

The diagnosis and reporting of Barrett's esophagus

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McMaster – 6 month ago

Three month later



Three month later





Thank you for bringing us to warm weather

OUTLINE

- Definitions
- GERD
- Dysplasia
- Markers

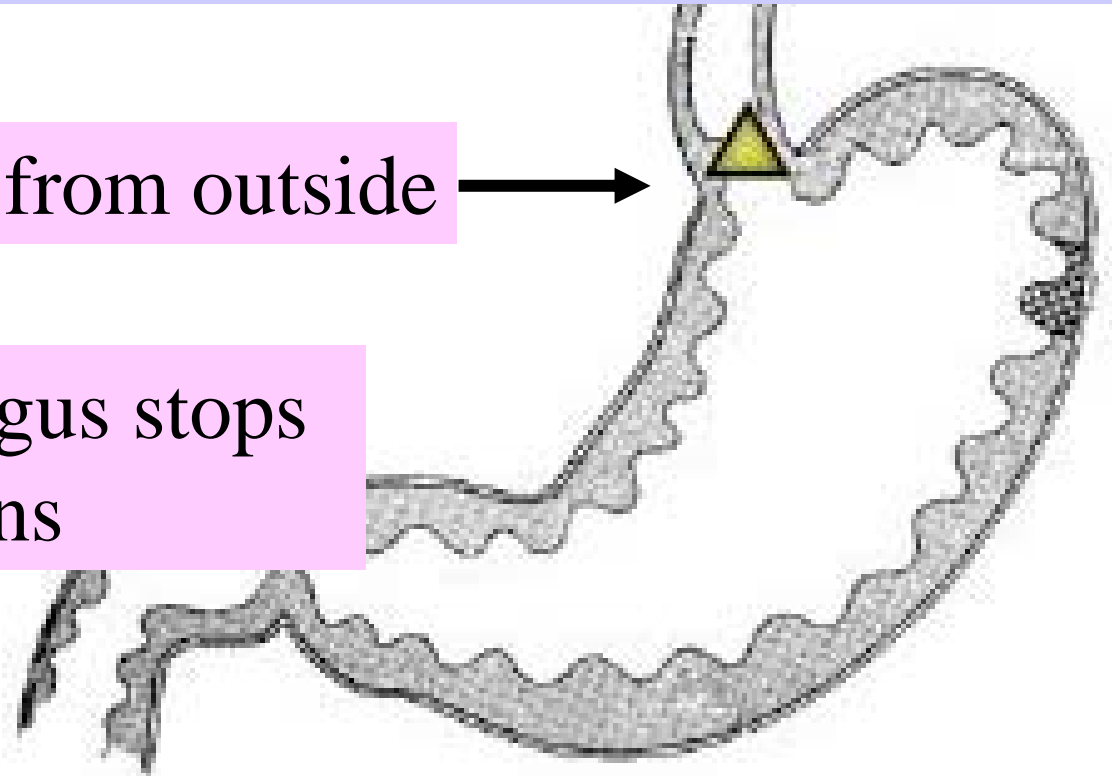
DEFINITIONS

- What is the GE junction?
- What is Barrett's?

