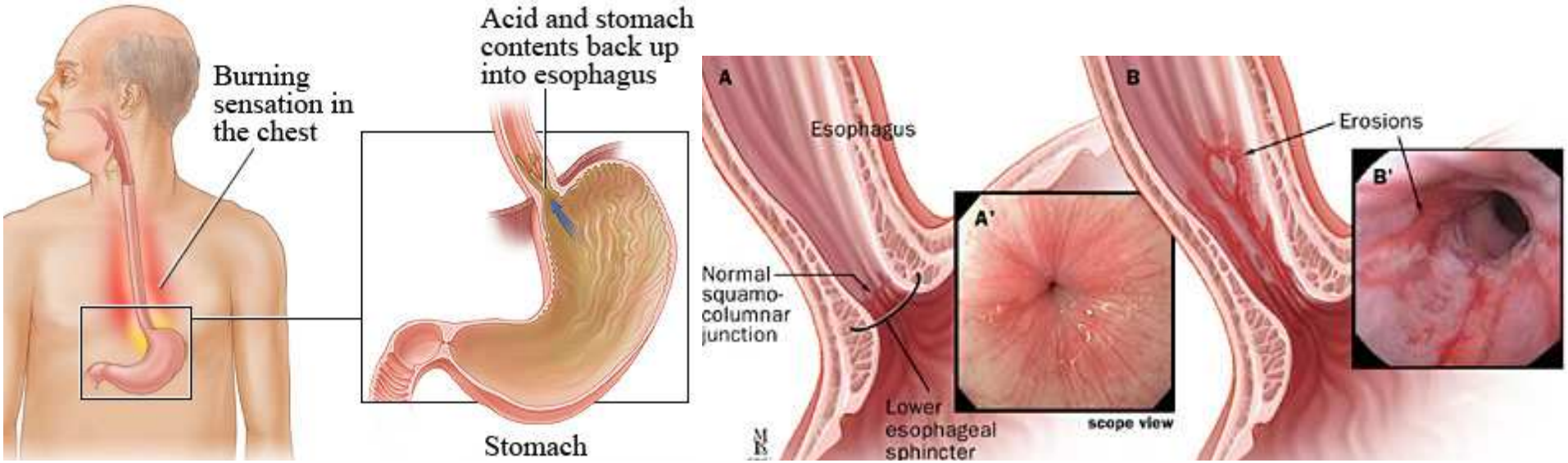
Barrett mucosa: histopathological assessment

A condition in which the normal stratified squamous epithelium of the oesophagus is replaced by metaplastic columnar epithelium

- The columnar-lined oesophagus was described by Norman Barrett in 1950
- Reported to be associated with gastroesophageal reflux disease in 1953

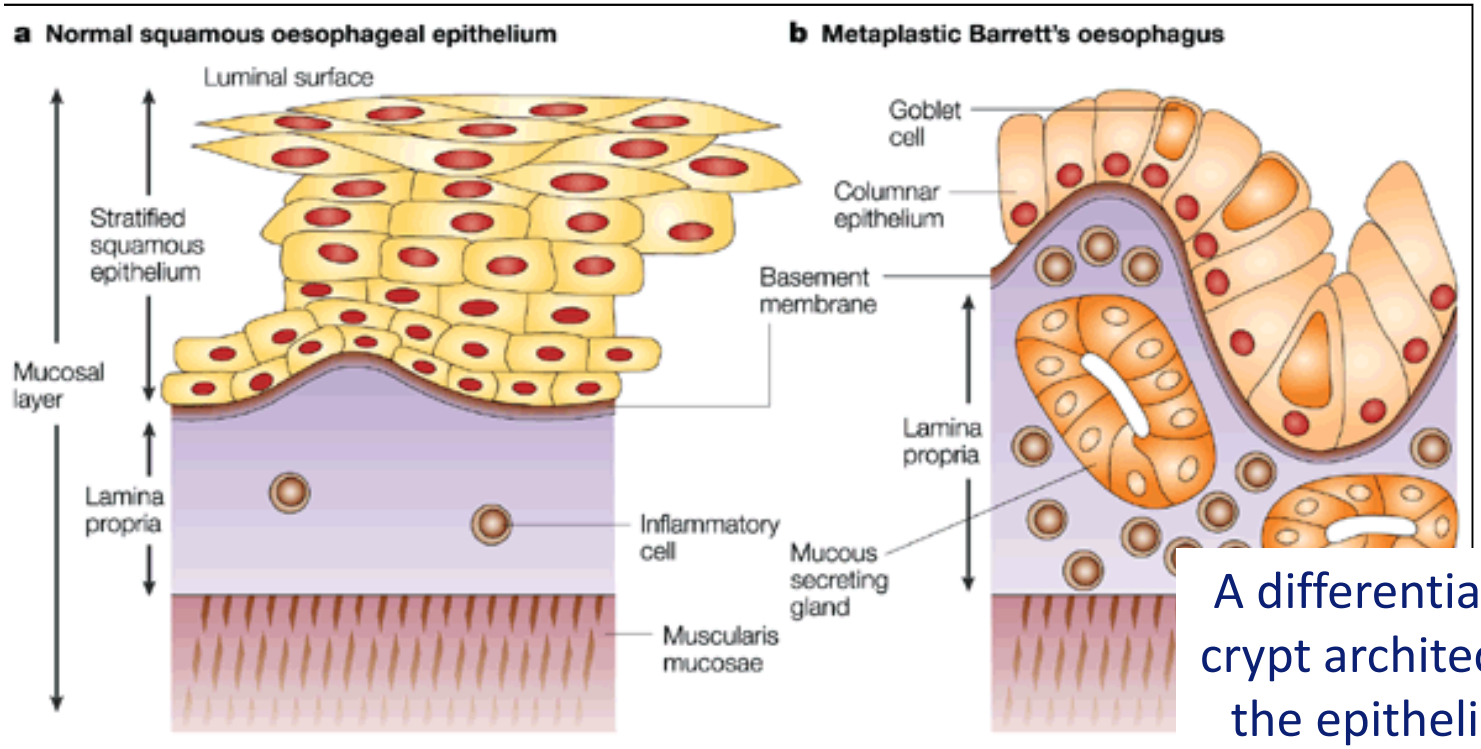


Barrett mucosa: histopathological assessment

The harsh intra-oesophageal environment of chronic GERD

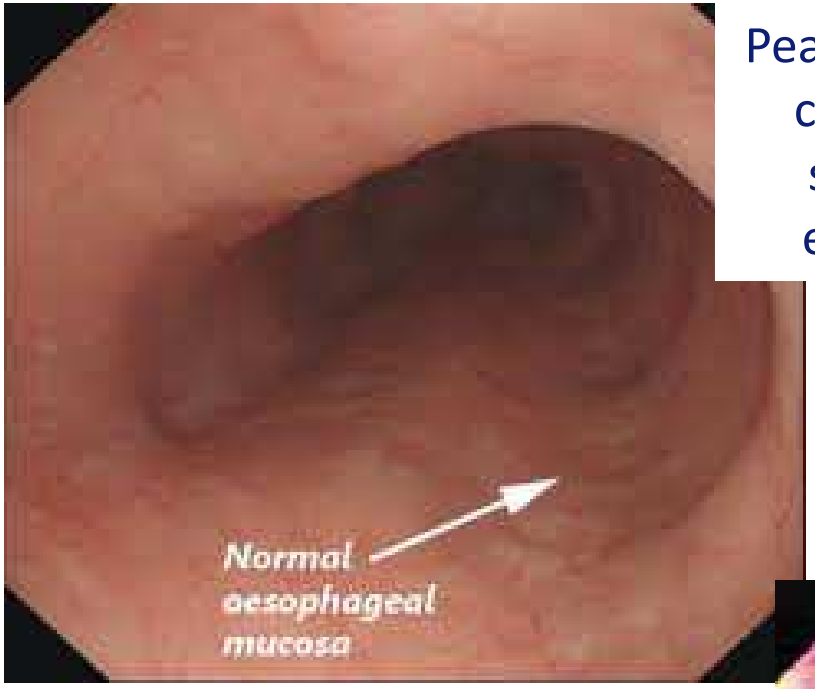
Adaptation of the epithelium

Specialized intestinal metaplasia

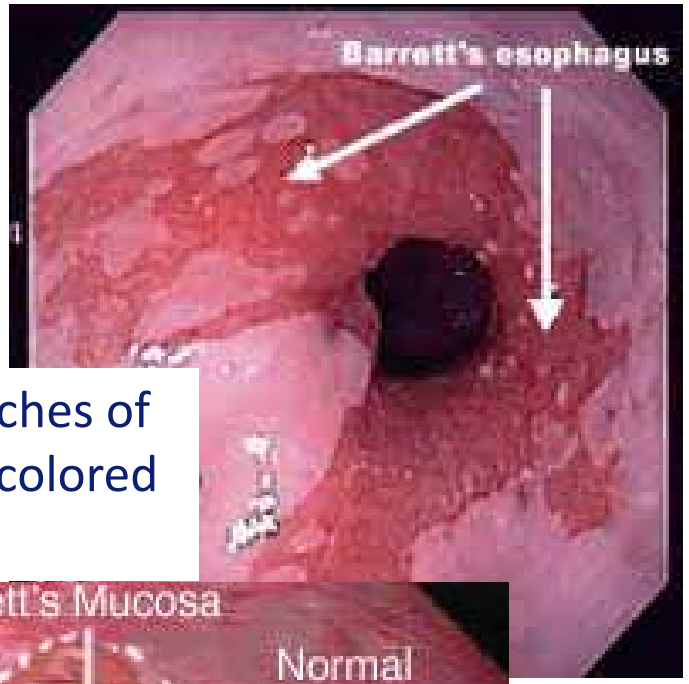


A differentiated epithelium with crypt architecture that resembles the epithelium of the intestine

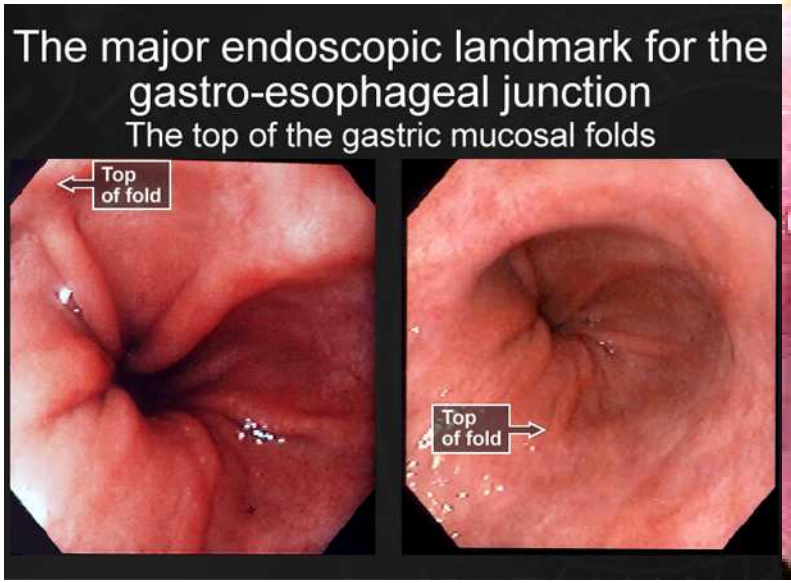
Barrett mucosa: histopathological assessment

