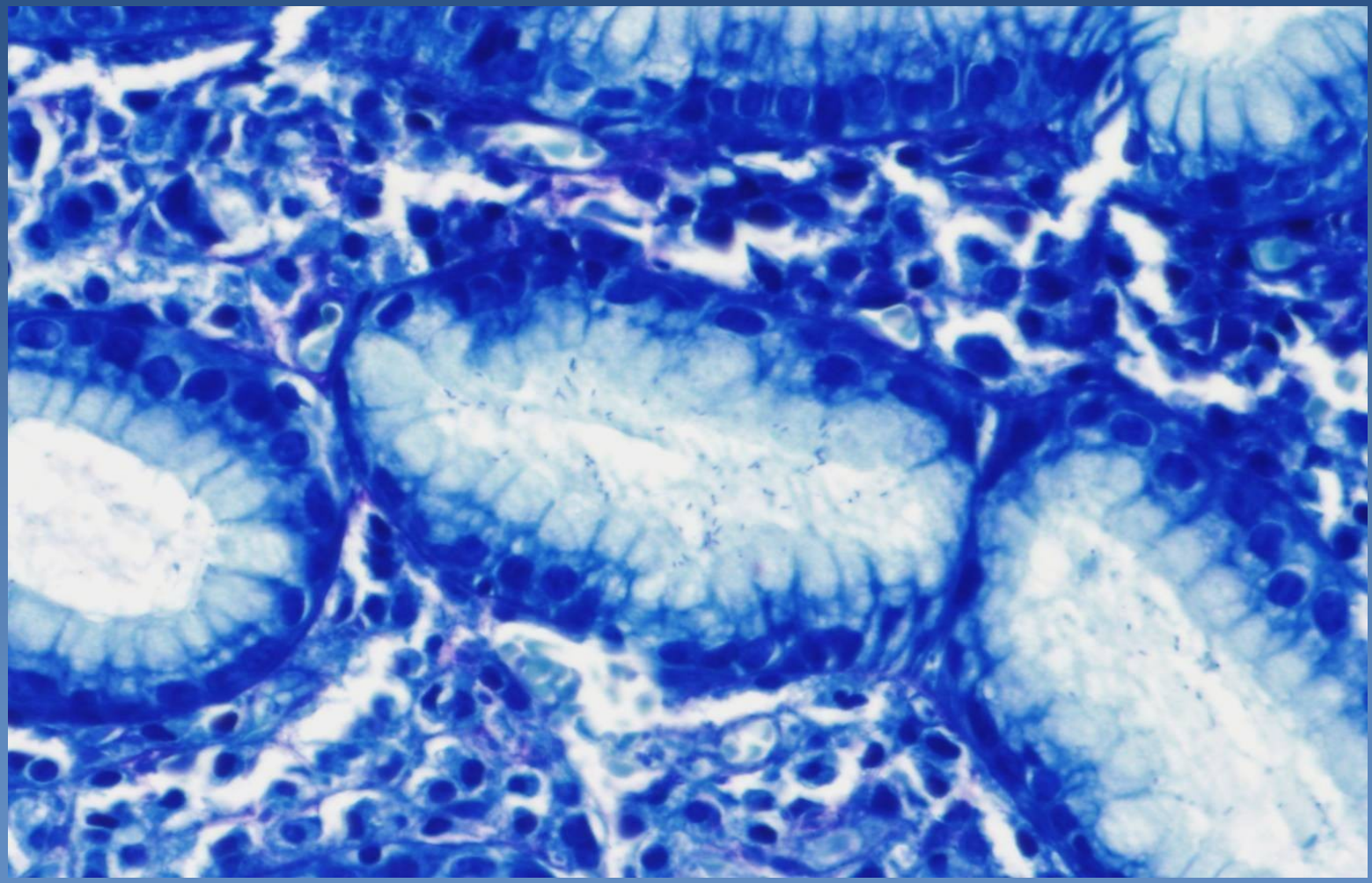


intraepithelial neutrophils

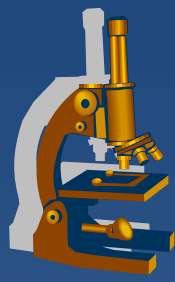
Chronic non-atrophic gastritis
Helicobacter pylori (Warthin-Starry)



Chronic non-atrophic gastritis Helicobacter pylori (Giemsa–Romanowski)



Chronic gastritis



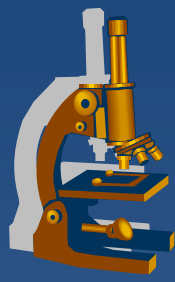
- **Chronic atrophic gastritis**

1/ Autoimmune chronic atrophic gastritis („A“)

⇨ ***autoimmune, anti-parietal cell and anti-intrinsic factor antibodies, hypochlorhydria, association with vitamin B12 deficiency and pernicious anemia***

- ***gross:*** mucosa of the gastric body and fundus atrophy
- ***micro:*** chronic non-active gastritis (severe mucosal atrophy with intestinal or pseudopyloric metaplasia, fibrosis)
- ***higher risk of developing adenocarcinoma!***

Chronic gastritis



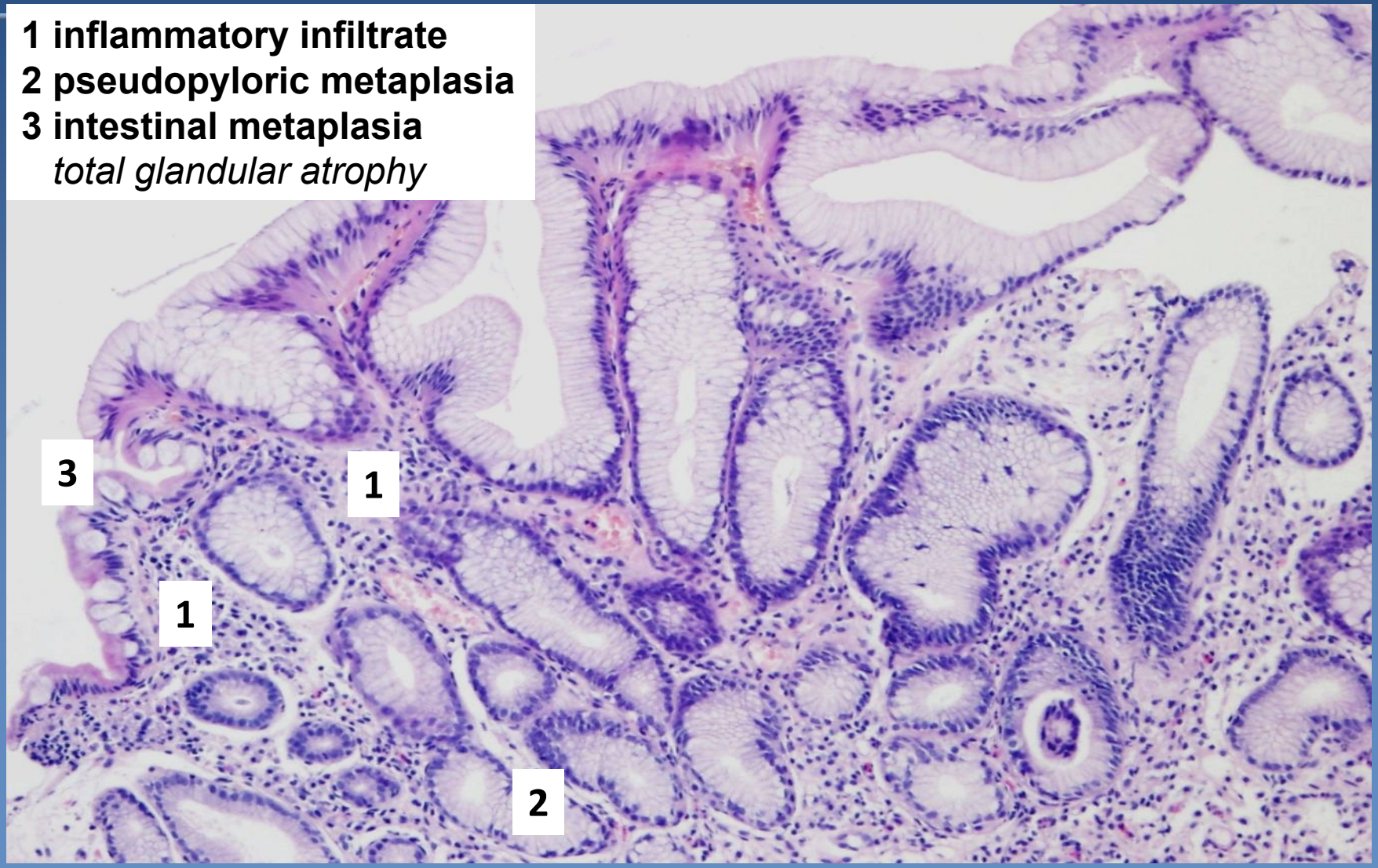
- **Chronic atrophic gastritis**

2/ Chronic multifocal atrophic gastritis (pangastritis)

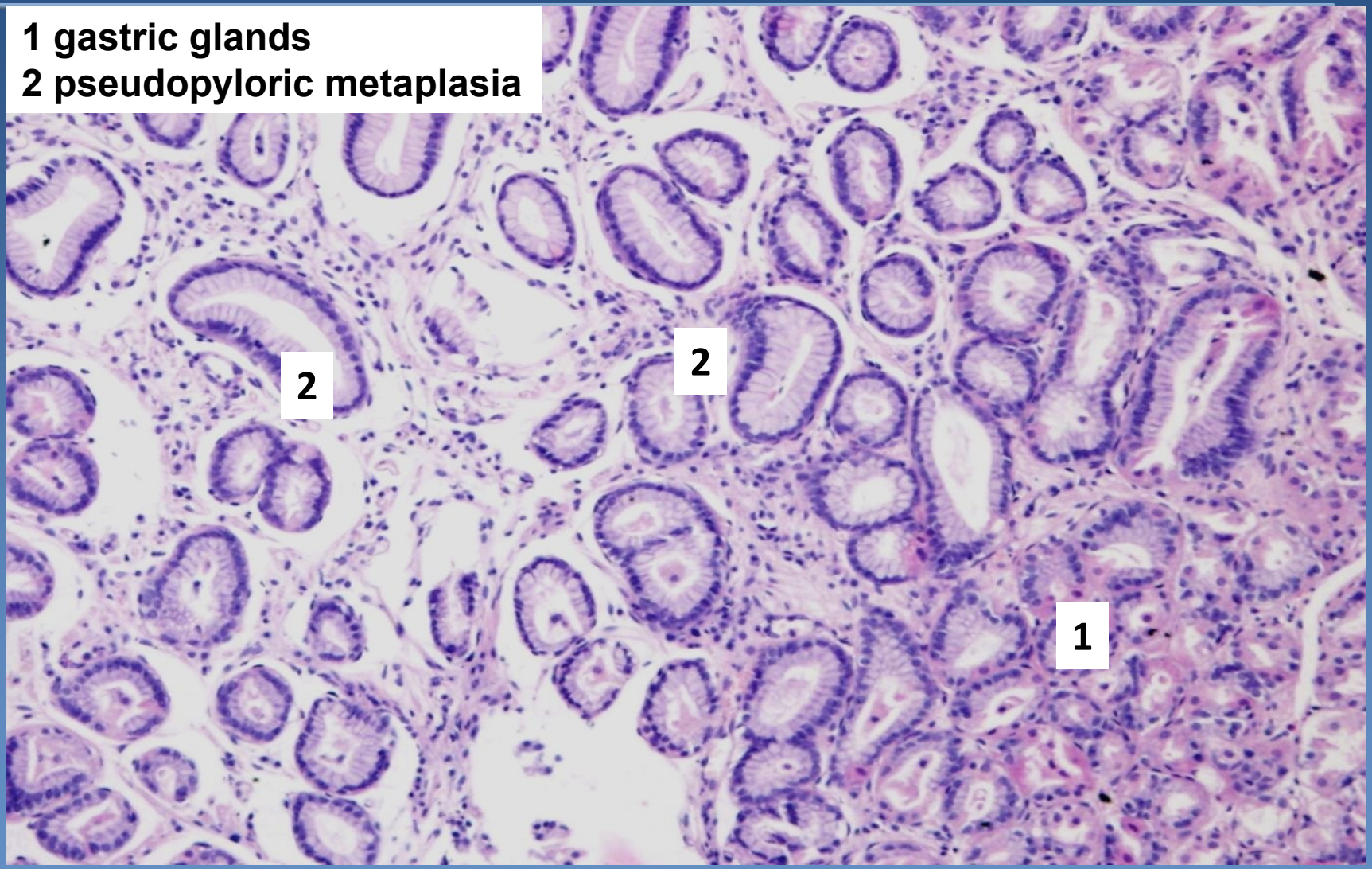
- ⇨ *Helicobacter pylori-associated*
- ⇨ *low grade of inflammation (body + antrum)*
- ⇨ *epithelial reactive changes, erosions*
- ⇨ *uneven distribution of atrophic foci*

Chronic atrophic gastritis (gastric body)

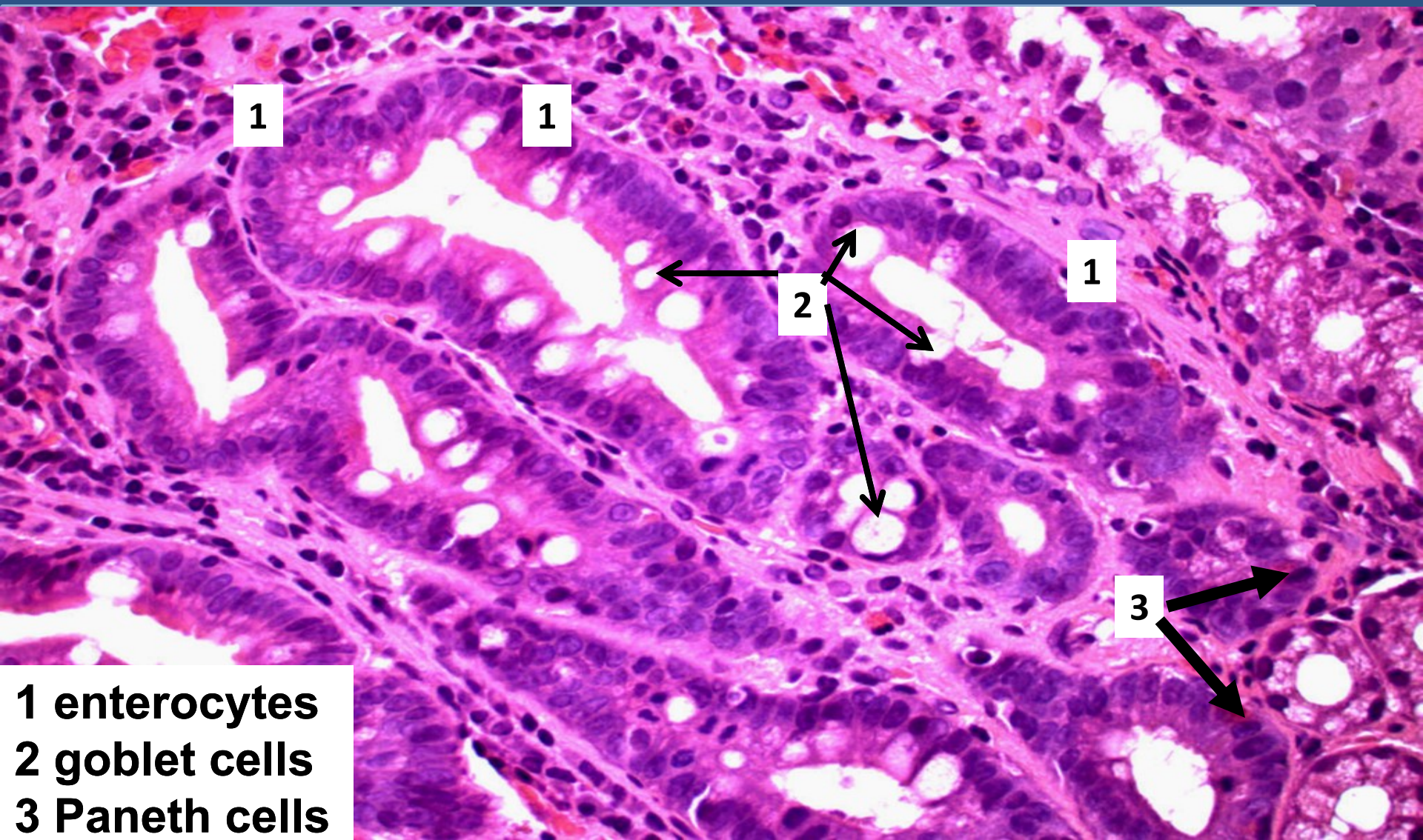
1 inflammatory infiltrate
2 pseudopyloric metaplasia
3 intestinal metaplasia
total glandular atrophy



Chronic atrophic gastritis (gastric body)

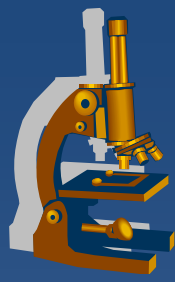


Chronic gastritis
- intestinal metaplasia



1 enterocytes
2 goblet cells
3 Paneth cells

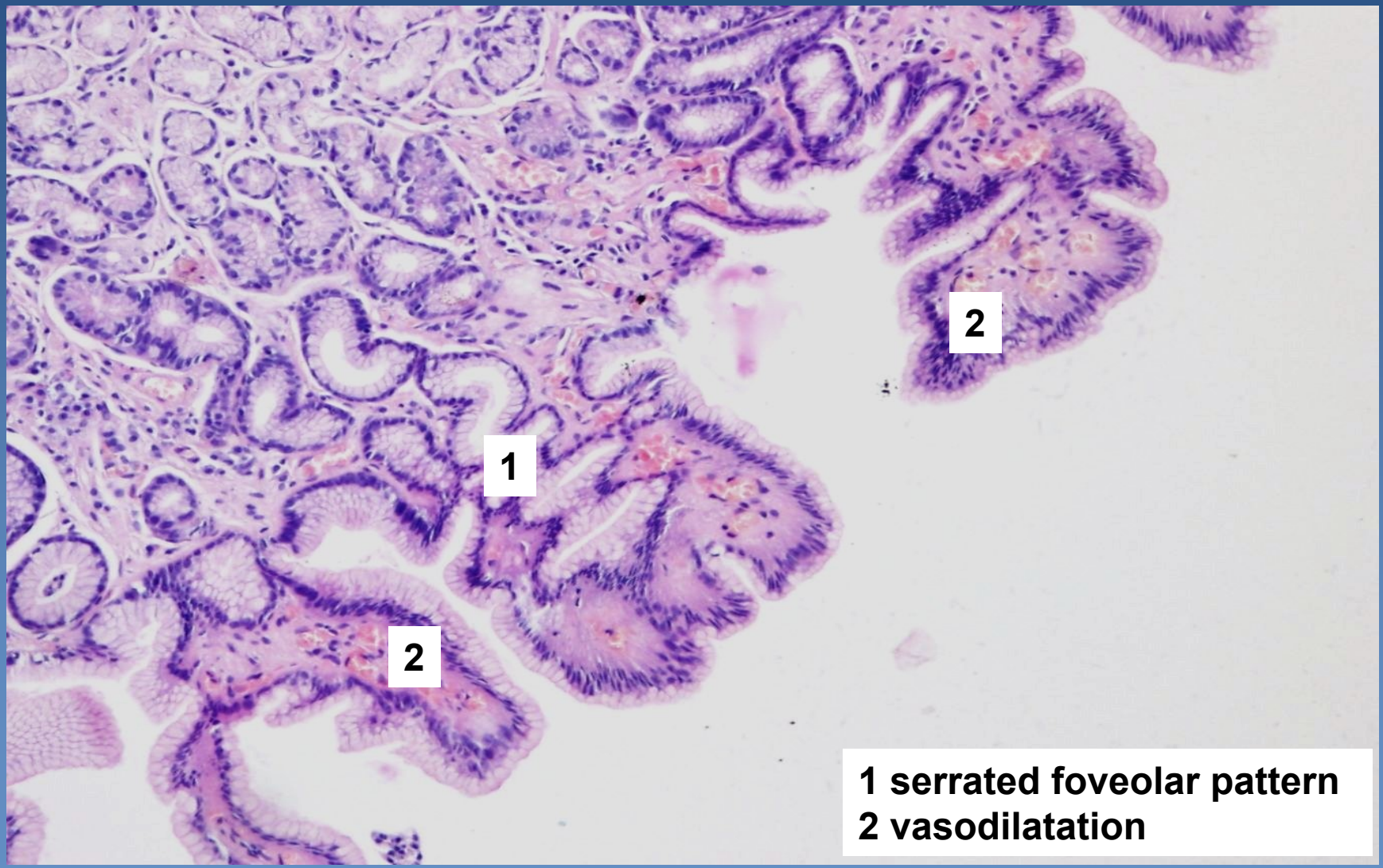
Chronic gastritis



Special forms:

- Chemical (reflux) gastritis / reactive gastropathy (former „C“)
  - ⇨ ***bile reflux, duodenal reflux after partial gastrectomy, NSAIDs***
  - ⇨ ***micro: hyperemic, oedematous mucosa, foveolar hyperplasia, vasodilatation, little inflammatory response***
- Lymphocytic, eosinophilic, granulomatous...

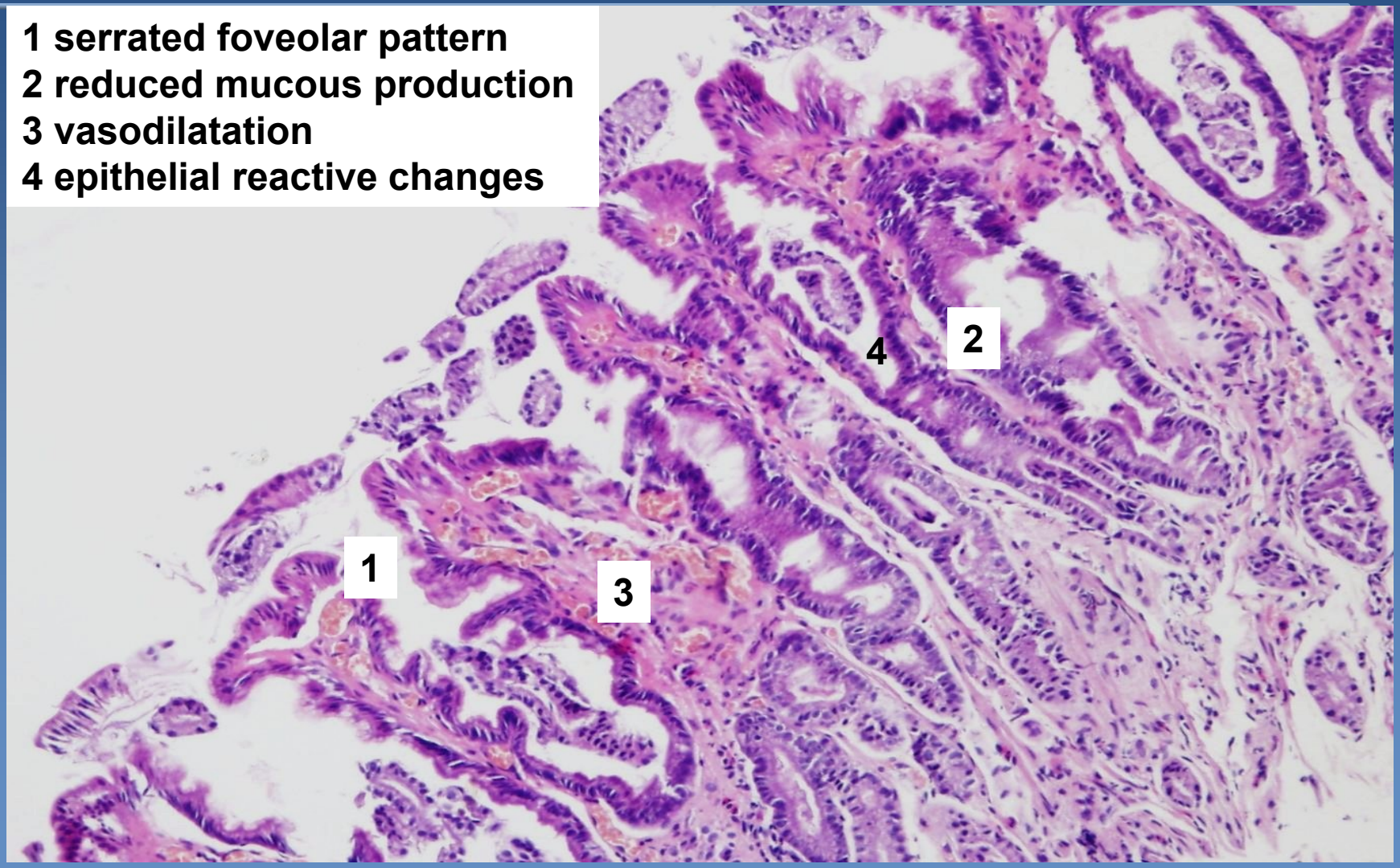
Reactive gastropathy (gastritis C)
mild changes



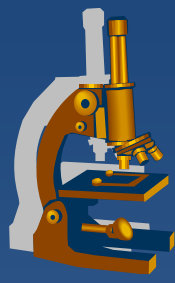
Reactive gastropathy (gastritis C)

severe changes

1 serrated foveolar pattern
2 reduced mucous production
3 vasodilatation
4 epithelial reactive changes

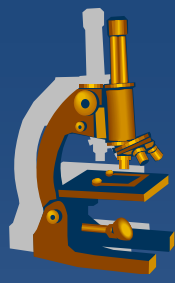


Hypertrophic gastropathy



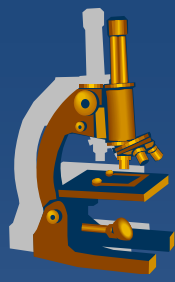
- uncommon, large mucosal folds
  - ⇨***marked epithelial hyperplasia (↑ growth factor release), may mimic a tumor:***
    - Ménétrier‘s disease (hyperplastic hypersecretory gastropathy with protein loss)
    - hypersecretory gastropathy (hyperplasia of parietal and chief cells)
    - glandular hyperplasia in Zollinger - Ellison syndrome (in neuroendocrine tumors with gastrin production)

Gastric erosions



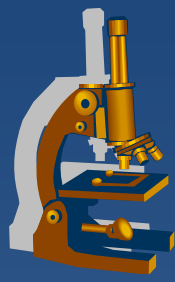
- definition:
  - ⇨ ***limited by m. mucosae, tiny superficial defects < 3 mm***
- causes:
  - ⇨ ***NSAIDs, alcohol, vomiting, stress, burns, infection***
- localisation:
  - ⇨ ***antrum and body***
- microcirculation disorder, capillary rupture
- complete regeneration within a few days

Peptic ulceration



- Ulcer definition: ***mucosal defect progressing through the m. mucosae into the submucosa or deeper***
- risk factors/causes:
  - ⇨ ***general: genetics, age, stress, alcohol, smoking***
  - ⇨ ***local: gastric hyperacidity, HP gastritis, NSAIDs***
- localisation:
  - ⇨ ***pylorus, lesser curvature, bulbus duodeni, (Meckel's diverticulum, stomic junction, GE junction)***

Gastric ulceration



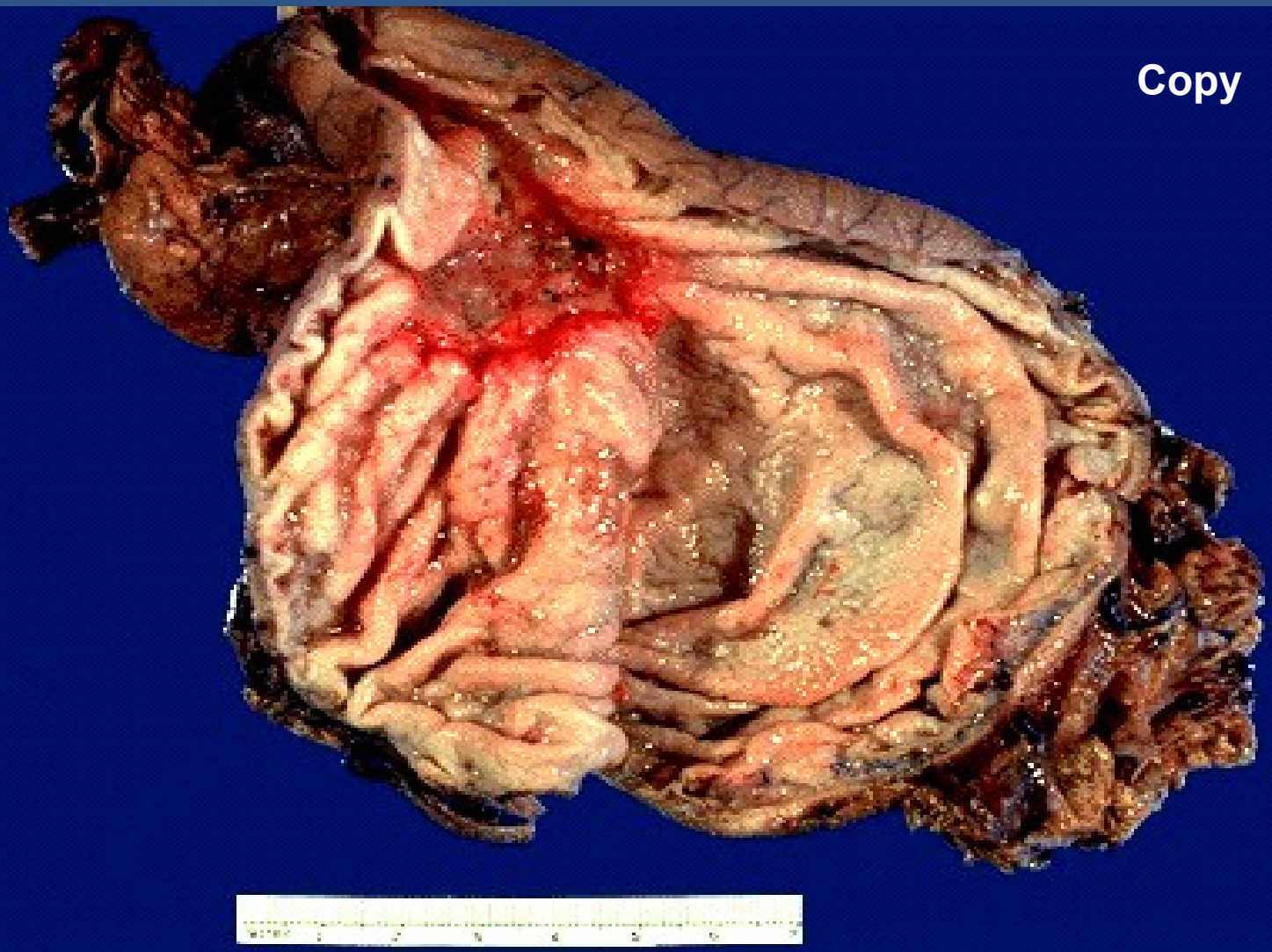
Acute ulcer:

- ***sharply demarcated defect 4 - 25mm; acute gastritis, severe stress (shock, trauma, burns), NSAIDs, severe hyperacidity***

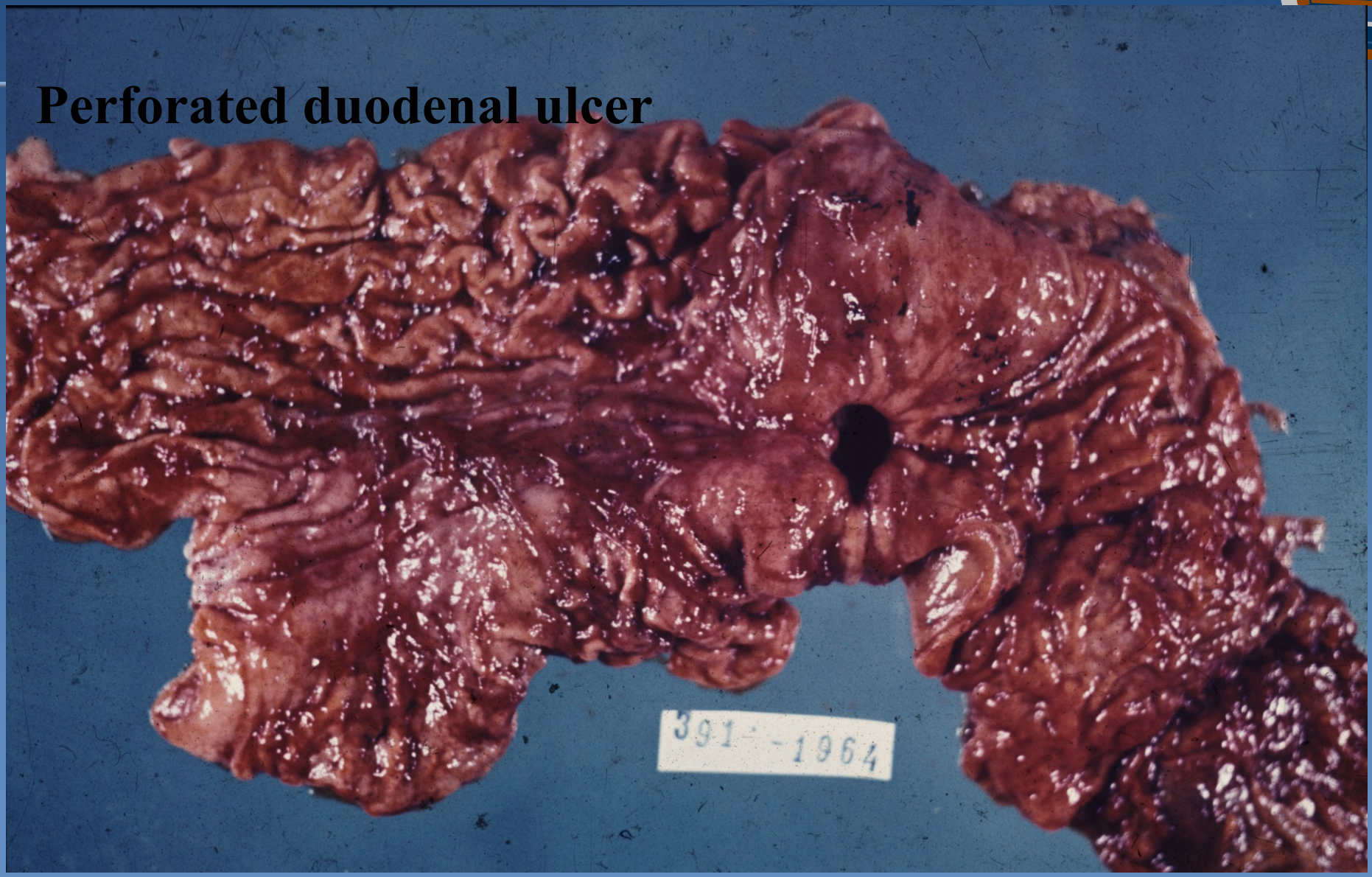
Chronic ulcer:

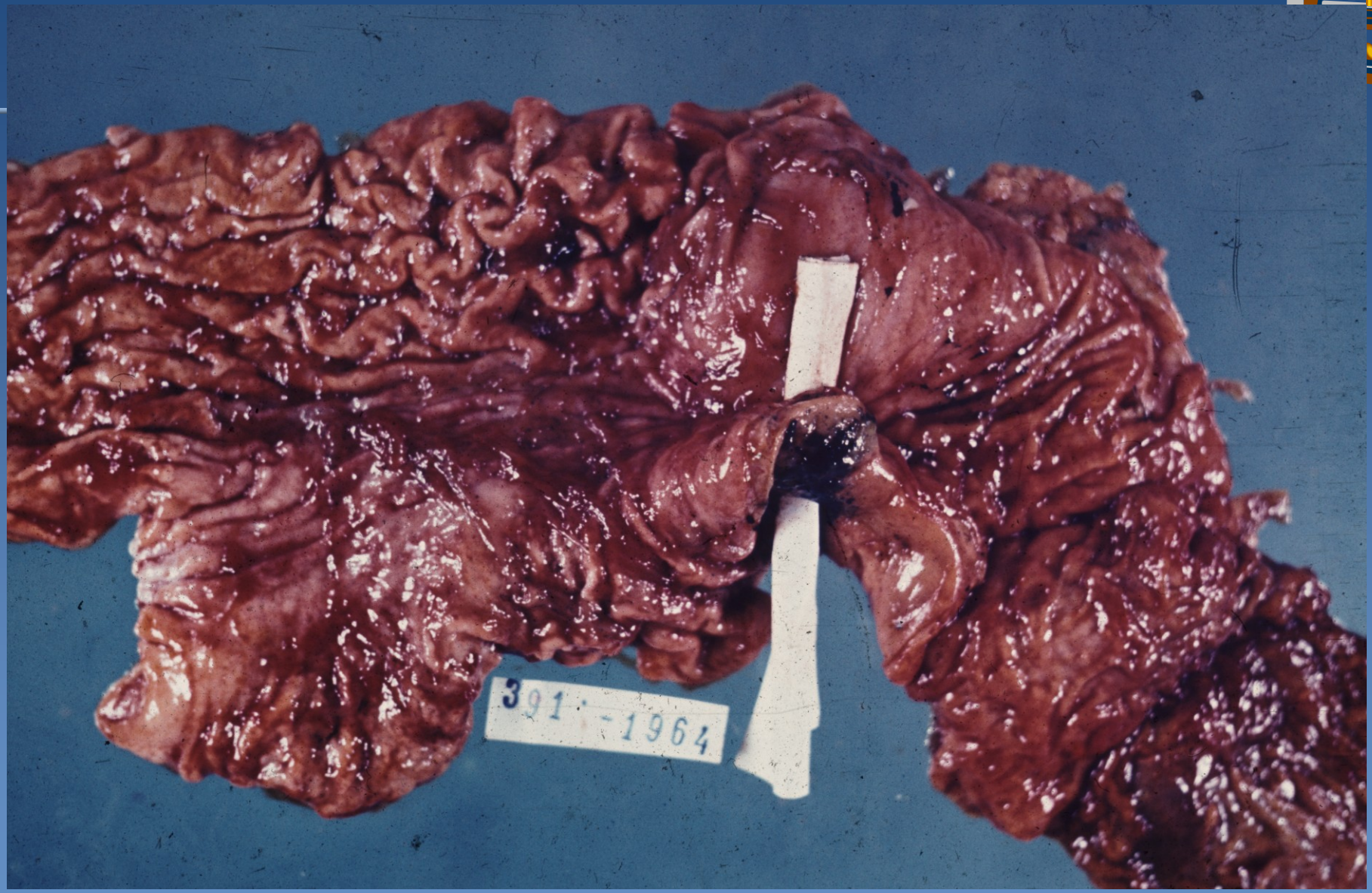
- ***slightly overhanging margins, radial adjacent mucosal folds***
- ***gross: smooth base***
- ***4 histologic zones: 1) fibrinoid necrosis and cell debris – active u. 2) mixed inflammatory infiltrate 3) granulation tissue 4) fibrous scar***
- ***complications: bleeding (overt, occult), penetration, perforation, scarring + obstruction, rare malignant transformation***