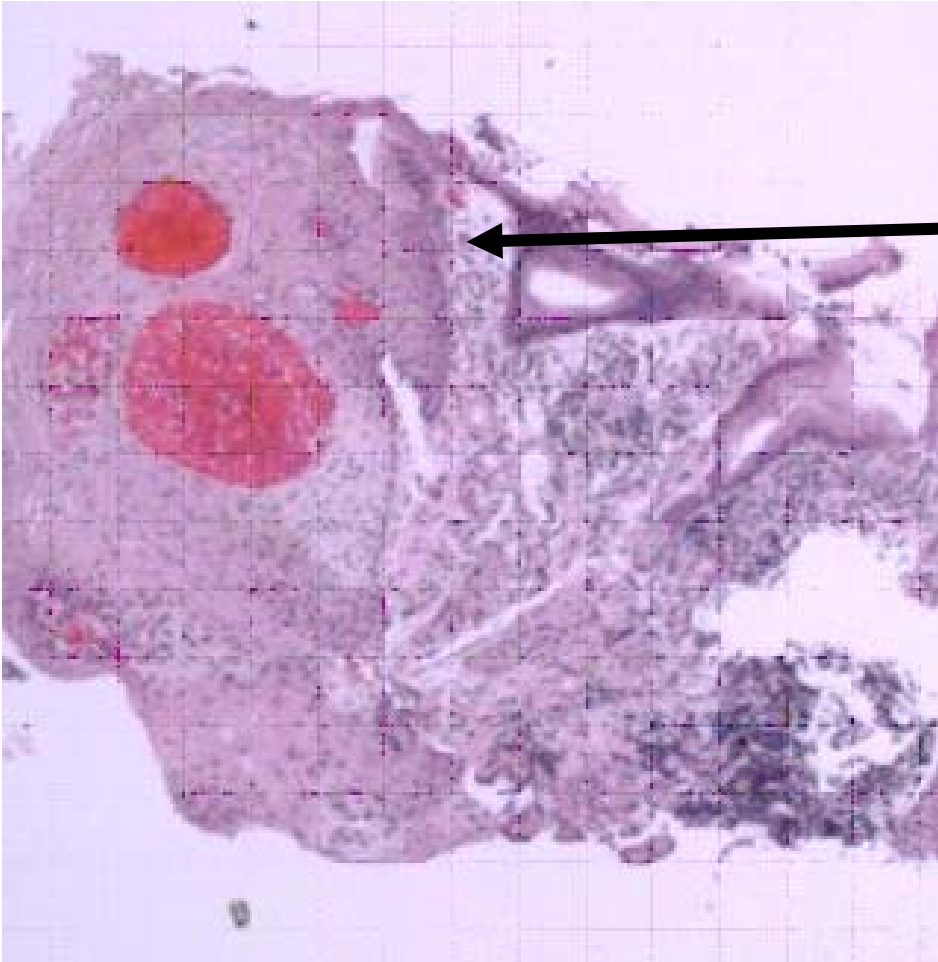
What is the **definition** of the distal end of the esophagus (gastro-esophageal junction GEJ)?