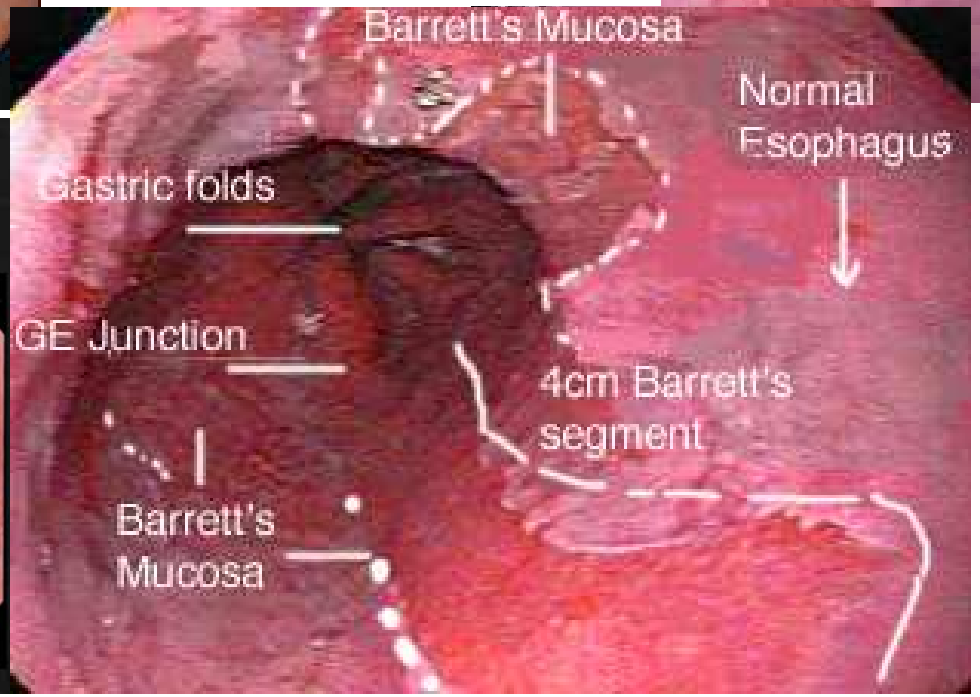


Pearly grey-pink color of the squamous epithelium

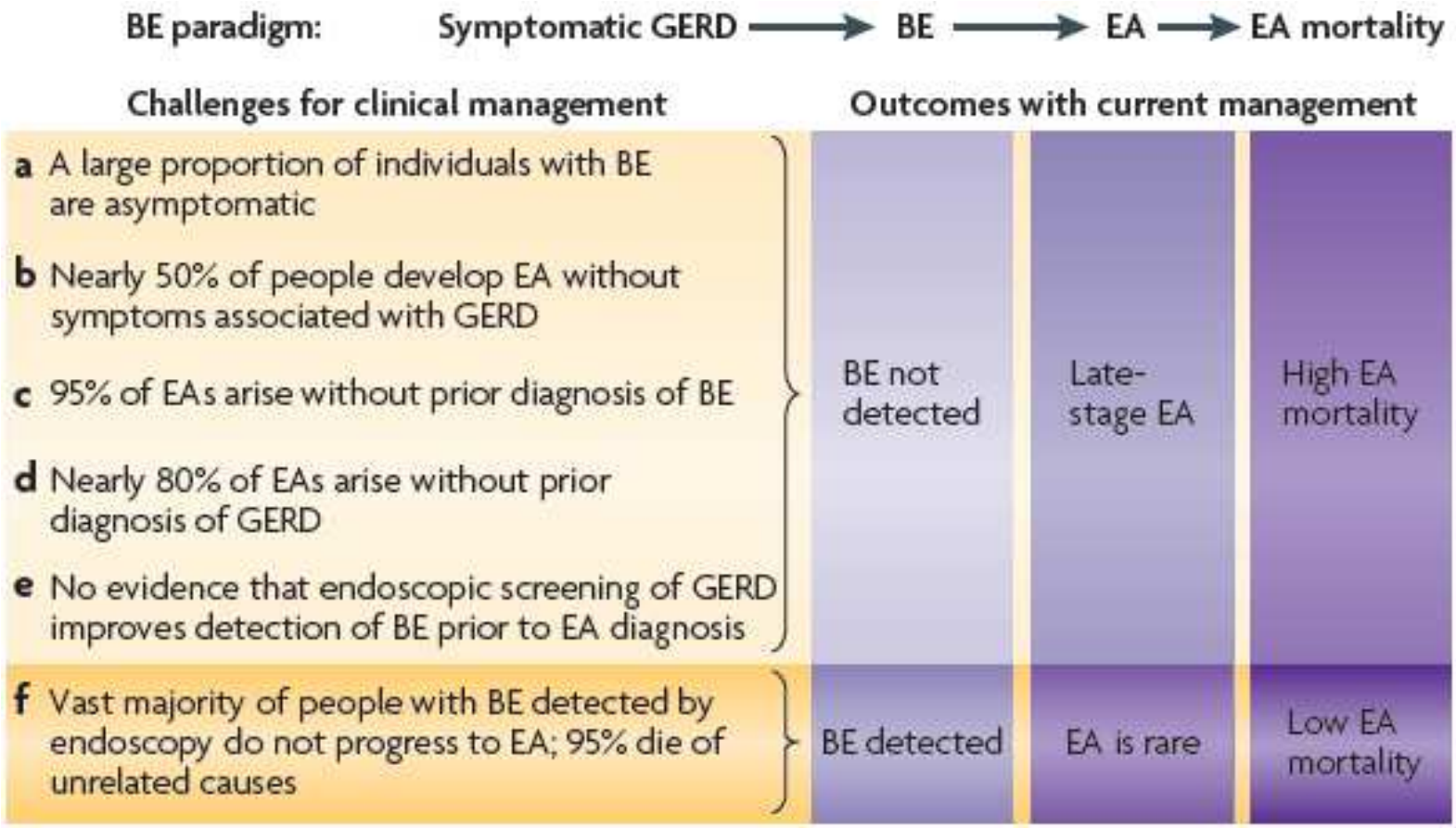


Tongues and patches of reddish, salmon-colored mucosa

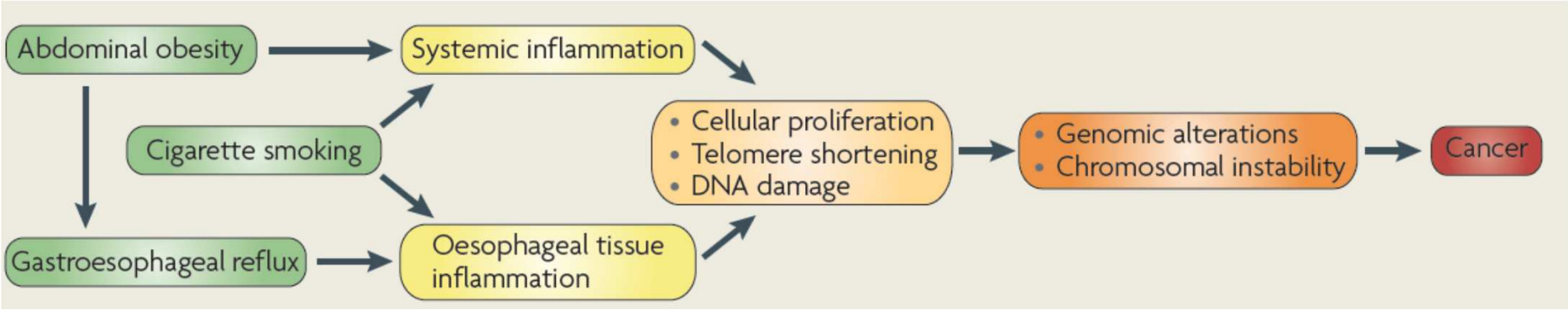




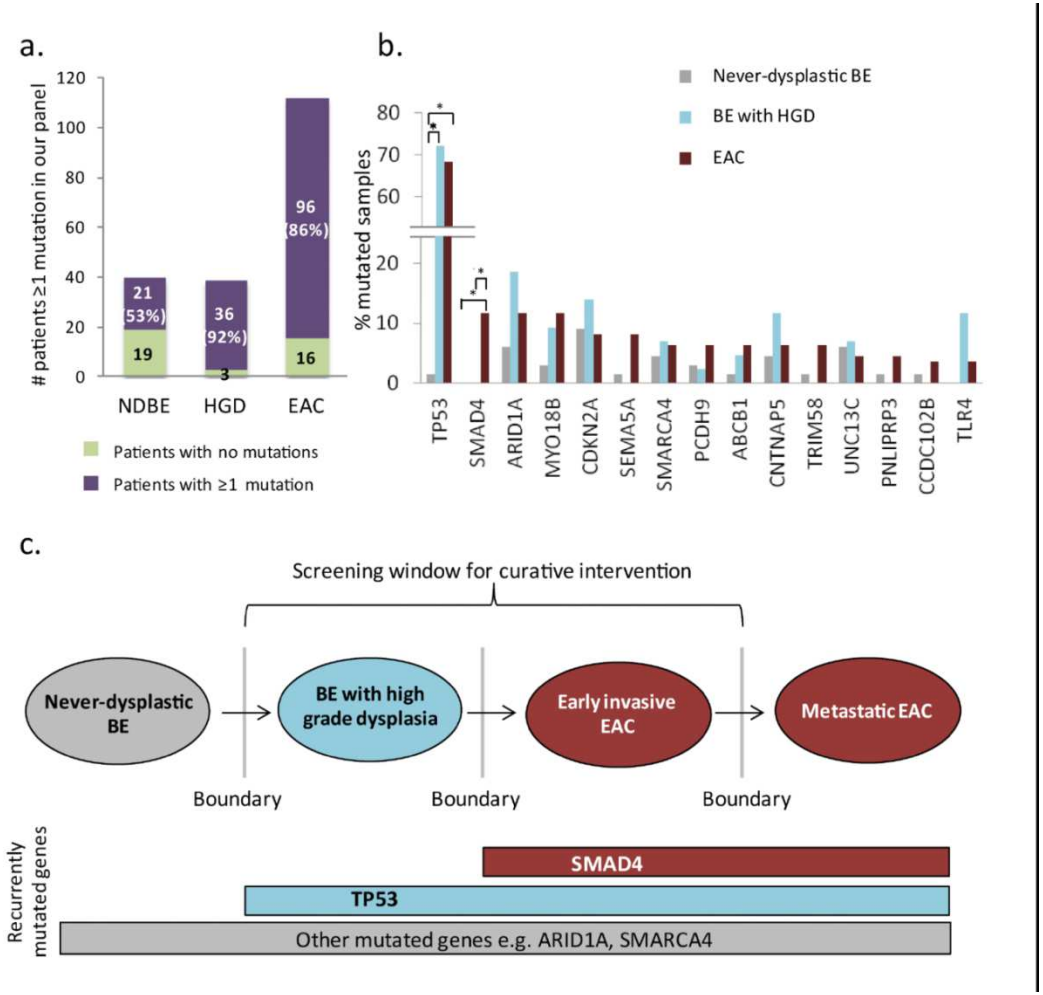
Problems in BE



Pathogenesis of BE

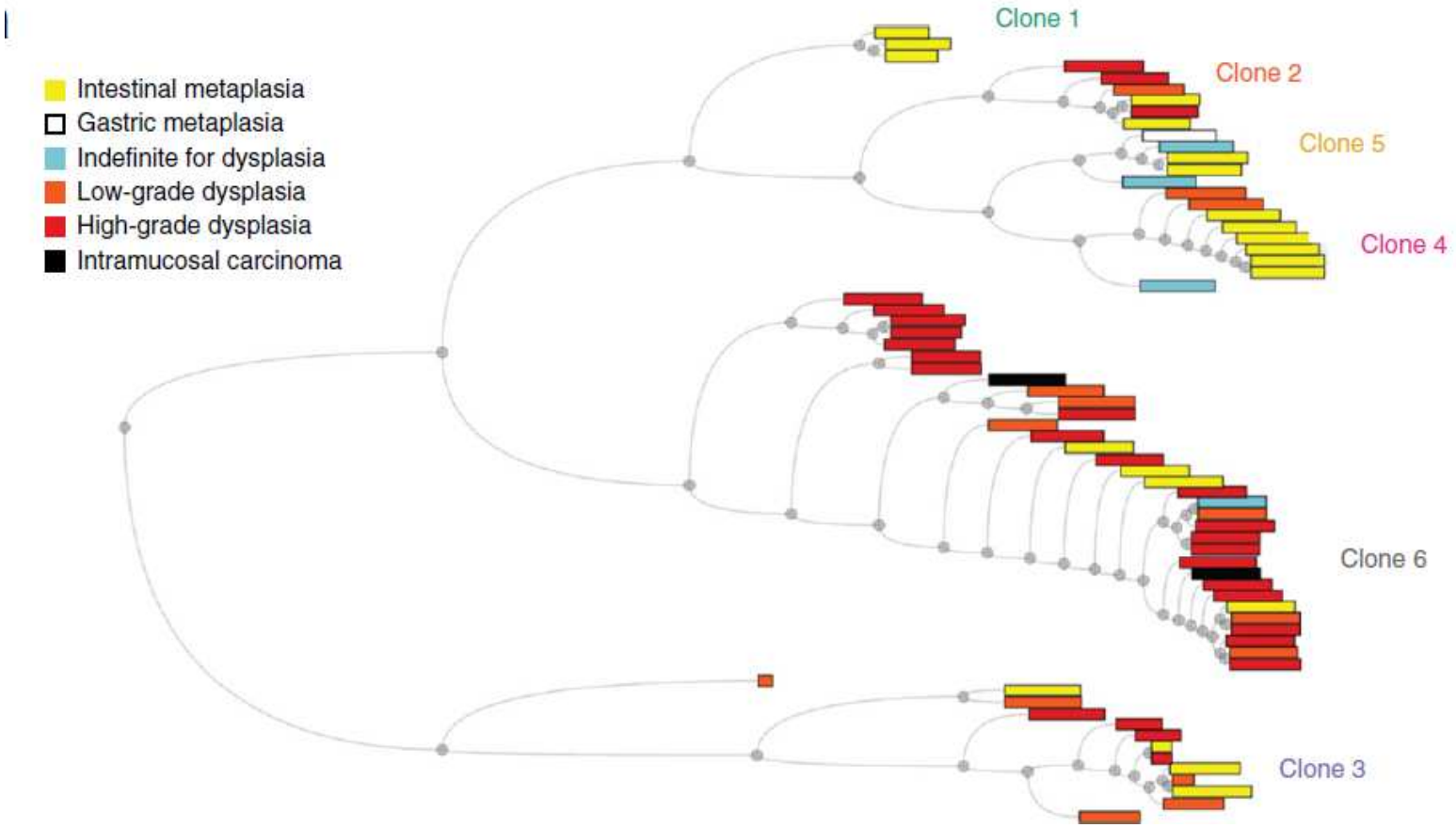


Complex landscape of mutations in preinvasive BE stages

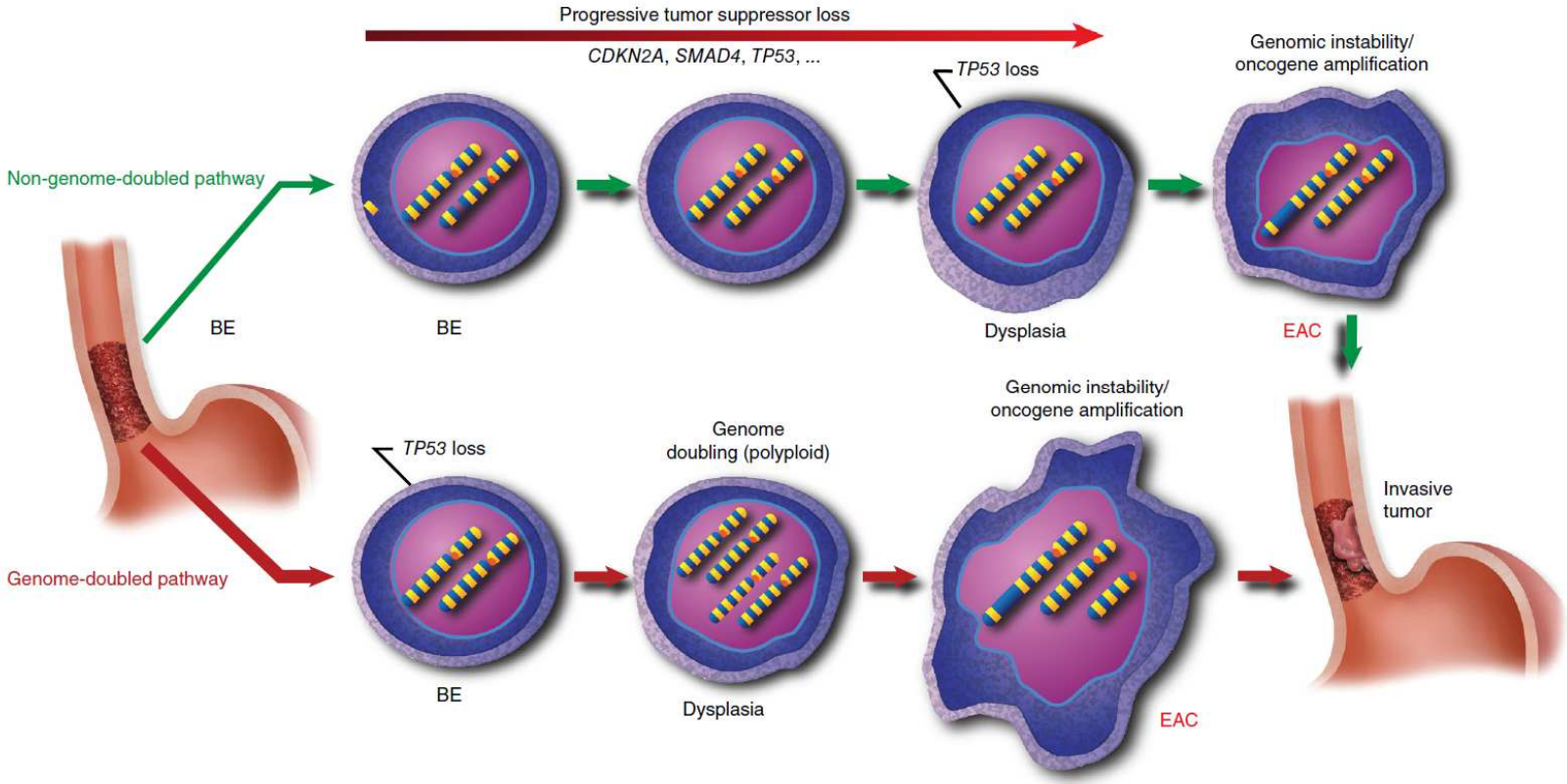


Ordering of mutations in preinvasive disease stages of esophageal cancer. Nat Genet 2014, Weaver et al.

WGS of BE patient



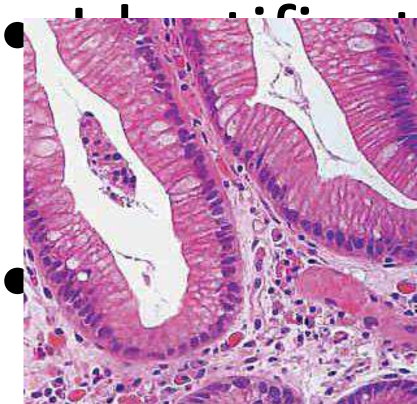
WGS of BE patient: different pathways



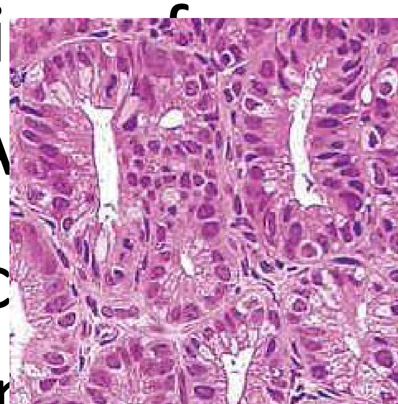
Neoplastic progression

- The development of EAC is a gradual process
- BE → Low-grade dysplasia → High-grade dysplasia → EAC

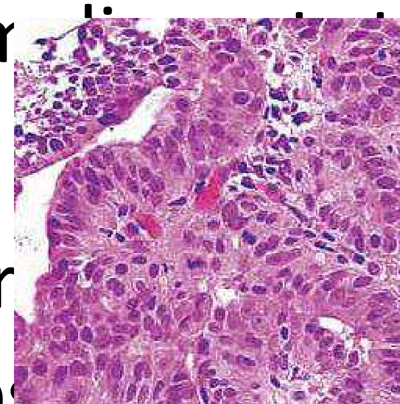
(gastroscopy with biopsy sampling)



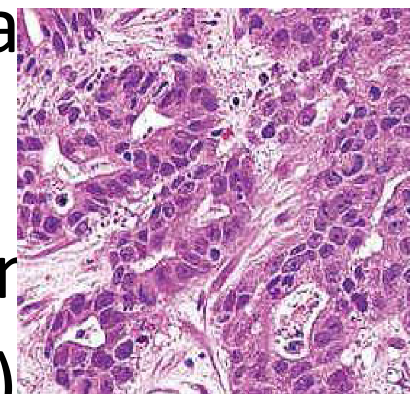
Barrett's esophagus (BE)



Low-grade dysplasia (LGD)