Chronic peptic ulcer of the stomach

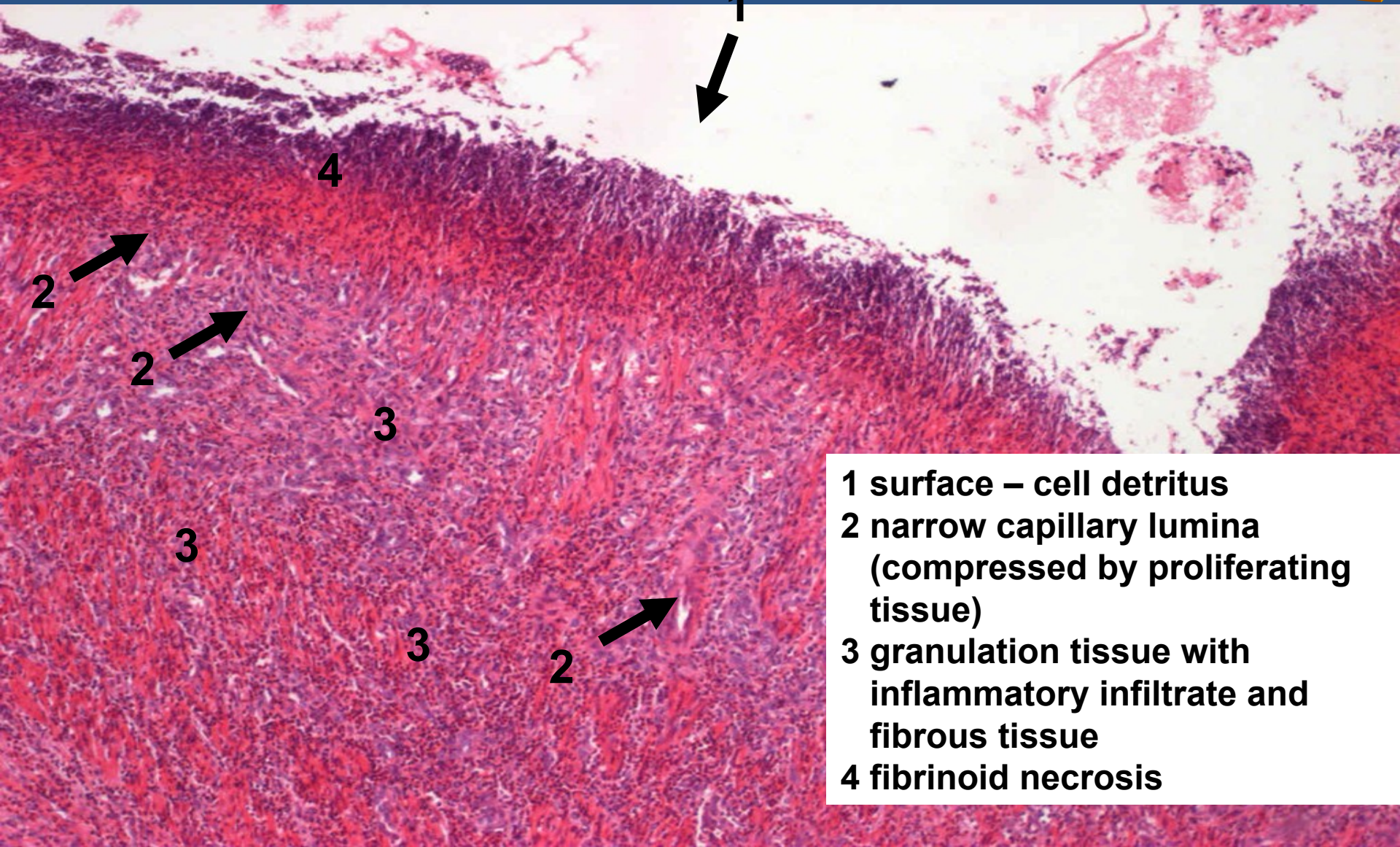


Perforated duodenal ulcer



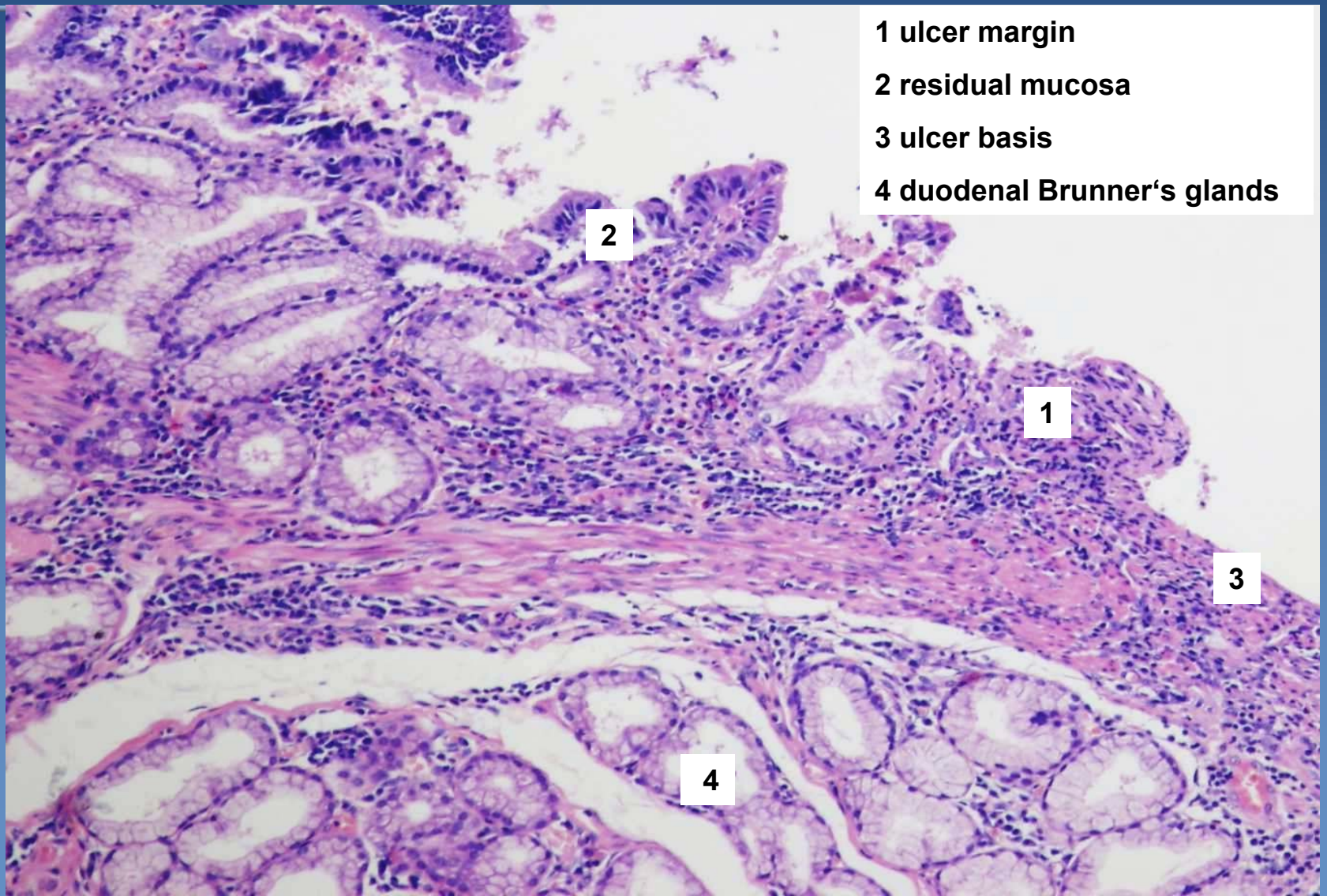

391 - 1964

Chronic peptic ulcer of the stomach
- basis

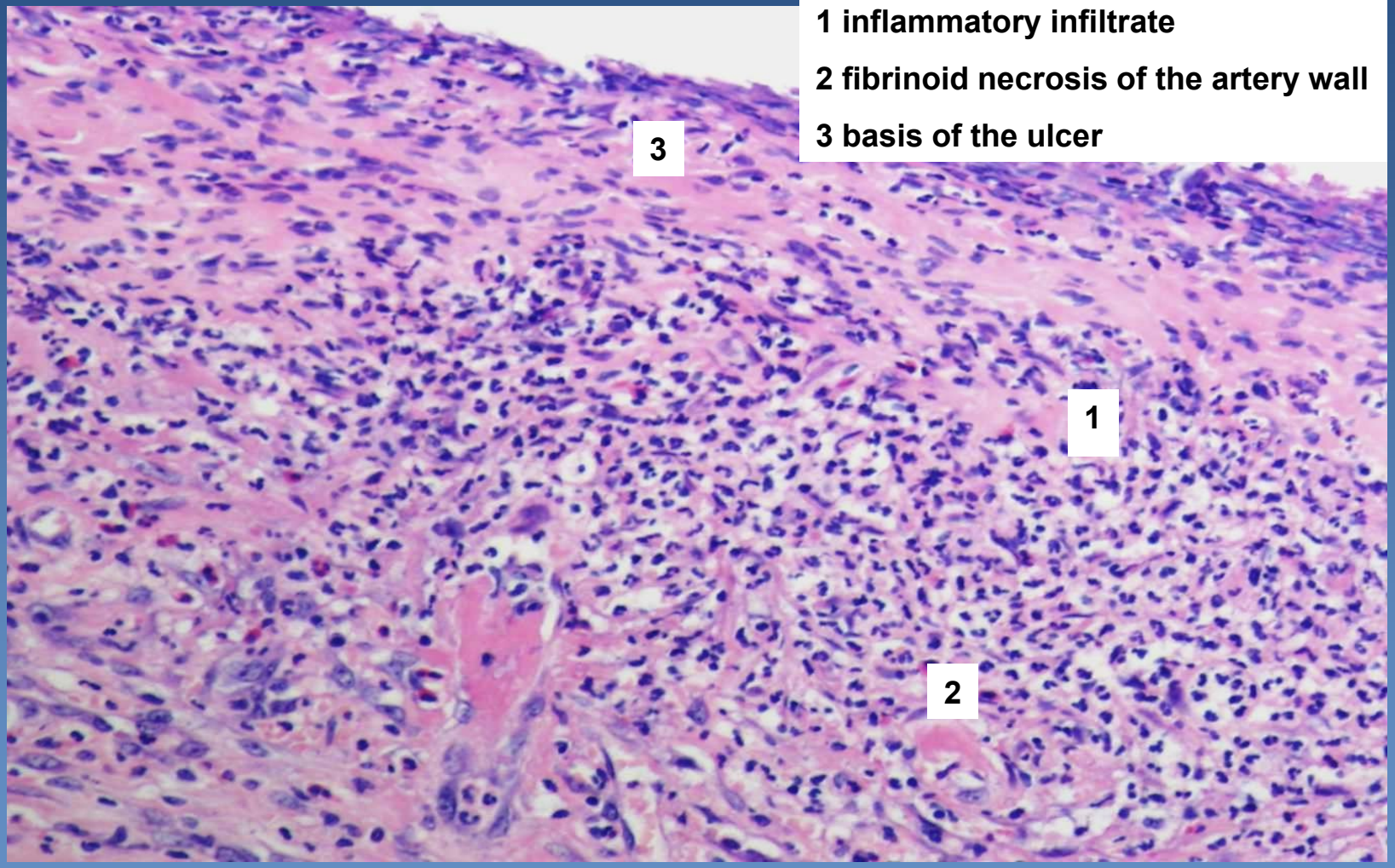


1 surface – cell detritus
2 narrow capillary lumina (compressed by proliferating tissue)
3 granulation tissue with inflammatory infiltrate and fibrous tissue
4 fibrinoid necrosis

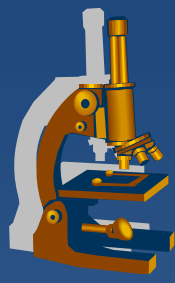
Peptic duodenal ulcer
- edges of the ulcer



Chronic peptic duodenal ulcer
- basis of the ulcer

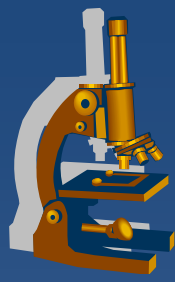


Important gastric tumors



- PSEUDOTUMORS
  - ⇨ *non-tumorous polyps (inflammatory, hyperplastic, fundic gland polyps)*
- EPITHELIAL
  - ⇨ *adenoma (in the setting of chronic gastritis/intest. metaplasia)*
  - ⇨ *malignant: carcinoma (adenoca, neuroendocrine ca, …)*
- NON-EPITHELIAL
  - ⇨ *gastrointestinal stromal tumors (GISTs)*
  - ⇨ *lymphomas (NHL: MALT, DLBCL)*

Gastric carcinoma

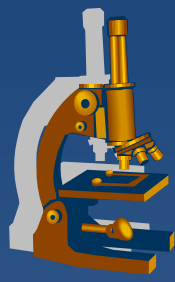


- most common malignant gastric tumor
- location: antrum, pylorus, lesser curvature
- risk factors:
  - ***precursor lesions: chronic gastritis with intestinal metaplasia, infection with HP, intraepithelial neoplasia***
  - ***EBV, dietary carcinogenes (salted, smoked food), familial***
- clinical features:
  - ***vomiting, abdominal discomfort, weight loss, anorexia***

  Direct spread into adjacent organs/tissues

  Metastases: LN regional, distant (Troisier's supraclavicular LN), portal circulation (liver), peritoneal dissemination, lung, ovarian Krukenberg tumor in females.

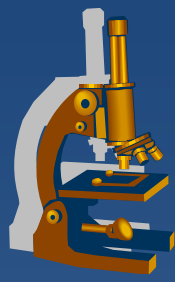
Gastric carcinoma



Classification:

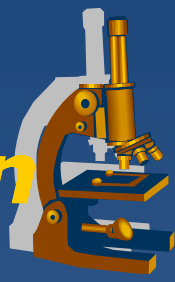
- macroscopical:
  - ⇨ ***exophytic (polypous)***
  - ⇨ ***excavated (ulcerated)***
  - ⇨ ***infiltrative (linitis plastica)***
- depth of invasion:
  - ⇨ ***early*: only in mucosa and submucosa**
  - ⇨ ***advanced*: extended into the muscular wall**
- histological type

WHO histological classification of gastric tumors



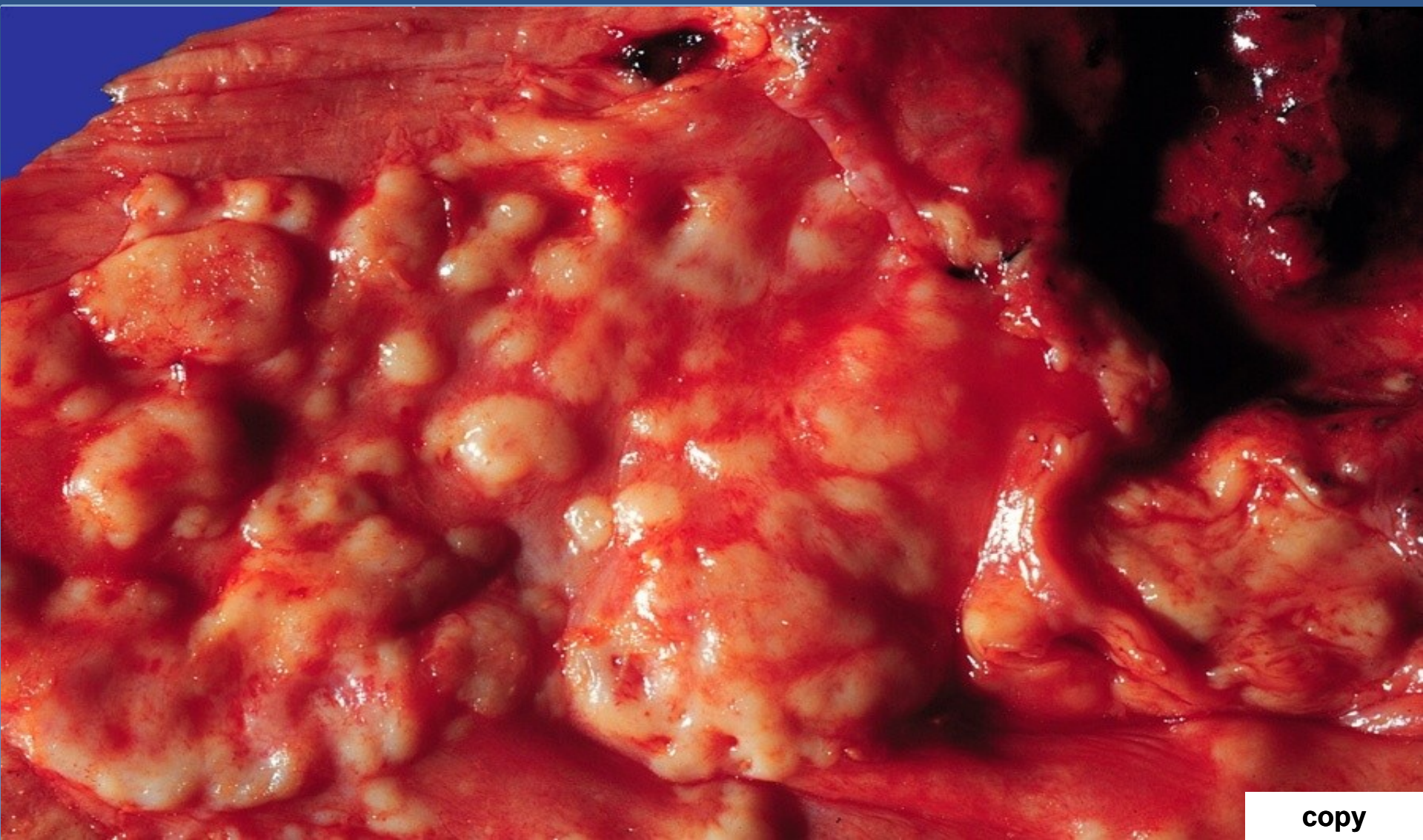
- Tubular
- Papillary
- Mucinous
- Signet-ring cell
- Adenosquamous
- Squamous
- Undifferentiated
- Neuroendocrine

Lauren's histological classification

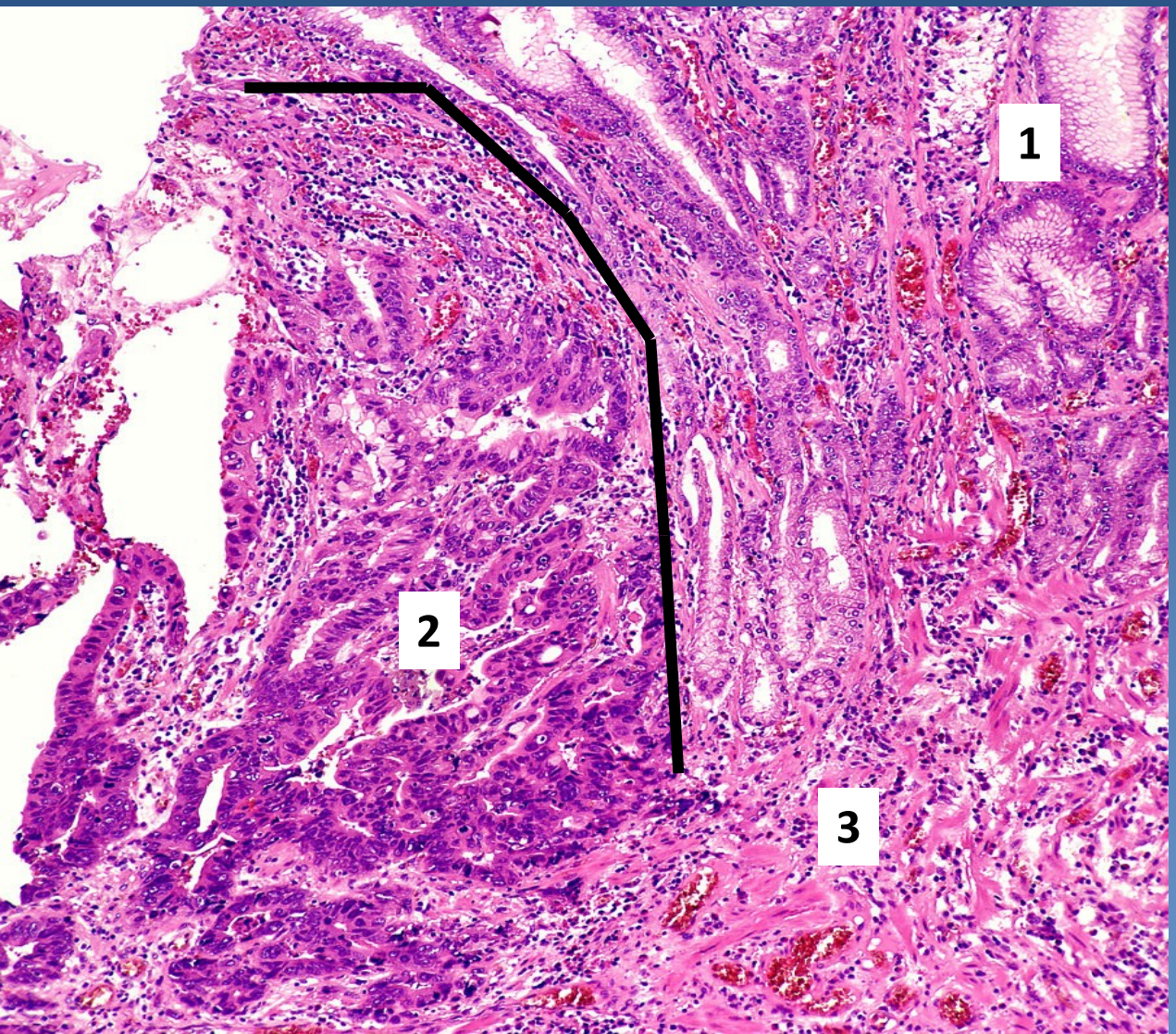


- Intestinal:
  - ***50%, HP chronic gastritis, ↓ tendency***
  - ***intestinal metaplasia-connected, neoplastic tubular glands/papillary formations, columnar epithelium, expansive growth***
  - ***> 50 yrs, M:F 2:1***
- Diffuse:
  - ***30%, ↑ tendency***
  - ***dissociated cells infiltrating singly / in small clusters into the stomach wall, signet-ring cells possible, reactive desmoplasia - fibrosis (scirrhus)***
  - ***earlier age, M:F 1:1***
- Mixed

Gastric adenocarcinoma
- exophytic growth



Gastric adenocarcinoma - intestinal type



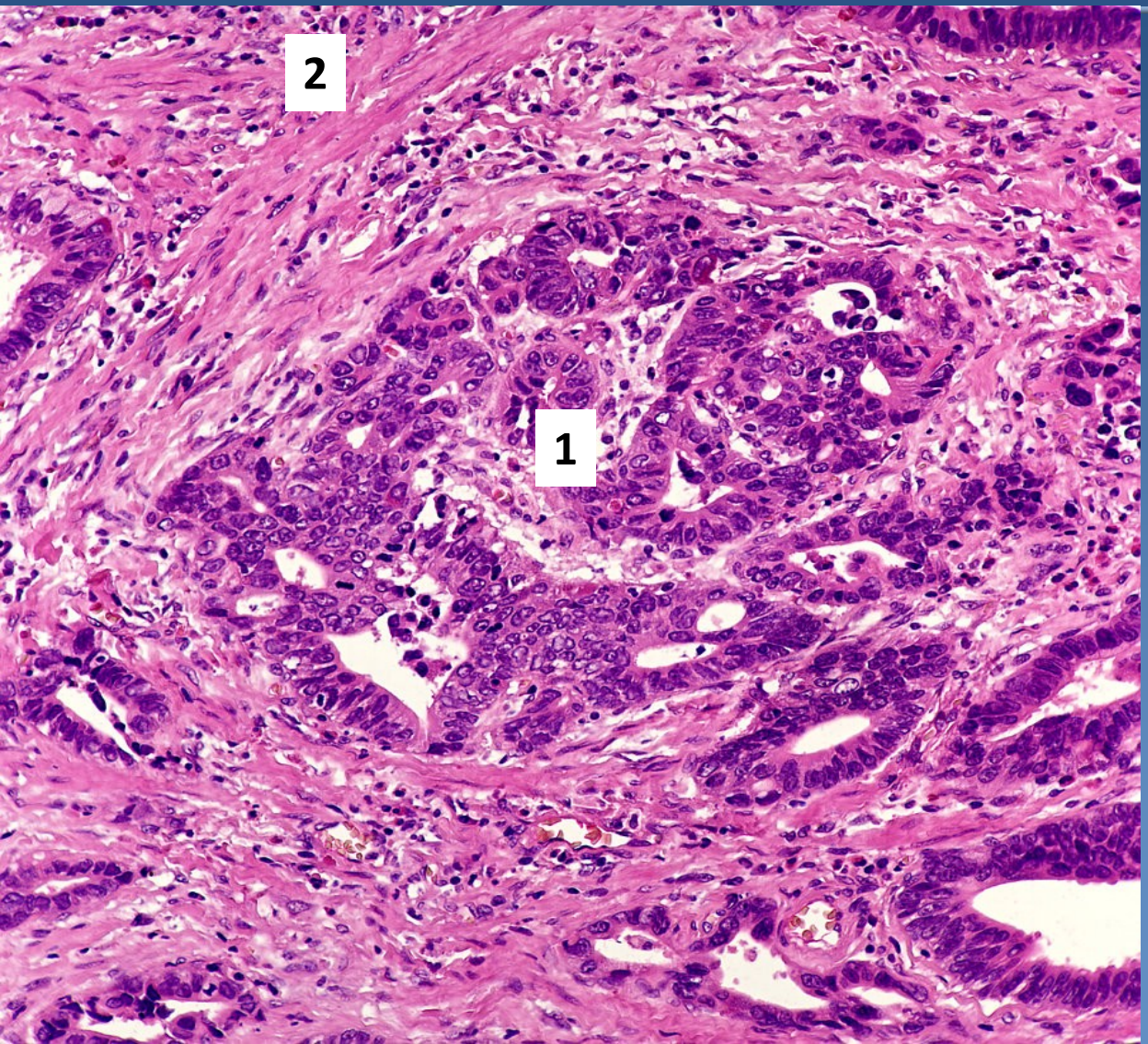
1 normal gastric mucosa

2 tubopapillary adenocarcinoma

3 muscularis mucosae

line - sharp demarcation of the tumor from normal mucosa

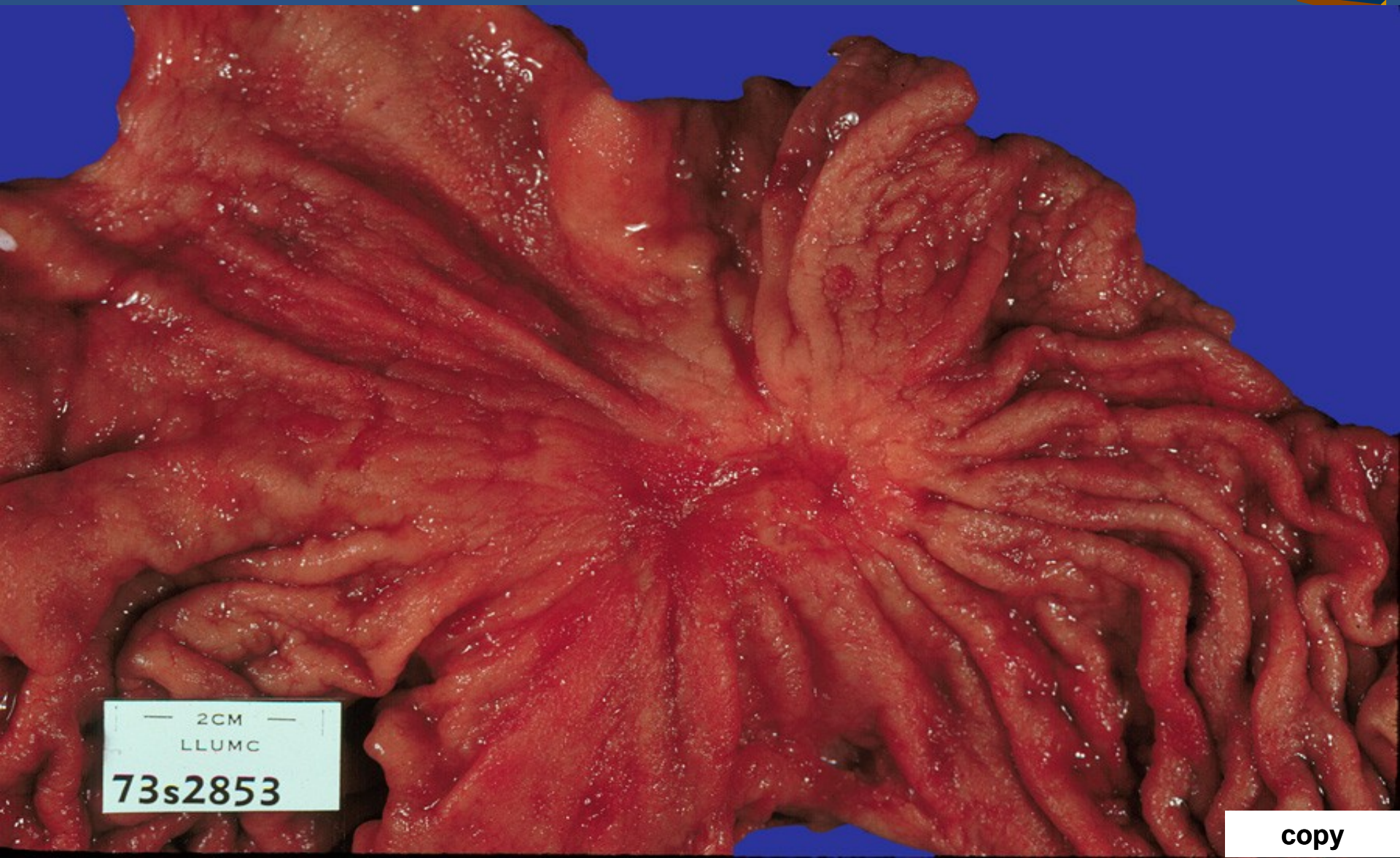
Gastric adenocarcinoma (intestinal type) infiltration into lamina muscularis propria



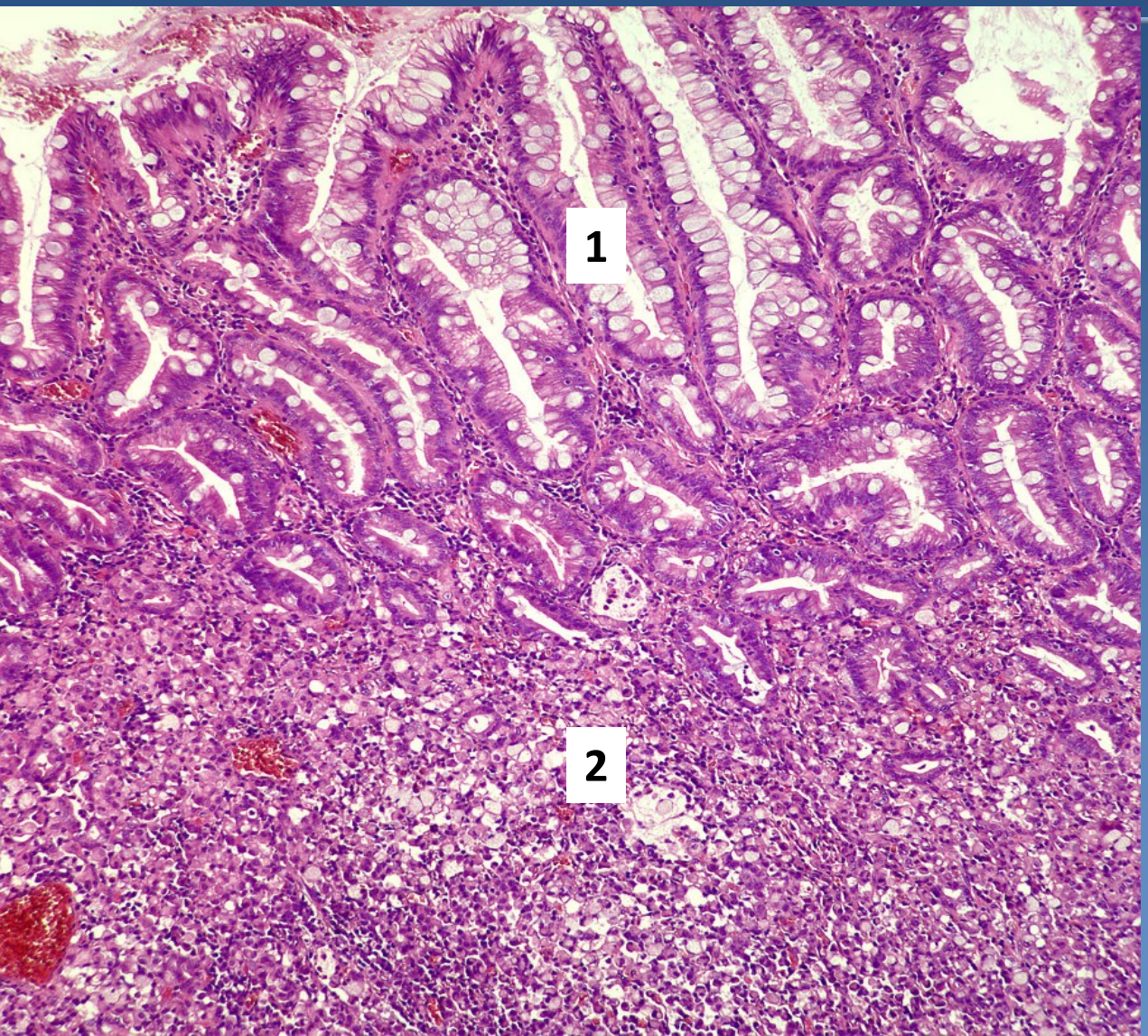
1 tumor cells

2 smooth muscle cells

Gastric adenocarcinoma
- diffuse type



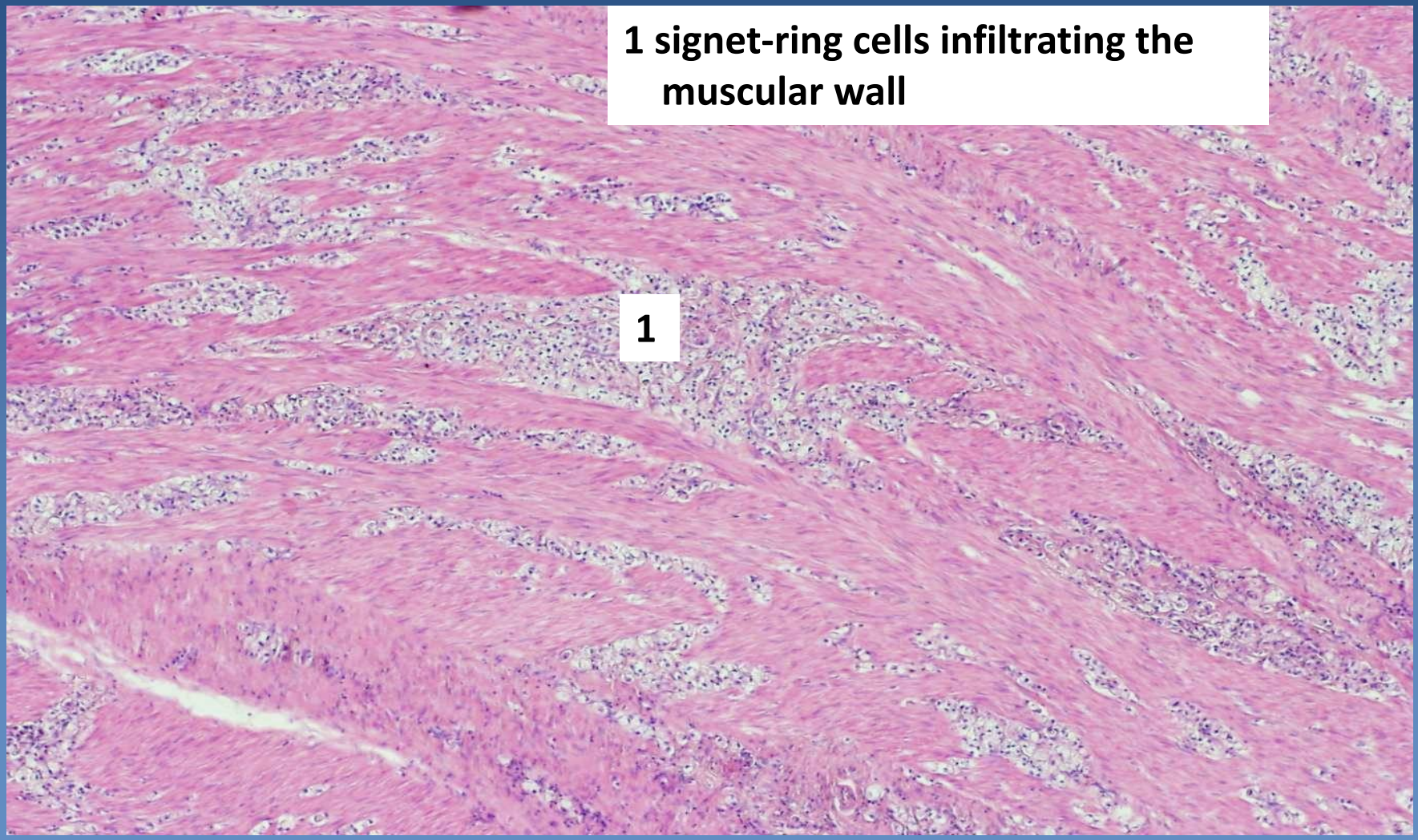
Gastric adenocarcinoma
- diffuse type



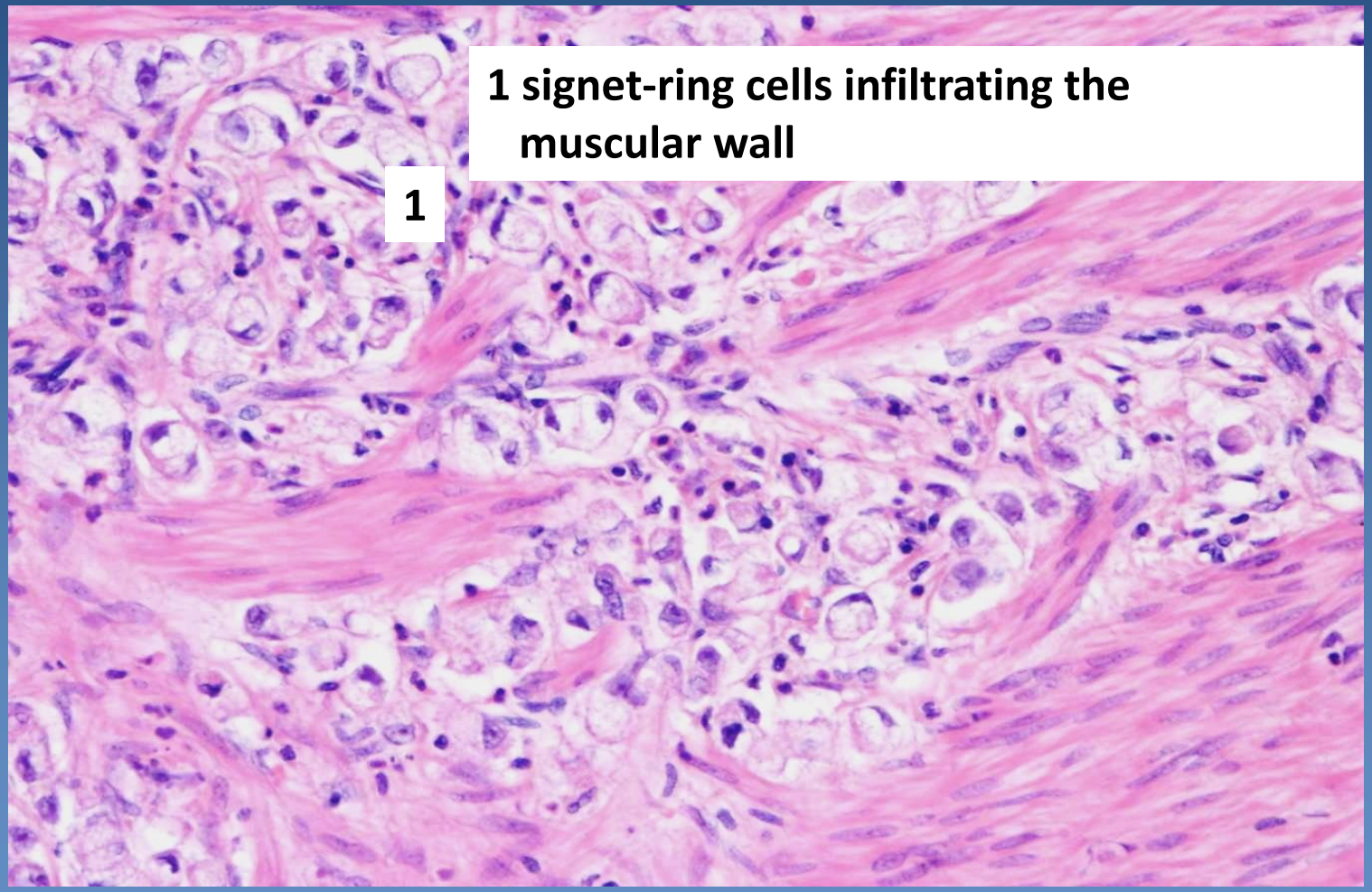
1 intestinal metaplasia of the mucosa

2 diffuse infiltration with signet-ring cells

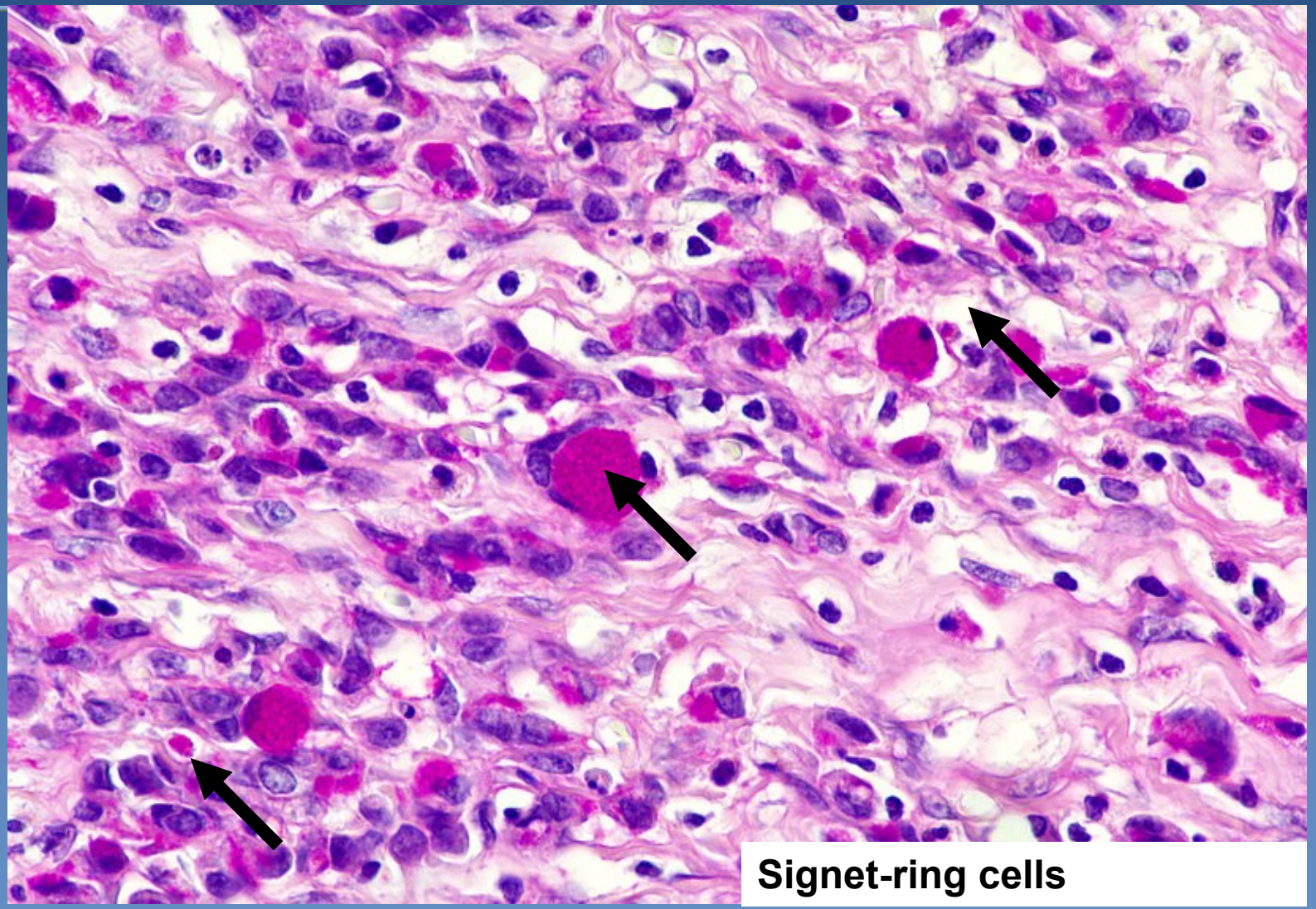
Gastric adenocarcinoma - diffuse type
– infiltration into lamina muscularis propria