Looking from outside →

It's where esophagus stops
and stomach begins



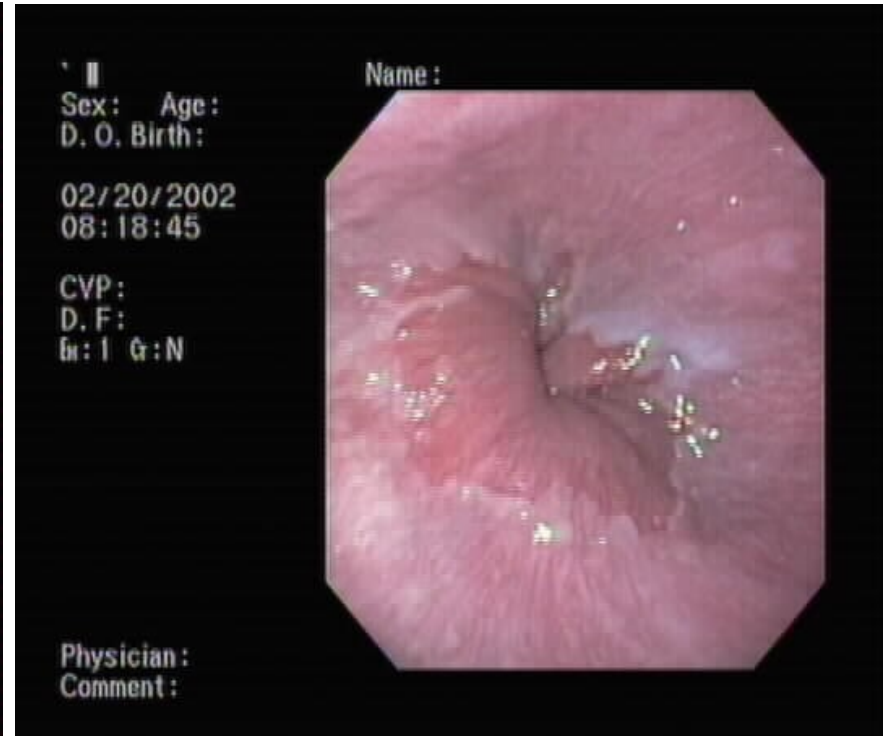
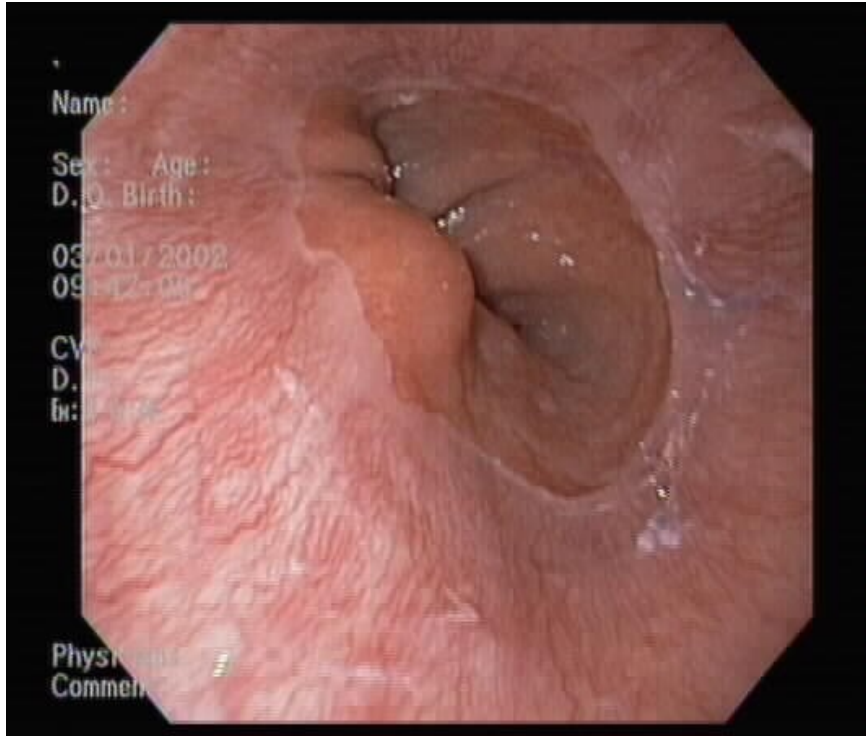
What is the **definition** of the distal end of the esophagus (gastro-esophageal junction GEJ)?