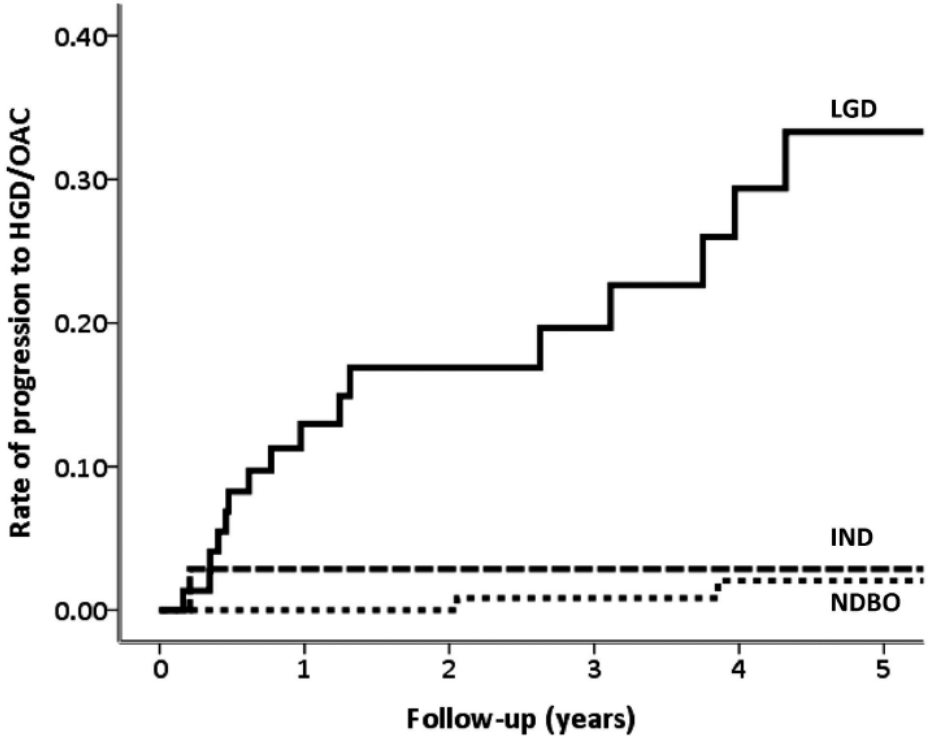


High-grade dysplasia (HGD)



Adenocarcinoma (EAC)

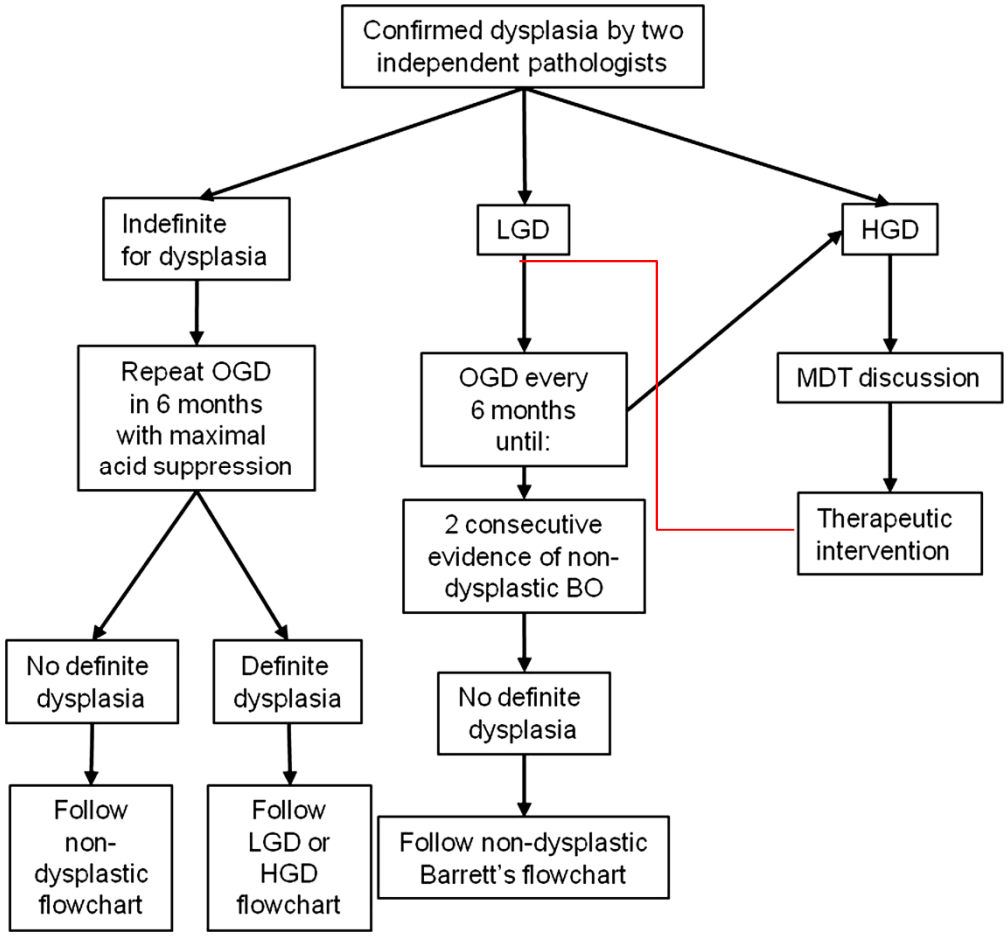
Progression in LGD over time



Number at risk at time (years)	1	2	3	4	5
LGD	49	33	27	21	16
IND	30	19	16	12	9
NDBO	137	125	104	75	59

Surveillance flow chart for dysplastic BE

Low overall incidence of EAC
Large screening base
(1 - 2% of the general population)



Barrett mucosa: histopathological assessment

Grading dysplasia according to mucosal features

- Surface maturation (compared to the underlying glands)
- Architecture of the glands
- Cytologic features
- Inflammation and erosions/ulcers

* Biopsy taken from oesophagus – Contain compatible endoscopic features of Barrett – Intestinal metaplasia is found

Barrett mucosa: histopathological assessment

Amongst the most common types of biopsies encountered in daily practice are esophageal biopsies to evaluate for Barrett esophagus

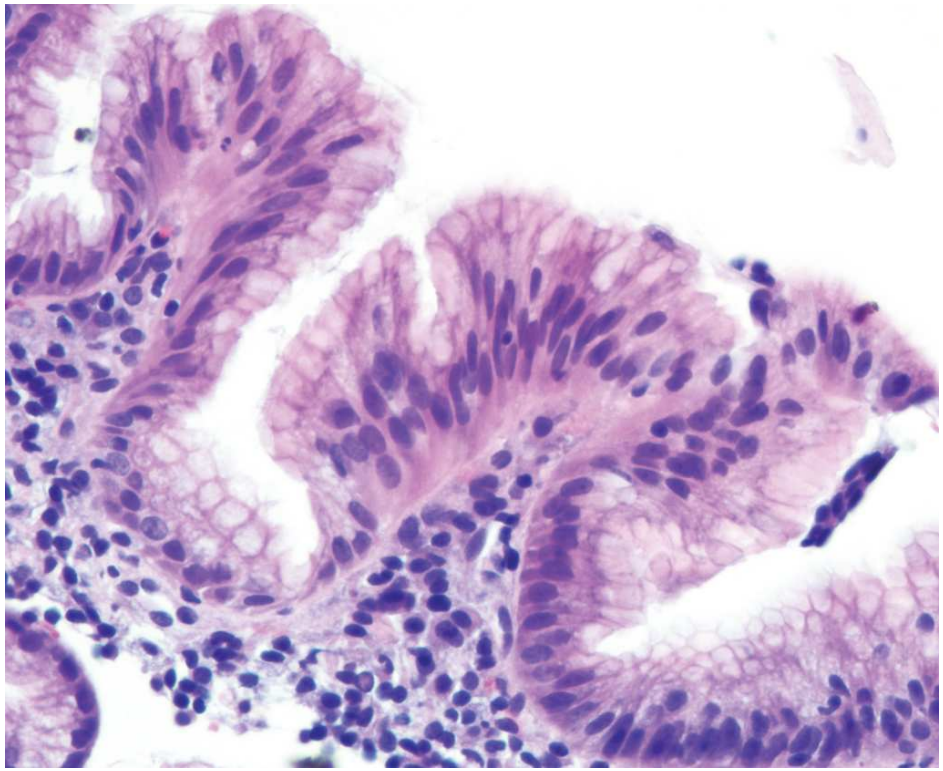
Difficulties in evaluation include:

- Duplicated muscularis mucosae in endoscopic mucosal resection (EMR)
- Distinguishing reactive changes from dysplastic ones
- Identifying intestinal metaplasia on H-E slides

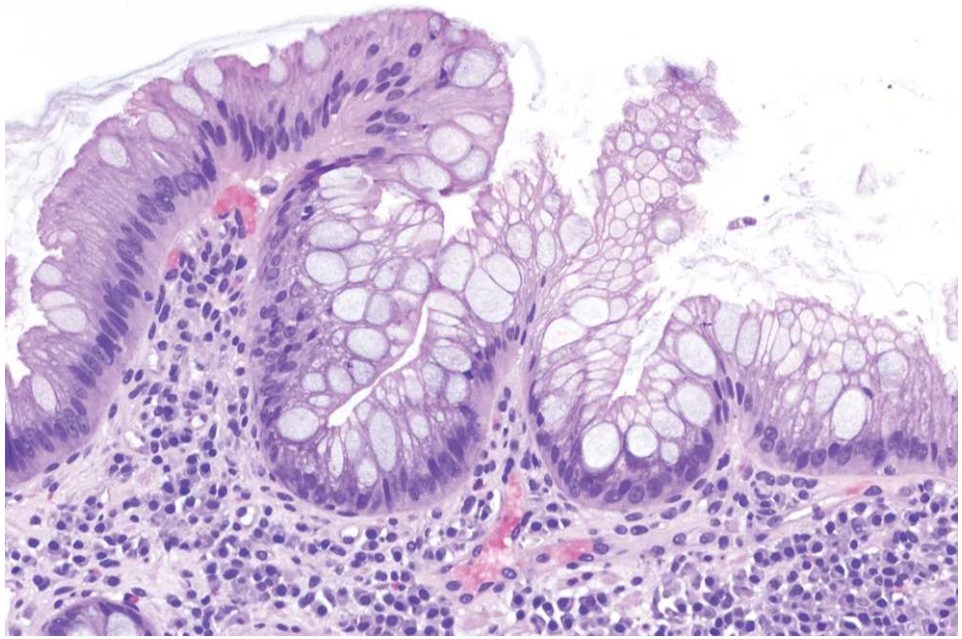
LGD criteria

Derivation set definition	Validation set definition	Weighted kappa Derivation/Validation set	P-value
Loss of surface maturation	**On low power, no maturation of the epithelium is seen from the proliferation zone until the surface**	**0.27/0.55**	**<0.001**
Clonal step	Abrupt transition of normal epithelium next to dysplastic epithelium	0.05/0.36	0.193
Loss of polarity	More than 45 degrees of deviation of the longitudinal nuclear axis	0.06/0.29	0.001
Mucin depletion	**On high power, almost total to total disappearance of mucus from the surface columnar cells, dystrophic goblet cells* can be permitted**	**0.11/0.51**	**<0.001**
Stratification of nuclei	Piling of nuclei with minimum of 2 nuclei on top of each; the nuclei do not overlap	0.04/0.29	<0.001
Nuclear enlargement	**Nuclear size at least 2x as large as nuclei of the normal columnar epithelium**	**0.07/0.41**	**<0.001**
Form of nuclei	Elongated (pencil shaped) or round-oval nuclei	0.02/0.13	0.034
Nuclear pleomorphism	Fluctuation of size and form of nuclei compared to nearby normal nuclei of the surface epithelium	0.13/0.36	0.001
Hyperchromasia	Nuclei with a darker hue in comparison to the nuclei of normal columnar epithelium, nucleolus is often not recognizable anymore	0.18/0.25	0.329
Prominent nucleolus	Multiple clearly enlarged nucleoli (macronucleoli)	-0.10/0.16	<0.001
Increase in apoptosis	More than 3 crypts in a hundred crypts with nuclear- or necrotic debris	0.03/0.13	0.154
Increase in mitoses	**One or more mitoses at the surface or in the neck of the crypts**	**0.13/0.48**	**<0.001**

Barrett mucosa: histopathological assessment

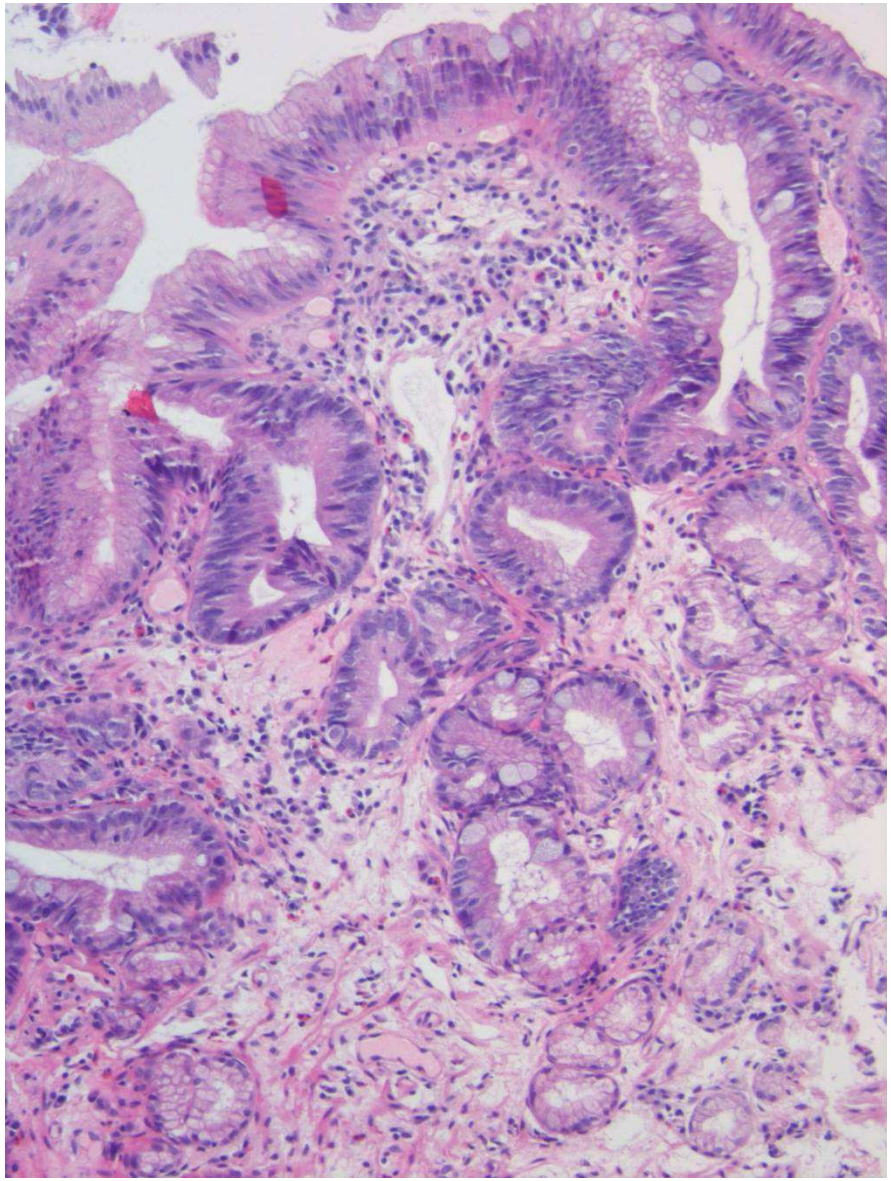


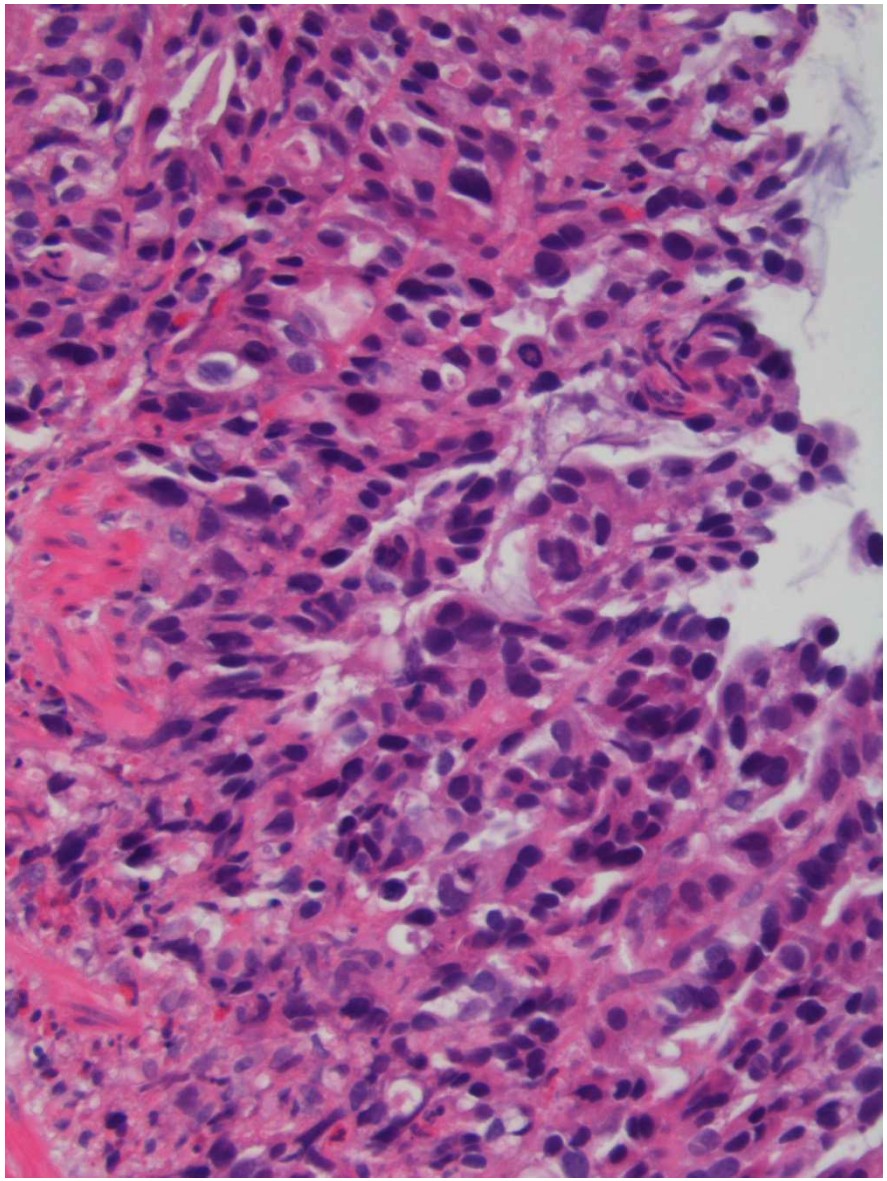
Foveolar Epithelium



Intestinal metaplasia

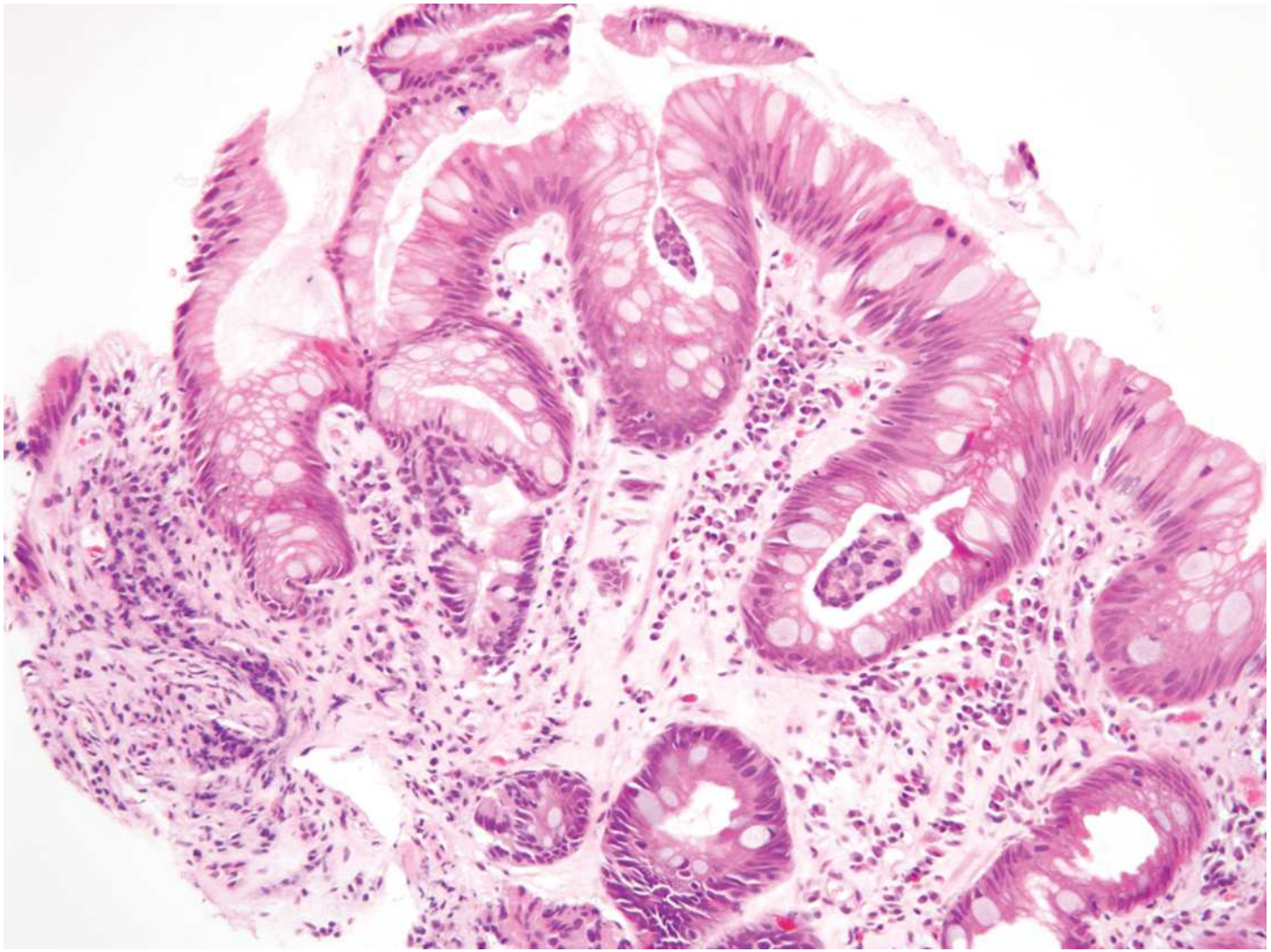
Barrett mucosa: histopathological assessment