Gastric adenocarcinoma - diffuse type detail

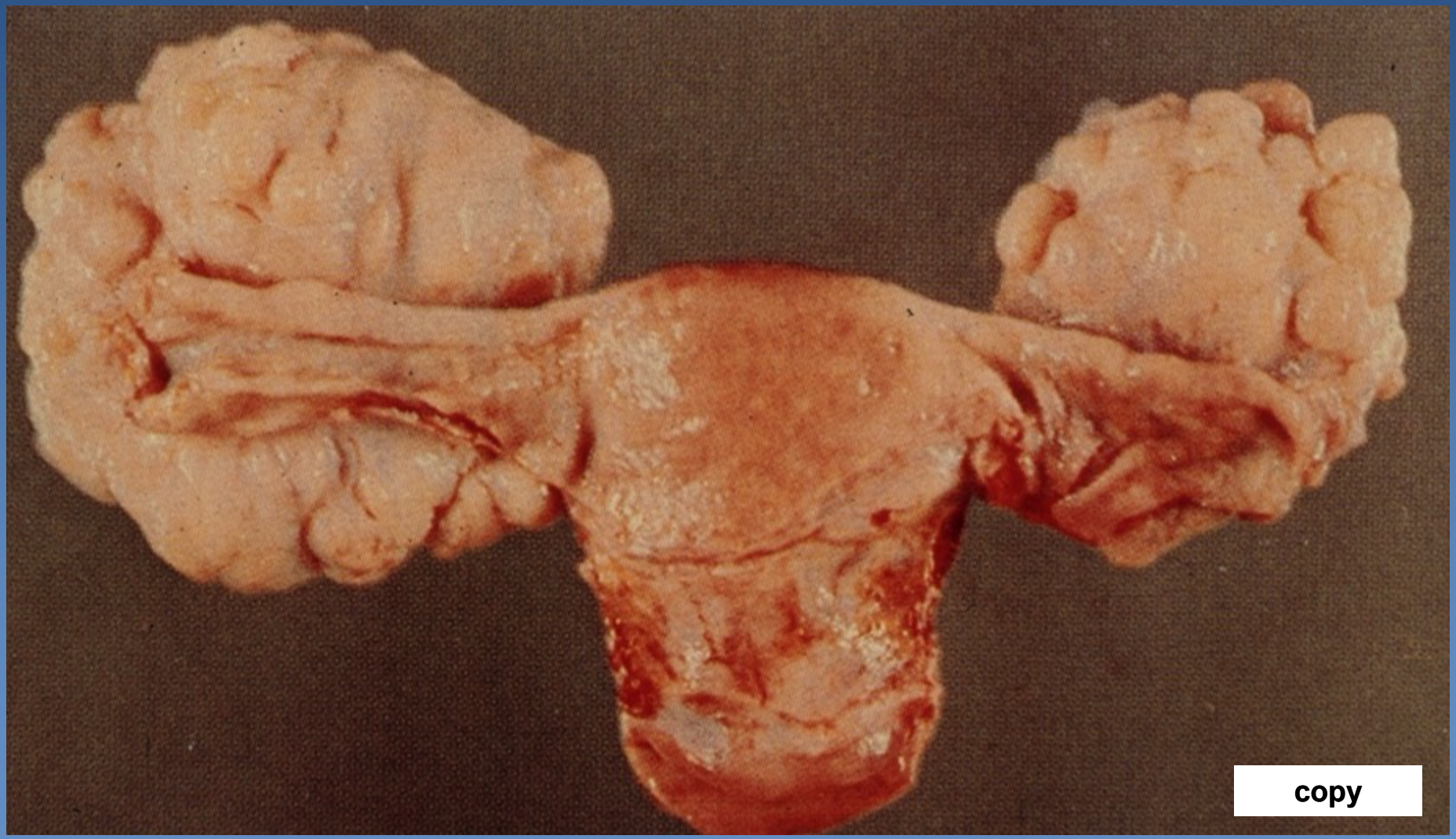


Gastric adenocarcinoma - diffuse type
detail (PAS)

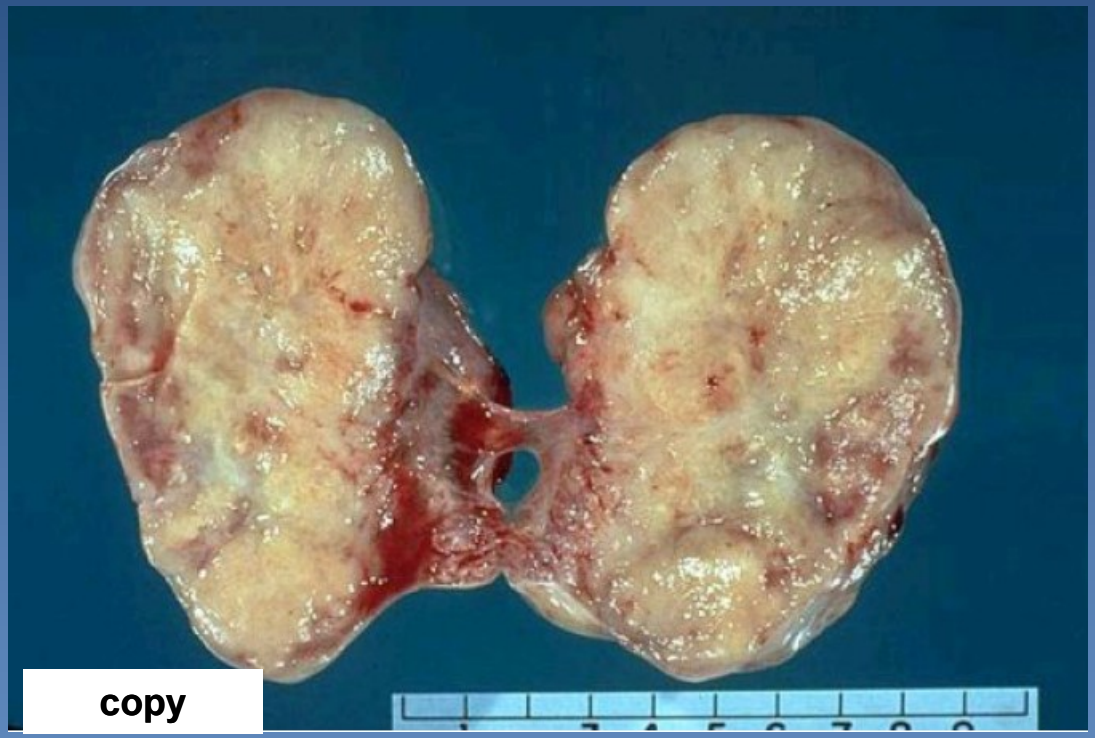


Signet-ring cells

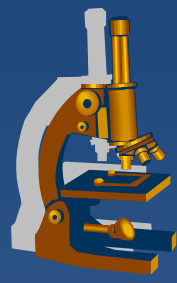
Krukenberg tumor



Krukenberg tumor

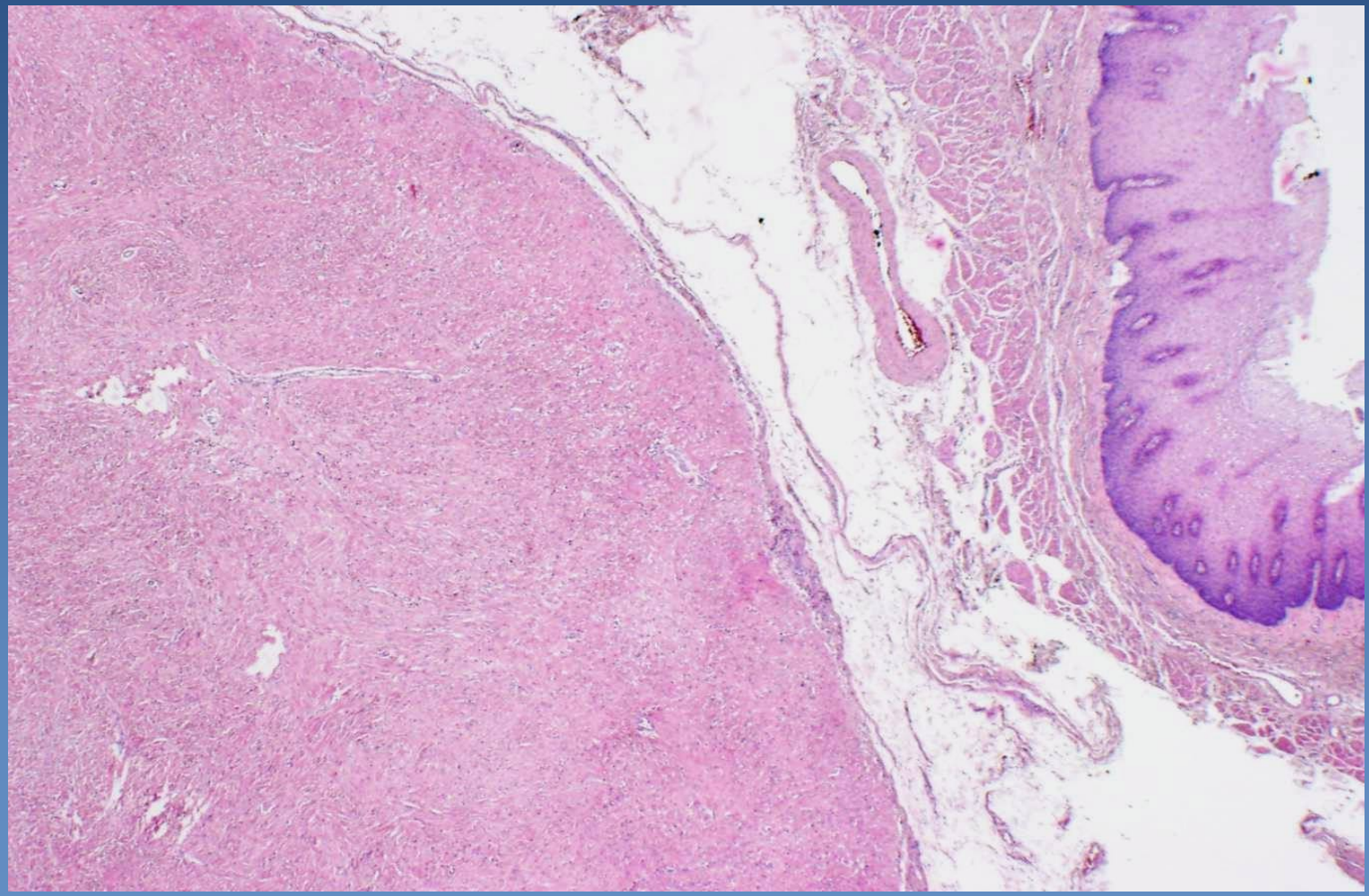


Gastrointestinal stromal tumors (GISTs)

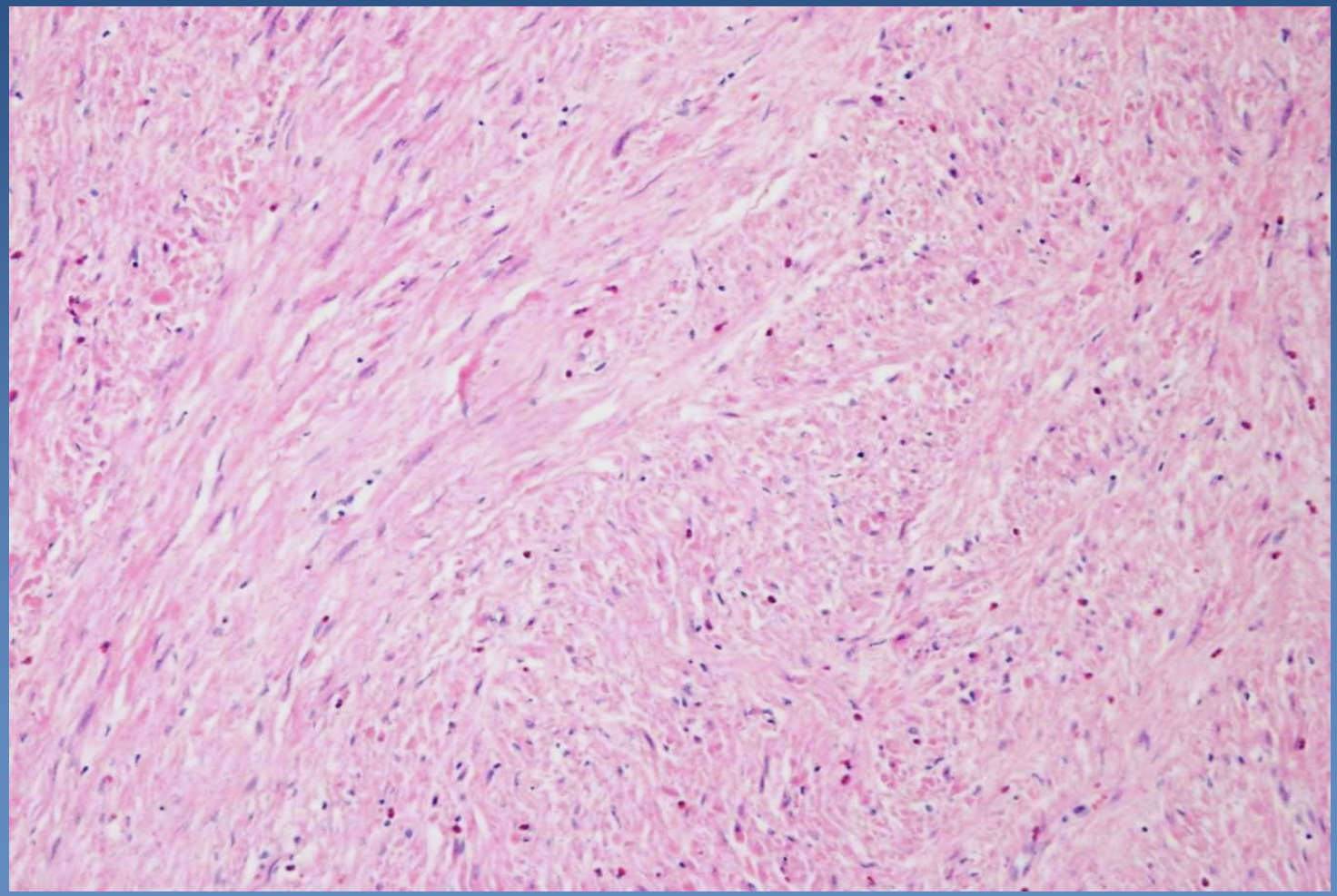


- mesenchymal tumors
- arising from intestinal cells of Cajal (pacemaker cells controlling peristalsis)
- origin anywhere in the GIT: predominantly the stomach and small intestine
- spindle-like or epitheloid cells, IHC CD117+,
- biologic behaviour prognosis :
  - ⇨ ***according to mitotic rate, size, localization***

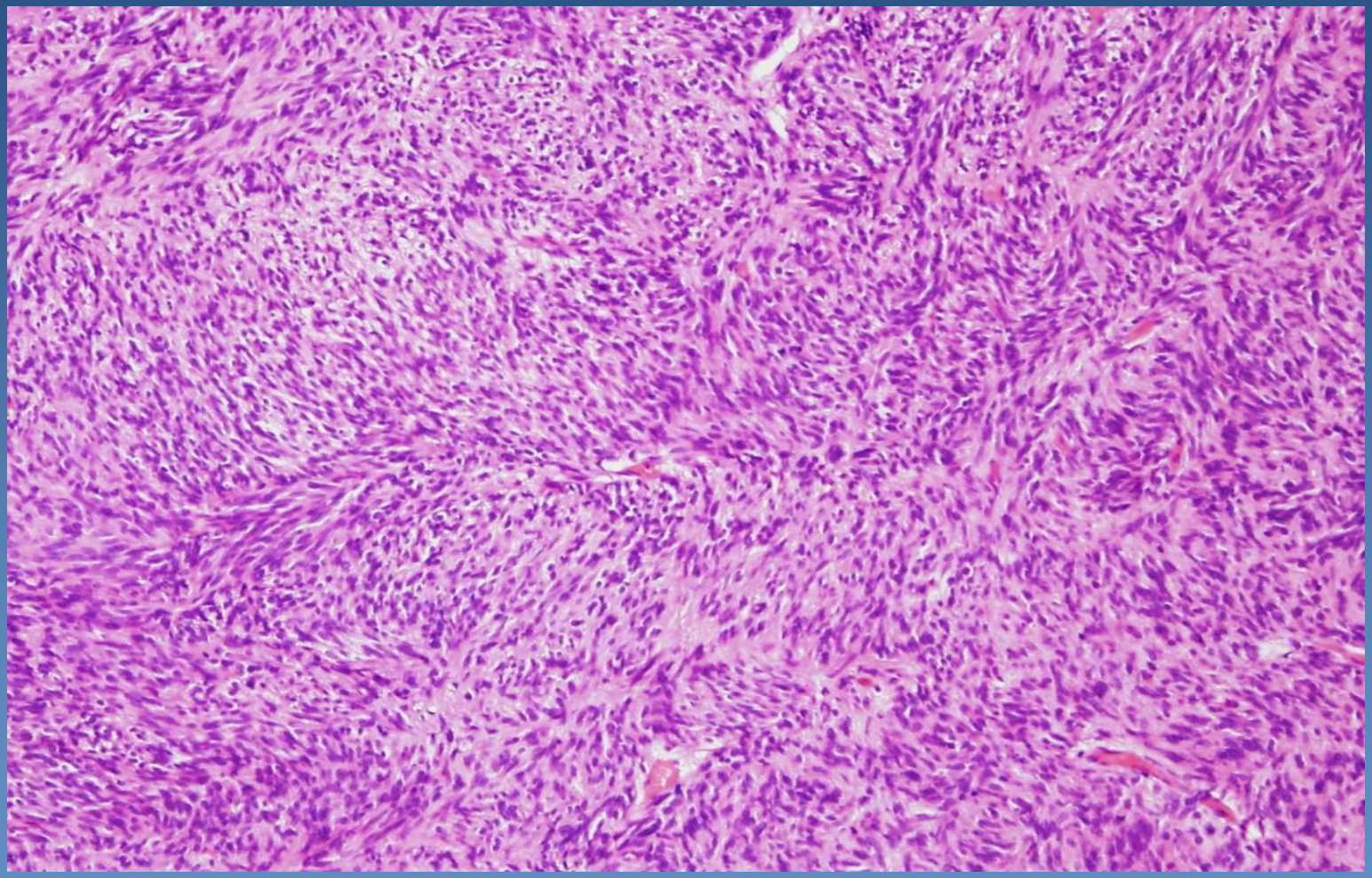
Oesophageal GIST



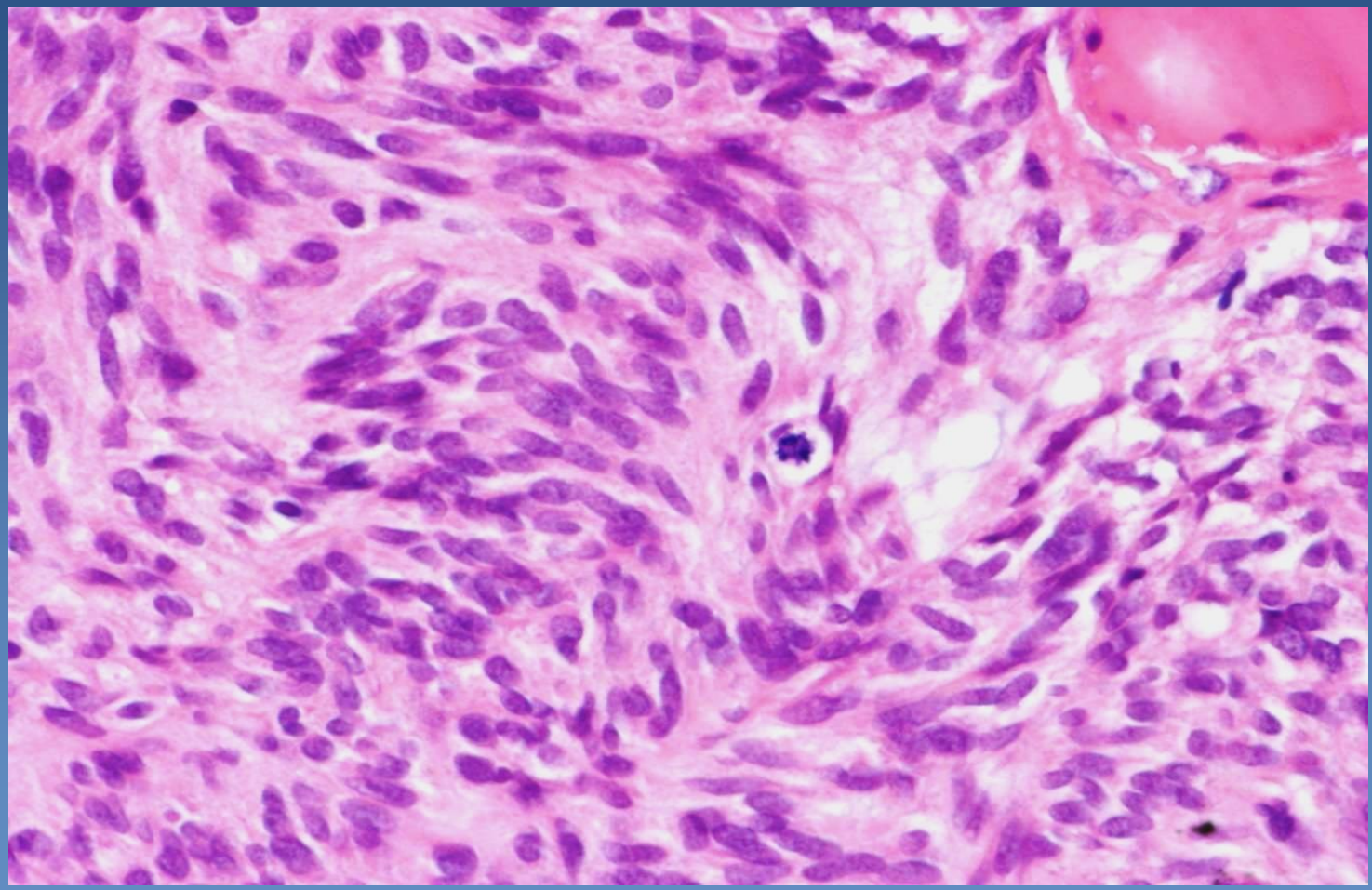
Oesophageal GIST - detail (spindle-like cells, low malignancy)



Oesophageal GIST - detail (spindle-like cells, highly malignant)

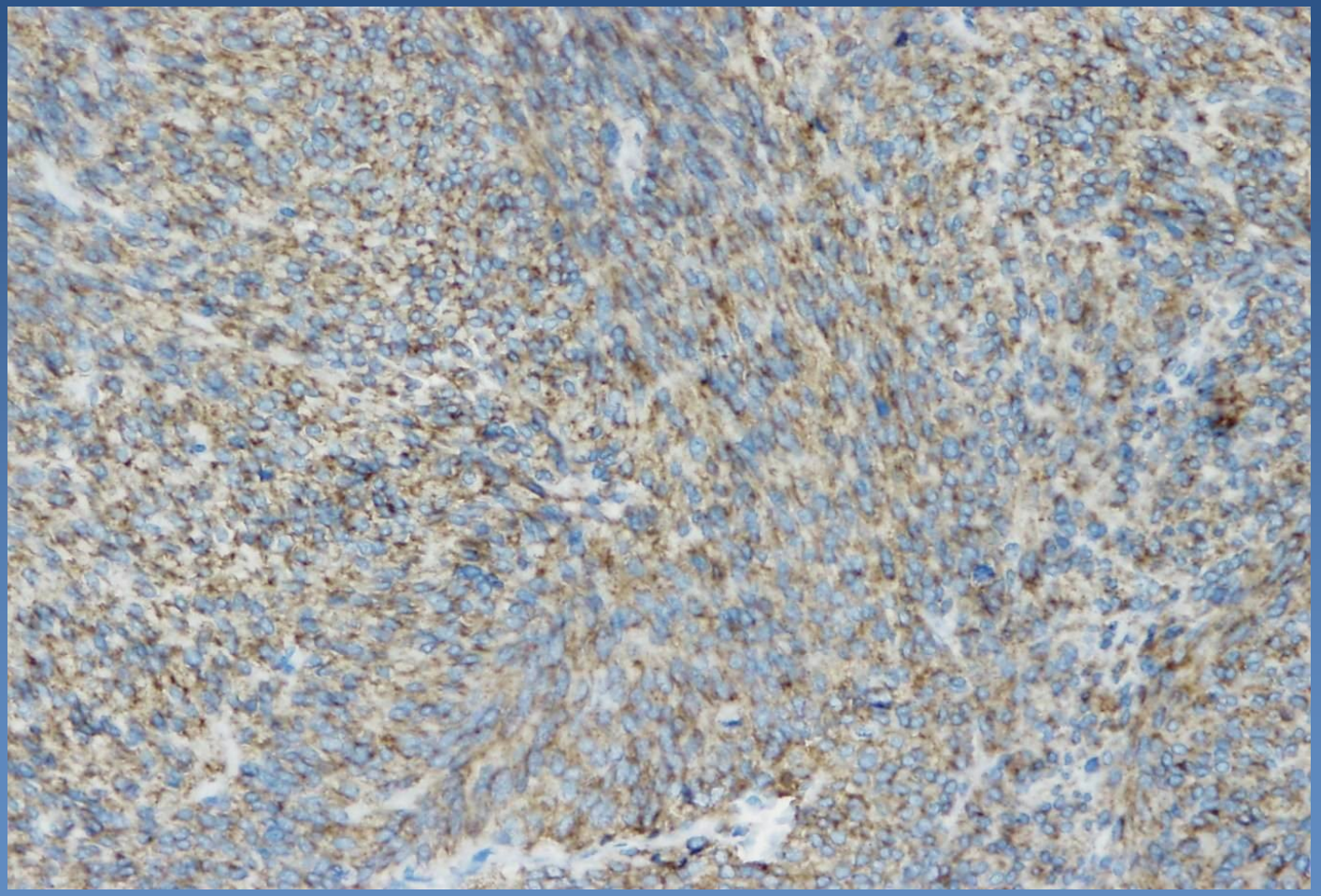


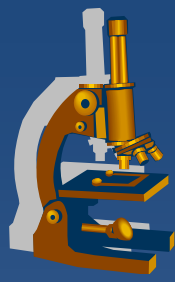
Intestinal GIST - detail (spindle-like cells, highly malignant)



Intestinal GIST

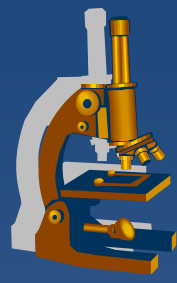
IHC CD117 positivity





INTESTINES

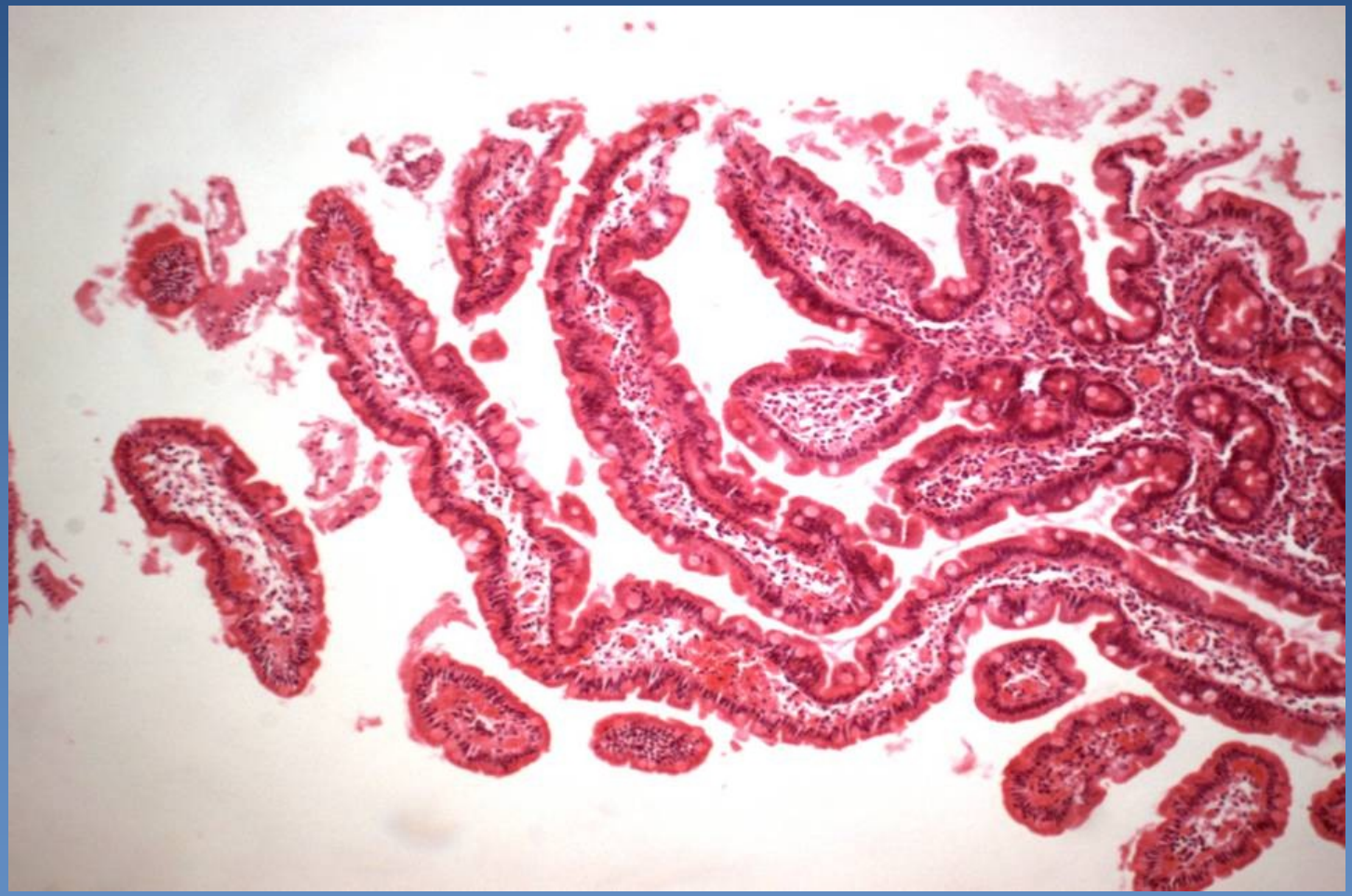
Normal mucosa of the small intestine



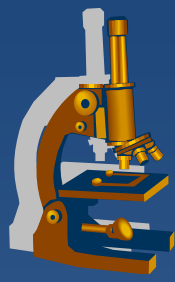
- **villi to crypts height ratio 3:1 – 5:1**
- **standard number of intraepithelial lymphocytes: 40 IEL / 100 enterocytes**

  - ⇨ *brush border – microvilli (PAS+, alkaline phosphatasis +)*
  - ⇨ *differentiated enterocytes*

Normal villi of the small intestine



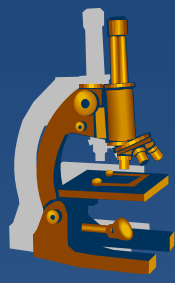
Malabsorption syndromes



- a group of symptoms resulting from an alteration in the digestion / absorption of nutrients mostly in the small intestine
- symptoms:
  - ***anorexia, diarrhea, steatorrhea, weakness, weight loss, abdominal distention,***
  - ***growth disturbances, eczema, neurologic/psychologic disturbances, bleeding disorders, anaemia, tetany***

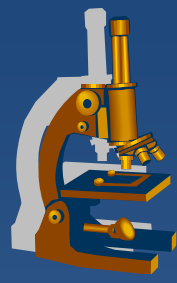
- disturbance of:
  - ***digestion intraluminal, terminal in the brush border***
  - ***mucosal absorption - enterocytes abnormalities, reduced intestinal surface area***
  - ***lymphatic transport***

Malabsorption syndromes



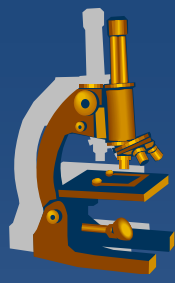
- Classification
  - ⇨ ***primary** – enterocytes‘ disorder (inborn, acquired)*
  - ⇨***secondary** – cause apart from enterocytes*
- commonly mixed causes

Defects of mucosal absorption



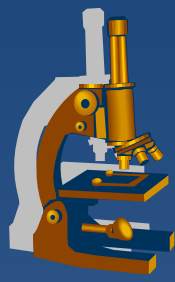
- Brush border enzymatic deficiency (lactose intolerance – lactase deficiency)
- Celiac disease gluten (gliadin)-sensitive enteropathy

Celiac disease



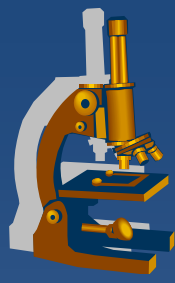
- prevalence 0,5-1% in Caucasian Europeans
- associated with dermatitis herpetiformis Duhring, DM I., Sjögren sy, etc.
- immunological sensitivity to gluten (component of wheat)
- antibodies EMA, TG (non-specific anti-gliadin), …
- genetic (HLA), immune, exogenous factors

Celiac disease



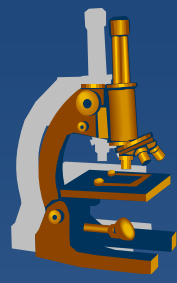
- gluten-free diet necessary, sm. lifelong
- risk of malignant disease:
  - ***malignant lymphomas (T-cell), carcinomas of the small intestine***
- clinical
  - ***infancy (6-24 m.), adults 30-60 yrs; silent, latent***
- symptoms:
  - ***irritability, diarrhoea, fatigue…***
- endoscopy:
  - ***loss of mucosal folds, mosaic mucosal pattern, prominence of the submucosal vessels***

Celiac disease



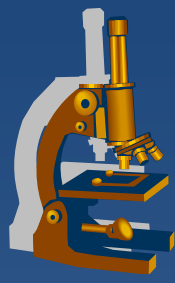
- micro: most changes in the proximal part of the small intestine
- basic histologic features:
  - ***increased number of intraepithelial T-cells***
  - ***inflammatory infiltrate (plasma cells, eosinophils, neutrophils, T-cells) in lamina propria mucosae***
  - ***villous atrophy***
  - ***reactive hyperplasia (elongation) of the crypts***

Marsh classification 0-IV



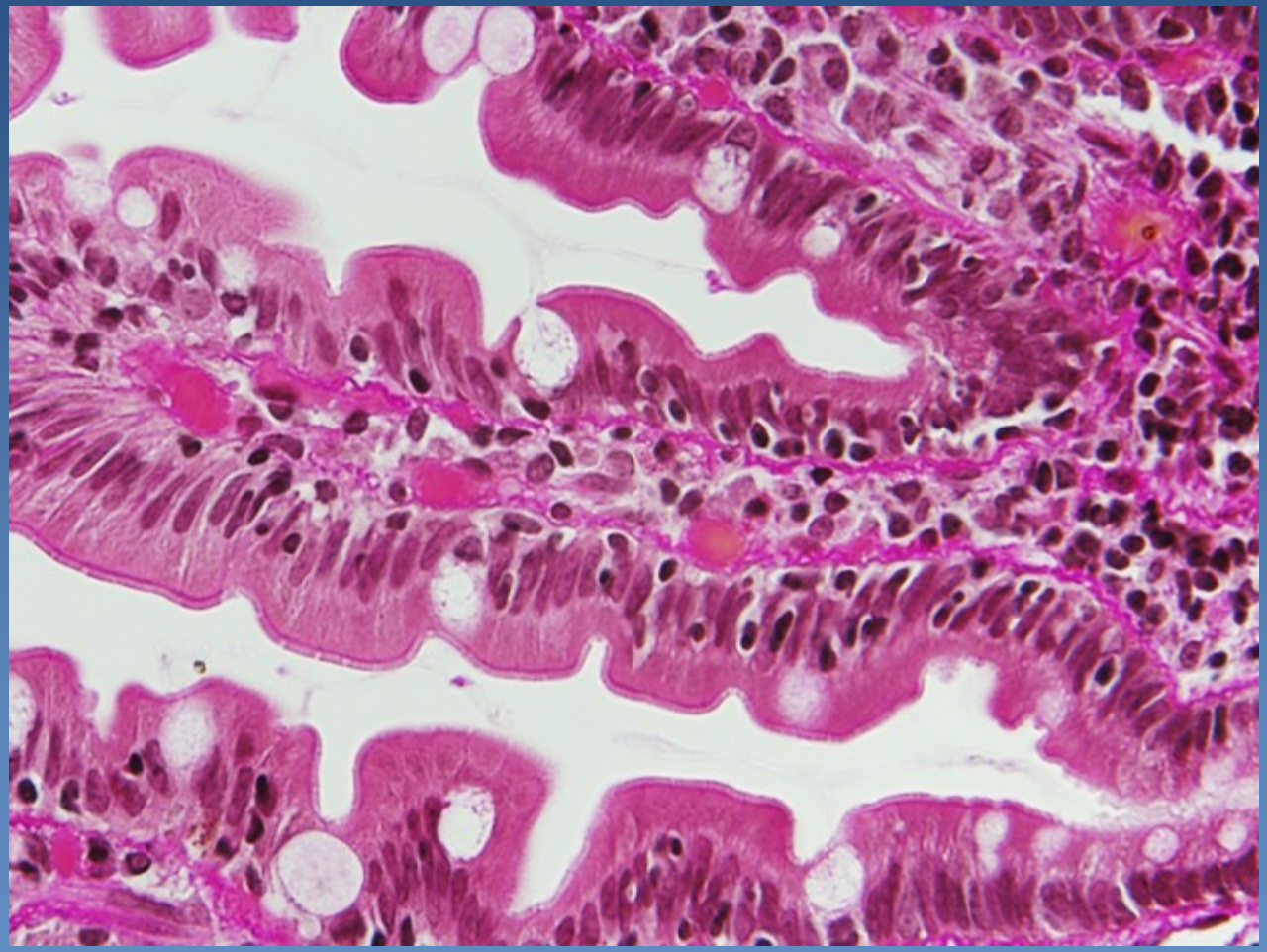
- Stage 0: normal mucosa
- Stage I: infiltrative
  - ⇨ ***increased number of IEL***
- Stage II: hyperplastic
  - ⇨ ***proliferation of the crypts***
- Stage III: destructive
  - ⇨ ***villous atrophy***
- Stage IV: hypoplastic
  - ⇨ ***crypt hypoplasia, loss of villi***