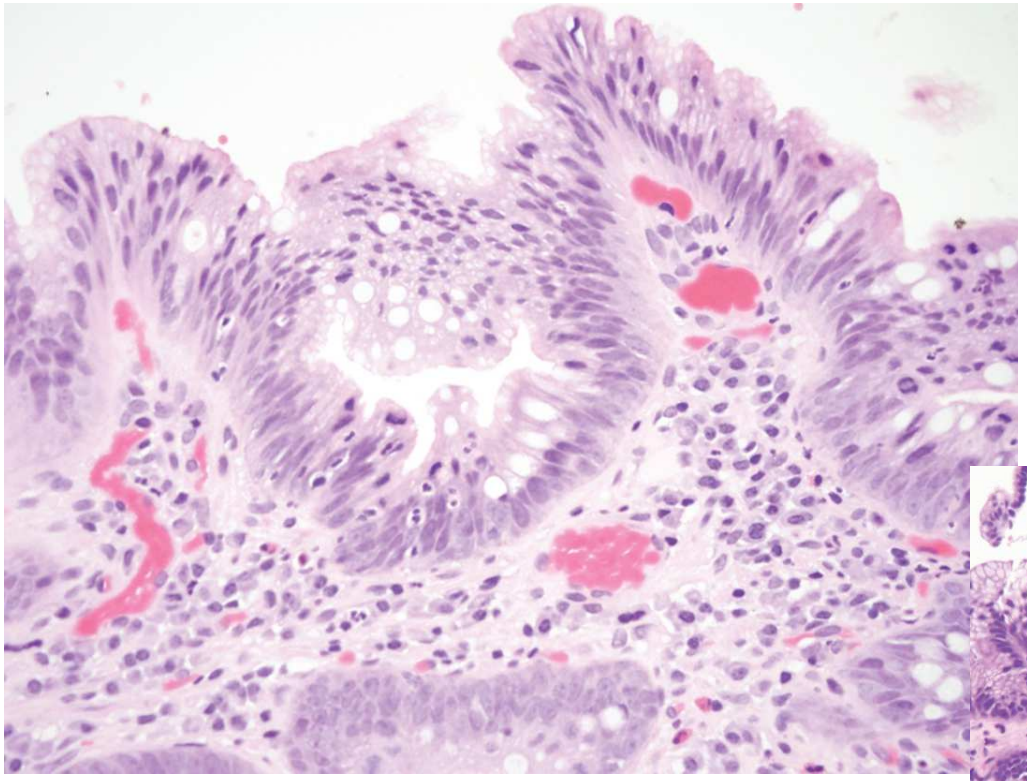
Barrett mucosa: histopathological assessment

Barrett oesophagus: **Negative** for dysplasia

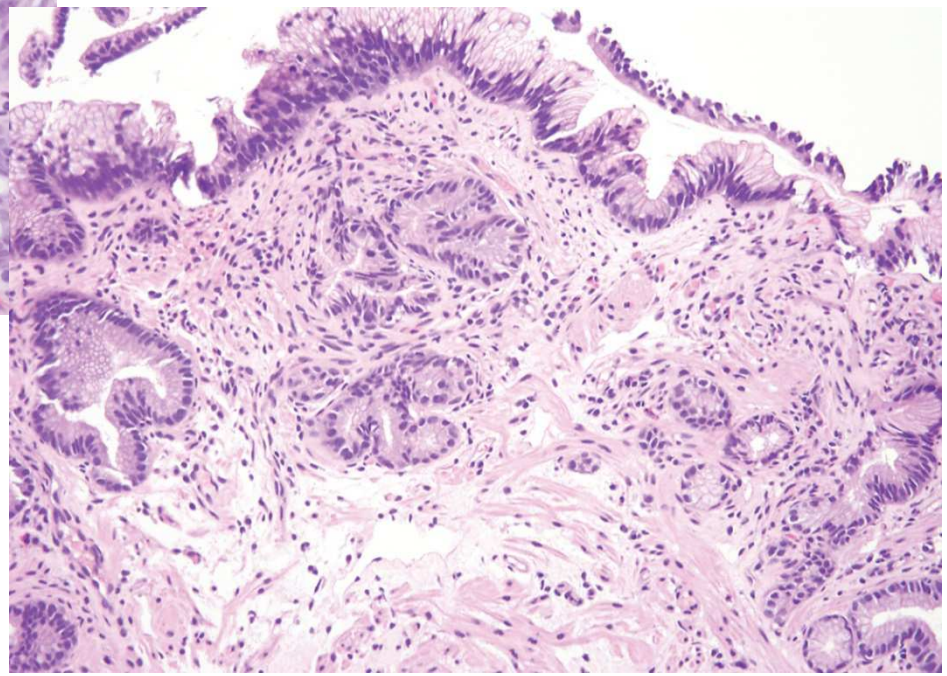


Barrett mucosa: histopathological assessment

Barrett oesophagus: **Indefinite** for dysplasia



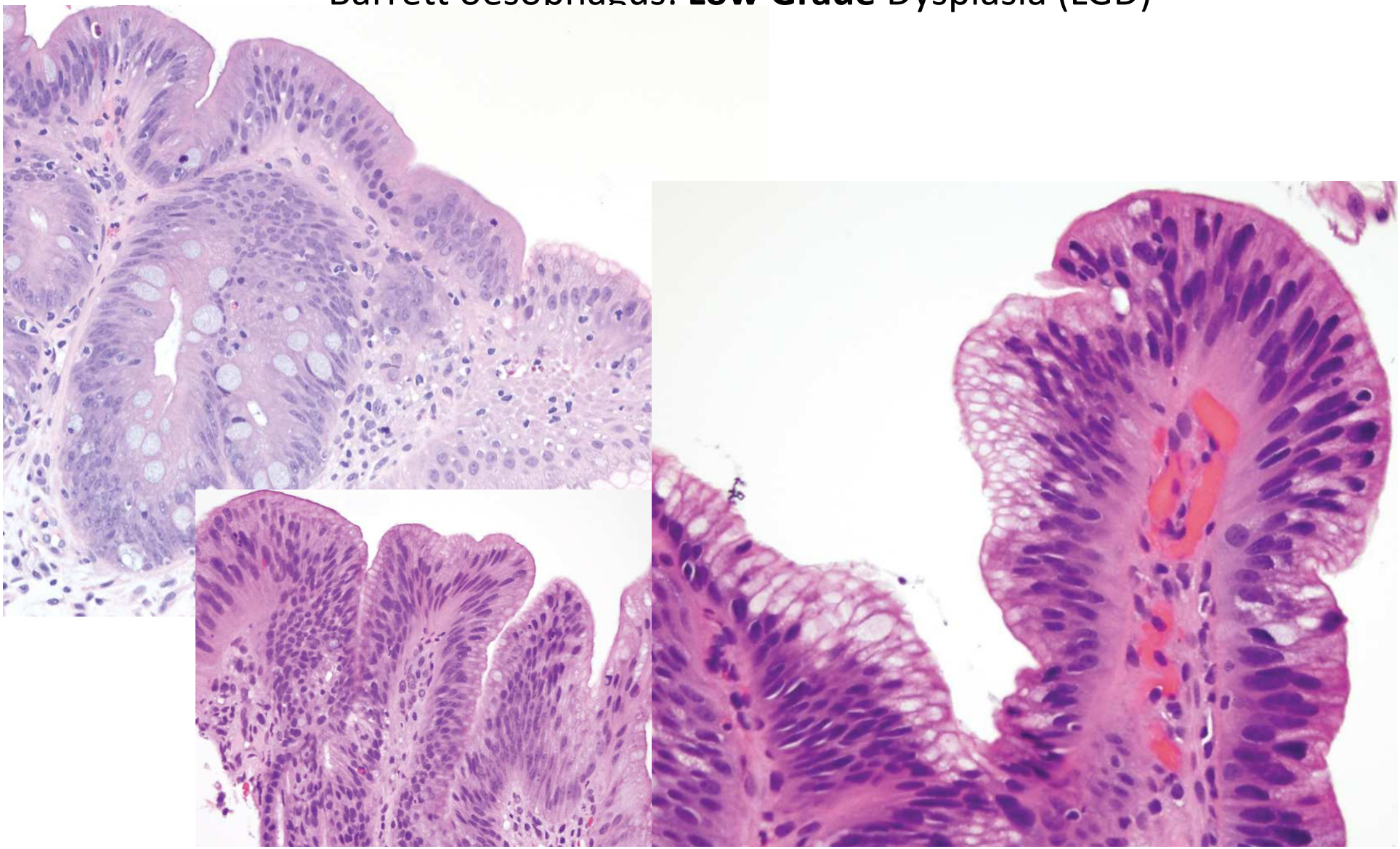
- Inflammation
- Tangential embedding-cutting
- Hypermucinous features



Offer an explanation

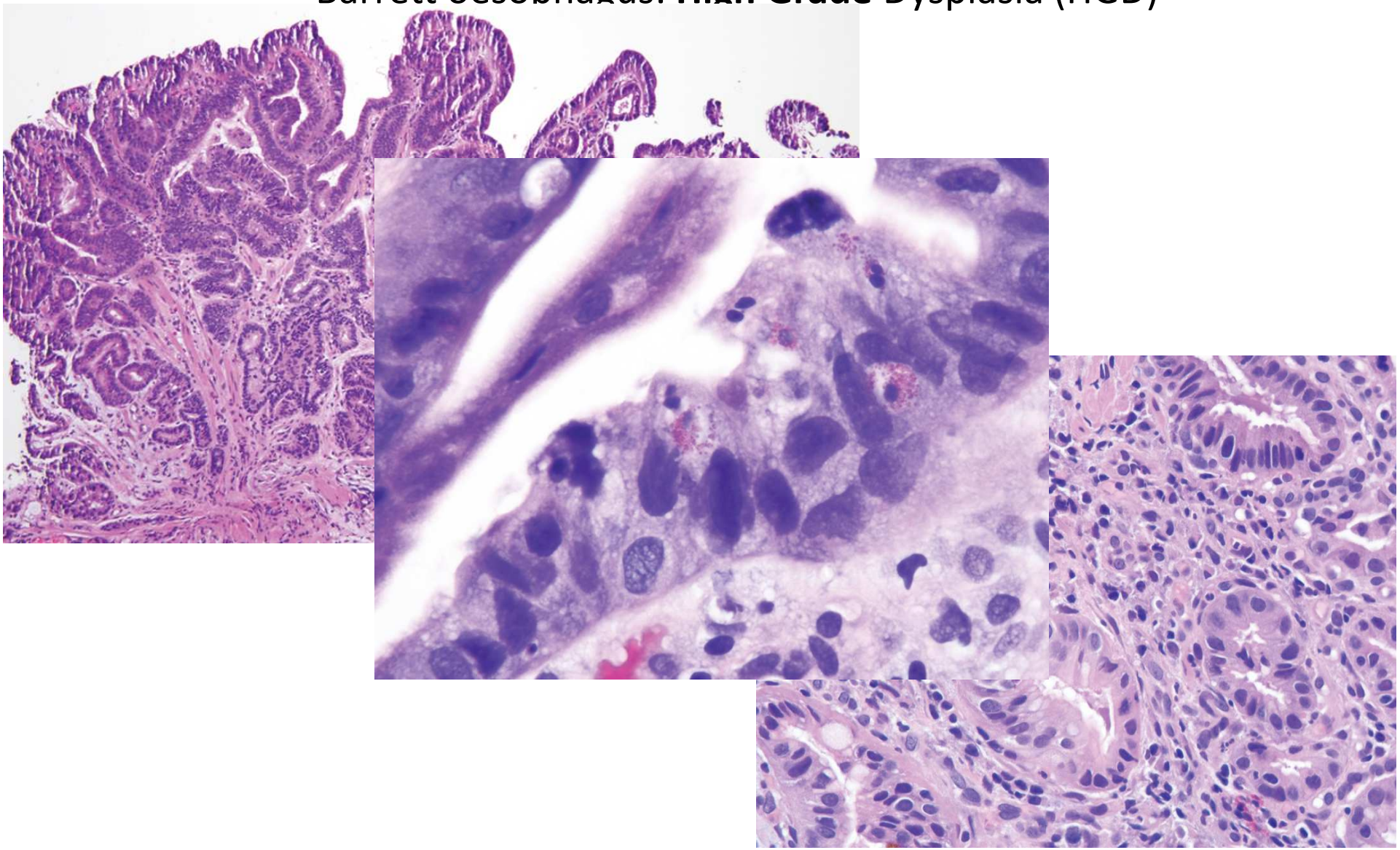
Barrett mucosa: histopathological assessment

Barrett oesophagus: **Low Grade** Dysplasia (LGD)



Barrett mucosa: histopathological assessment

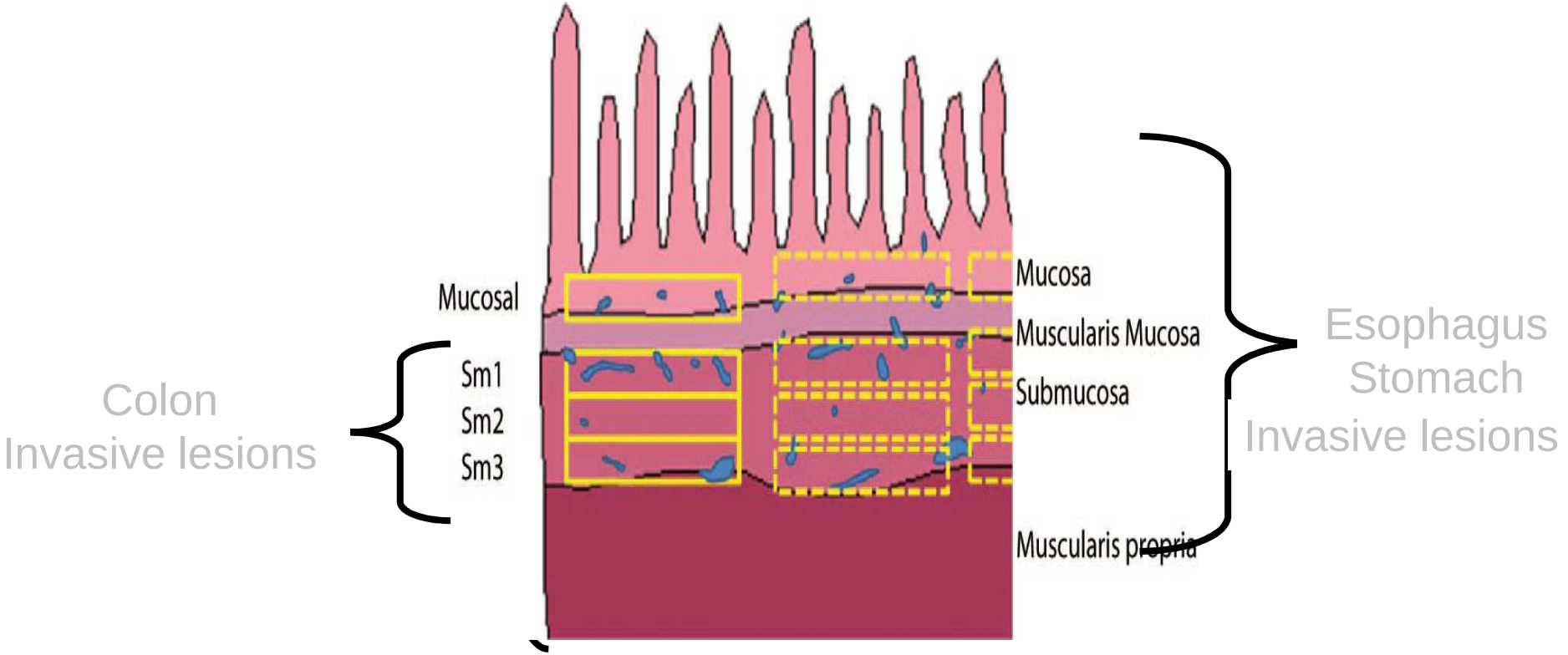
Barrett oesophagus: **High Grade** Dysplasia (HGD)



Barrett mucosa: histopathological assessment

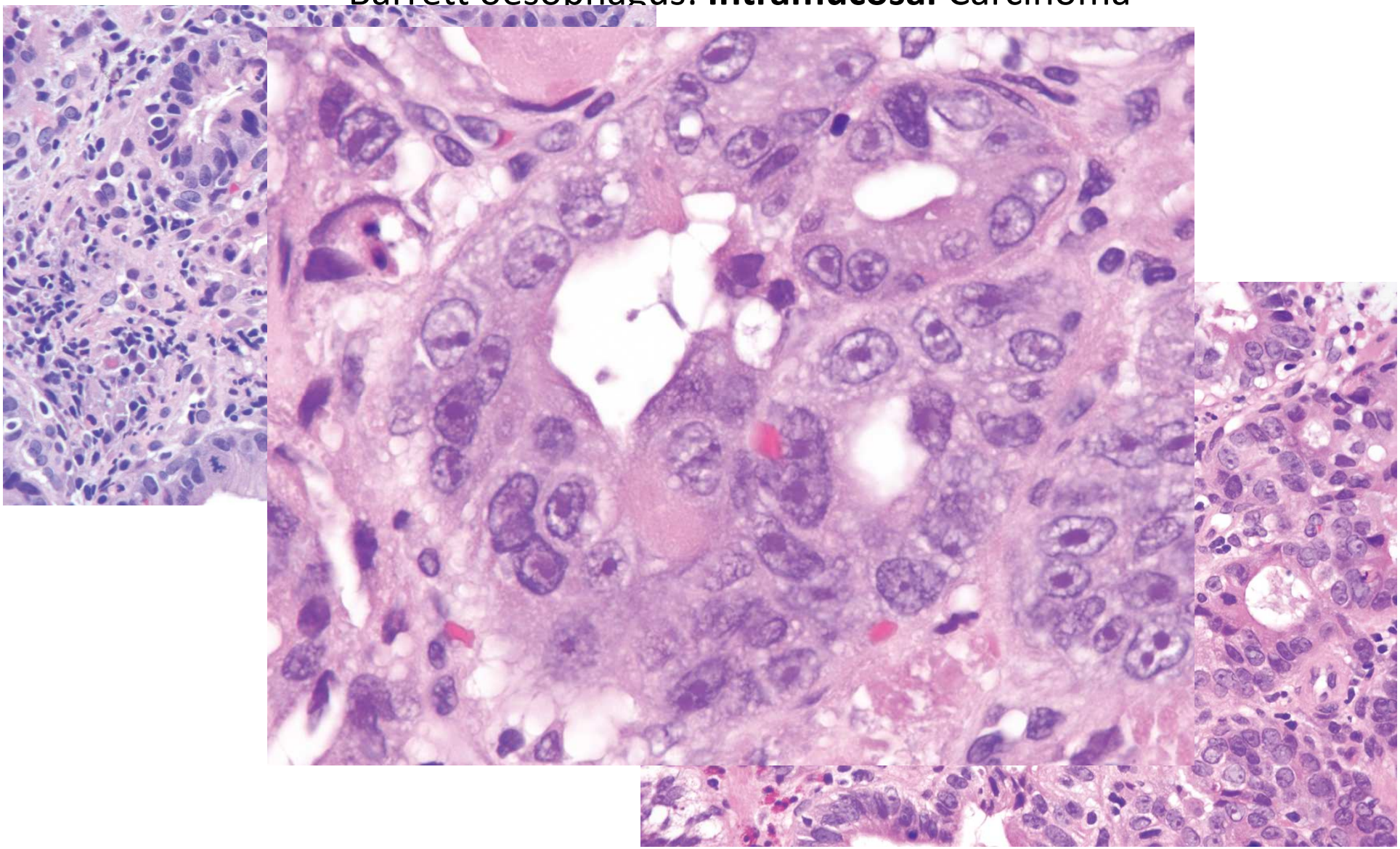
Barrett oesophagus: **Intramucosal** Carcinoma

(invasion through the basement membrane into the lamina propria or muscularis mucosae but not beyond)



Barrett mucosa: histopathological assessment

Barrett oesophagus: **Intramucosal** Carcinoma



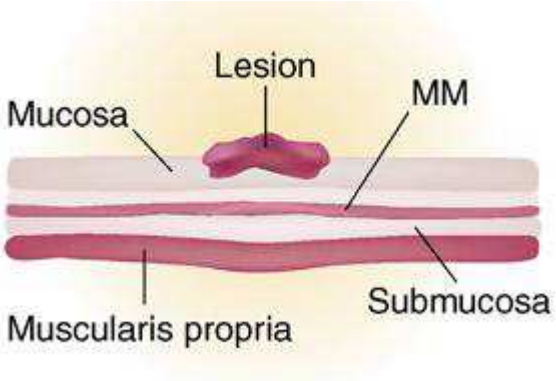
Barrett mucosa: histopathological assessment

Using modern techniques, endoscopic treatment for HGD and intramucosal carcinoma has become the standard

Surveillance epidemiology and end results data show that patients with HGD and early carcinomas have the same mortality whether managed endoscopically or surgically

Endoscopic Mucosal Resection (EMR)

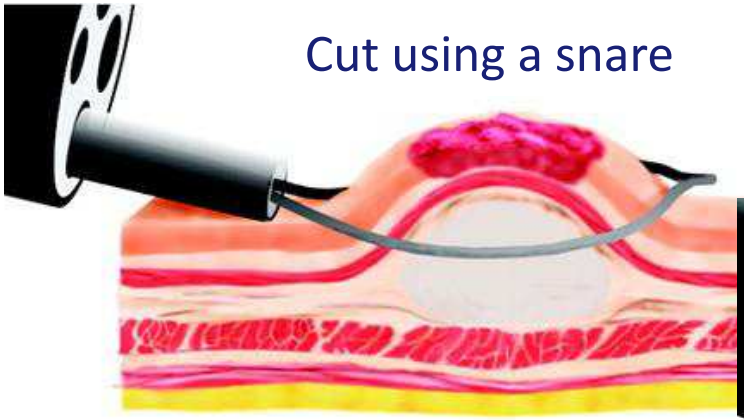
Barrett mucosa: histopathological assessment

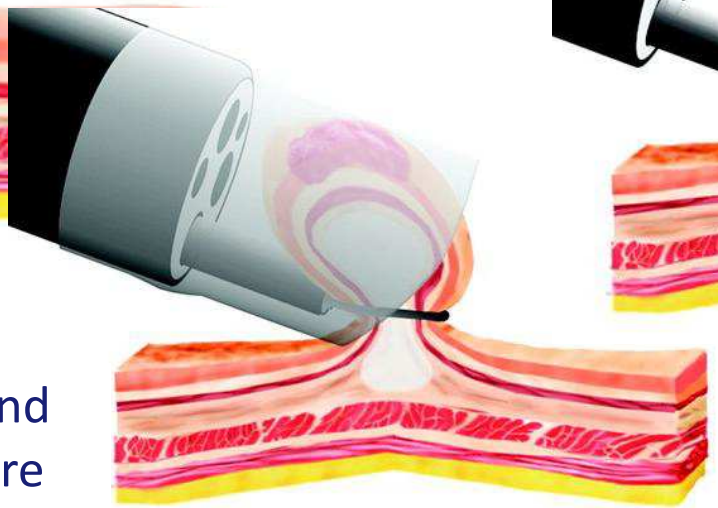


Lift the mucosa by injecting in the submucosa fluid

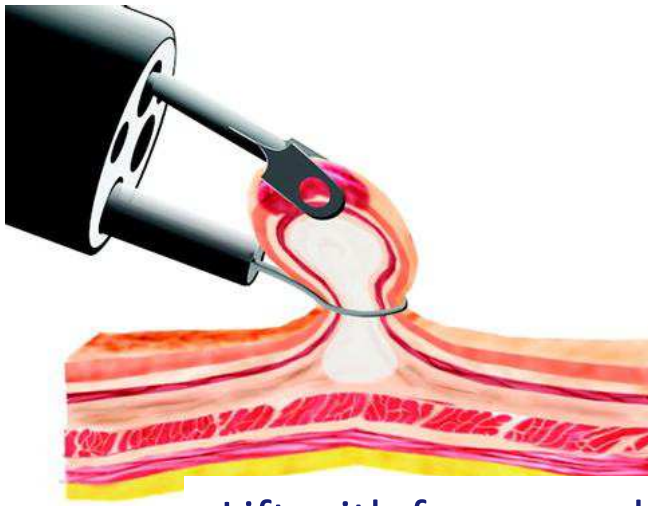
This creates an artificial “polyp” that is then resected using a cauterizing snare