Celiac disease

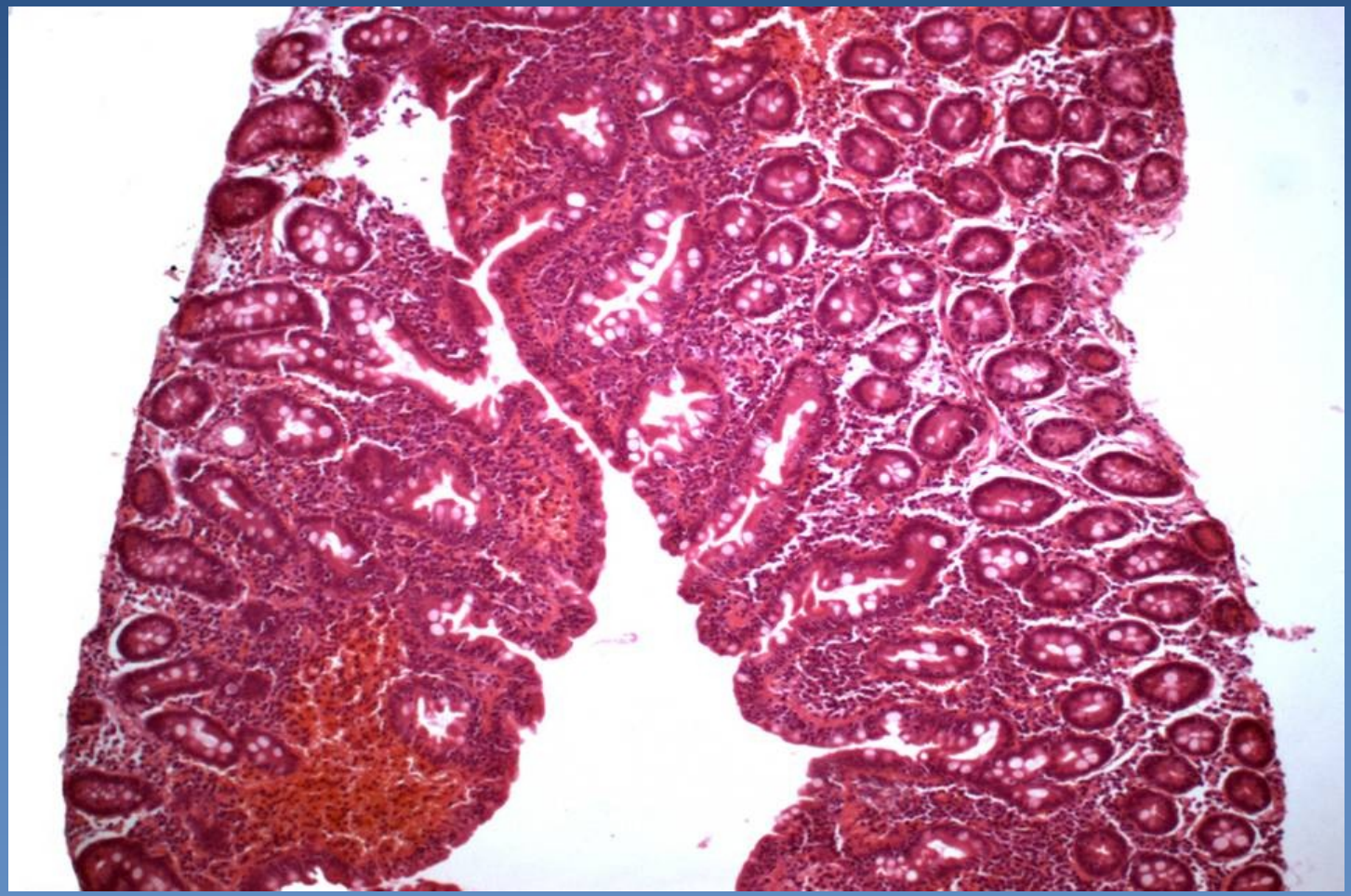


- IEL – specific activated CD8+ T-cell subpopulation
- direct cytotoxic activity – killing of enterocytes
- increased enterocytes‘ turnover
- non-specific histology – diff. dg. alimentary allergies, viral infections, giardiasis, tropical sprue

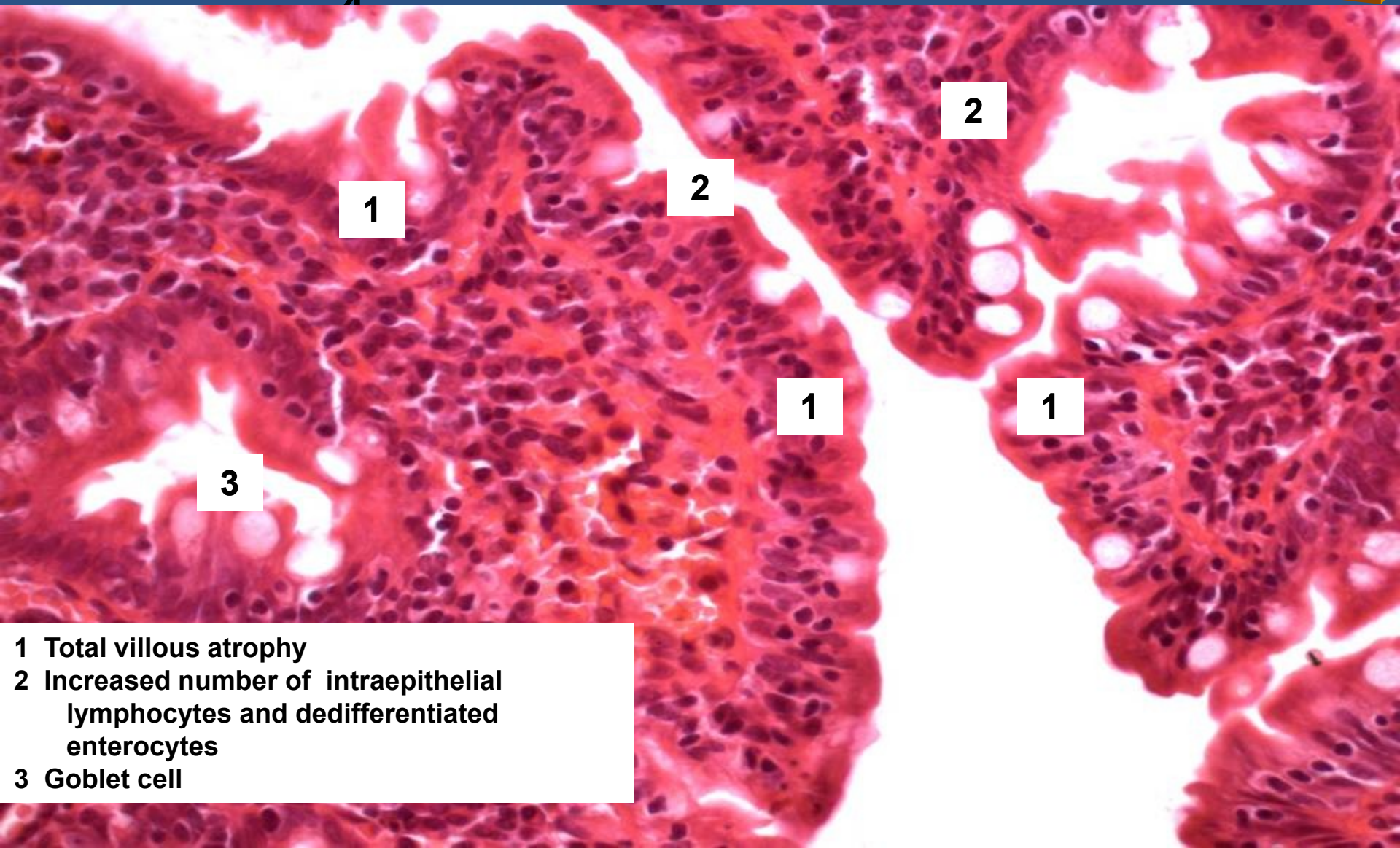
Celiac disease
Marsh I



Celiac disease
Marsh IIIc

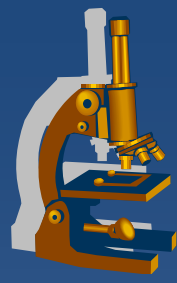


Celiac disease
atrophic mucosa - detail



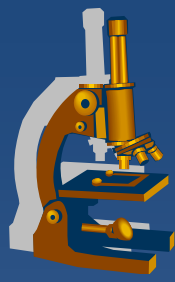
1 Total villous atrophy
2 Increased number of intraepithelial lymphocytes and dedifferentiated enterocytes
3 Goblet cell

Inflammatory bowel disease (IBD)



- idipathic, chronic relapsing inflammatory disorders of not completely known origin
- genetic predisposition, immunologic factors
- etiology:
  - ⇨ ***aberrant local immune response to exogenous stimulus (microbiome)→ increased transepithelial permeability → inflammation acceleration***
- **Crohn disease**
- **Ulcerative colitis**
- **Indeterminated colitis (10-15%)**

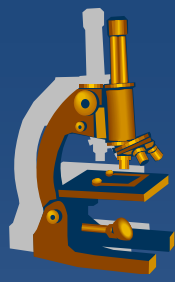
IBD



- common histologic features:

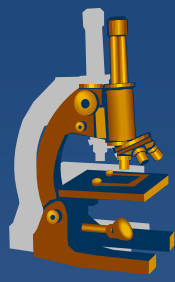
1) abnormal crypt architecture
2) crypt atrophy
3) dense inflammatory infiltrate in lamina propria, basal plasmacytosis
4) Paneth cell metaplasia in the left colon

Crohn's disease



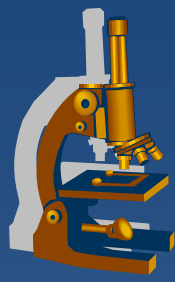
- Clinical features:
  - ***recurrent attacks of diarrhea, abdominal pain, fever***
  - ***abrupt beginning, lasting days to weeks, symptom-free intervals,***
  - ***common other AI diseases:***
    - iritis, ankylosing spondylitis, erythema nodosum, PSC
- Gross:
  - ***terminal ileum****, or anywhere else in the GIT (oral-anus)*
  - ***sharply demarcated , segmental lesions and skip lesions:***
    - shallow → longitudinal ulcers
    - wall stenosis and thickening, fissuring, fistulae

Crohn's disease



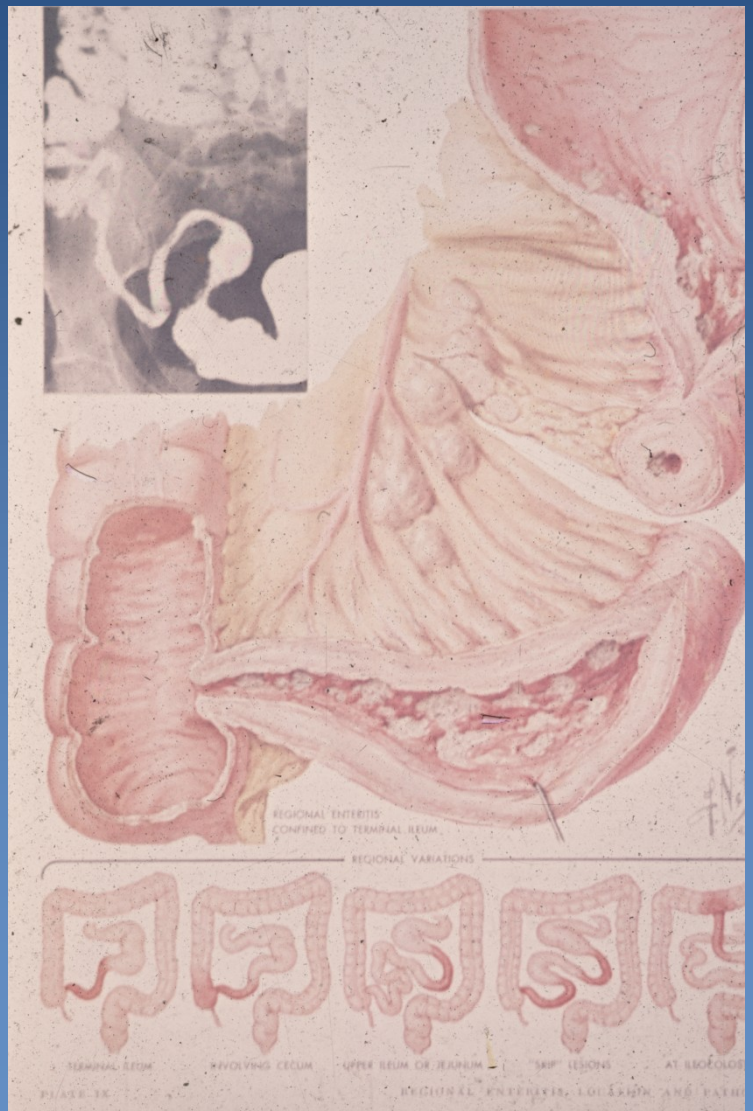
- Histology:
  - ⇨ ***transmural** inflammatory infiltrate*
  - ⇨ *formation of lymphatic follicles/germinal centres*
  - ⇨ ***non-caseating granulomas** (not always present) in submucosa, subserosa and regional lymph nodes*
  - ⇨ *fissuring, ulceration*
  - ⇨ *fibrosis*

Crohn's disease

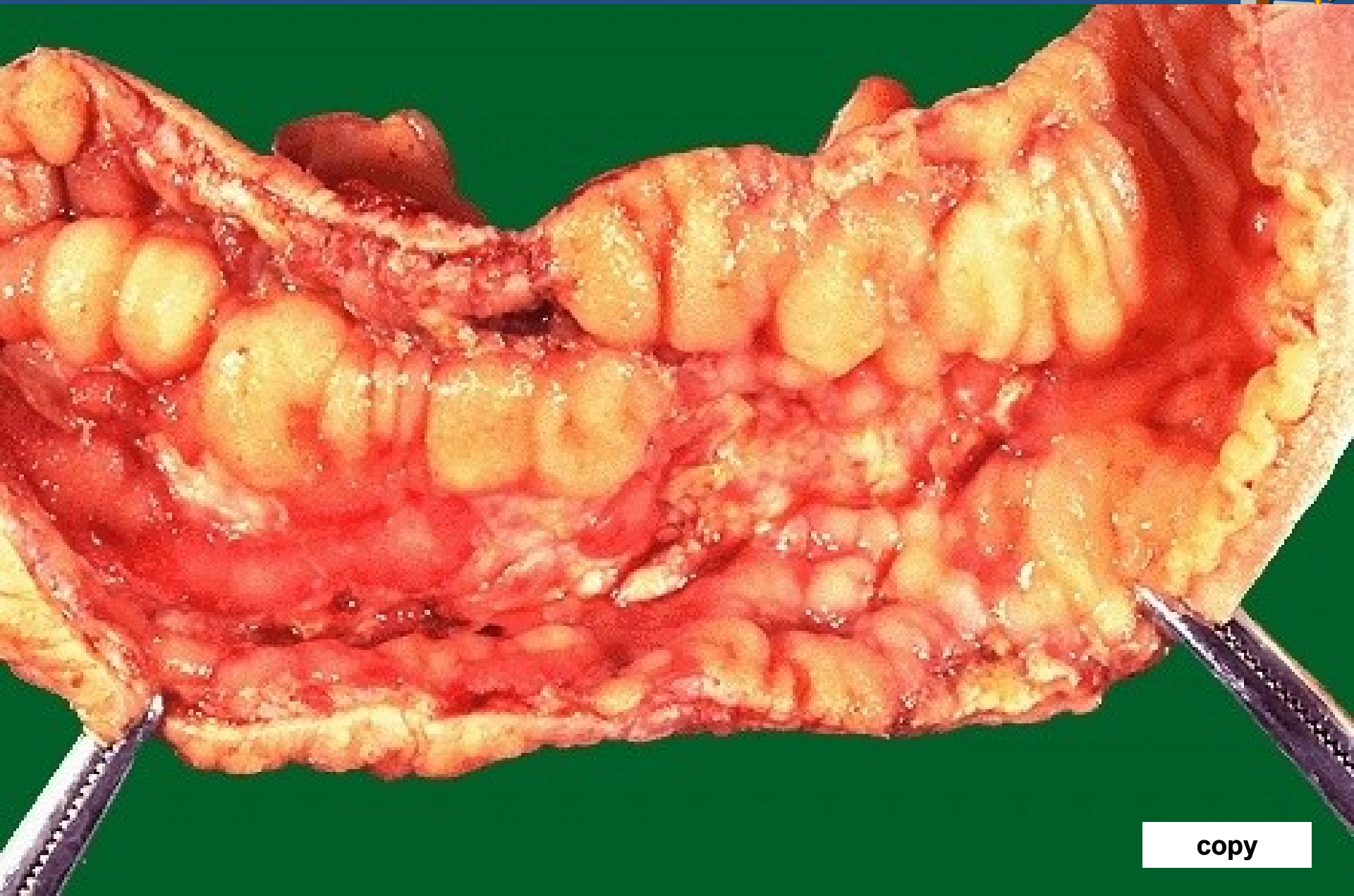


- Complications:
  - ⇨ *narrowed lumen, intestinal strictures, obstruction*
  - ⇨ *malabsorption, protein loss*
  - ⇨ *perforation, peritonitis, fistulae formation*
  - ⇨ *hemorrhage*
  - ⇨ *systemic AA amyloidosis*
  - ⇨ *carcinoma*

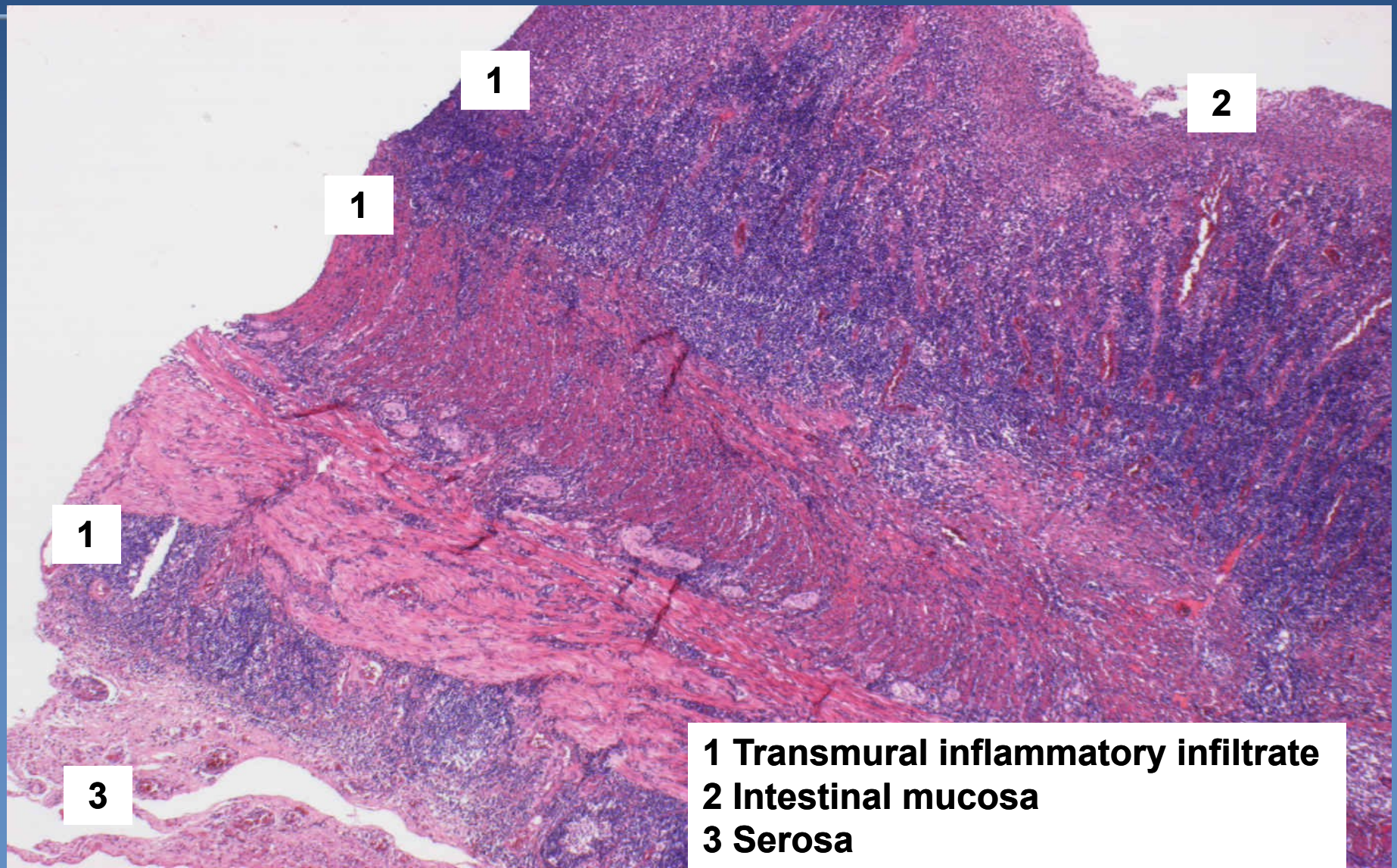
Crohn's disease



Crohn's disease

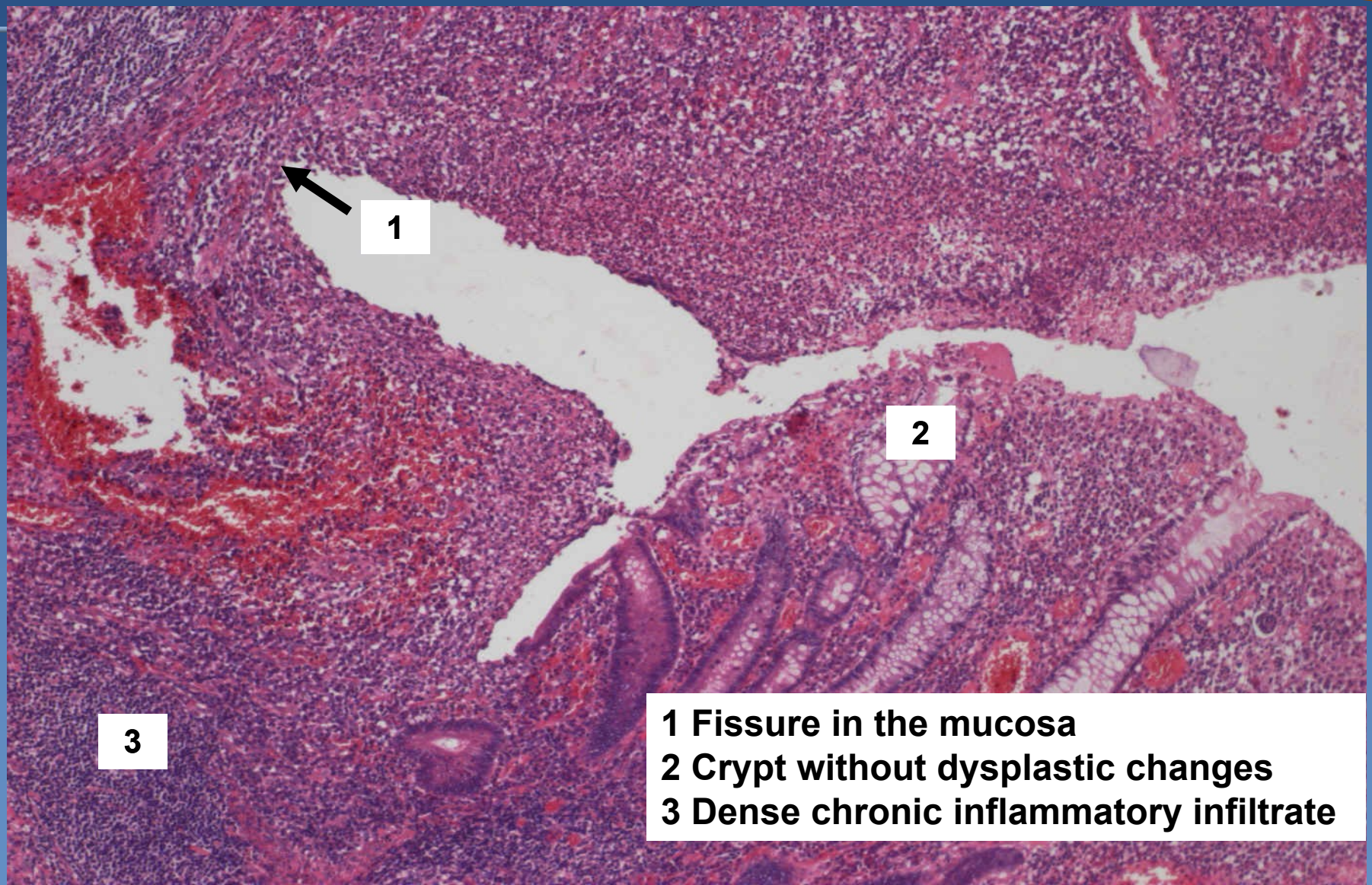


Crohn's disease in the colon
(transmural chronic inflammatory infiltrate)



1 Transmural inflammatory infiltrate
2 Intestinal mucosa
3 Serosa

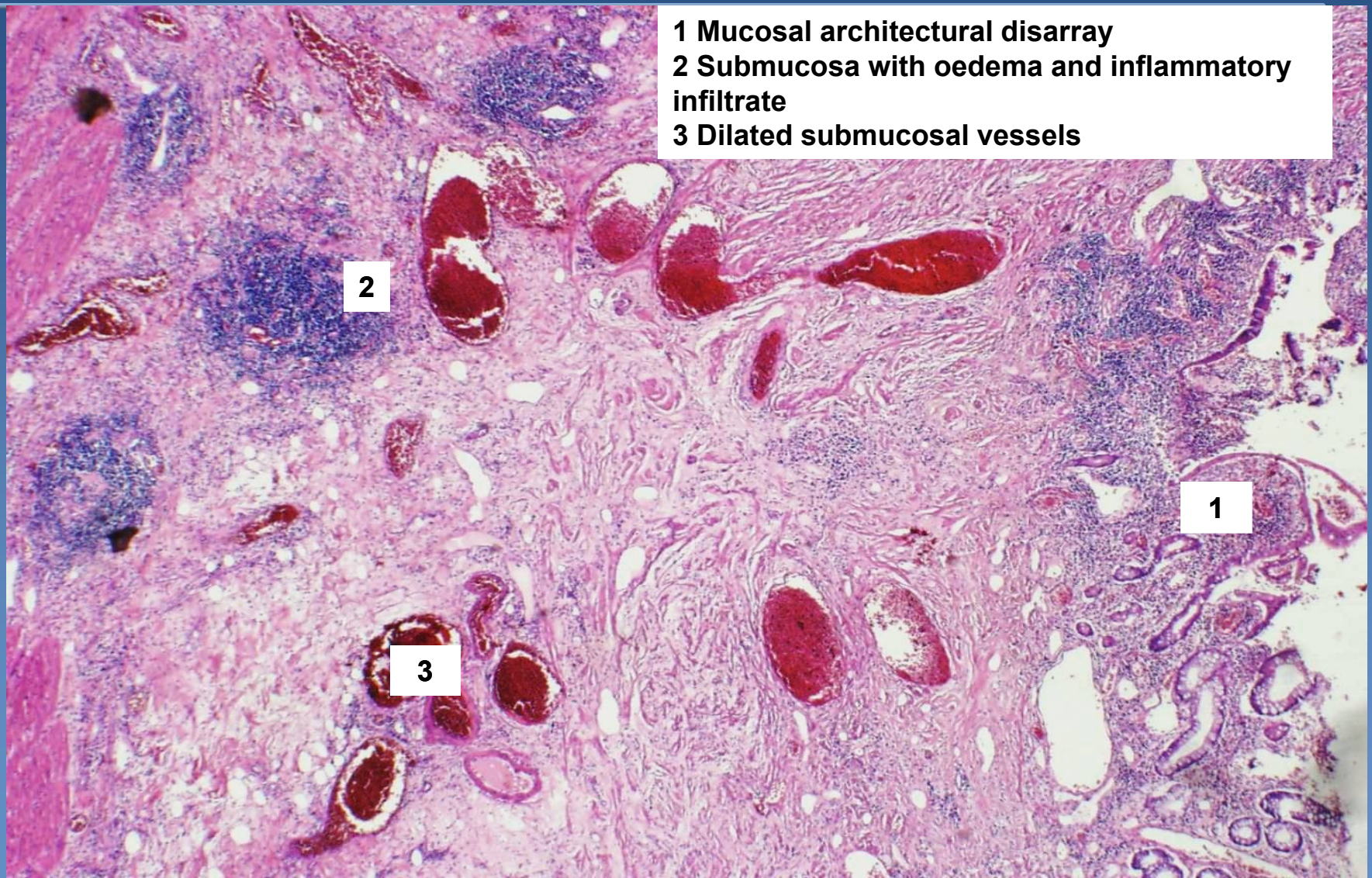
Crohn's disease - Enteritis regionalis



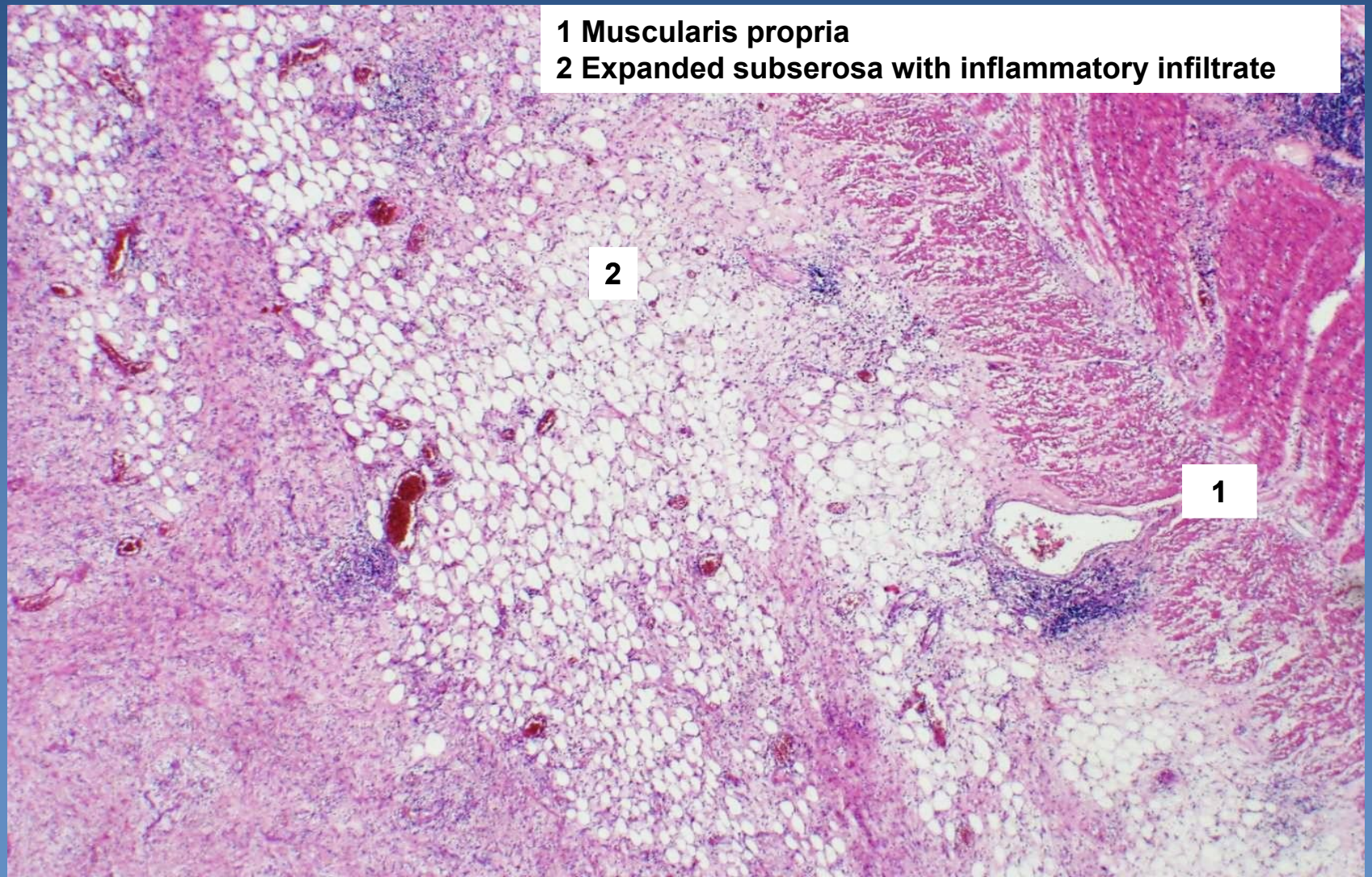
1 Fissure in the mucosa
2 Crypt without dysplastic changes
3 Dense chronic inflammatory infiltrate

Crohn's disease

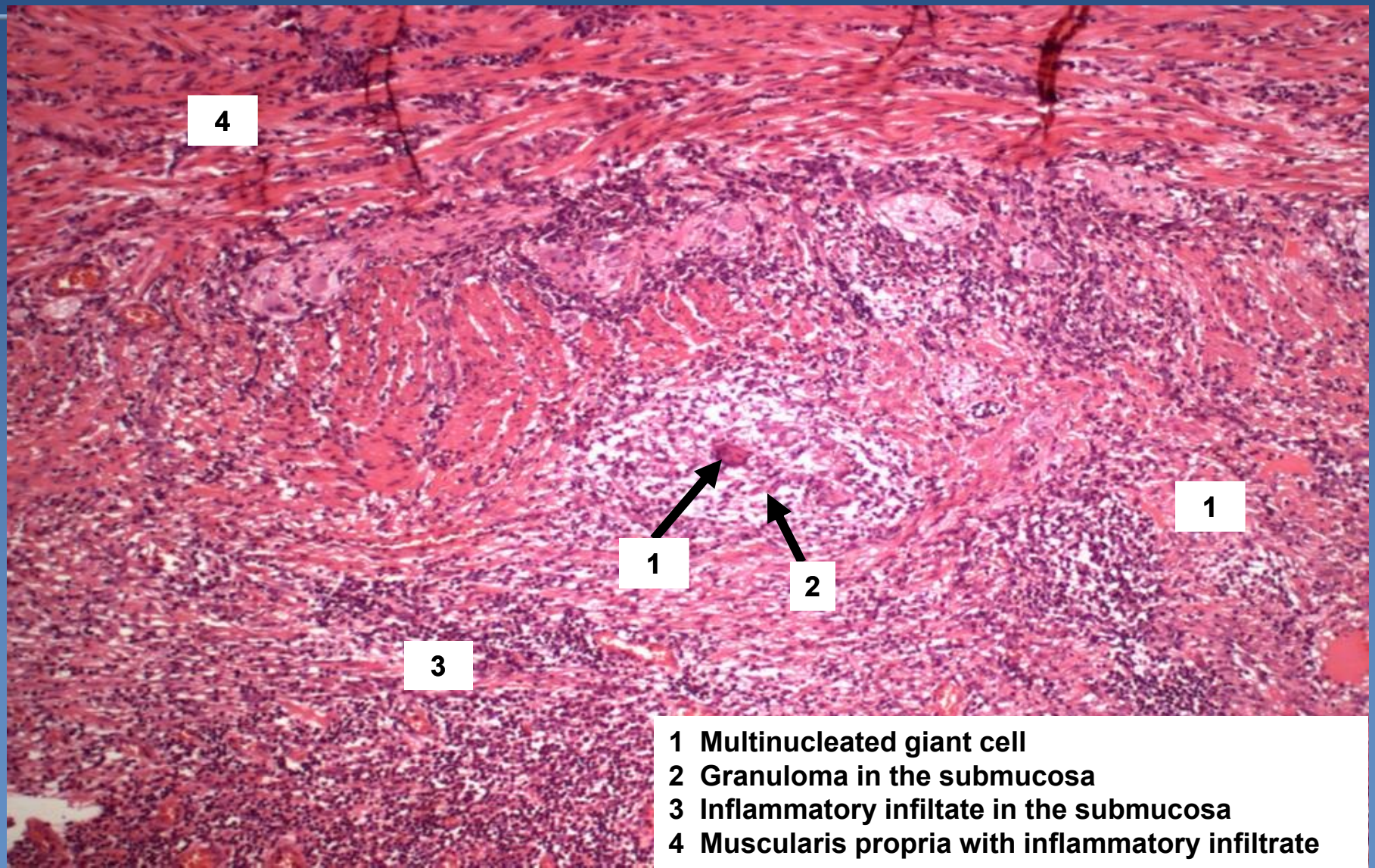
inflammatory infiltrate in the submucosa



Crohn's disease
inflammatory infiltrate in the subserosa

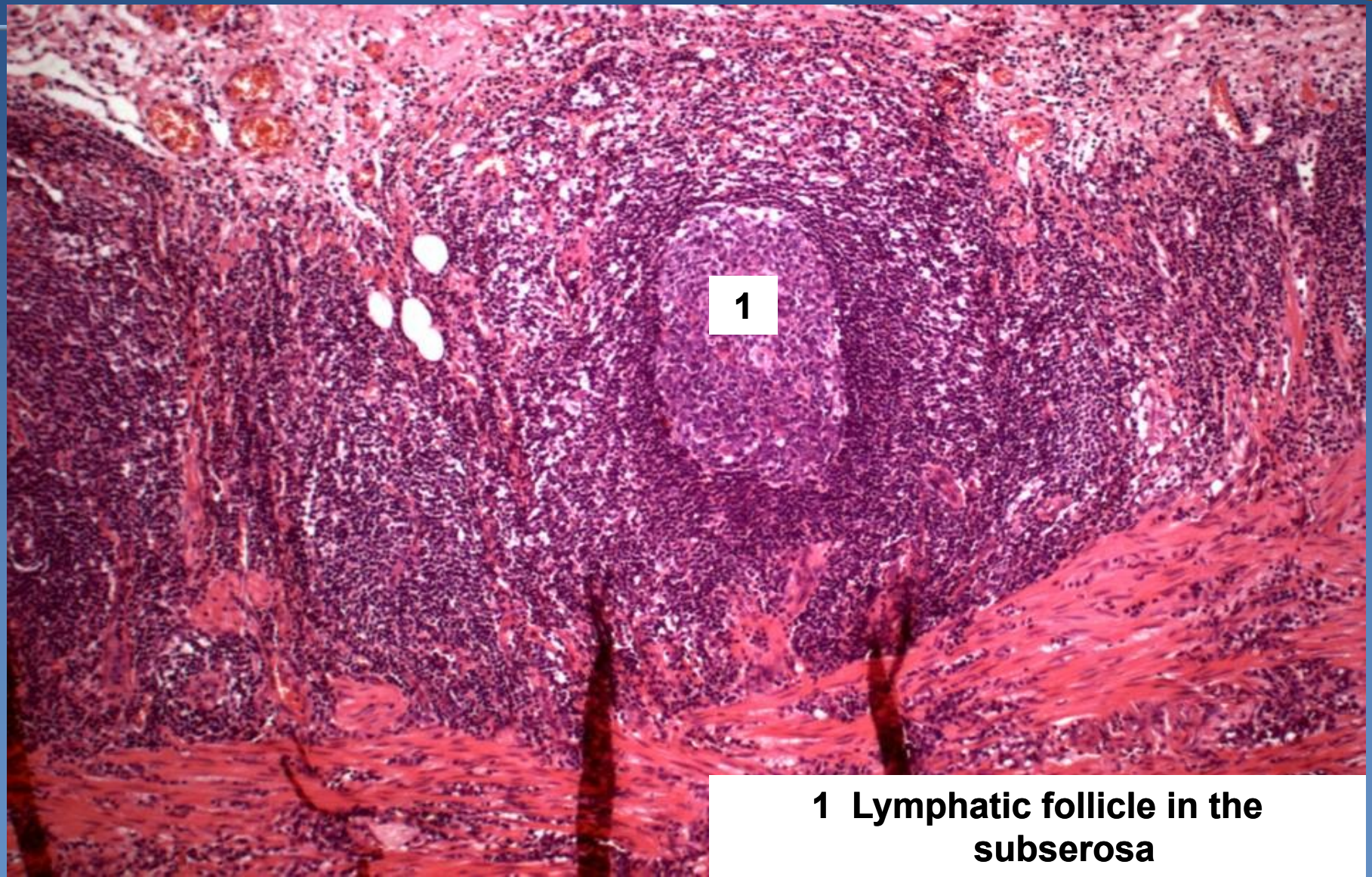


Crohn's disease
- granuloma in the submucosa



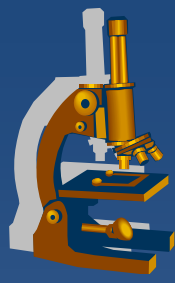
1 Multinucleated giant cell
2 Granuloma in the submucosa
3 Inflammatory infiltate in the submucosa
4 Muscularis propria with inflammatory infiltrate