Cut using a snare



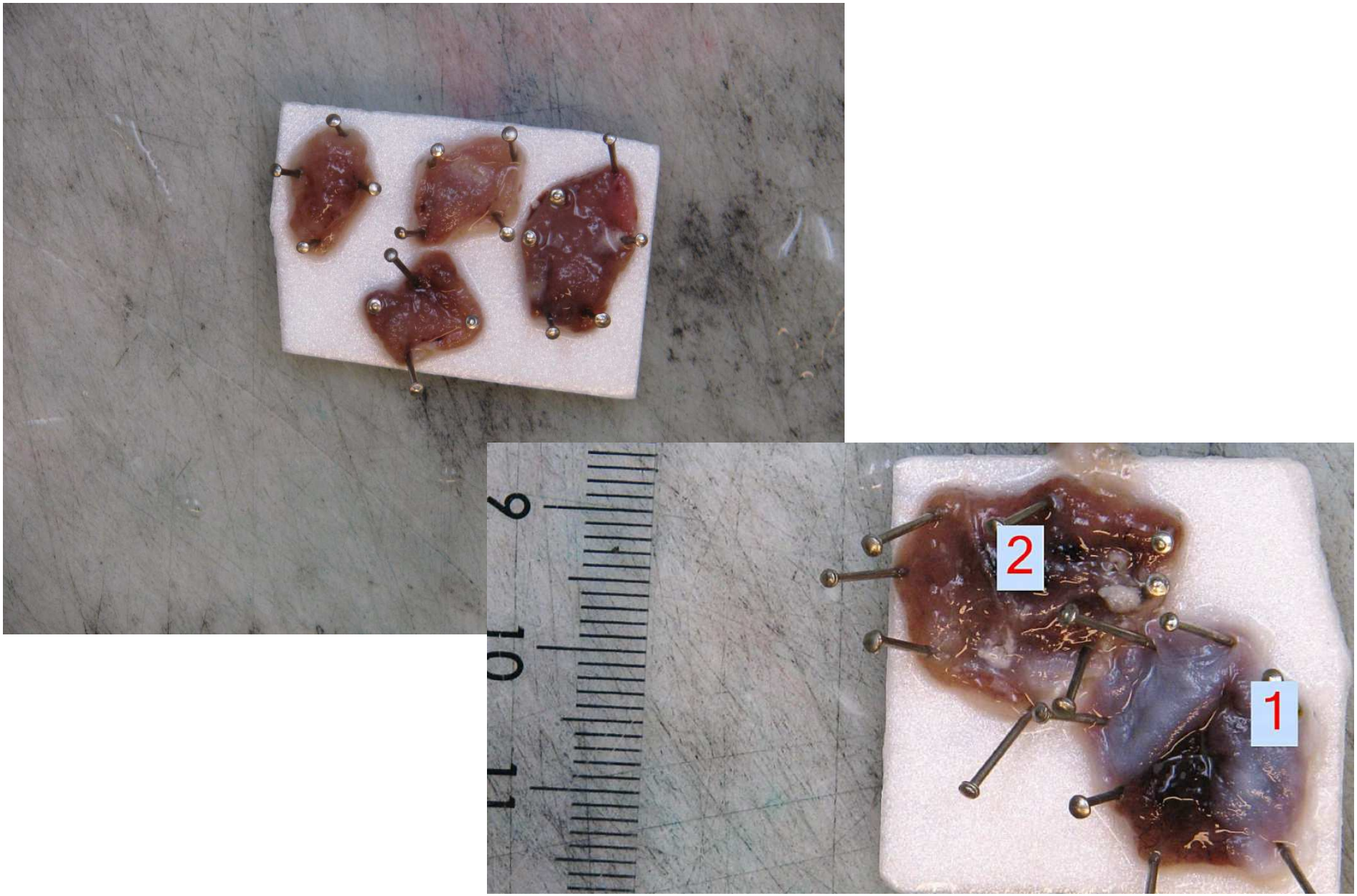


Suck into cup snd cut using a snare

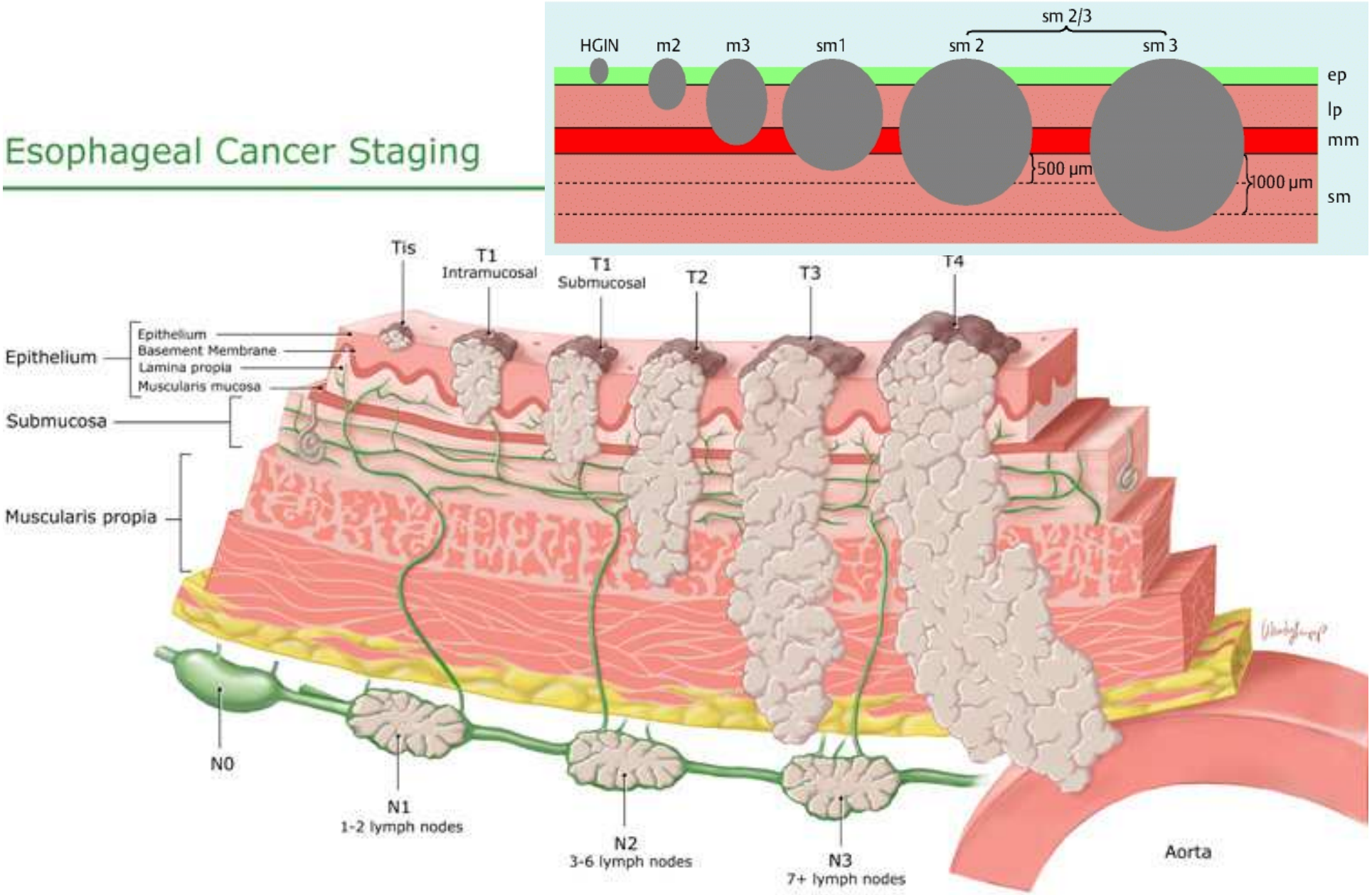


Lift with foecps and cut using a snare

Barrett mucosa: histopathological assessment

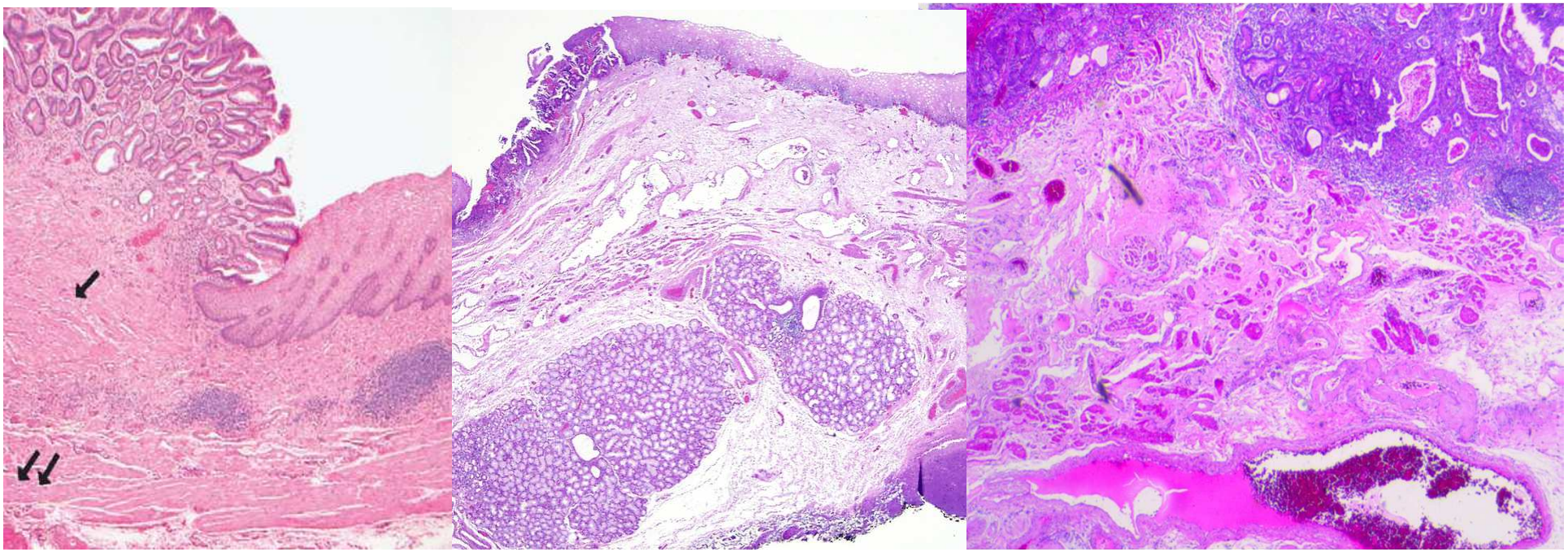


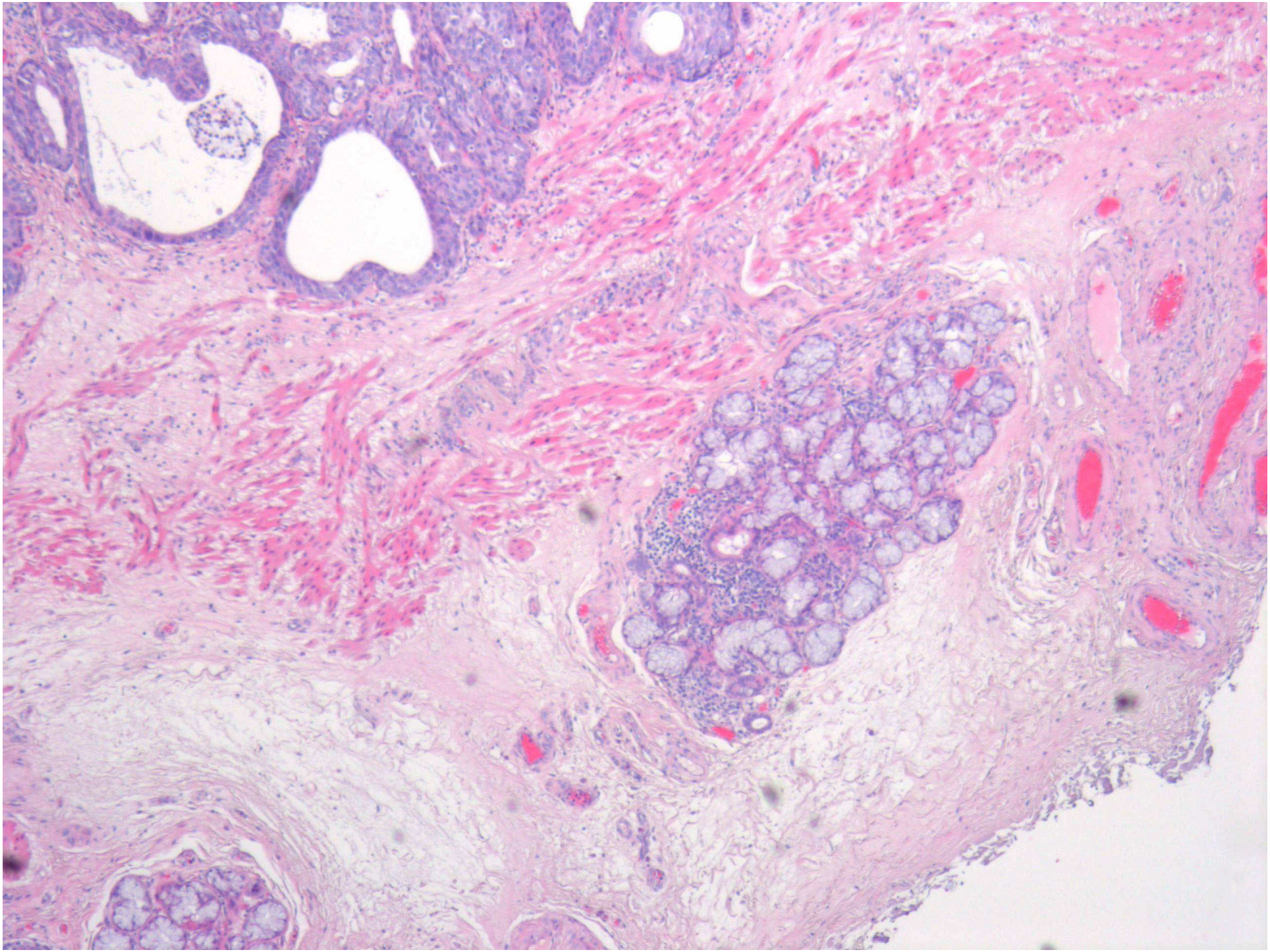
Barrett mucosa: histopathological assessment



Histologic assessment

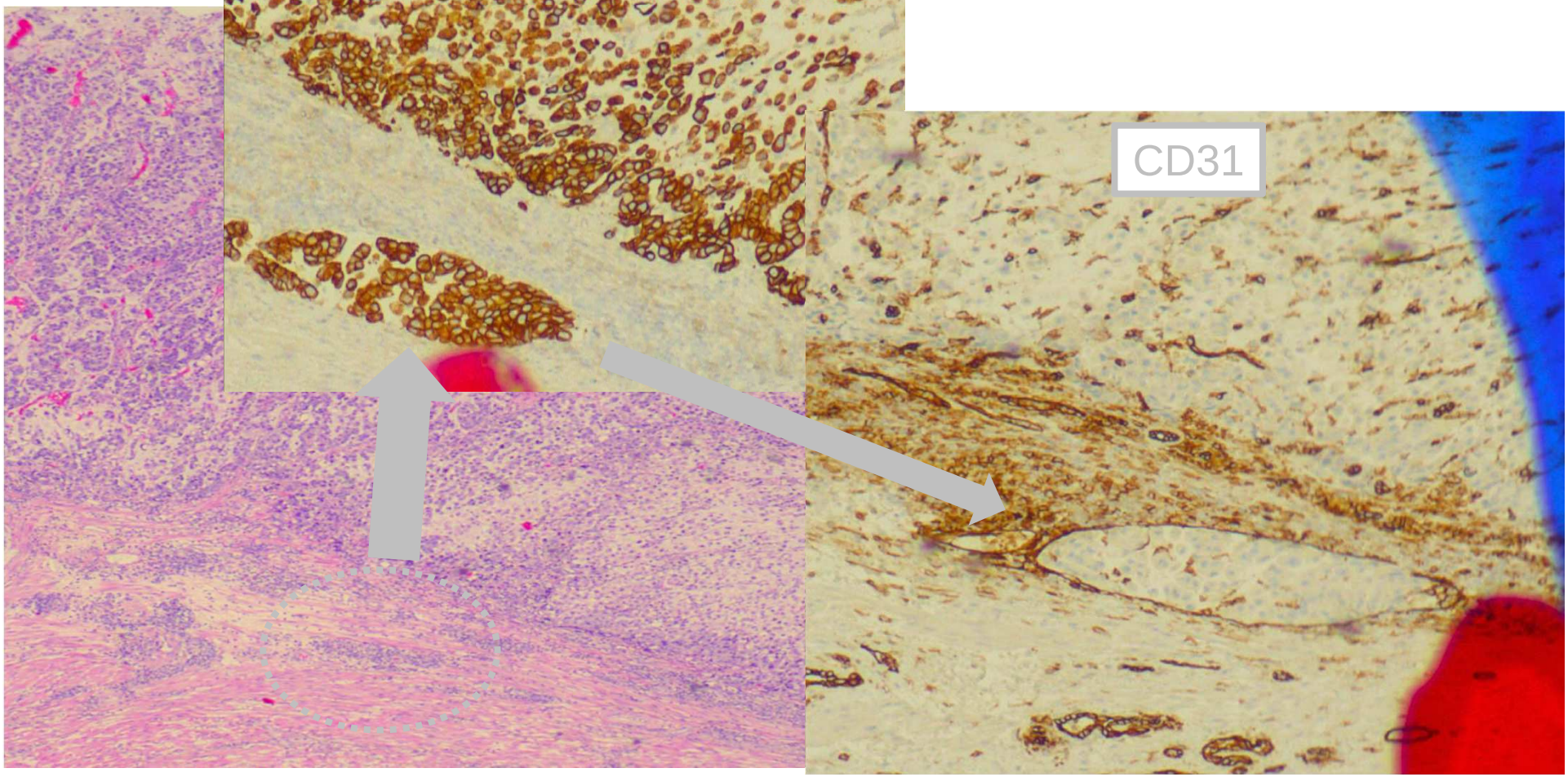
- In the esophagus lesion: double layer of muscularis mucosae





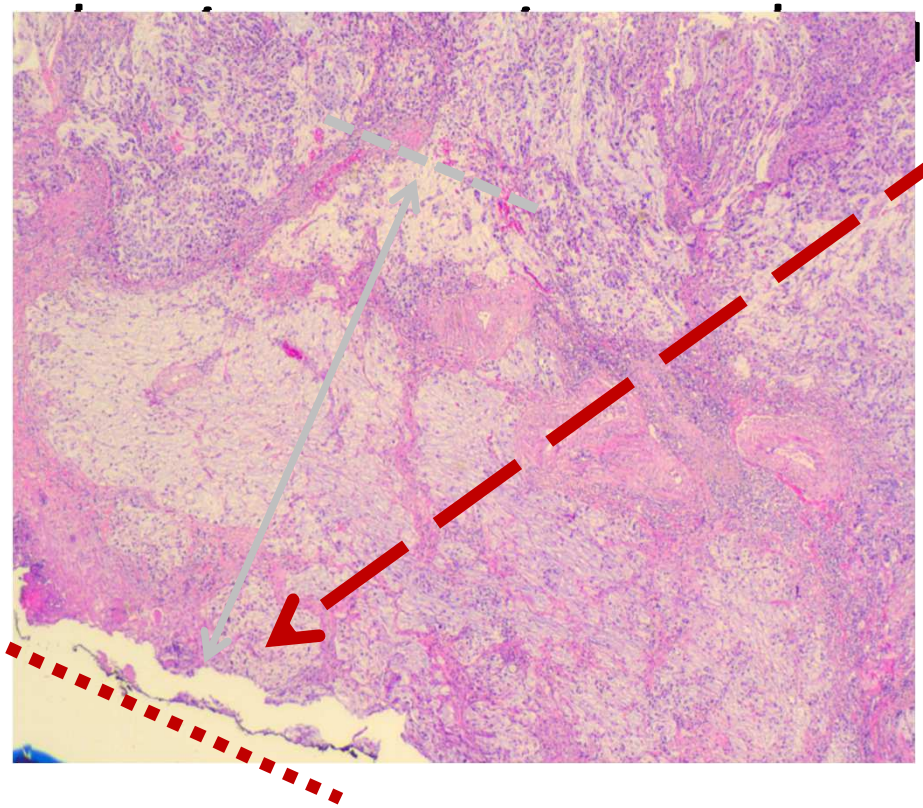
Lym essel invasion

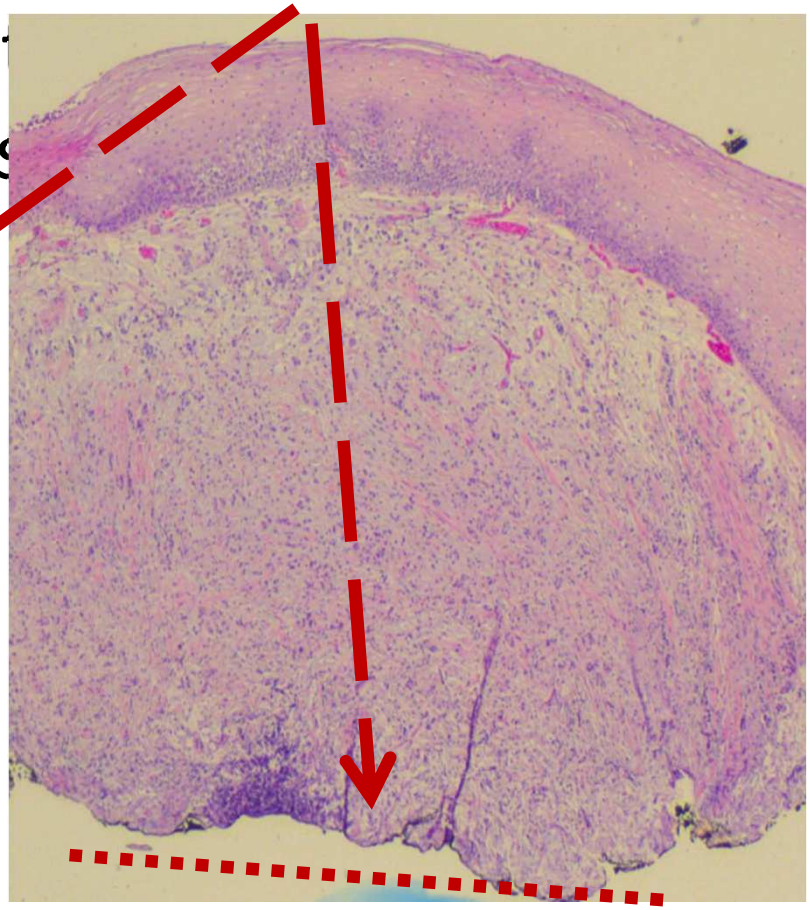
vascular invasion



Histological assessment: Surgical margins

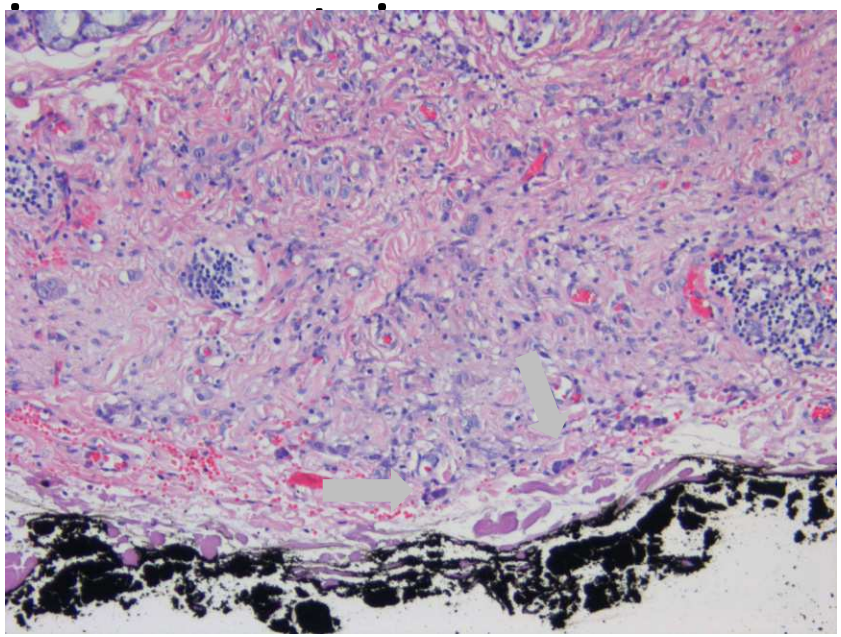
- In positive cases describe t
  ico

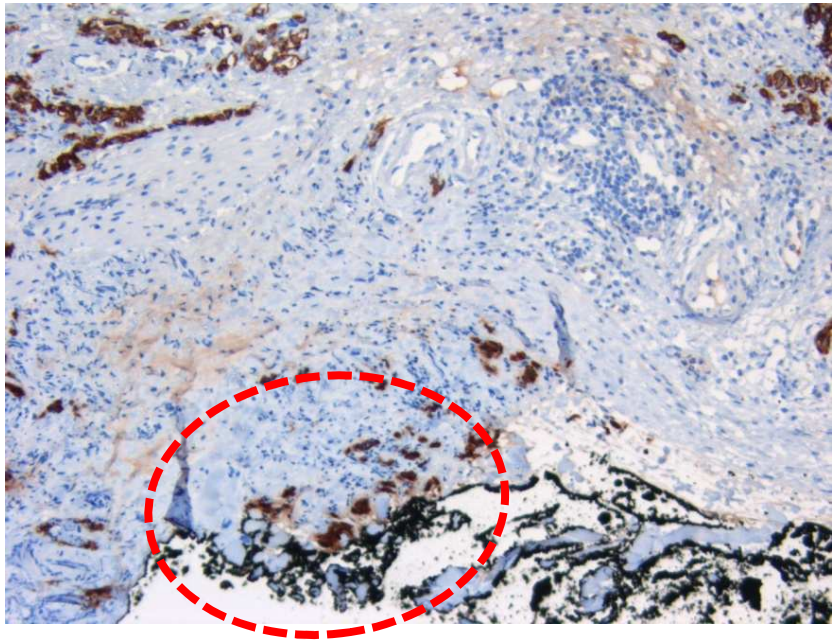




Histological assessment: Surgical margins

- If tumor cells are hard to identify due to cauterization-





if the positive margin shows no cauterization effect → **false positivity should be considered** → deeper cut section should be obtained

Conclusion

1. **Macroscopy**
2. **Size** of the lesion
3. **Differentiation** of the tumor
4. **Depth** of invasion
5. **Lymphovascular/Venous** invasion
6. **Margin** status

Relevant to prognosis and additional treatment decisions

Esophagus: ESGE Guideline

- BE with adenocarcinoma:
- No surgical treatment
  - G1-3, m1-3, LVI-, R0
  - G1-2, sm1 (≤ 500 µm), LVI-, R0
  - If the horizontal margin is positive or there is piecemeal resection with no other high risk criteria, endoscopic surveillance/re-treatment is recommended rather than surgery
- Treatment:
  - G3sm1
  - G1-2>sm1 (> 500 µm)
  - LVI+
  - R1 (vertical)