Crohn's disease
- inflammatory infiltrate



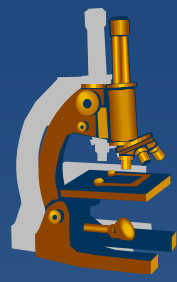
1 Lymphatic follicle in the subserosa

Ulcerative colitis



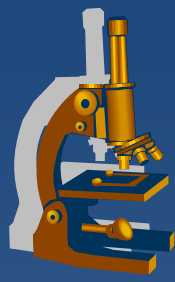
- Clinical features:
  - ⇨ *relapsing attacks of bloody mucoid diarrhea, cramps, lower abdominal pain*
  - ⇨ *start - rectum + sigmoid, continuous retrograde extension, may affect the entire colon (pancolitis)*
  - ⇨ *unclear etiology, autoimmune and genetic factors, variable triggers*
  - ⇨ *associated with systemic disorders (eye, skin, joint, bile tract – primary sclerosing cholangitis)*
- Gross:
  - ⇨ *hyperemia, oedema, flat ulcerations, regenerative hyperplastic mucosa forming pseudopolyps*

Ulcerative colitis



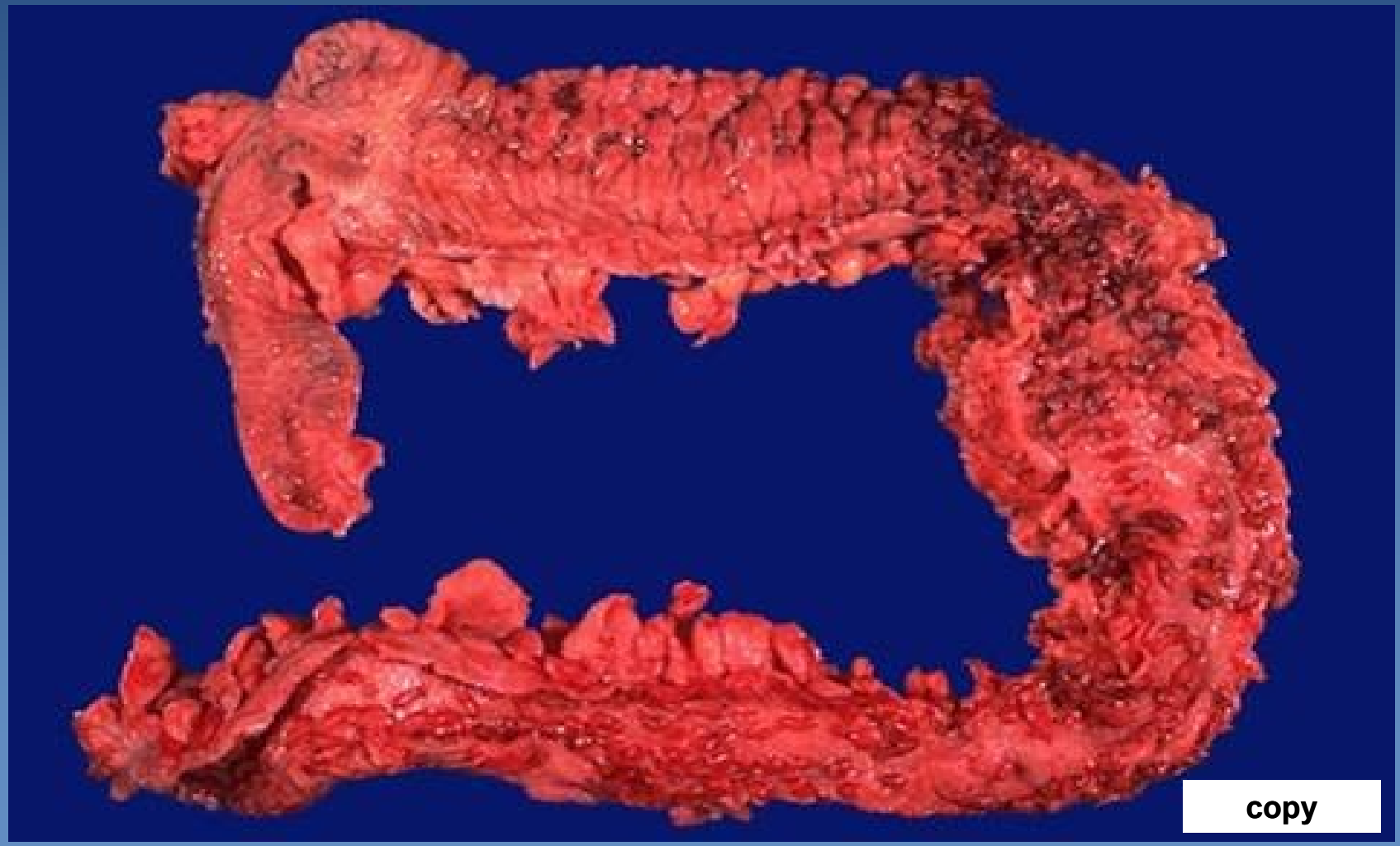
- Micro:
  - ⇨ ***non-specific inflammatory infiltrate only in the mucosa and submucosa***
  - ⇨ ***crypt abscesses, crypt destruction***
  - ⇨ ***no granulomas, no skip lesions***
  - ⇨ ***very little fibrosis, no mural thickening***
  - ⇨ ***high risk of carcinoma development***

Ulcerative colitis

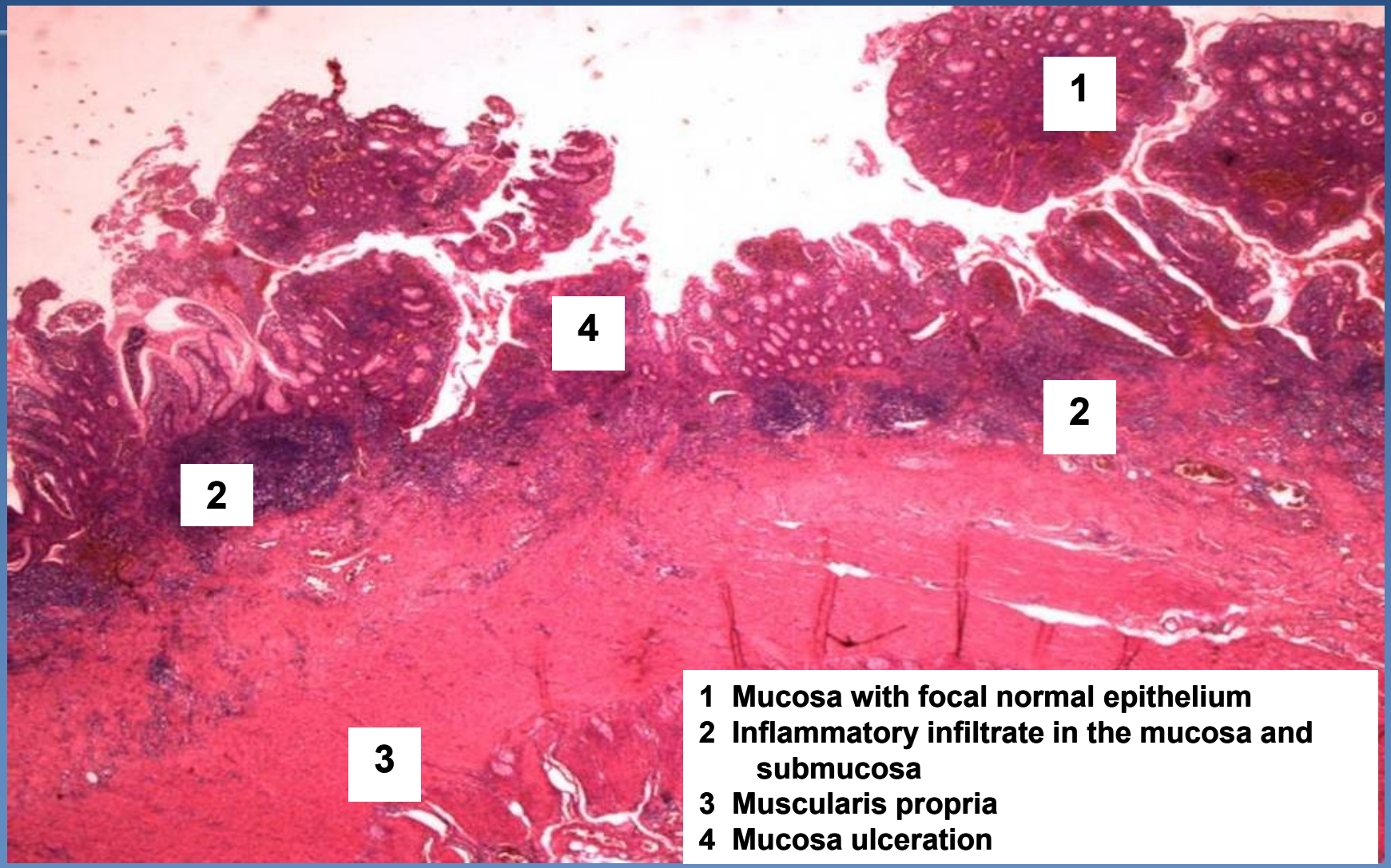


- Microscopic phases of the inflammation:
  - ⇨ ***1. active***
    - hyperemia, mixed inflammatory infiltrate, crypt abscesses
  - ⇨ ***2. healing***
    - less neutrophils, no crypt abscesses, epithelial regeneration
  - ⇨ ***3. remission***
    - mucosal architectural disarray, atrophy, inflammatory changes sm. only in the **rectum**
- Complications:
  - ⇨ ***toxic megacolon, hemorrhage, perforation, peritonitis, carcinoma development***

Ulcerative colitis
- gross

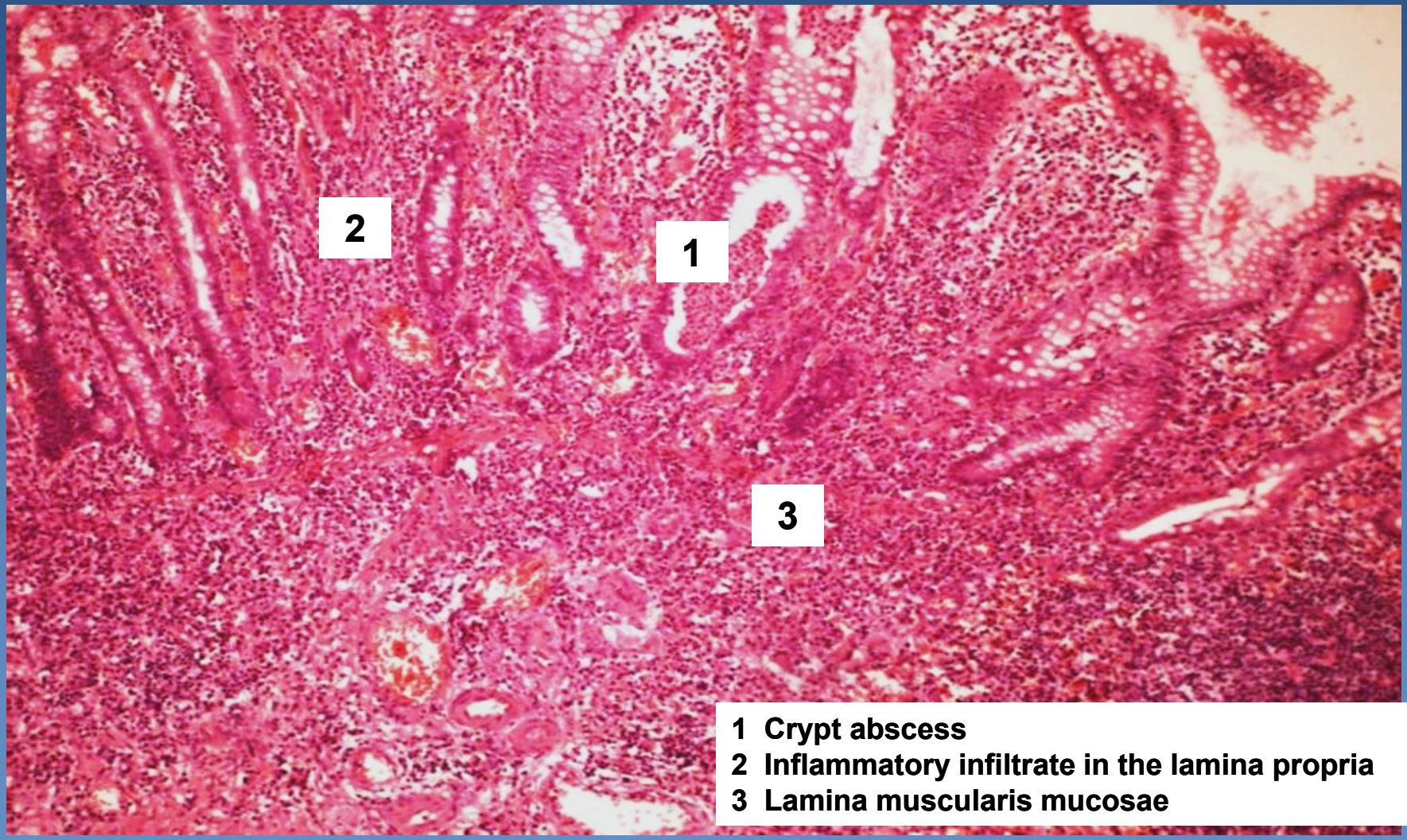


Ulcerative colitis
superficial inflammatory infiltrate



1 Mucosa with focal normal epithelium
2 Inflammatory infiltrate in the mucosa and submucosa
3 Muscularis propria
4 Mucosa ulceration

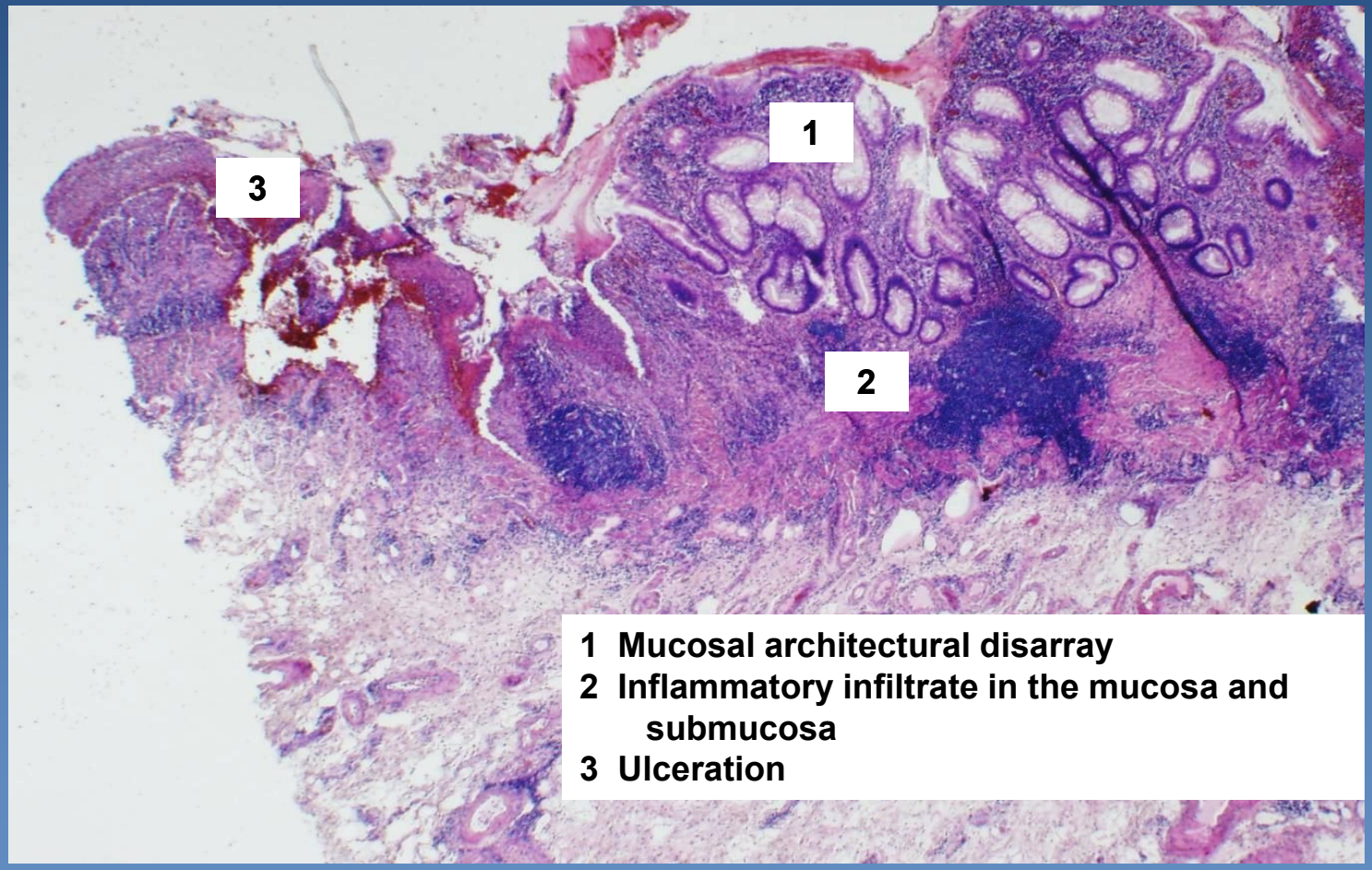
Ulcerative colitis - crypt abscess



Ulcerative colitis - dysplastic changes in the epithelium

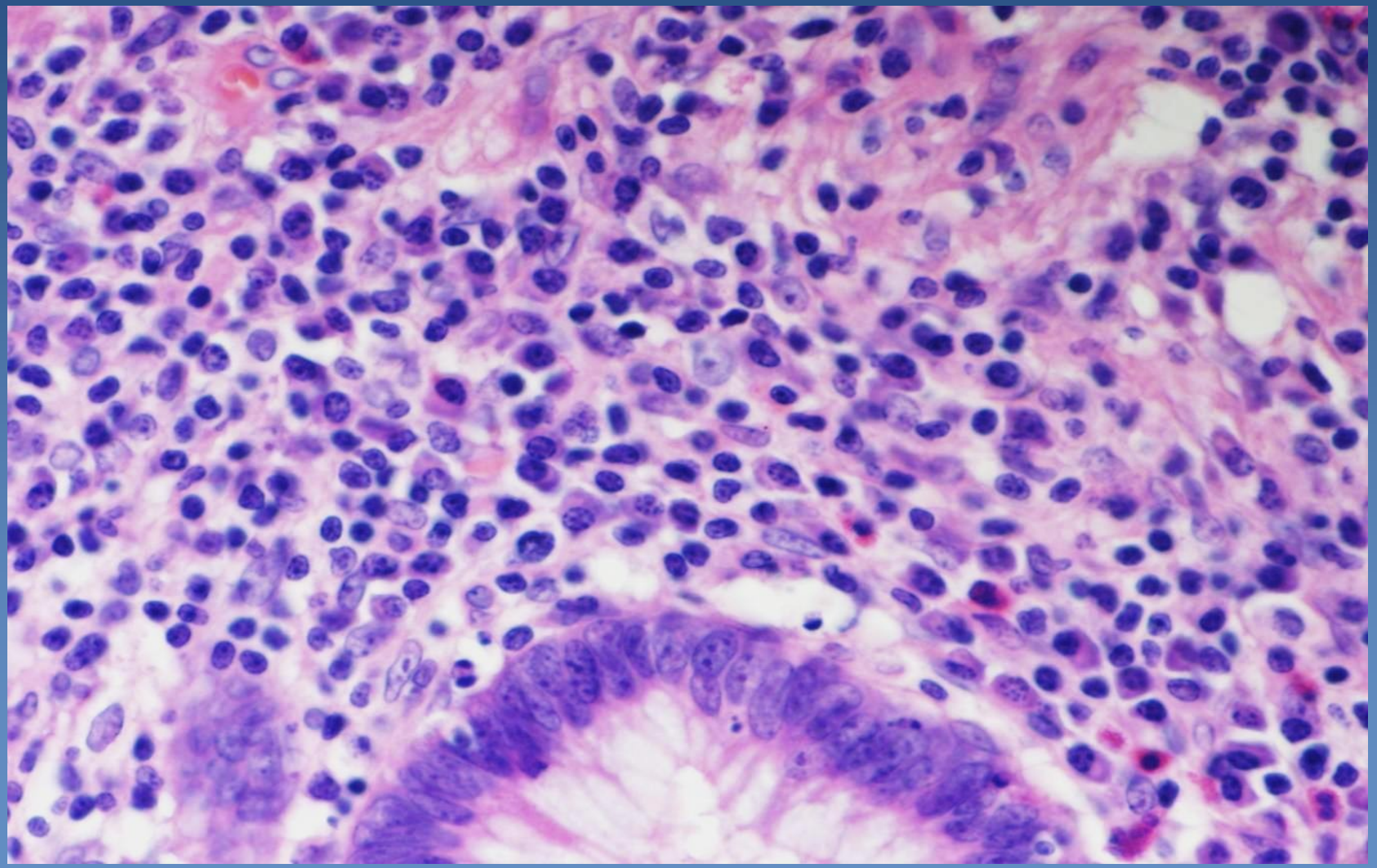
1 Dysplastic changes in the epithelium
2 Mixed inflammatory infiltrate

Ulcerative colitis

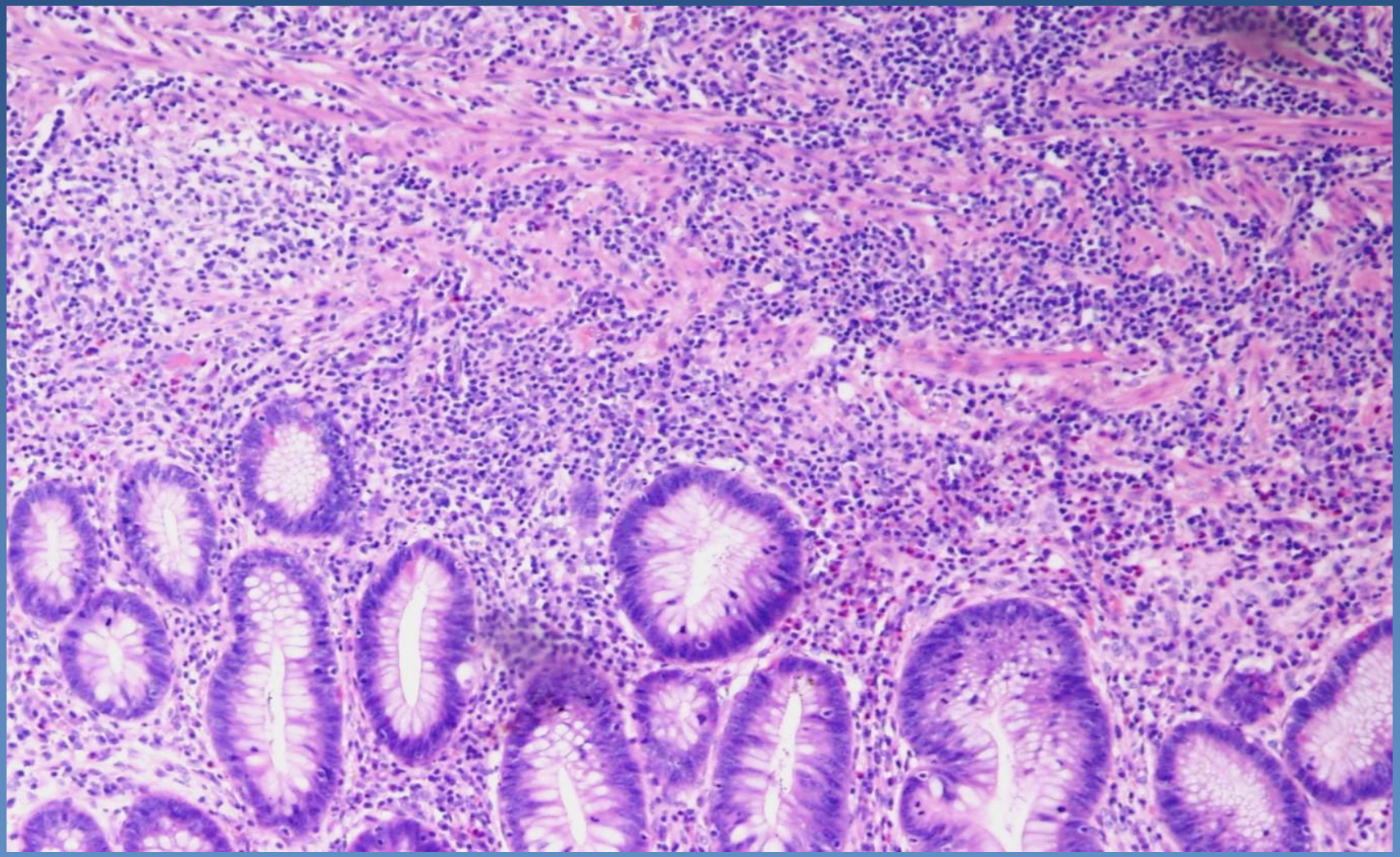


1 Mucosal architectural disarray
2 Inflammatory infiltrate in the mucosa and submucosa
3 Ulceration

Ulcerative colitis
basal plasmacytosis

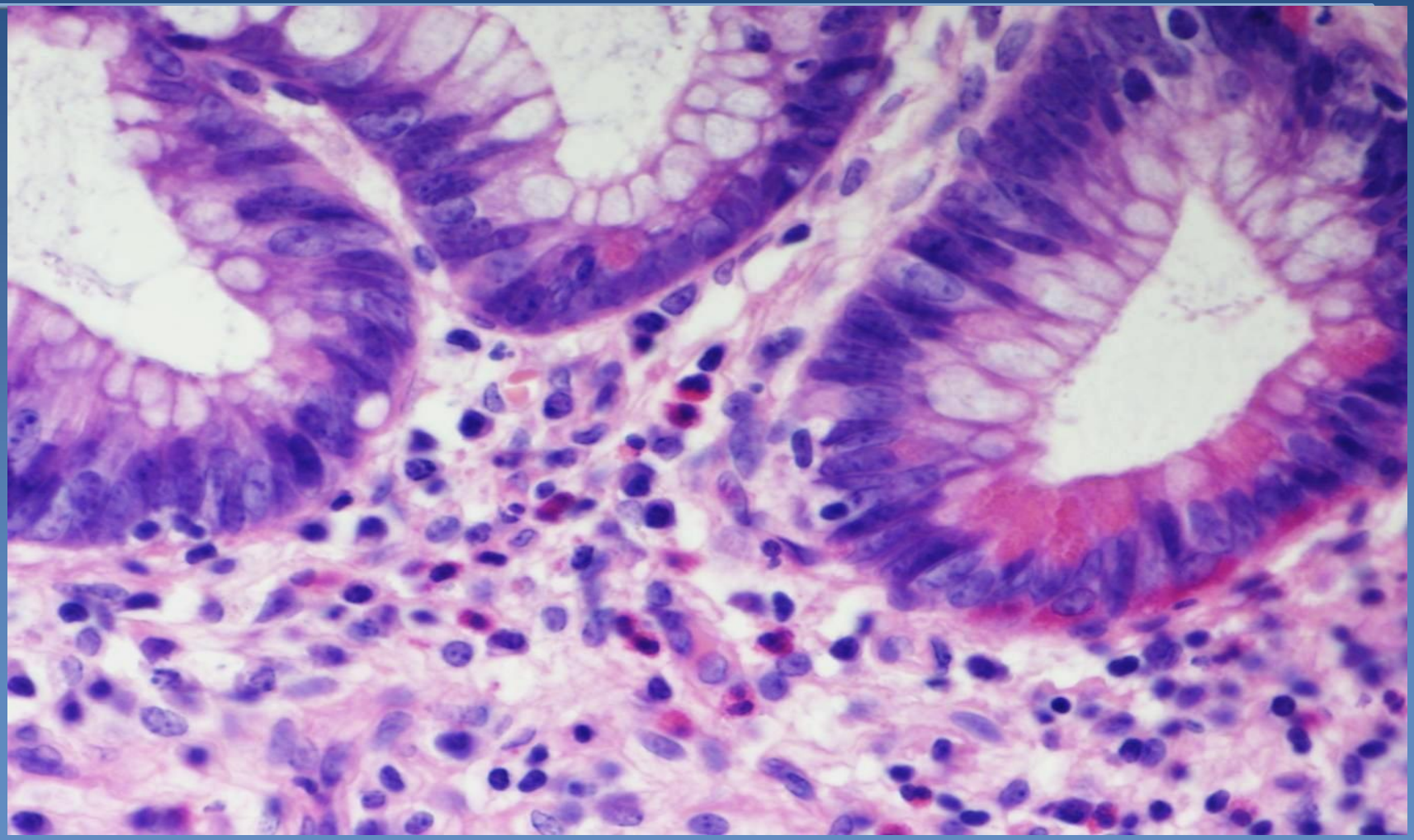


Ulcerative colitis
basal plasmacytosis



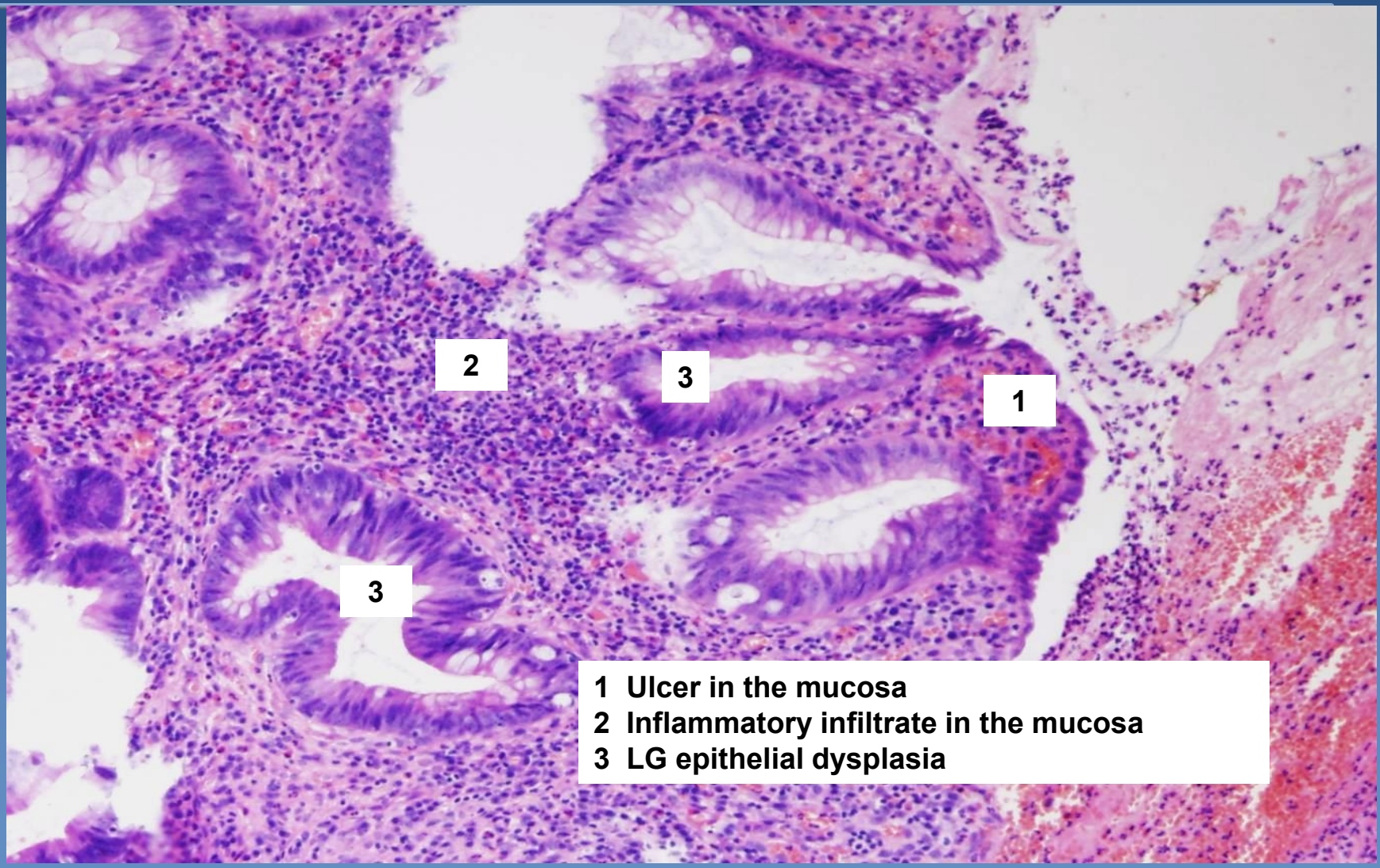
Ulcerative colitis

Paneth cell metaplasia in the left colon

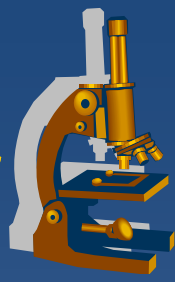


Ulcerative colitis

epithelial dysplasia

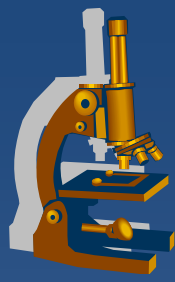


Further types of enterocolitis



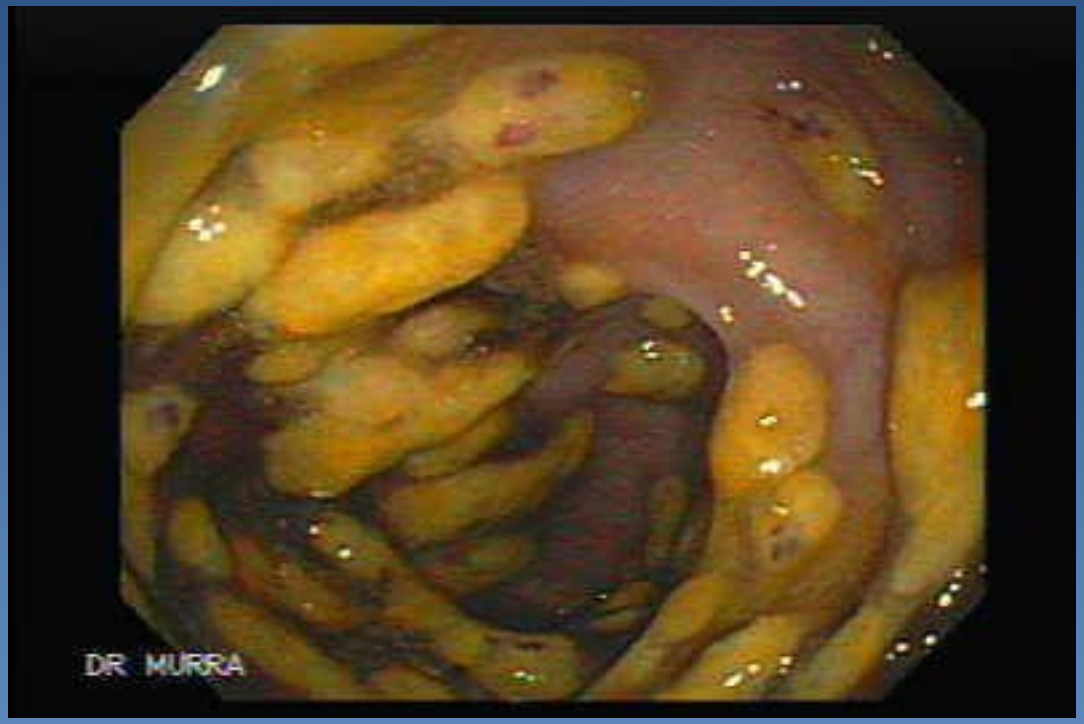
- pseudomembranous
- ischemic
  - ⇨***short-term decreased blood supply to the intestine (shock, trauma, surgery)***
- microscopic (collagenous, lymphocytic)
  - ⇨***chronic watery diarrhea, normal colonoscopy, associated with autoimmune diseases***
- infectious
- postradiation
- others

Pseudomembranous colitis



- etiology:
  - ***infection – bacterial (Clostridium difficile, Salmonella, Staph. aureus)***
  - ***antibiotic-associated***
  - ***uremia***
- gross:
  - ***greyish pseudomembranes on the mucosal surface, ulcers***
- micro:
  - ***fibrinous pseudomembrane with neutrophils, bacteria and macrophages, adherent to the necrotic mucosa***

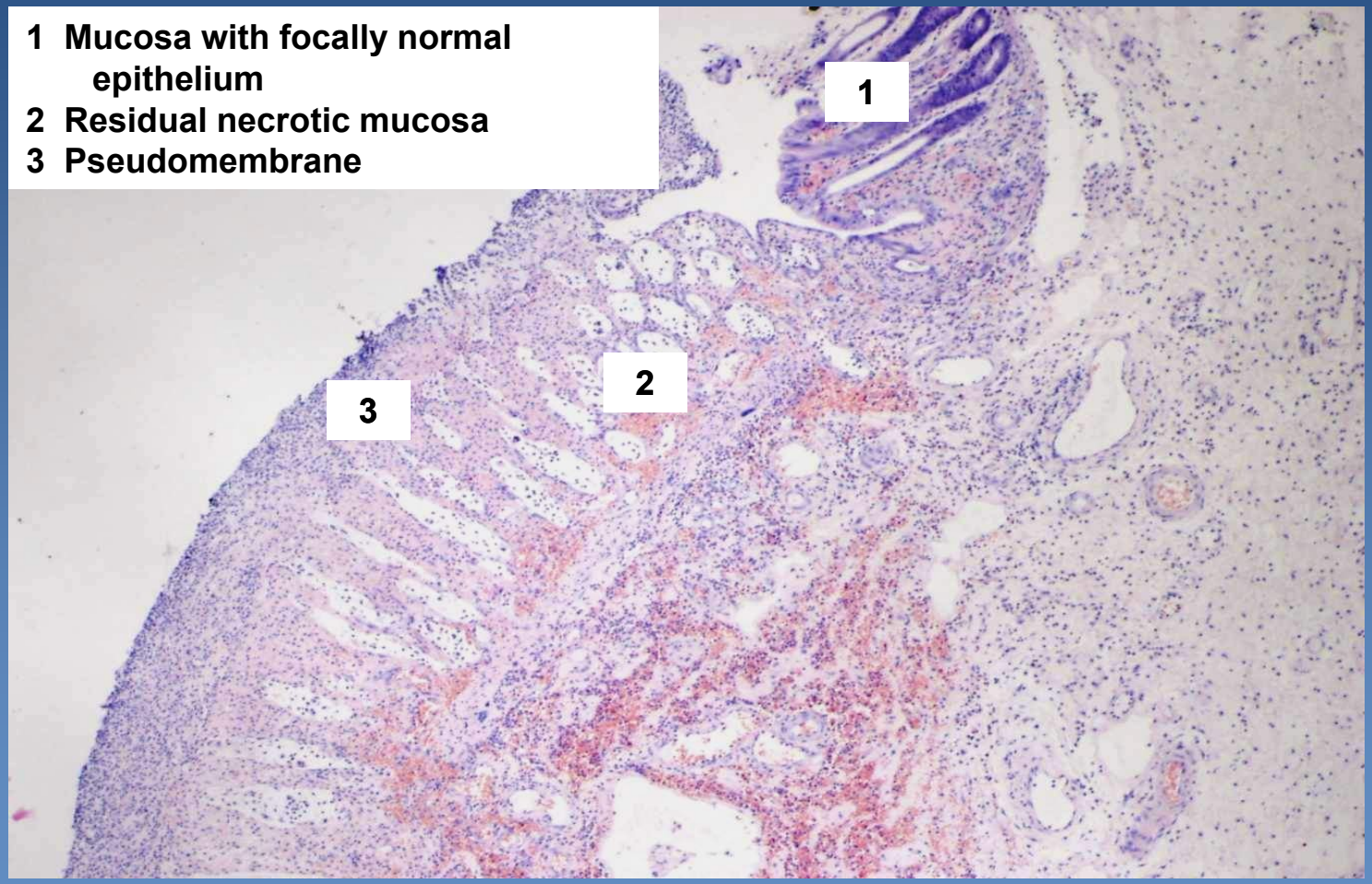
Pseudomembranous colitis



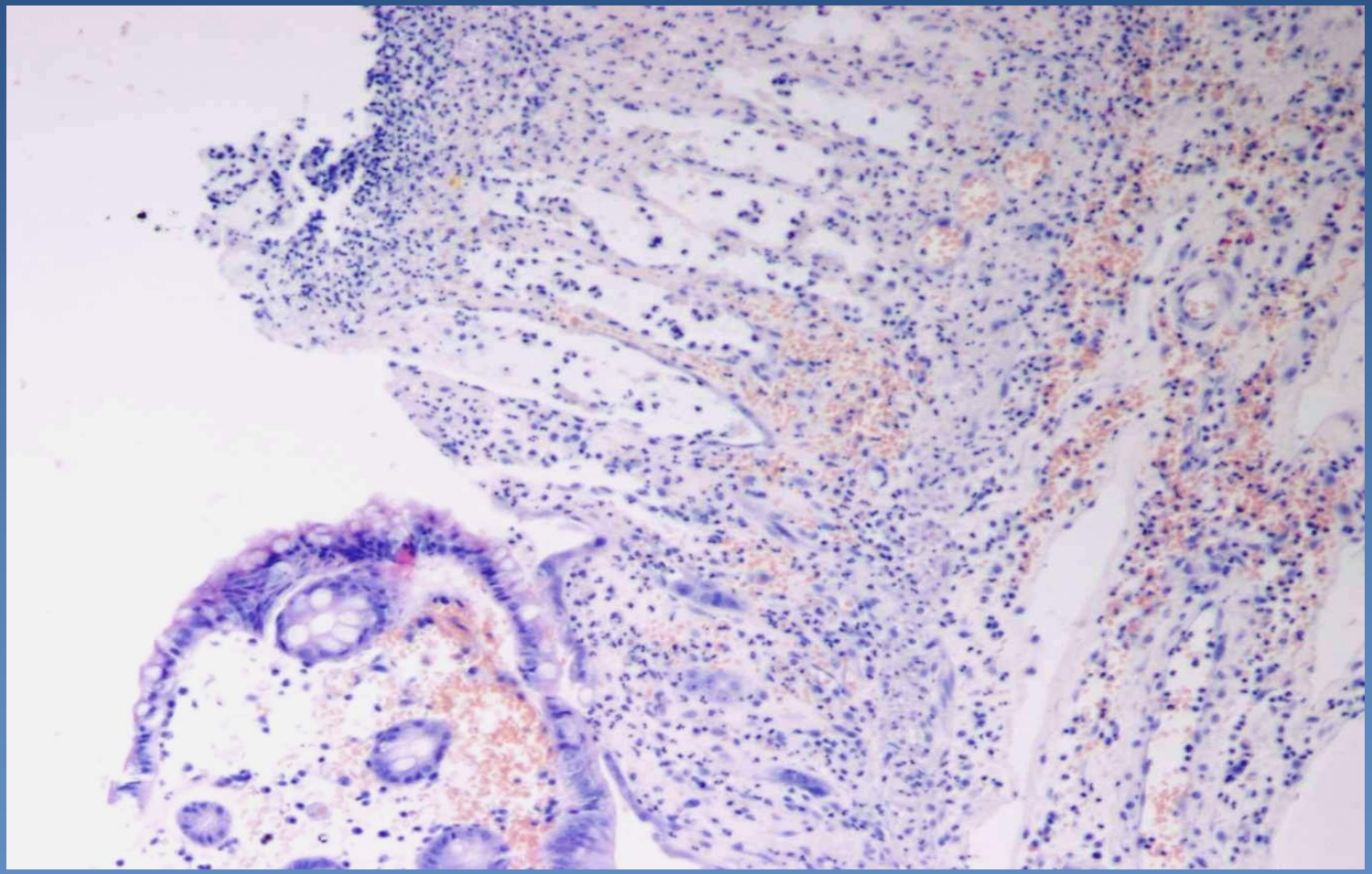
- Endoscopy (copy)

Pseudomembranous colitis

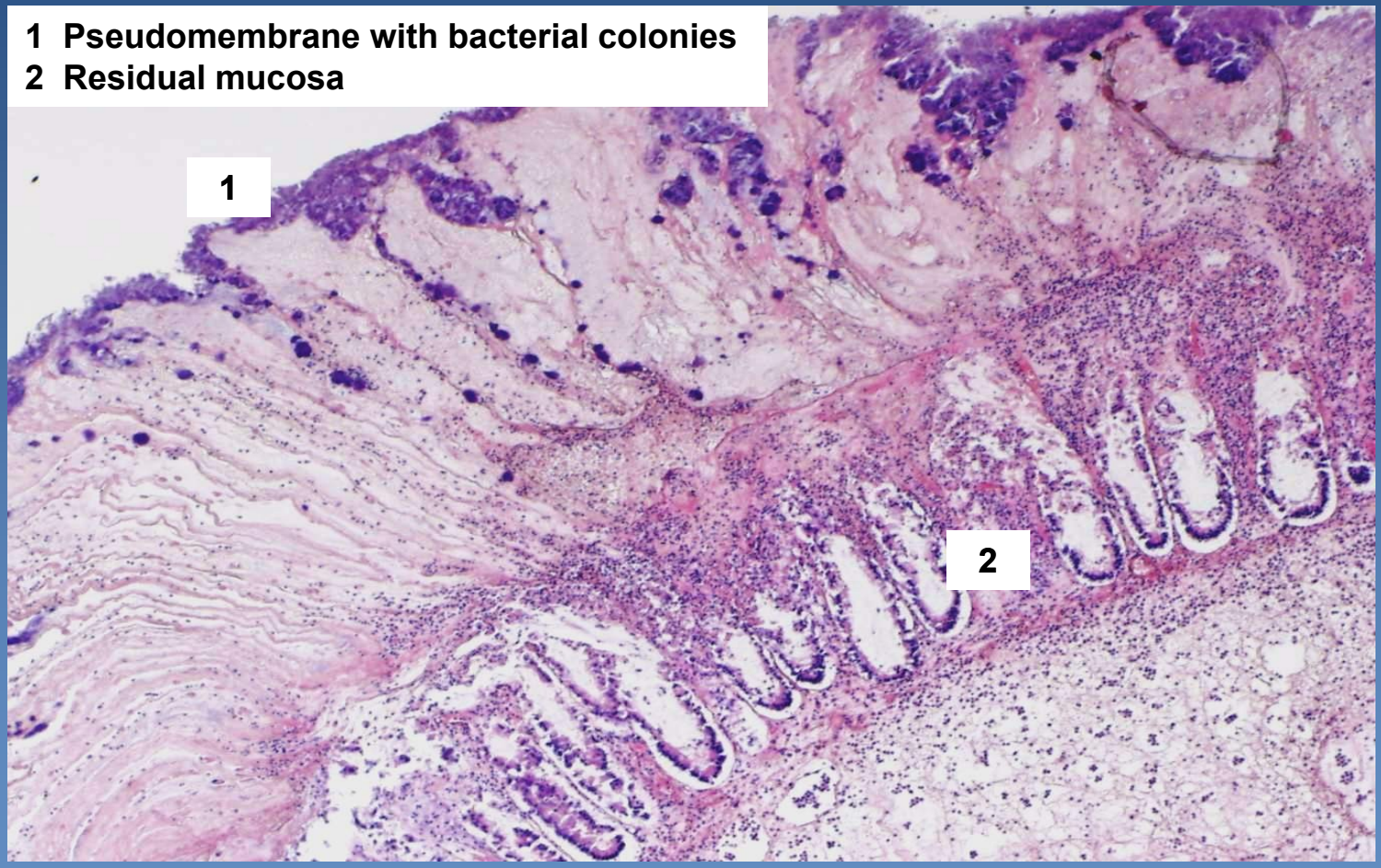
1 Mucosa with focally normal epithelium
2 Residual necrotic mucosa
3 Pseudomembrane



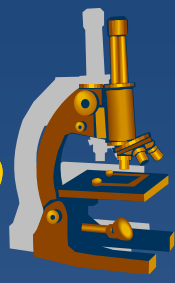
Pseudomembranous colitis - detail



Pseudomembranous colitis
(Clostridium difficile etiology)

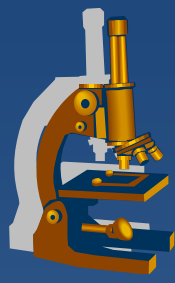


Ileus – intestinal obstruction/disruption of the normal motility



- mechanic (strangulation, obturation)
  - ⇨ ***Adhesions***
  - ⇨ ***hernias***
  - ⇨ ***volvulus***
  - ⇨ ***invagination***
  - ⇨ ***tumors***
  - ⇨ ***obstruction (foreign body)***
  - ⇨ ***congenital atresia***
  - ⇨ ***meconial in cystic fibrosis***
- dynamic
  - ⇨ ***paralytic: toxic-infective, drugs, peritonitis, post-operative***
  - ⇨ ***vascular: hemorrhagic infarction***
  - ⇨ ***myopathy, neuropathy***
  - ⇨ ***Hirschprung‘ disease***

Ileus

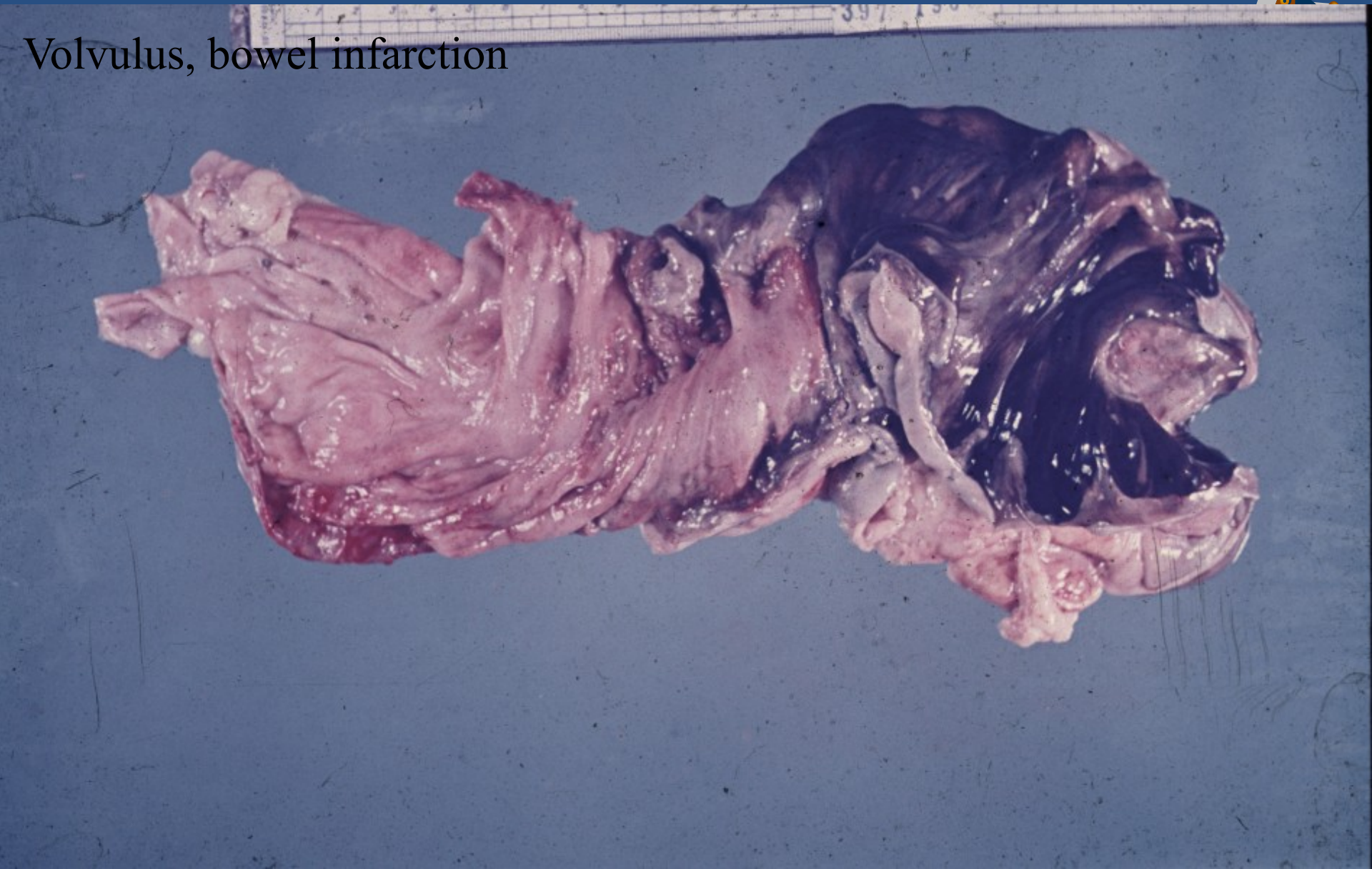


- Clinical features: signs of „acute abdomen“ with acute pain, cramps, abdominal distention, nausea and vomiting, stop of the stool/gases passage
- Type / severity of the signs acccording to localisation + stage of obstruction

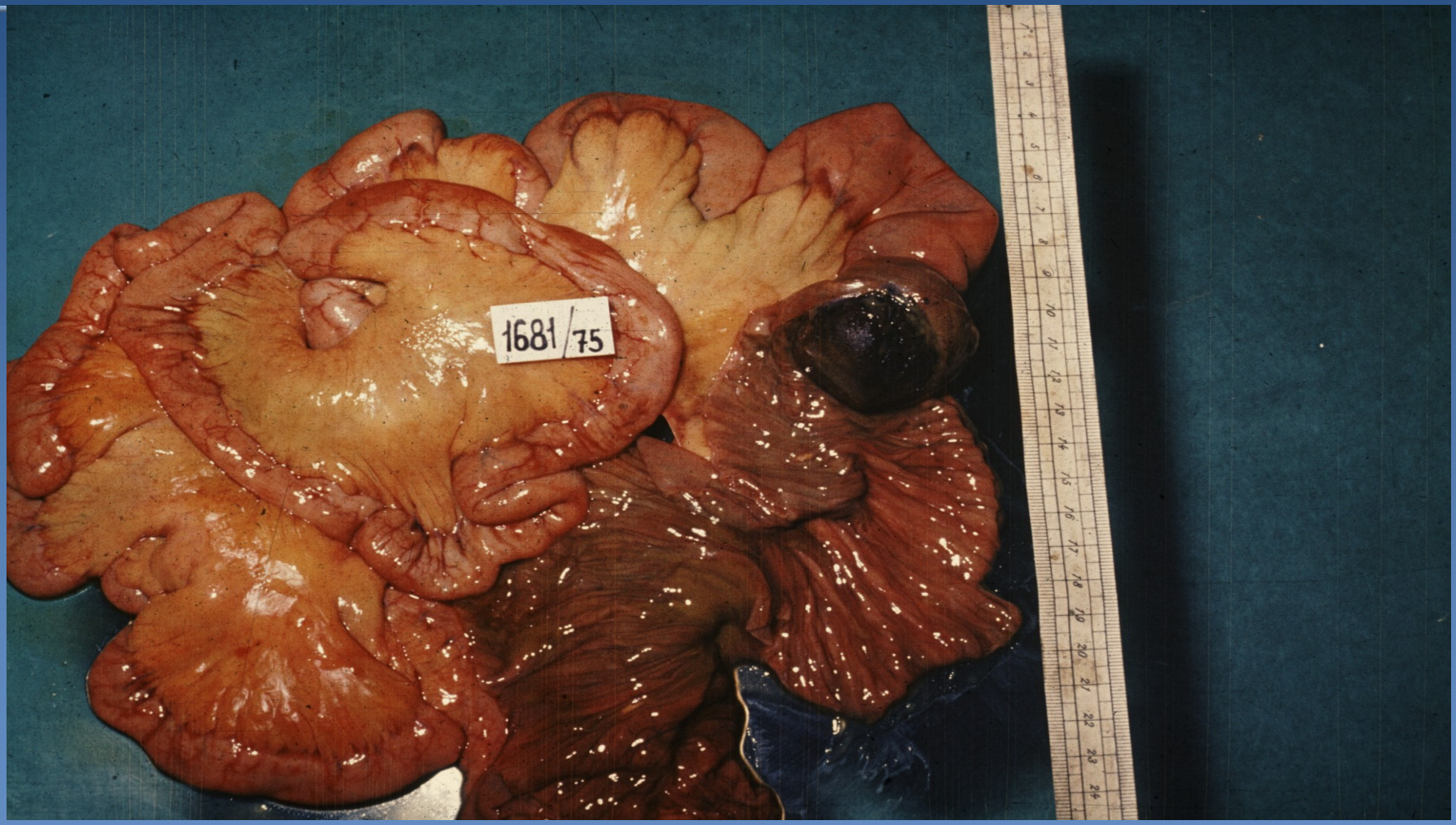
- Intestinal wall in/above the obstruction:

  dilatation → inflammation → (peritonitis, sepsis) → mural necrosis → perforation → stercoral (fecal) peritonitis

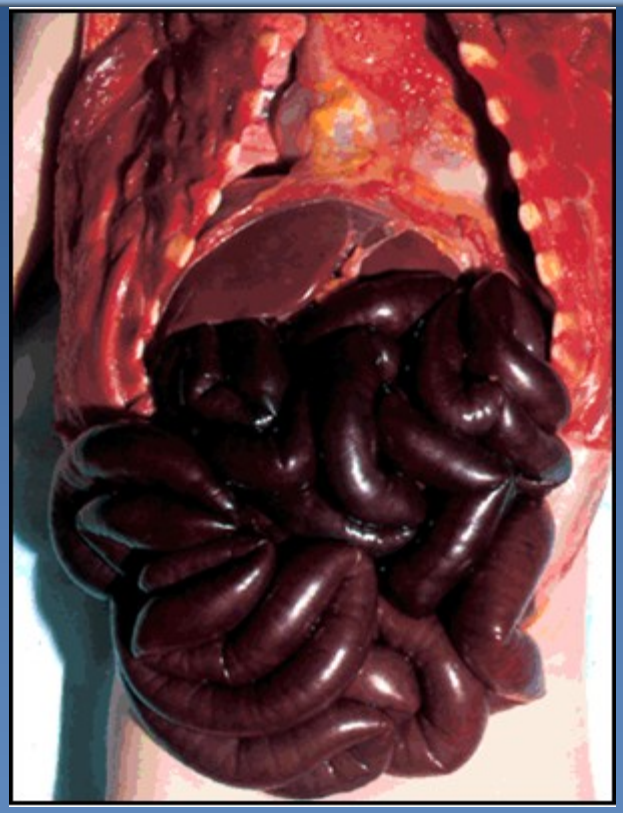
Volvulus, bowel infarction



Gallstone ileus



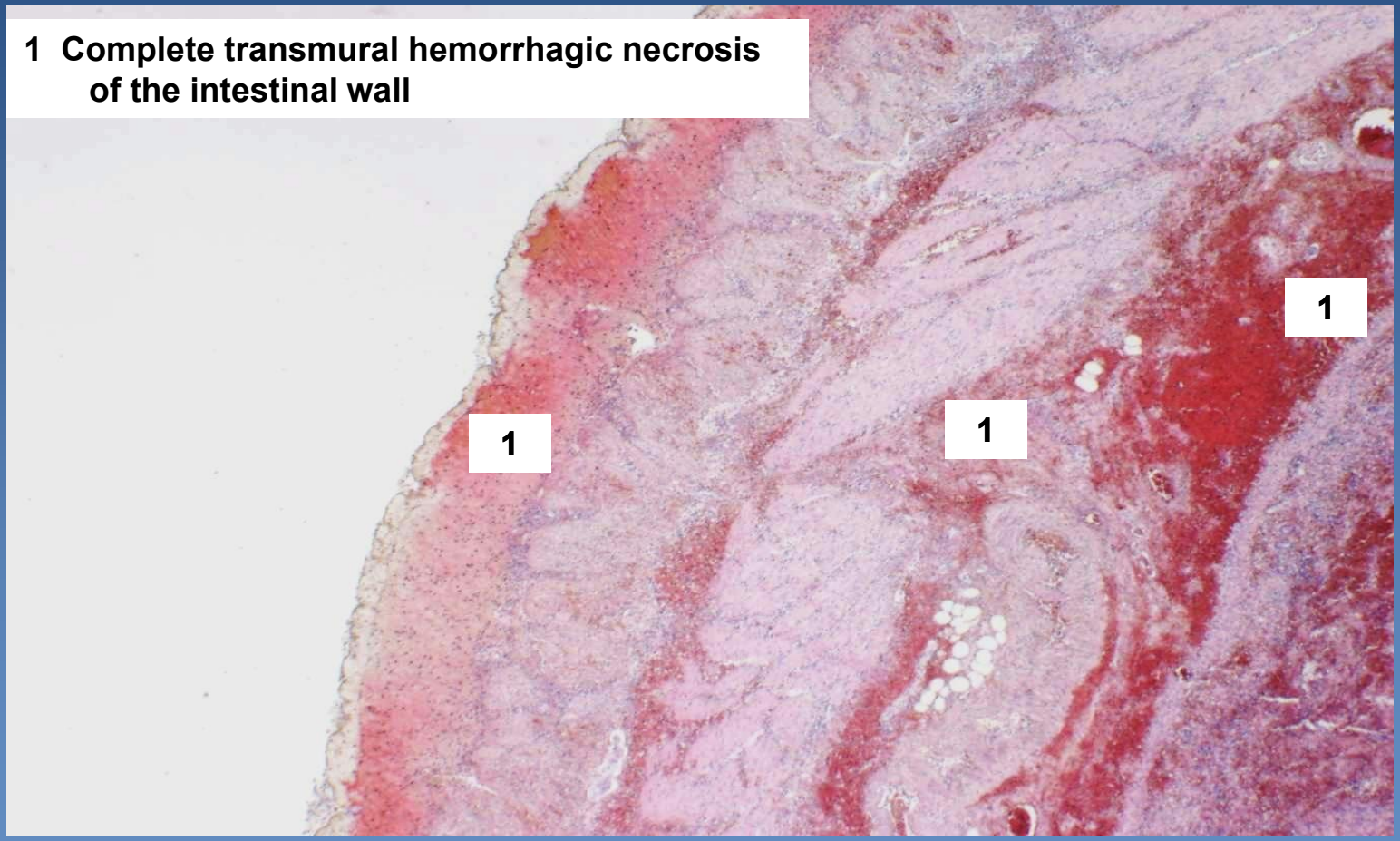
Hemorrhagic infarction of the intestine



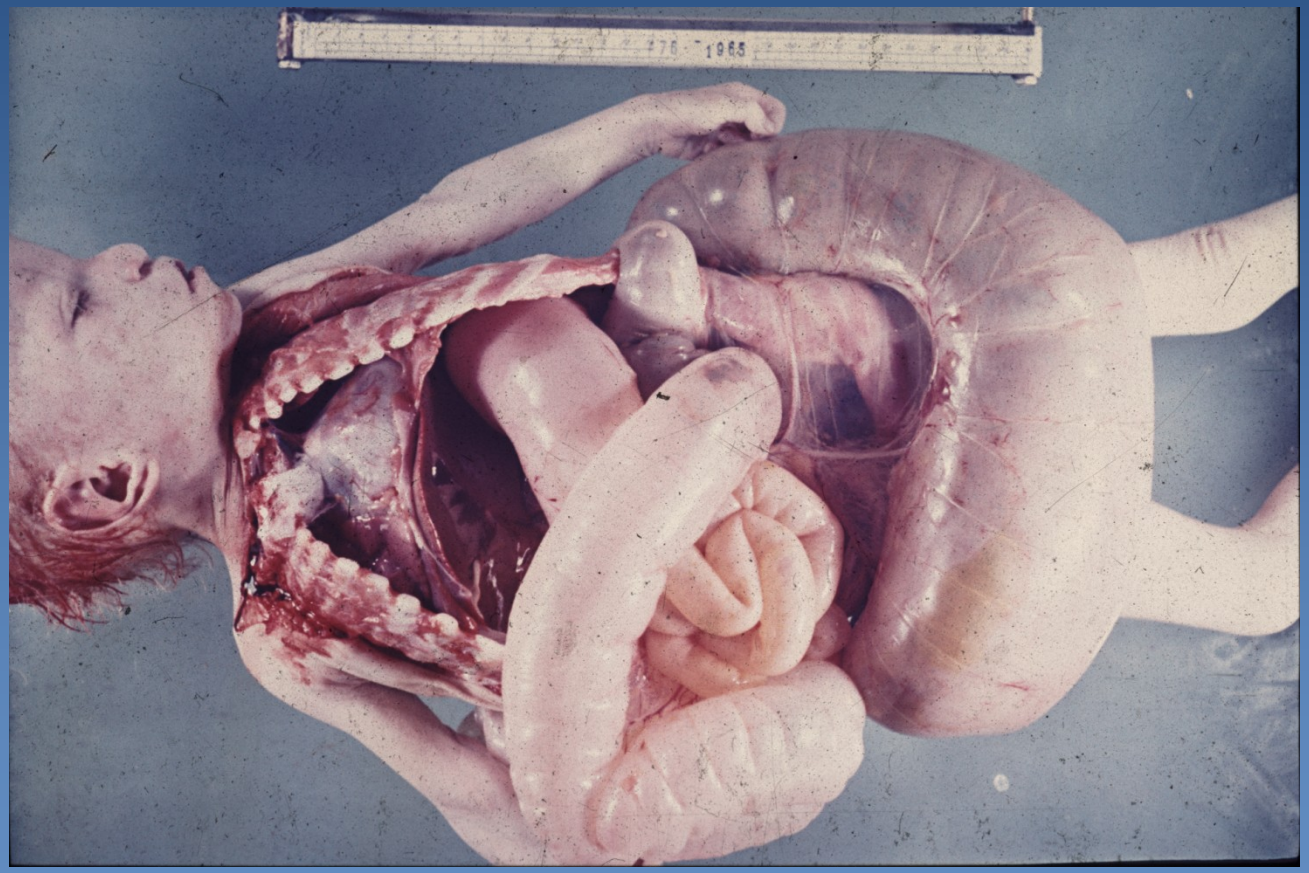
copy

- result of intestinal ischemia

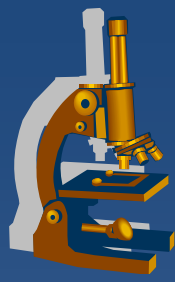
Hemorrhagic infarction of the intestine



Hirschprung‘ disease

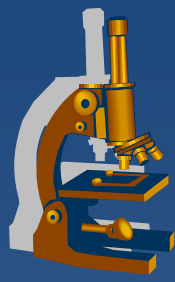


Intestinal polyps



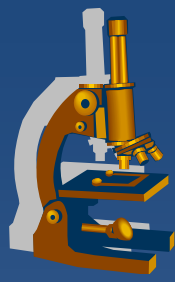
- **Non-neoplastic polyps**
  - ⇨ ***hyperplastic polyp*** *(<5 mm) minimal malignant potential, part of group of serrated lesions*
  - ⇨ ***juvenile polyp*** *- hamartoma; in children under 5 years, in the rectum, sporadic or part of juvenile polyposis sy (AD, haemorrhage, ↑ risk of ca)*
  - ⇨ ***Peutz - Jeghers*** *hamartoma polyps + mucocutaneous hyperpigmentation; single/multiple (P-J syndrome - ↑ risk of pancreatic, pulmonary, ovarian, breast cancer)*

Intestinal polyps



- **Neoplastic sporadic adenomatous polyps**
  - ⇨ ***tubular adenoma*** *(smaller, spheric, pedunculated)*
  - ⇨ ***villous adenoma*** *(large, flat, sessile, often HG dysplasia and high malignant potential)*
  - ⇨ ***tubulovillous adenoma***

Familial syndromes



1/ Familial hereditary polyposis syndromes

⇨**familial adenomatous polyposis (FAP):**

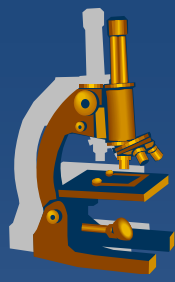
AD, mutation of suppresor APC gene, 100-2500 colonic adenomas, teenagers, 100% risk of cancer

⇨**Gardner syndrome:** *FAP variant, dental anomalies*

extraintestinal tumors: osteomas, gliomas, lipomas, fibromas

⇨**Peutz - Jeghers syndrome** *:*

melanotic mucosal and cutaneous pigmentation with hamartomatous intestinal polyps

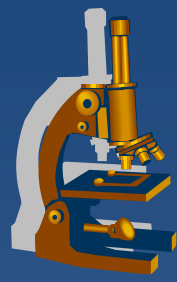


2/ Lynch syndrome

(hereditary non-polyposis colorectal cancer, AD), DNA mismatch repair defect + increased rate of mutations; younger age, right colon.

Increased risk of multiple tumors of the stomach, small intestine, liver, gallbladder tract, urinary tract, brain, skin, prostate.

Serrated lesions



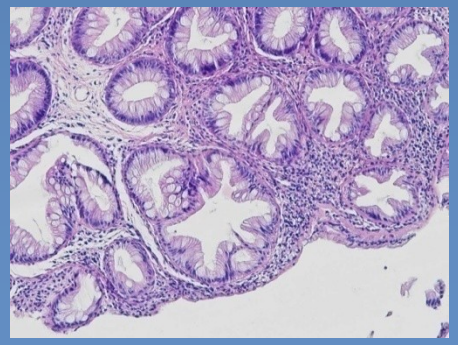
⇨ *special heterogenous group of polypous lesions, serrated (sawtooth, stellate) morphology, part of intraepithelial neoplasias*

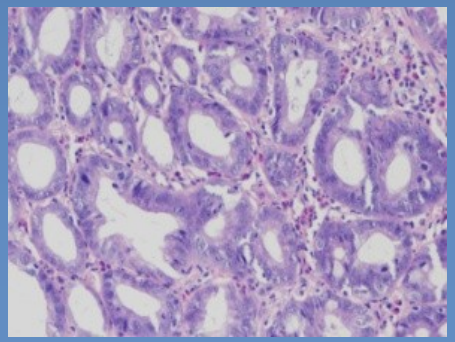
⇨ *precursors of perhaps one third of colorectal cancers*

⇨ *classification: dysplastic, non-dysplastic*

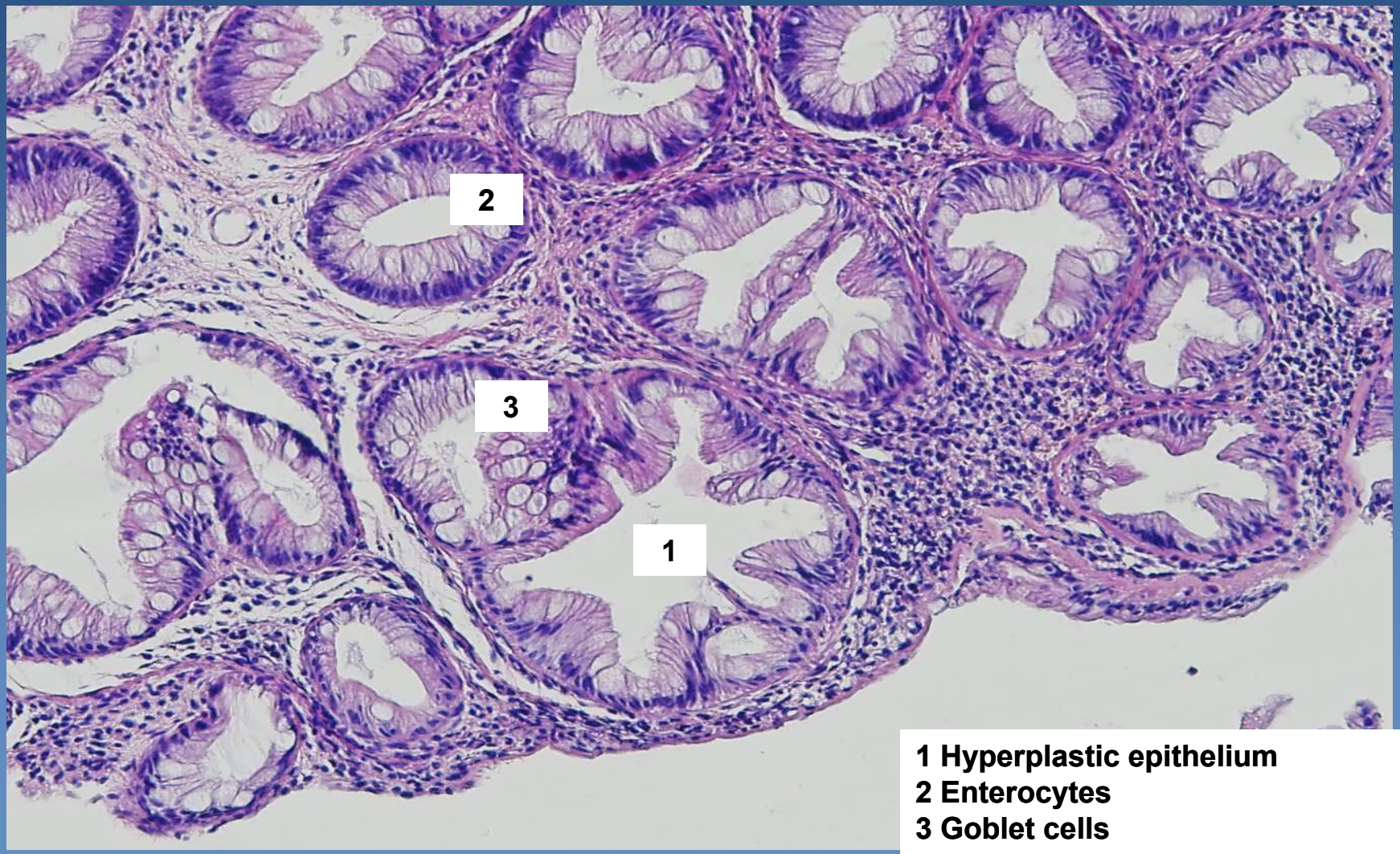
Classification of serrated lesions/polyps

- Non-dysplastic
  - ⇨ ***hyperplastic polyp***
  - ⇨ ***sessile serrated adenoma/polyp***
- With dysplasia
  - ⇨ ***sessile serrated adenoma/polyp w. dysplasia***
  - ⇨ ***traditional serrated adenoma***



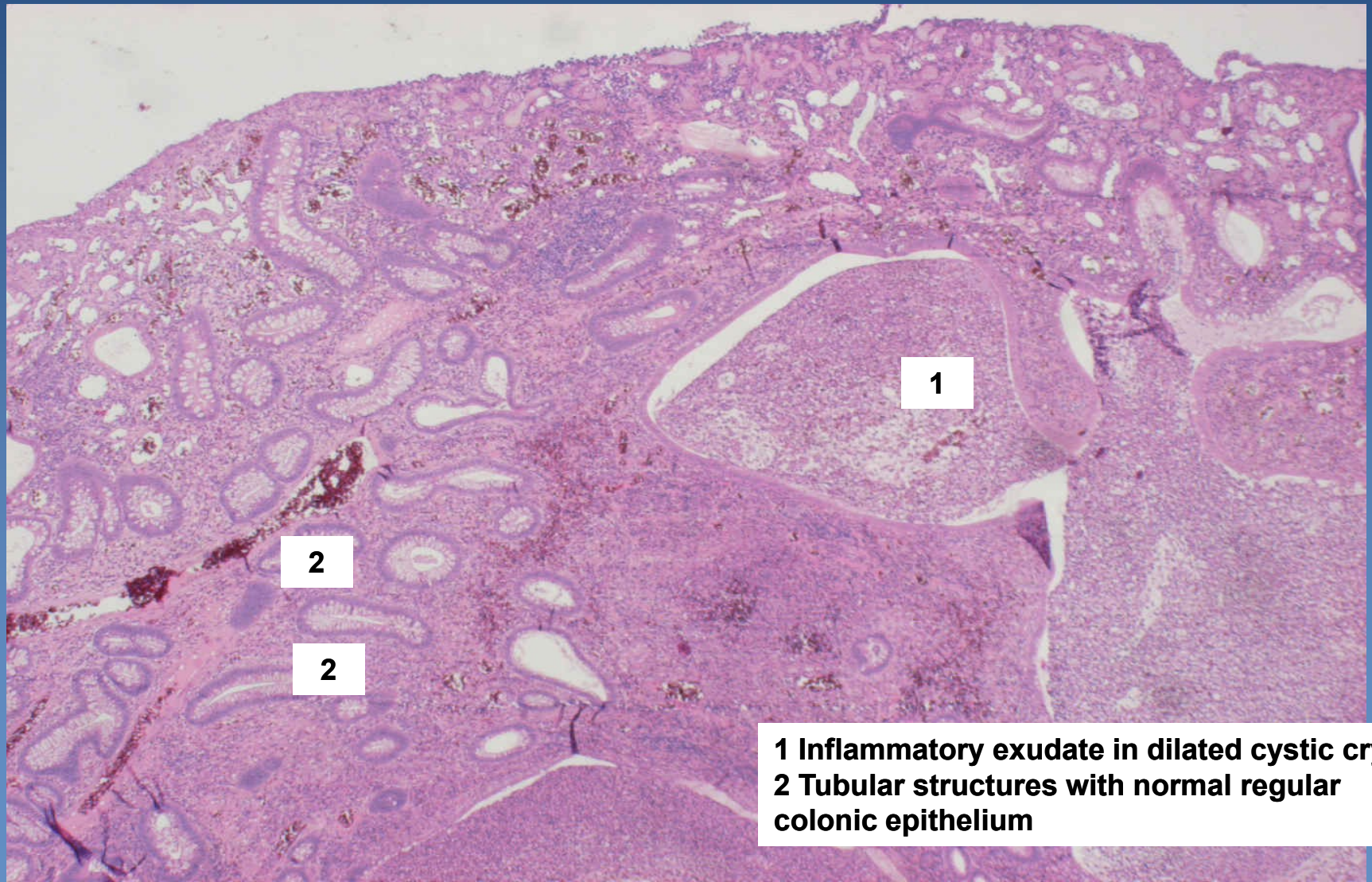


Colon – hyperplastic polyp



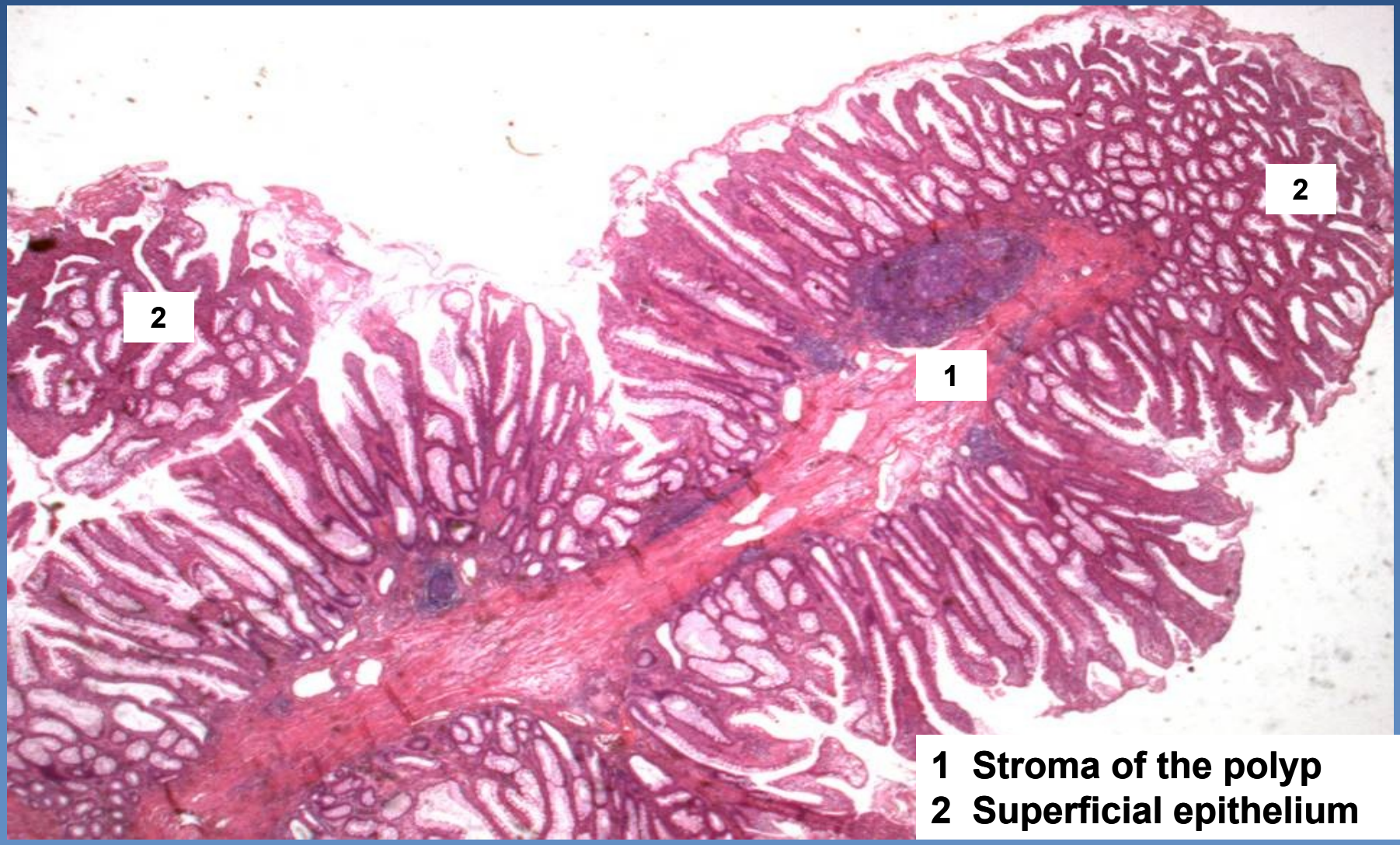
1 Hyperplastic epithelium
2 Enterocytes
3 Goblet cells

Colon - juvenile polyp



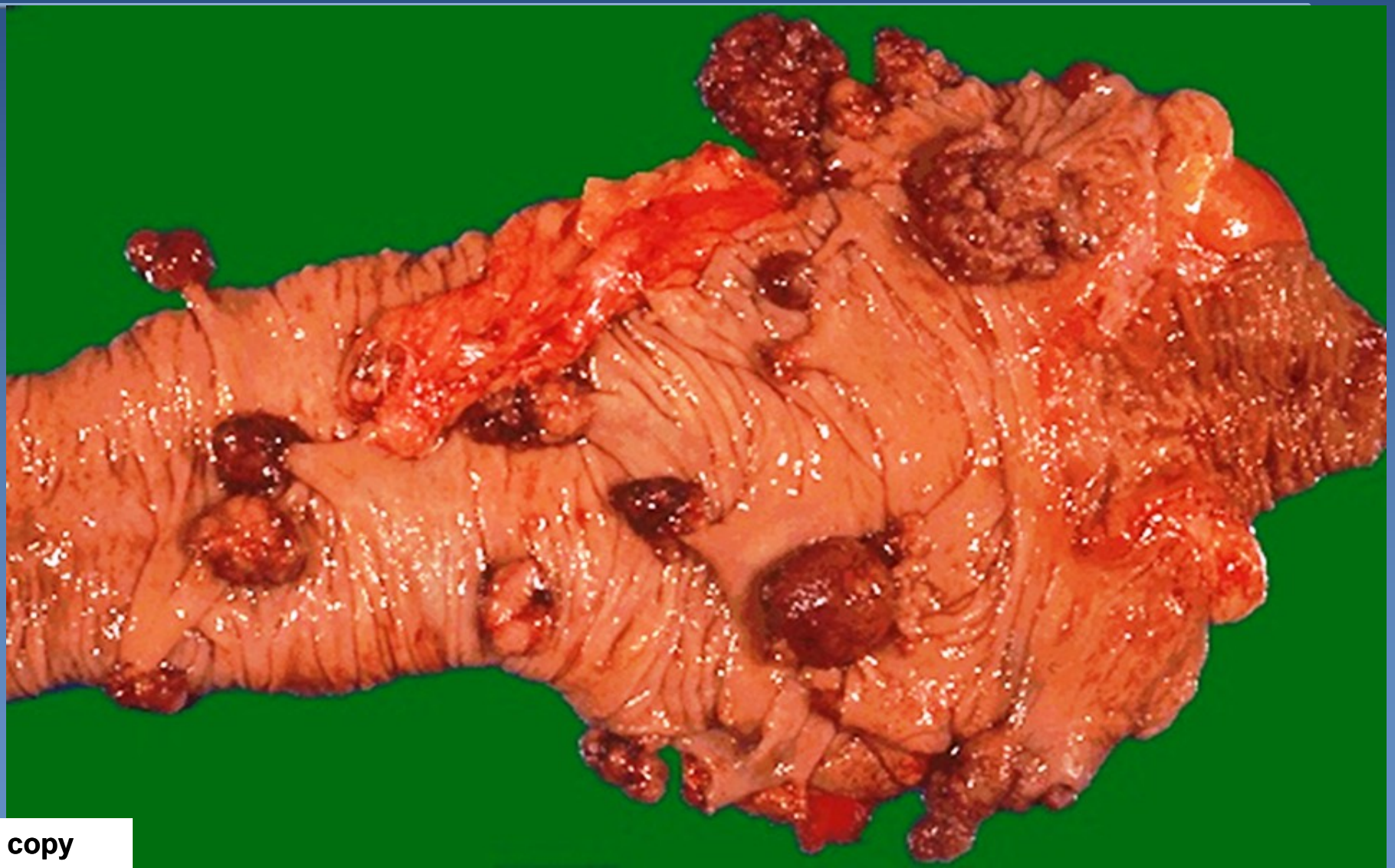
1 Inflammatory exudate in dilated cystic crypt
2 Tubular structures with normal regular colonic epithelium

Colon - hamartomatous P-J polyp



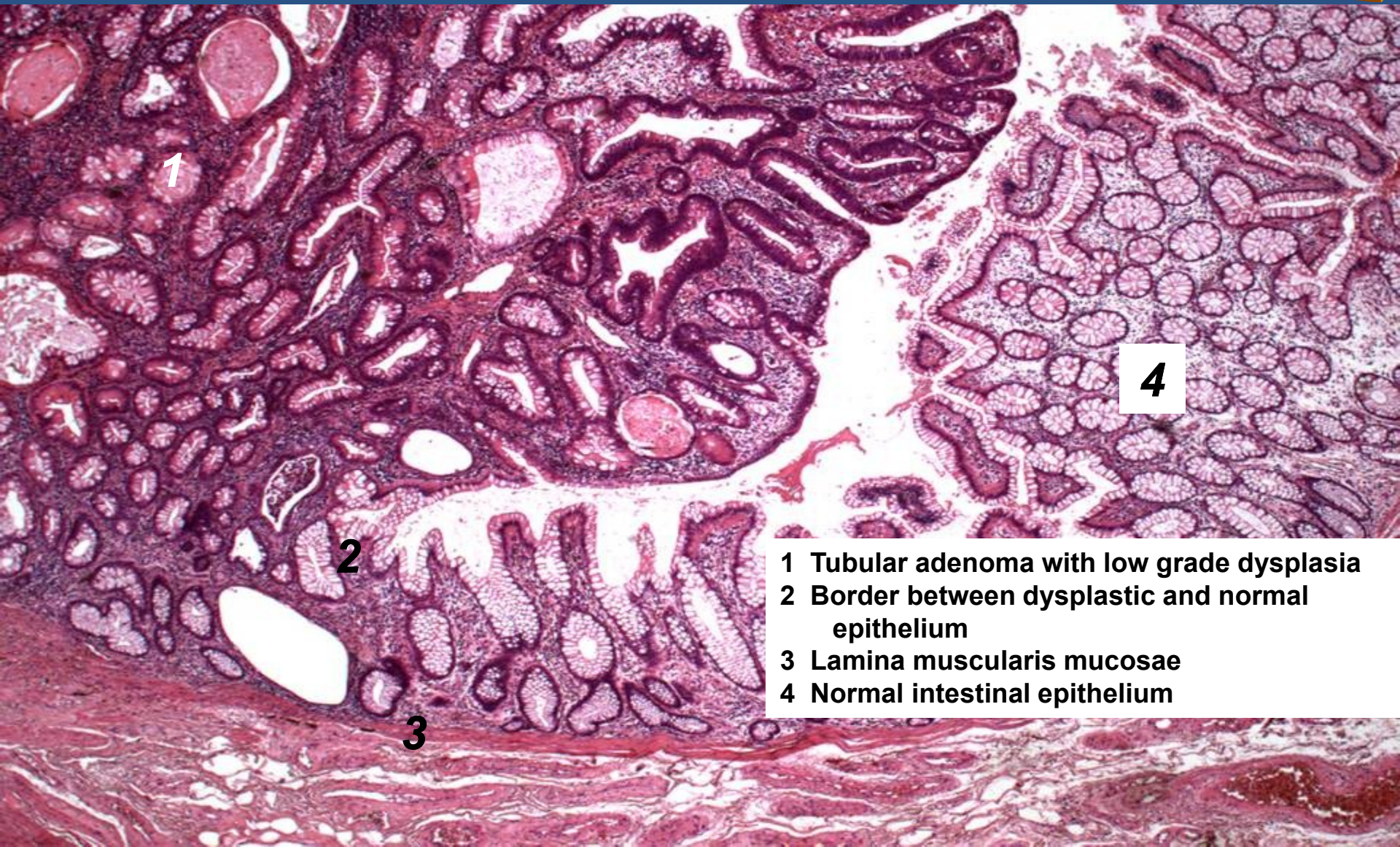
1 Stroma of the polyp
2 Superficial epithelium

Adenomas



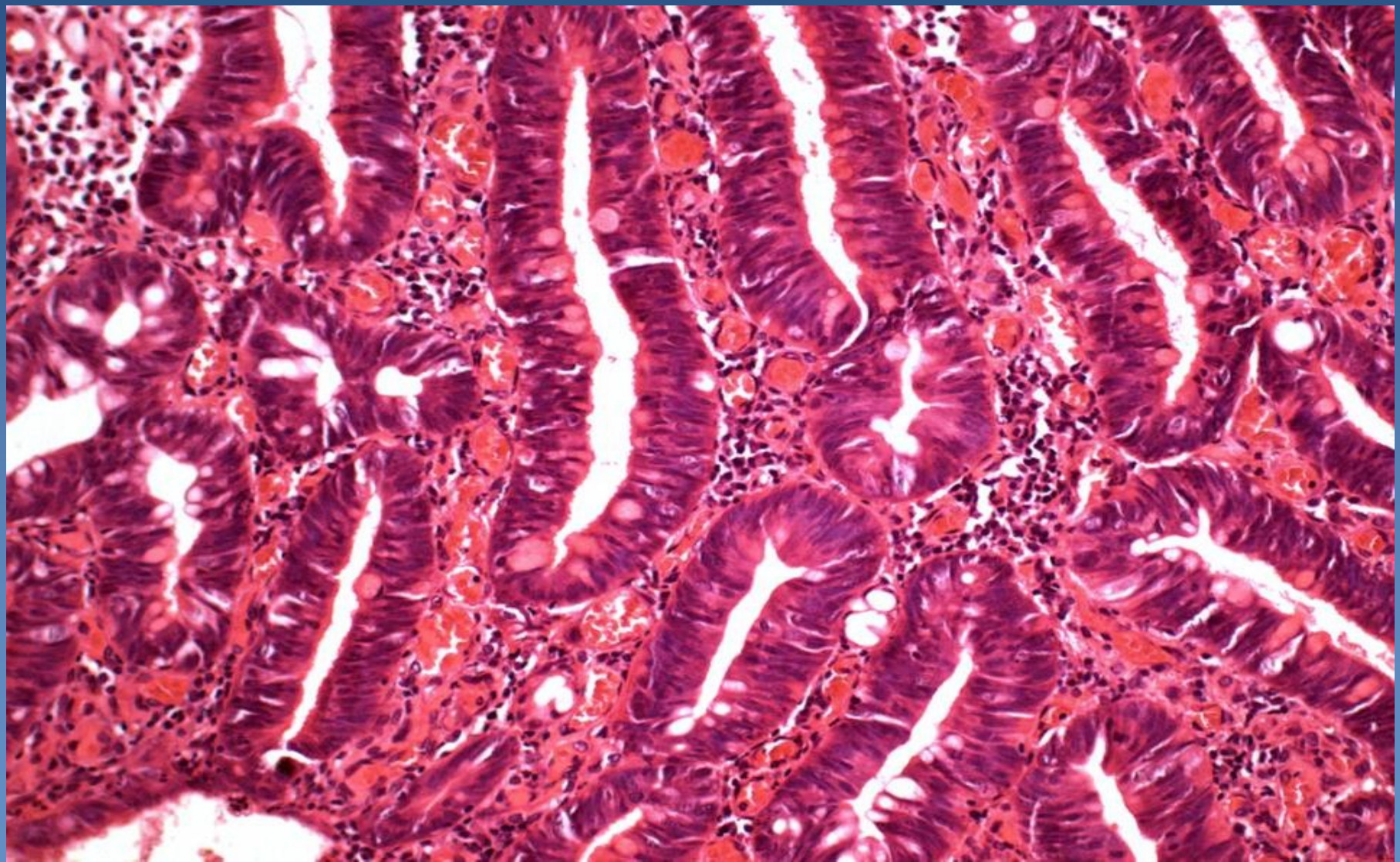
Polyposis of the colon

Tubular adenoma

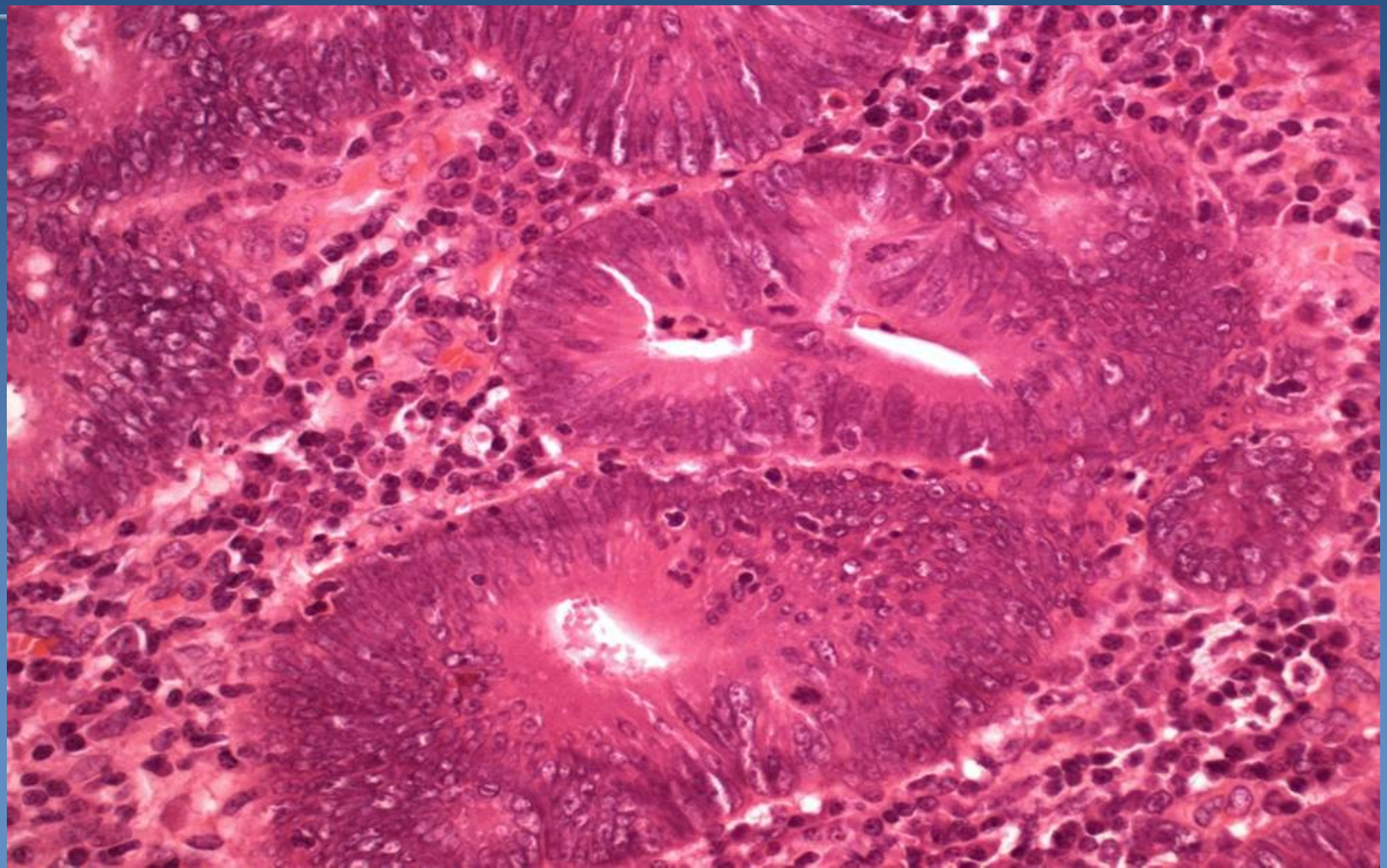


1 Tubular adenoma with low grade dysplasia
2 Border between dysplastic and normal epithelium
3 Lamina muscularis mucosae
4 Normal intestinal epithelium

Tubular adenoma – low grade dysplasia

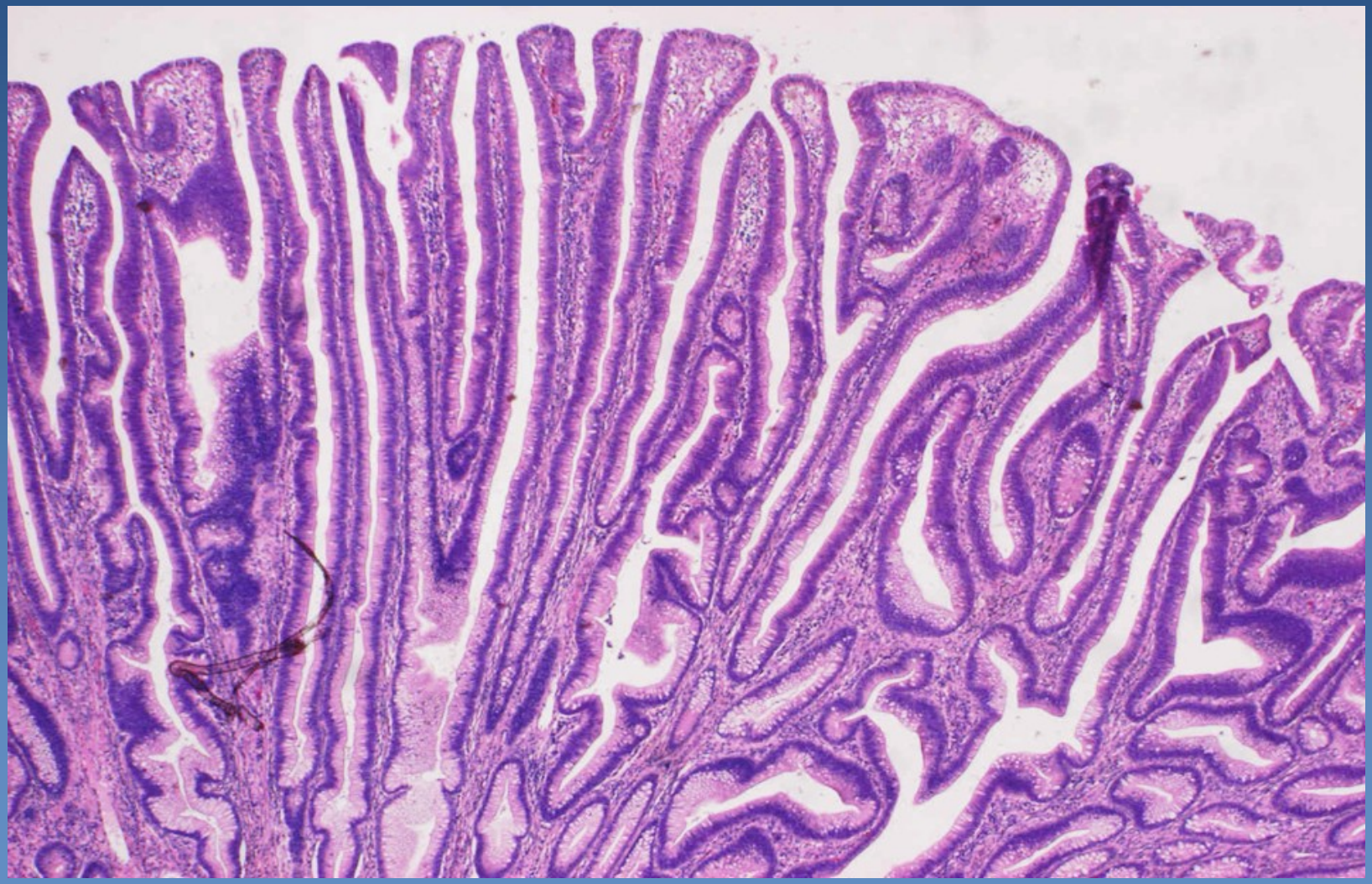


Tubular adenoma – high grade dysplasia

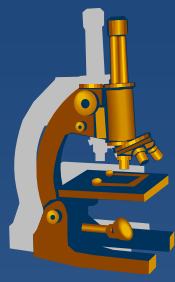


Villous adenoma

Villous adenoma

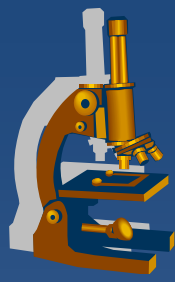


Colorectal carcinoma



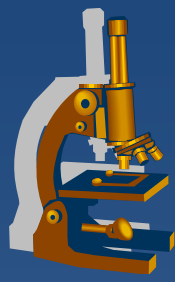
- high incidence in the Czech Republic and other developed countries
- 60 - 70 % in the rectum and sigmoid (50% detectable by per rectum examination)
- Risk factors: lifestyle + diet, smoking, alcohol
  - ⇨ ***high intake: refined carbohydrates, fat, red meat***
  - ⇨ ***decreased intake: unabsorbable vegetable fiber, protective micronutrients (vtamins A,C,E)***
- predisposing factors: genetic
  - ⇨ ***polyposis***
  - ⇨ ***ulcerative colitis***

Colorectal carcinoma



- Gross:
  - ⇨ ***exophytic, polypous***
    - proximal colon - long time asymptomatic
  - ⇨ ***endophytic, ulcers with heaped-up edges***
    - distal colon - early stenosis
  - ⇨ ***annular***
    - encircling lesions
  - ⇨ ***infiltrative***
    - rare, linitis plastica type

Colorectal carcinoma



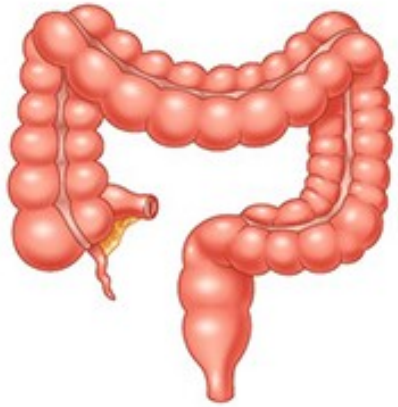
- Micro:
  - ⇨ ***tubular adenocarcinoma (most frequently)***
  - ⇨ ***other adenocarcinoma types:***
    - cribriform comedo-type
    - micropapillary
    - medullary
    - mucinous
    - serrated
    - signet ring cell
  - ⇨ ***adenosquamous, spidle-like, squamous cell, undifferentiated***

Colorectal carcinoma

Pathological Distinctions Between CRC Tumors

MSI pathway 15%

- Right-sided, proximal colon
- Diploid; associated methylation (CIMP)
- Poorly differentiated; often mucinous
- Presence of Crohn-like lymphocyte infiltrate
- Often large (ie, T3)
- More often N0, M0
- More often ≥ 12 nodes in specimen
- Prognosis may be less favorable

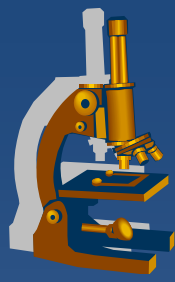


CIN pathway 85%

- Left-sided, distal colon
- Aneuploid; polyploidy (CIN)
- Highly differentiated; rarely mucinous
- No peritumoral lymphocytic infiltrate
- More often N+, M+
- May have lower number of harvested lymph nodes
- Prognosis may be more favorable

Söreide K, et al. *Br J Surg*. 2006;93:392-406.

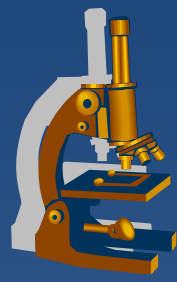
Colorectal carcinoma



- TNM classification and tumor progression:
  - ⇨ ***pTis intraepithelial/intramucosal (100% 5-year survival, no metastases)***
  - ⇨ ***pT1 submucosa (90% survival)***
  - ⇨ ***pT2 into the muscularis propria (+LN metastases possible);***
  - ⇨ ***pT3 subserosa (+ metastases common), 35% survival in LN meta - pT3N1***
  - ⇨ ***pT4 transperitoneal/invasion into adjacent organ***

Distant metastases present - 8% survival.

Colorectal carcinoma

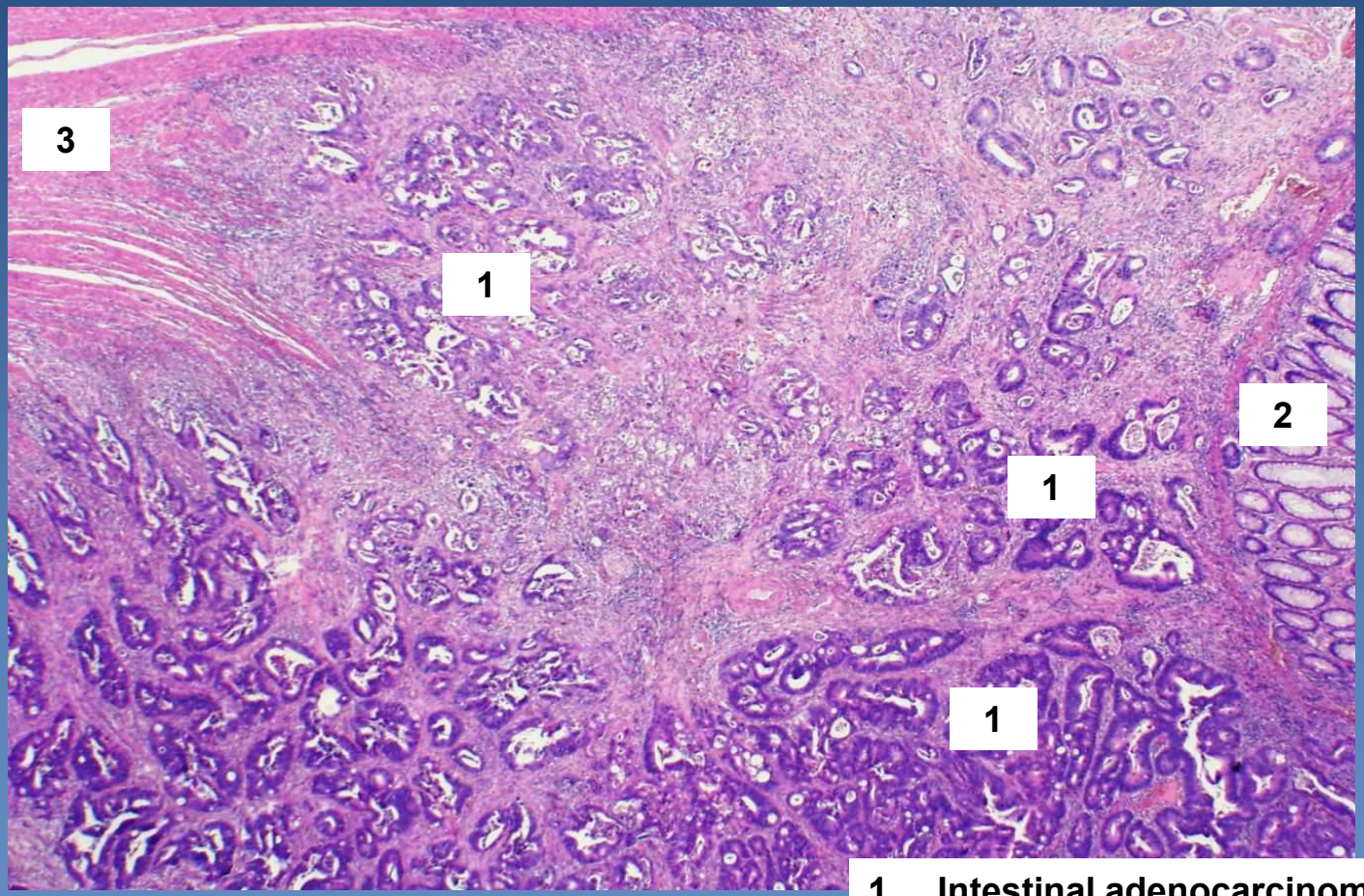


Staging

- stage I: T1, T2, no meta
- stage II: T3, T4, no meta
- stage III: any T, LN meta, no distant meta (M0)
- stage IV: any T, any N, M1

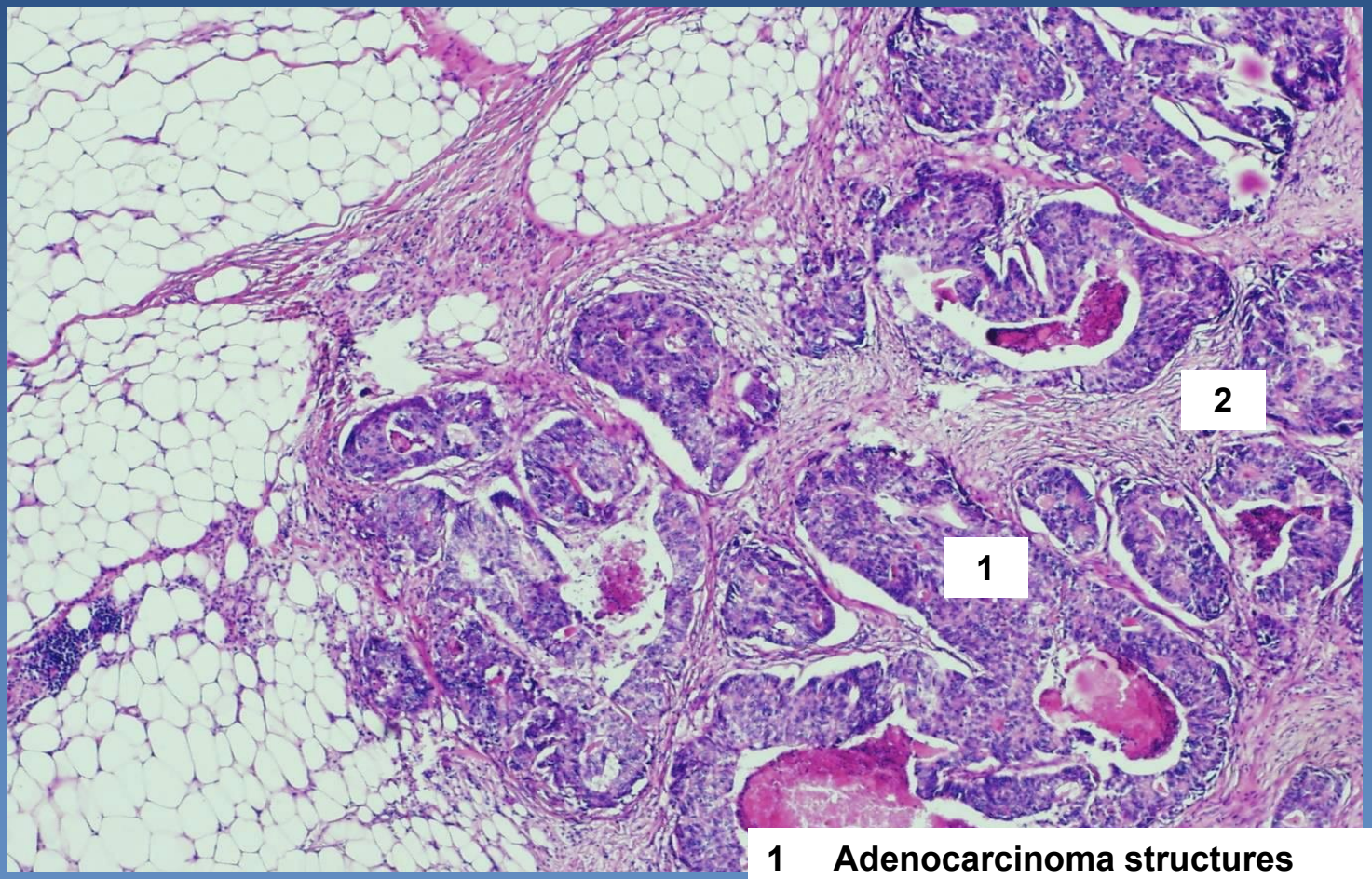
Colorectal carcinoma

Adenocarcinoma of the colon



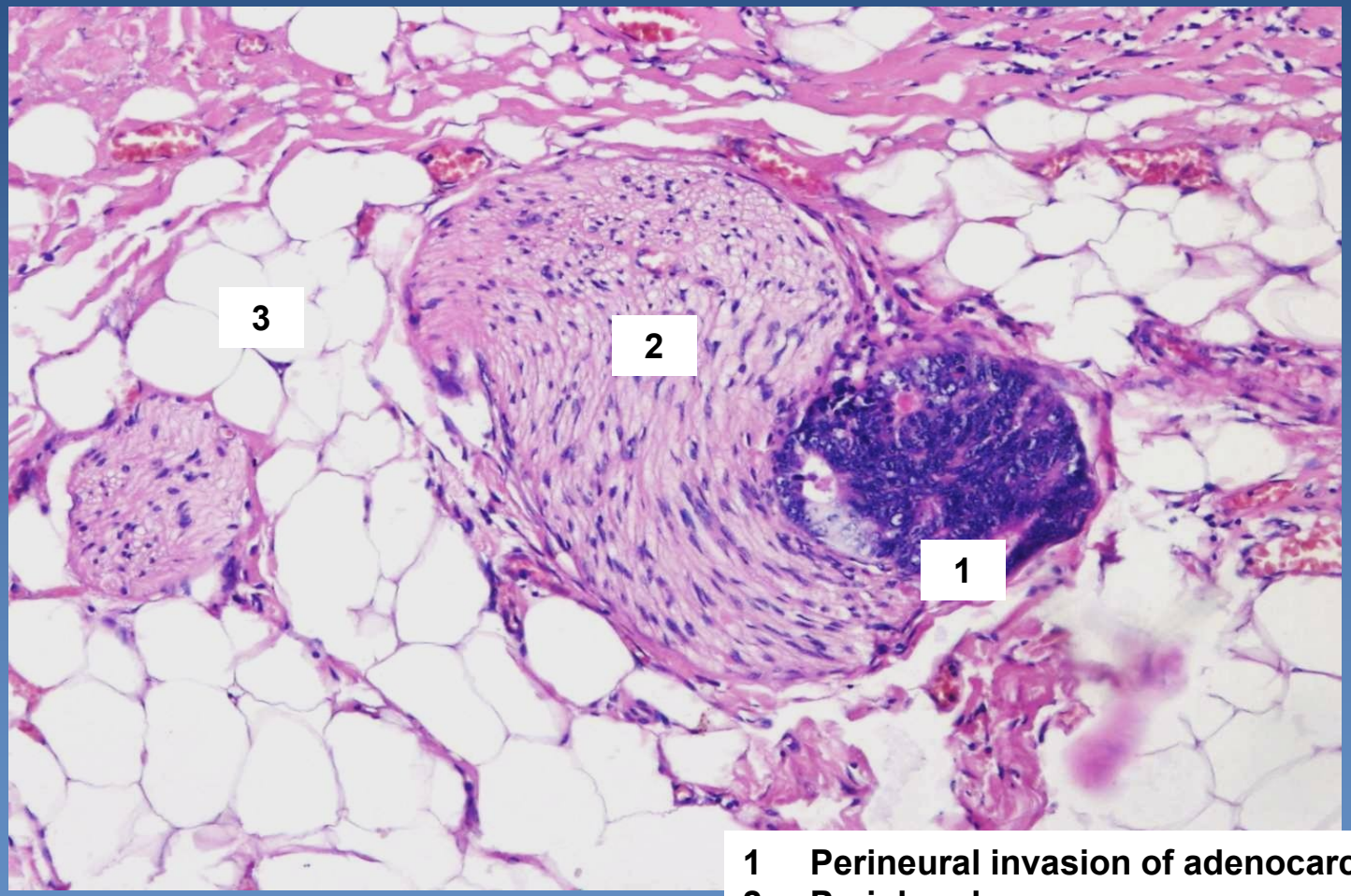
1 Intestinal adenocarcinoma structures
2 Normal colonic epithelium
3 Muscularis propria

Adenocarcinoma of the colon



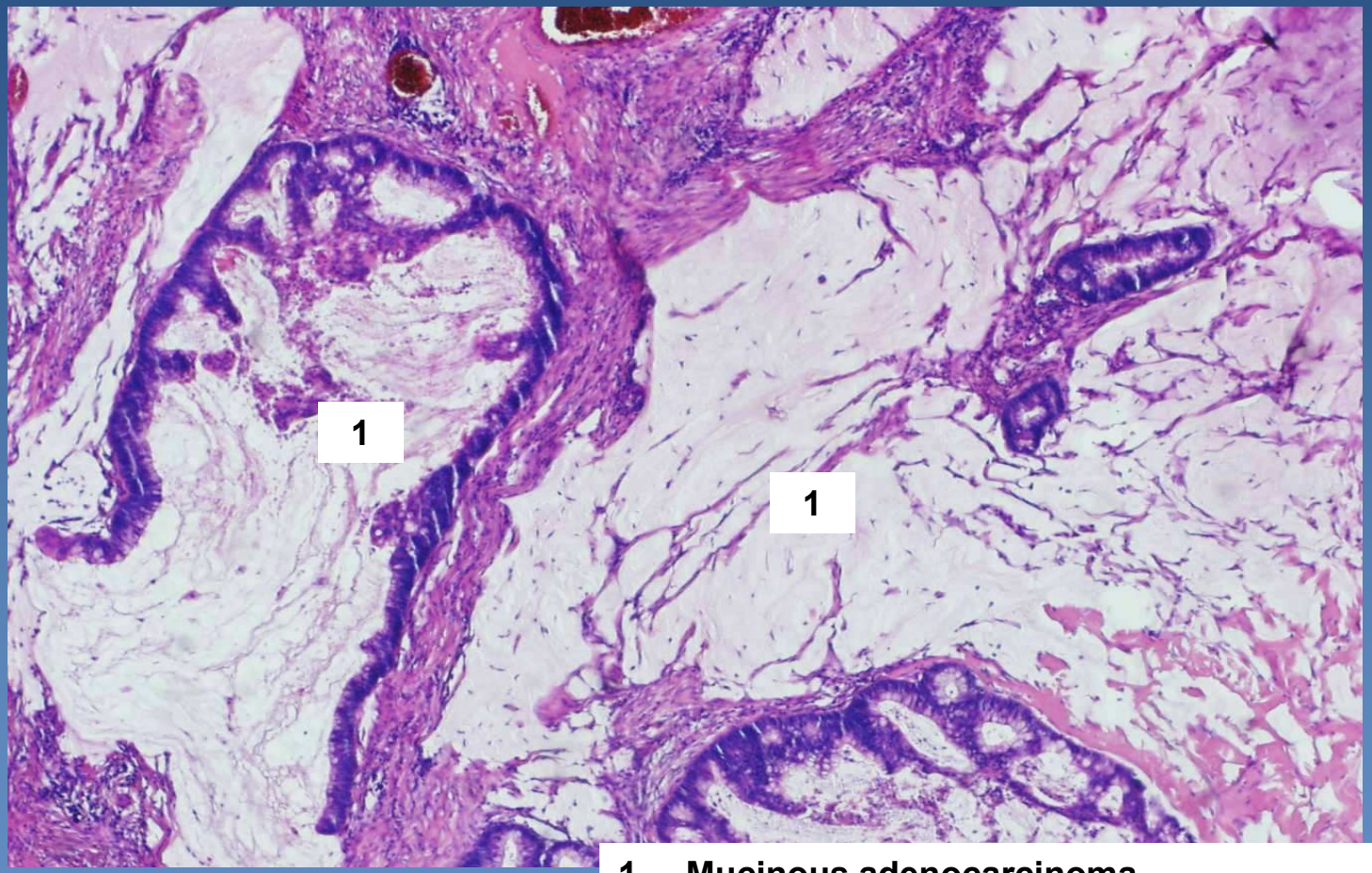
1 Adenocarcinoma structures
2 Pericolonic fat and fibrous tissue

Adenocarcinoma of the colon



1 Perineural invasion of adenocarcinoma
2 Peripheral nerve
3 Pericolonic fat

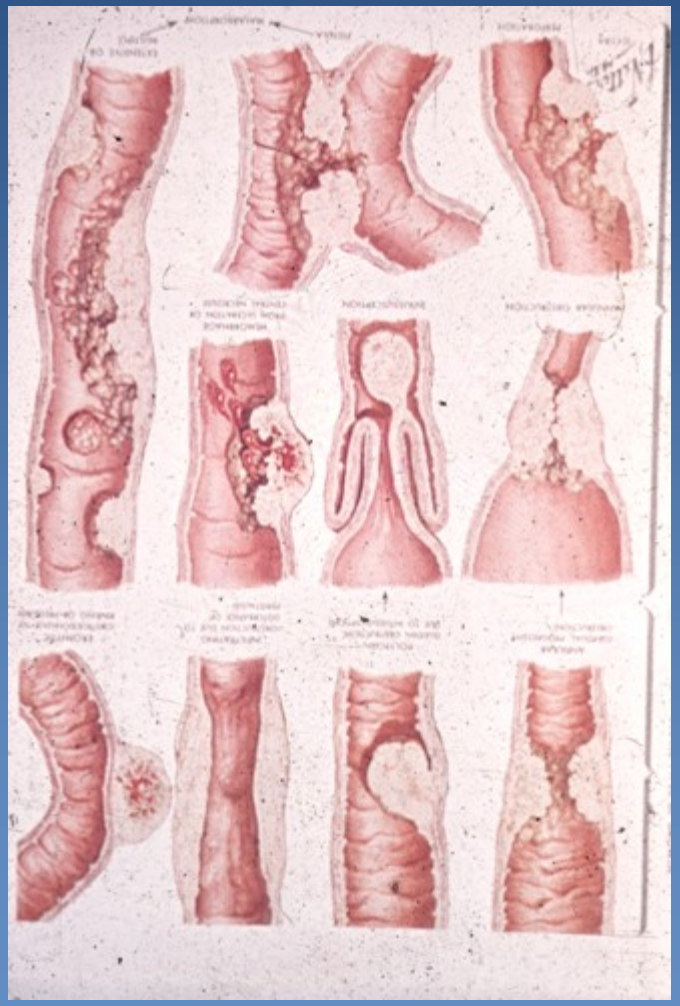
Adenocarcinoma of the colon



1 Mucinous adenocarcinoma

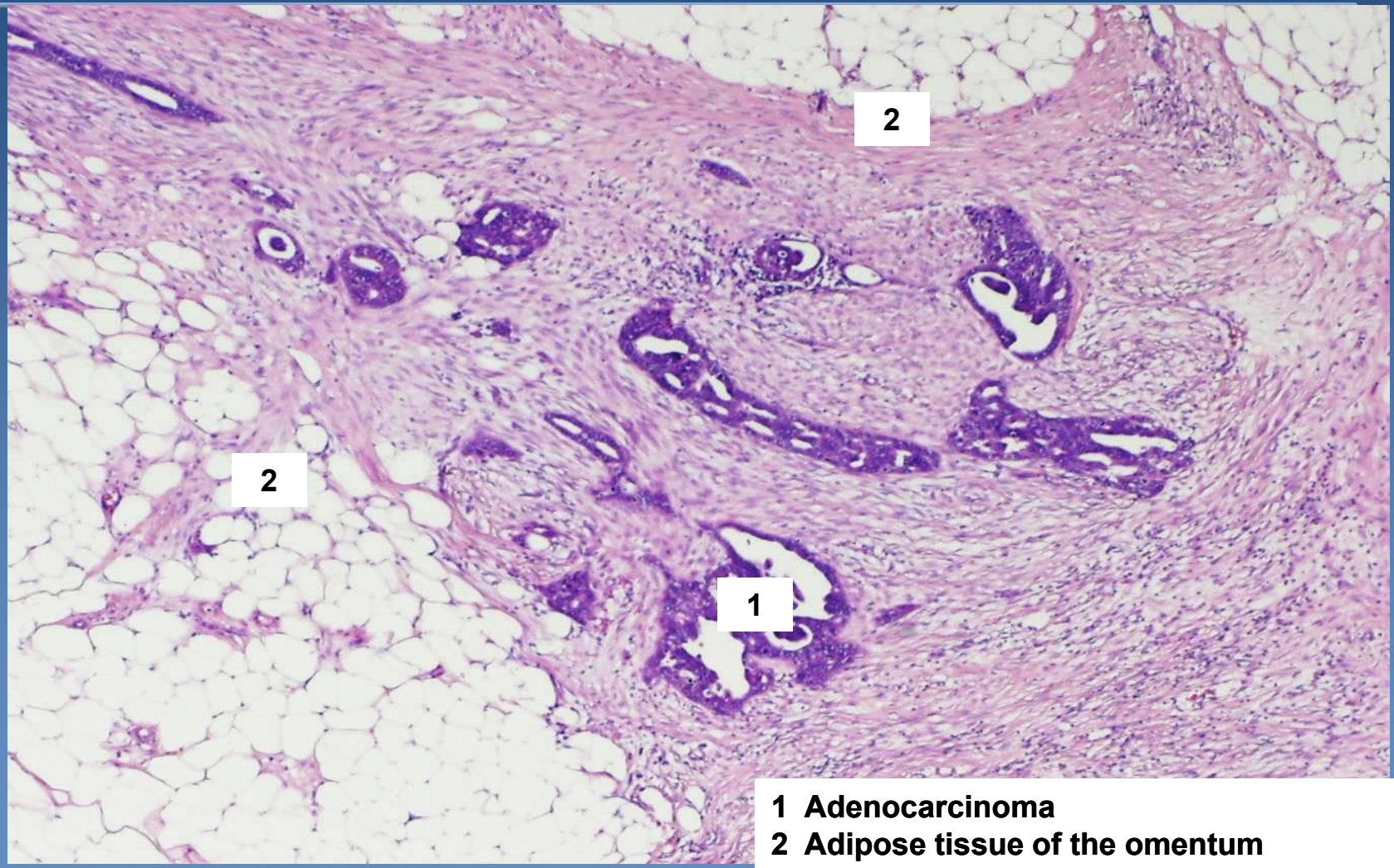
Colorectal carcinoma - complications

- stenosis
- obstructive ileus
- hemorrhage (occult!, overt)
- perforation
- penetration
- stercoral peritonitis



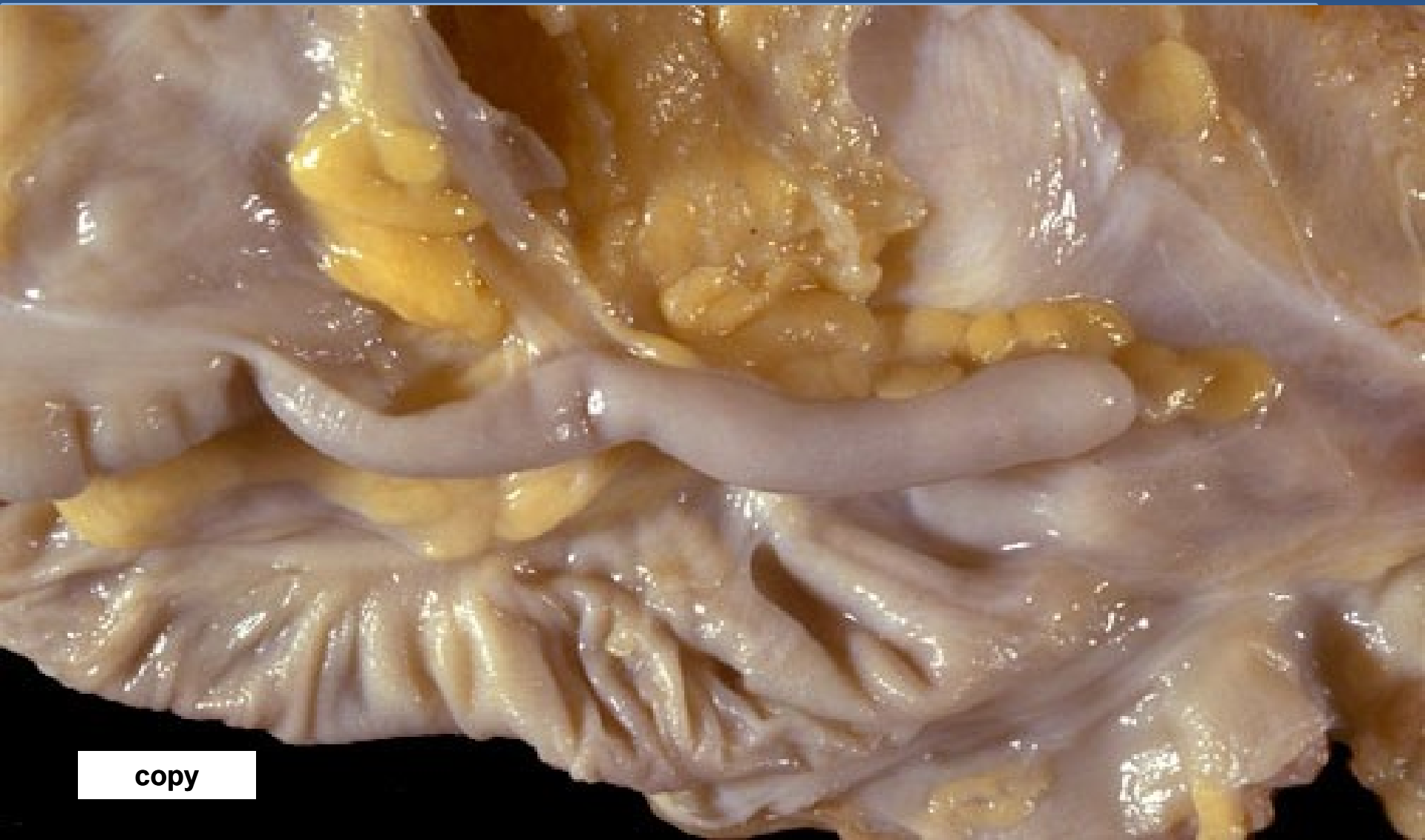
Peritoneal carcinomatosis

widespread metastases in the peritoneum/ omentum

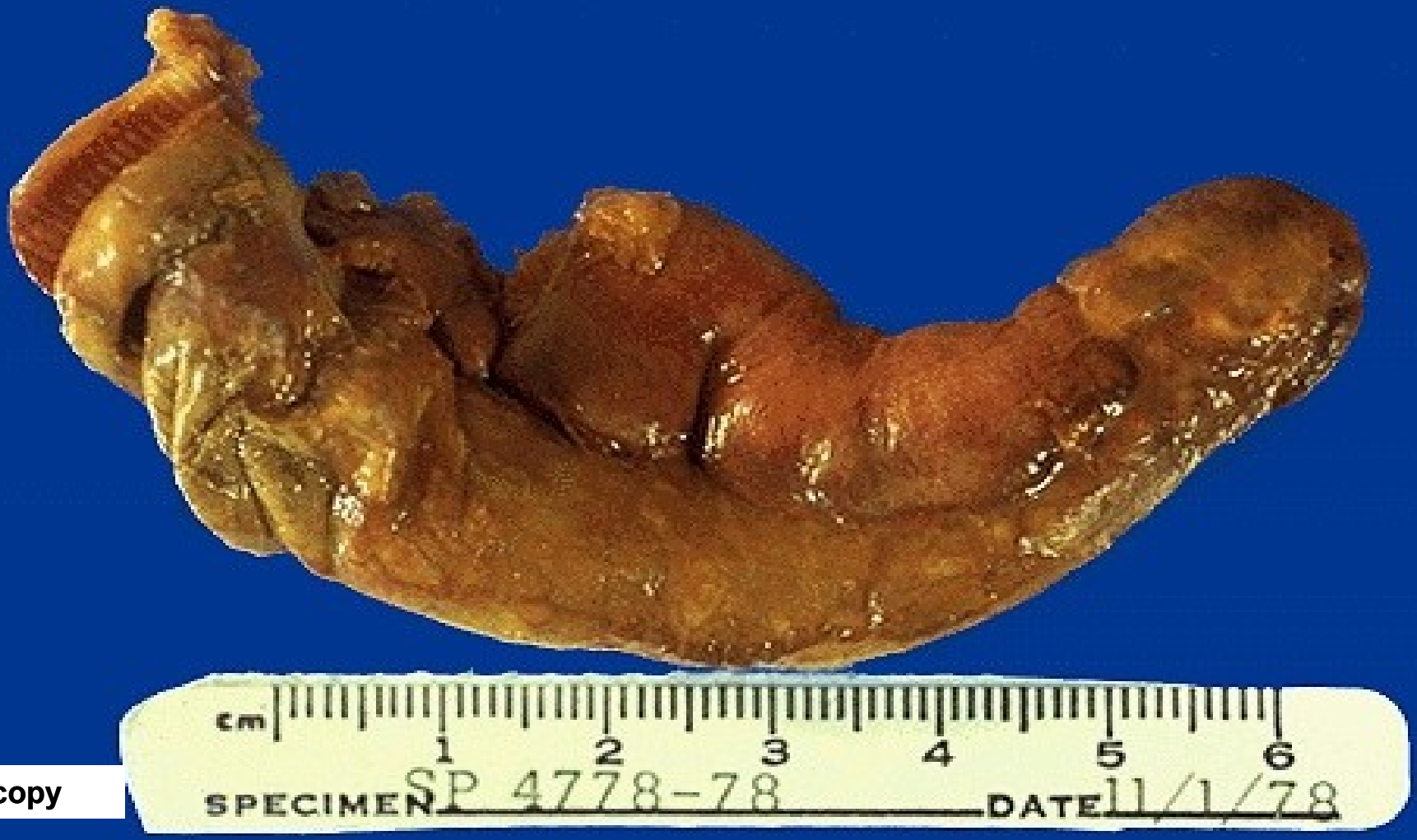


1 Adenocarcinoma
2 Adipose tissue of the omentum

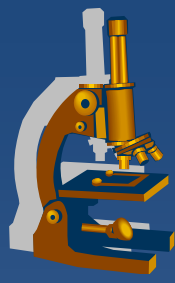
Appendix - normal



Appendix - periappendicitis

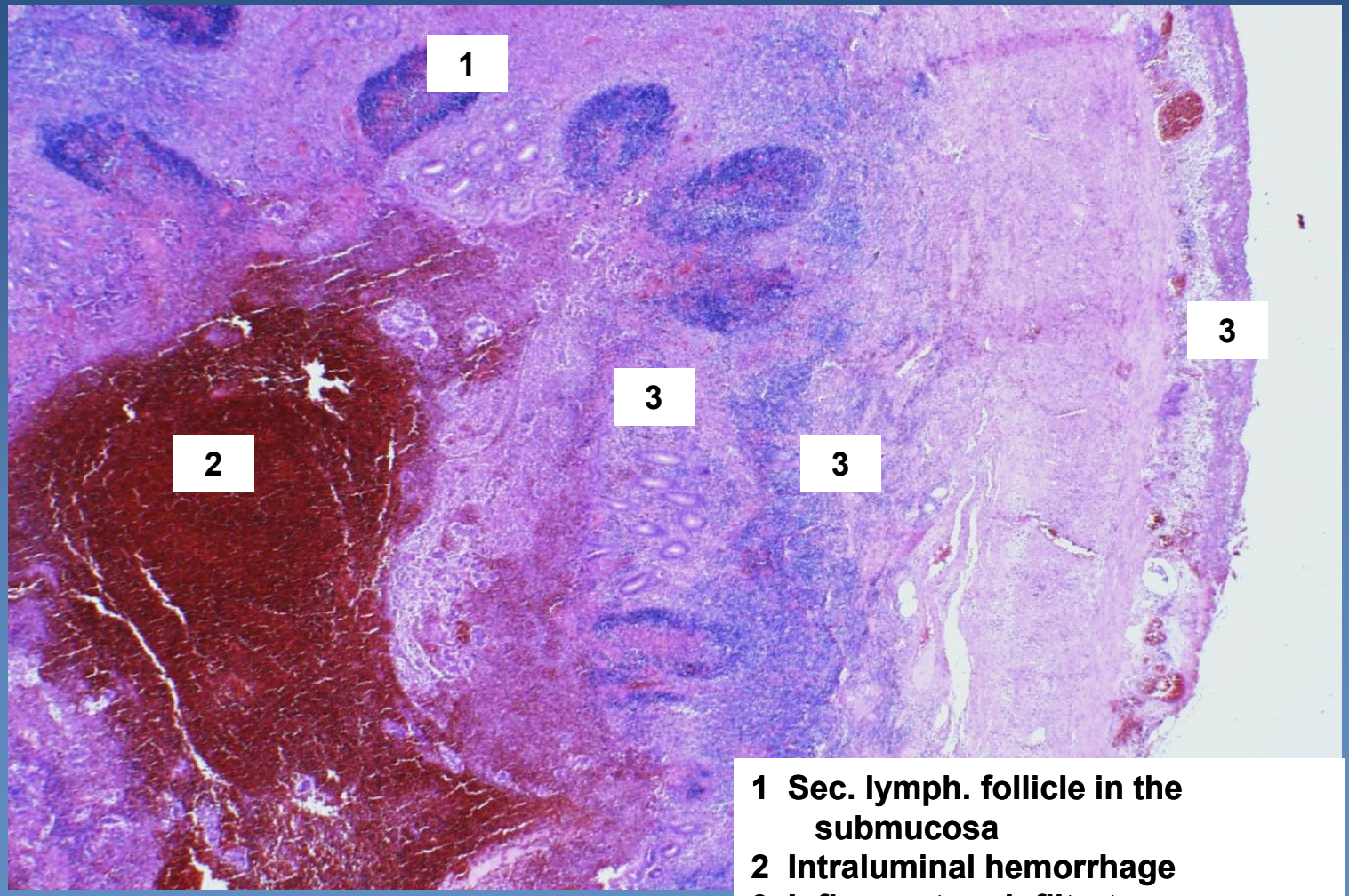


Appendicitis



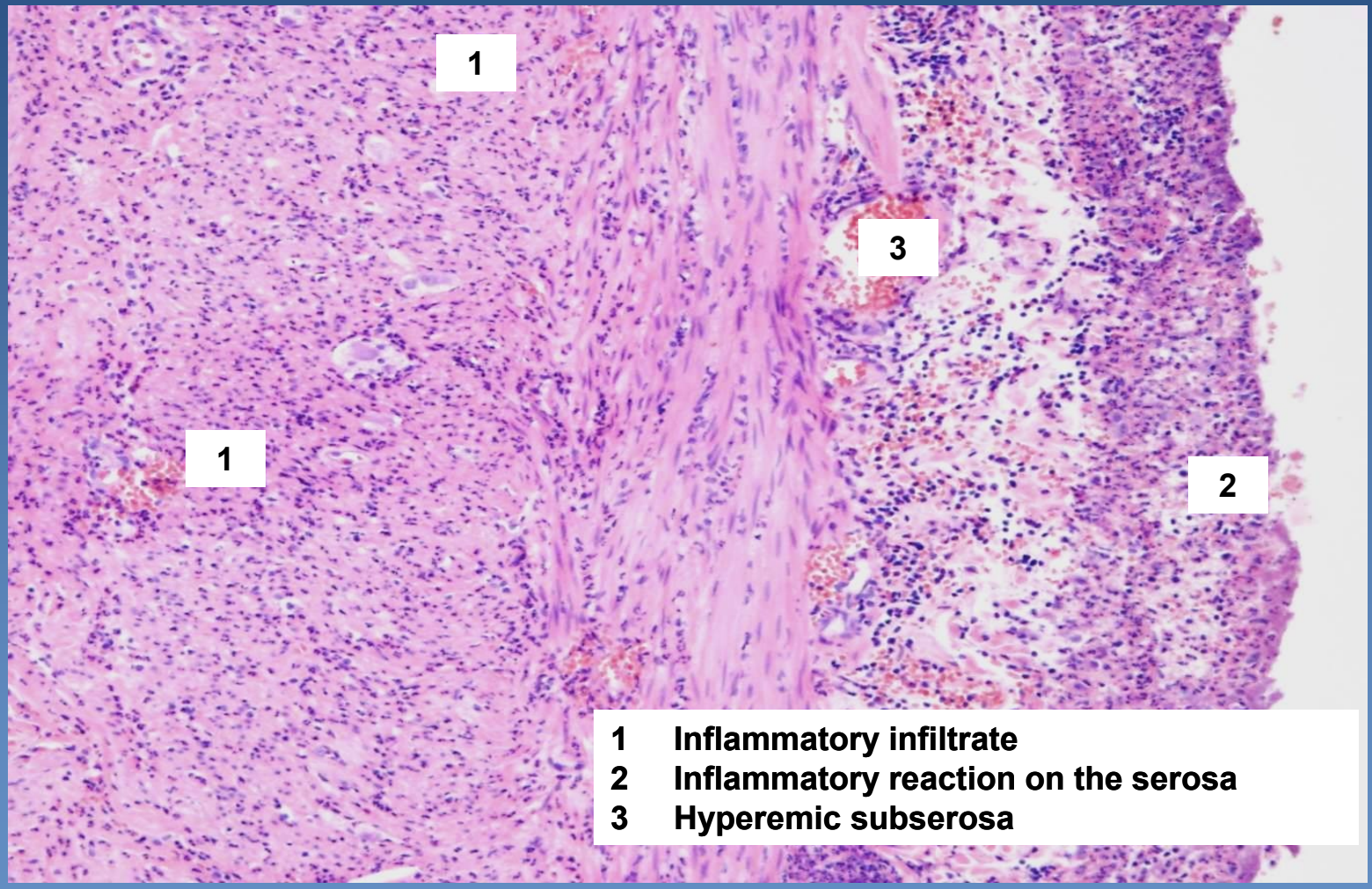
- Causes: ?obstruction, stool stagnation→ collapse of the draining veins → ischemia of the wall → bacterial proliferation → inflammation (catarrhal, phlegmonous)
- Trombosis of mesenteriolar veins → ischemic necrosis of the appendiceal wall → secondary bacteria invasion → gangrenous inflammation
- Complications:
  - ***peritonitis***
  - ***periappendiceal abscess***
  - ***portal pyemia***
  - ***adhesions***

Phlegmonous appendicitis

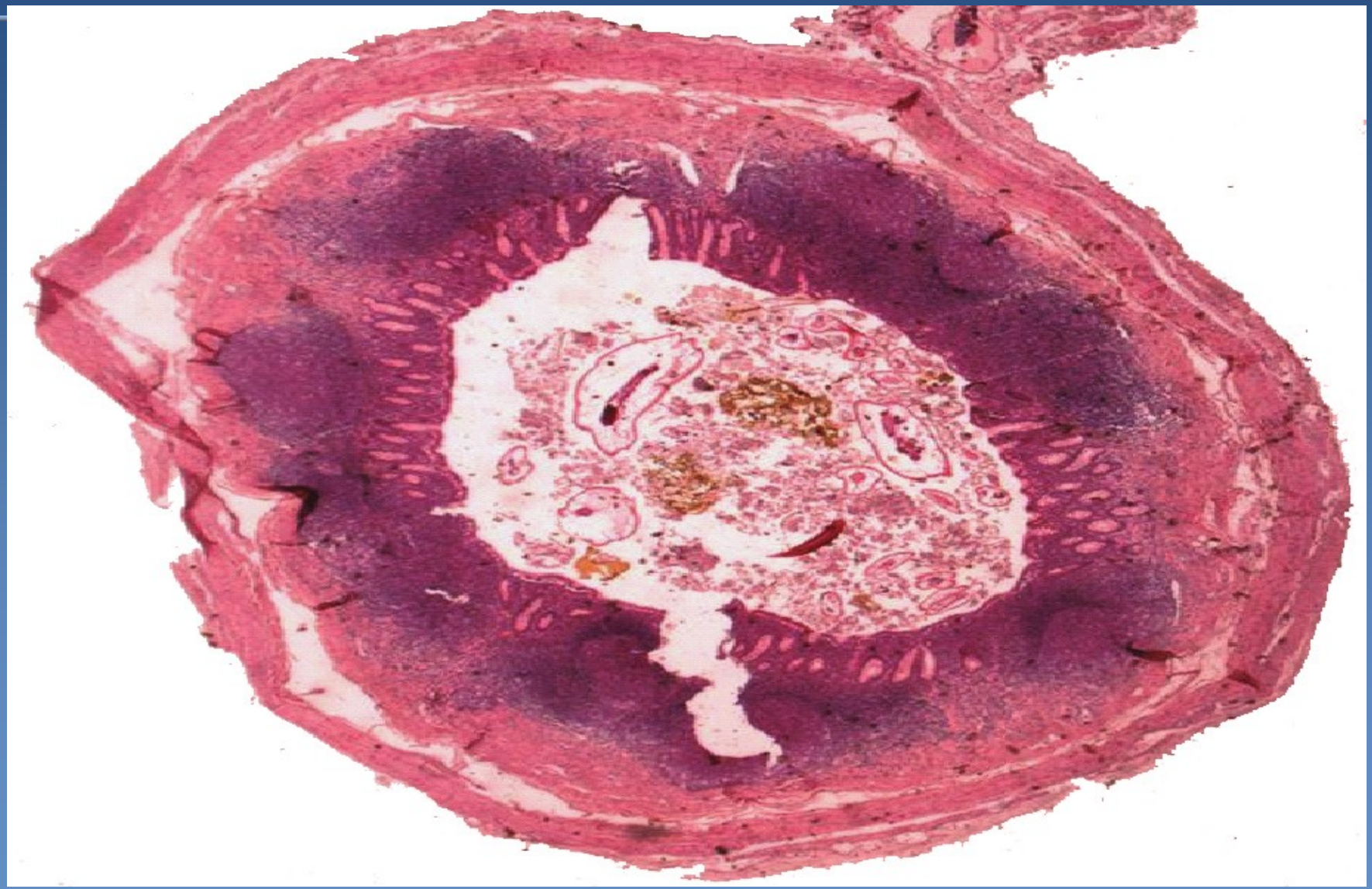


1 Sec. lymph. follicle in the submucosa
2 Intraluminal hemorrhage
3 Inflammatory infiltrate

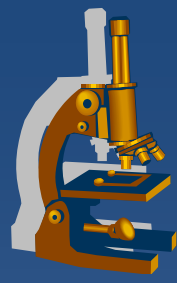
Phlegmonous appendicitis
- detail



Parasitic appendicitis - Oxyuriasis vermicularis (pinworm) in the lumen



Neuroendocrine tumors (NETs)

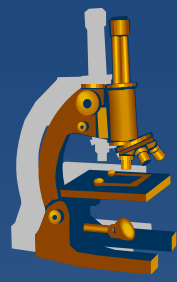


- **arise from neuroendocrine cells of the gastro-entero-pancreatic system (GEP-NET)**

- **histologic classification WHO 2010:**

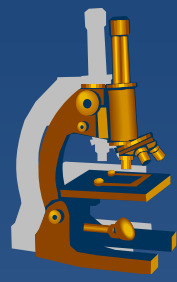
  - ⇨ ***NET G1 (carcinoid)***
  - ⇨ ***NET G2***
  - ⇨ ***NEC G3 large cell or small cell type***
  - ⇨ ***compound adenoneuroendocrine carcinoma***

Neuroendocrine tumors (NET)



- **arise from neuroendocrine or precursor cells of the GIT mucosa**
- mostly in the **ileum and appendix** (80%)
- **all NETs** (except for a very few) **are considered malignant** in various grade

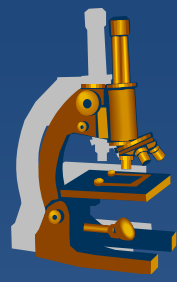
GEP-NET



- **classification** *depends on:*
  - ⇨ *location*
  - ⇨ *type of the endocrine product*

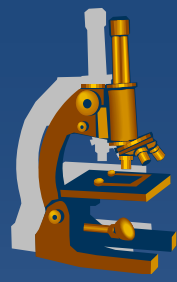
- **gross:**
  - ⇨ *small, round-shaped, flat nodules of yellowish colour, infiltrating the wall to different depth, superficially ulcerated or covered with normal mucosa, sometimes exophytic*

GEP-NET



- **micro:**
  - ⇨ *trabecular, glandular structures - tubules, palisading or compound structure*
  - ⇨ *regular cells with clear cytoplasm and round or oval-shaped nucleus; slight nuclear polymorphism*
  - ⇨ *low mitotic activity*
  - ⇨ *chromogranin A in cytoplasm*

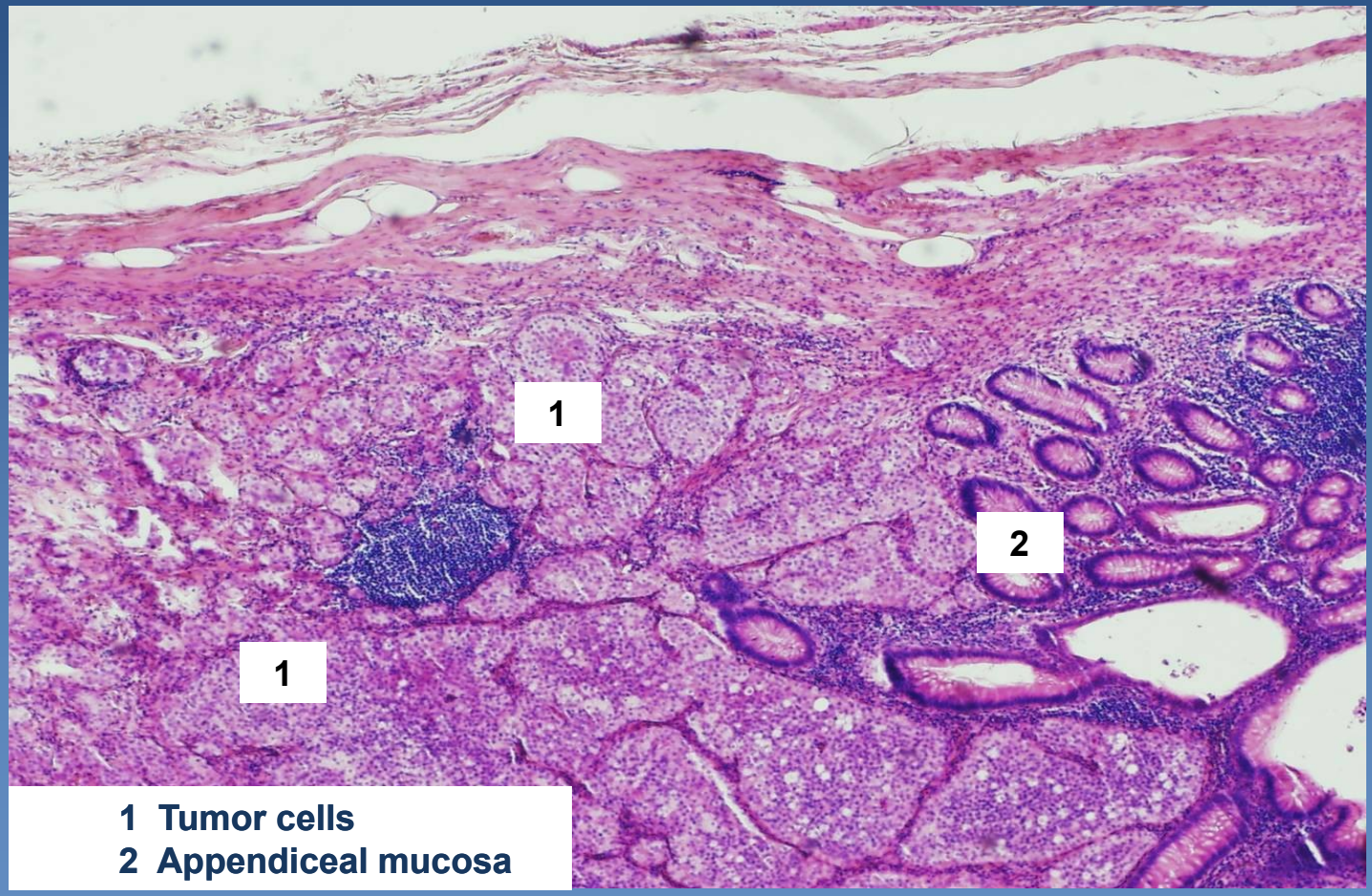
GEP-NET



- possible production of various endocrine substances: serotonin, somatostatin, gastrin
- *serotonin active only locally in intestine → intestinal hypermotility with diarrhea*
- liver metastases → carcinoid syndrome*:*

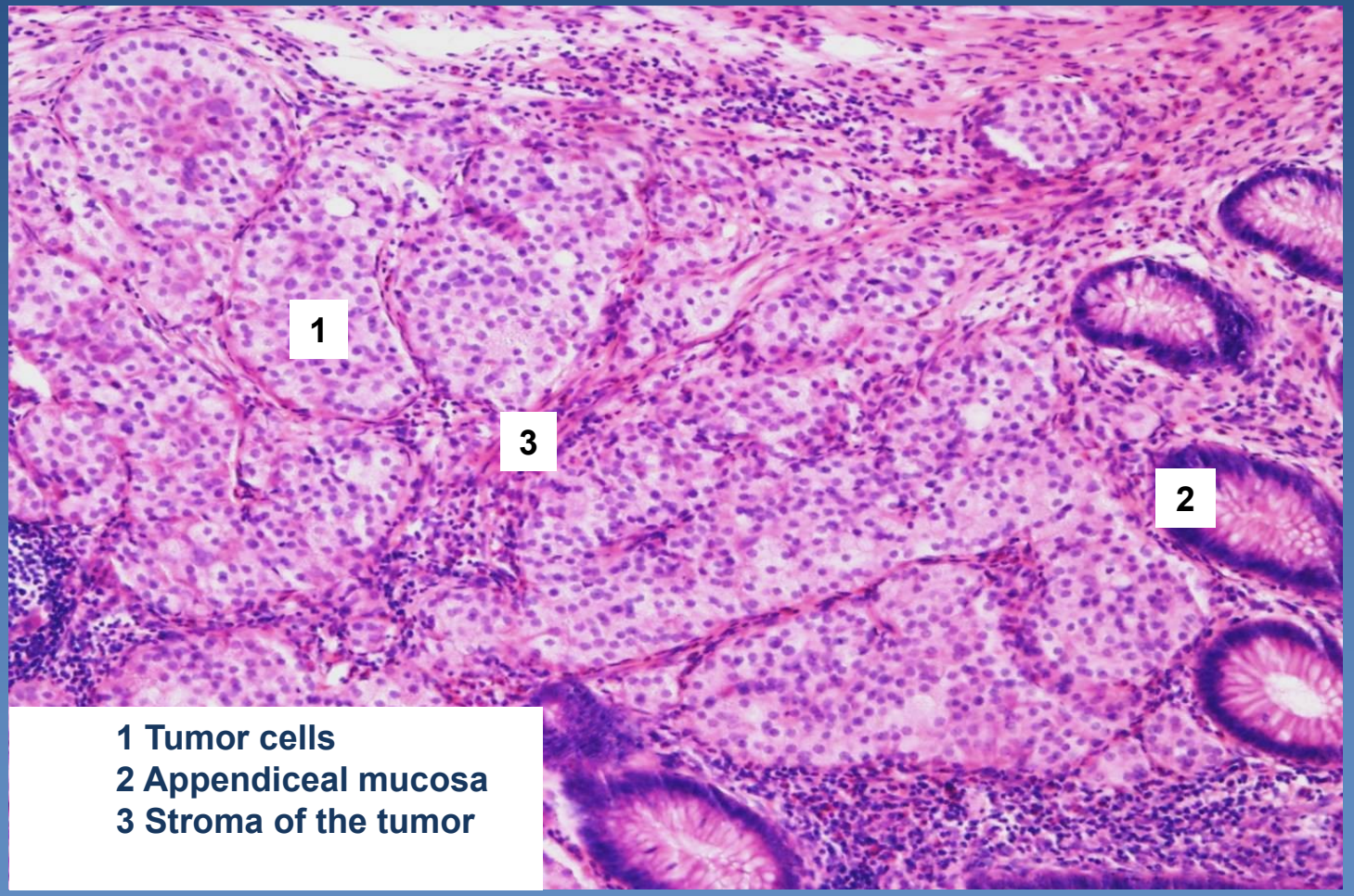
  cutaneous „flush“ and cyanosis, nausea and vomiting, astmatic bronchoconstrictive attacks, endocardial fibrosis in right ventricle, hepatomegaly

Carcinoid of the appendix



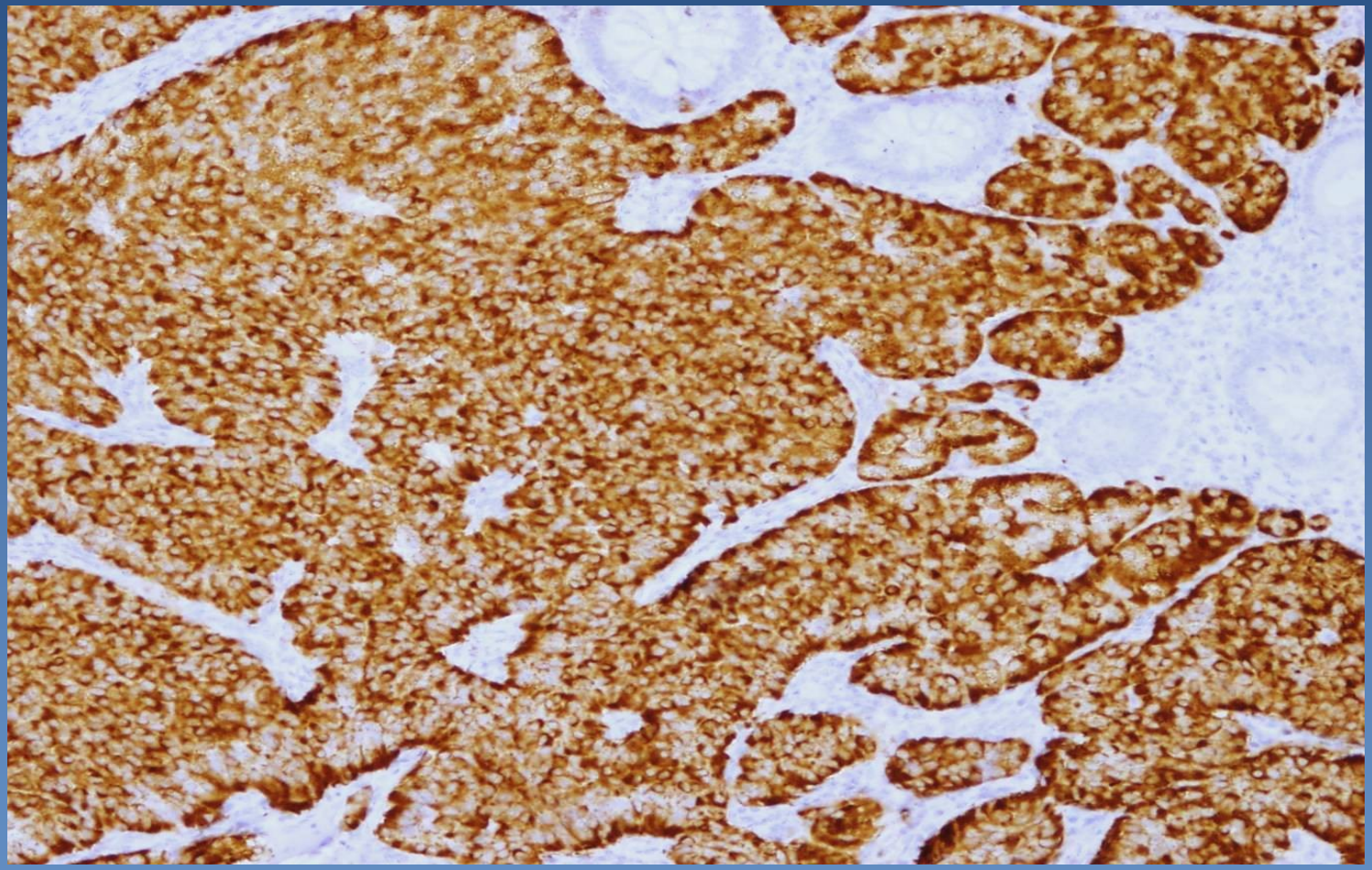
1 Tumor cells
2 Appendiceal mucosa

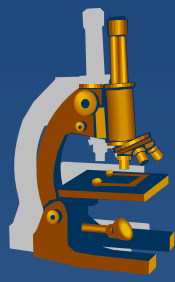
Carcinoid of the appendix
detail



1 Tumor cells
2 Appendiceal mucosa
3 Stroma of the tumor

Carcinoid of the appendix
(IHC chromogranin)





THANK YOU FOR ATTENTION