Looking from inside

GEJ is where
squamous
epithelium stops
and columnar
starts

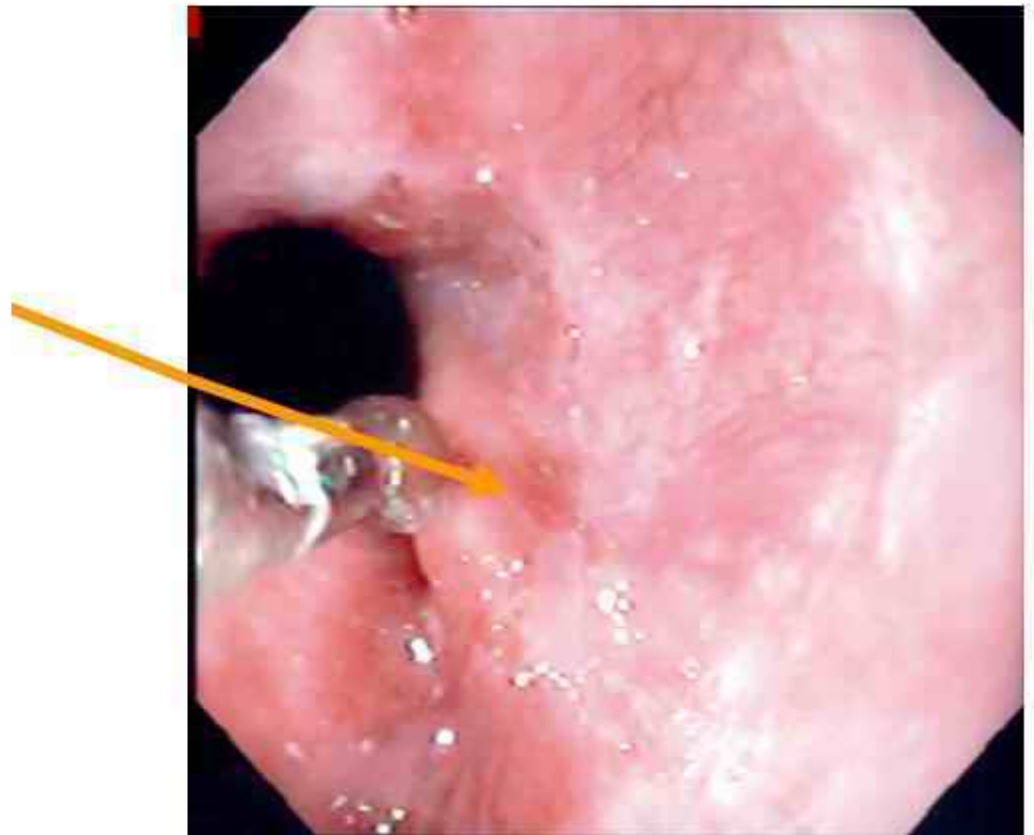
What is the **definition** of the distal end of the esophagus (gastro-esophageal junction GEJ)?

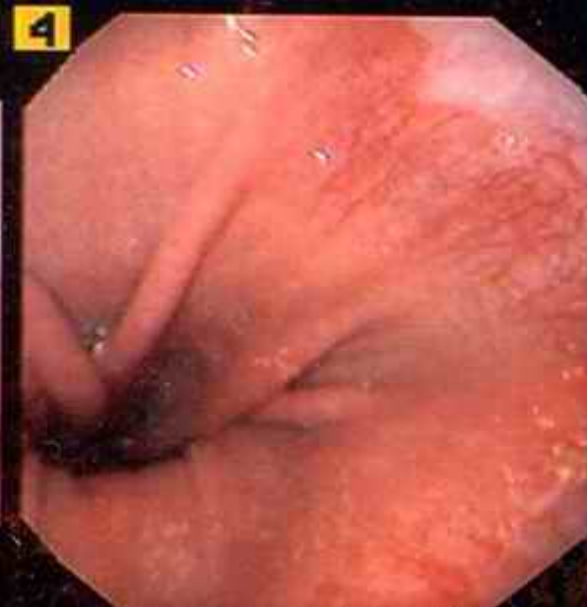
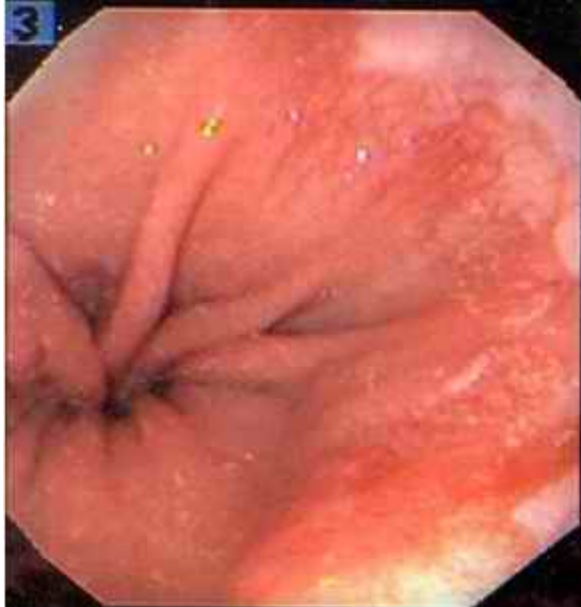


Normal: GEJ (squamo-columnar) are the same looking from outside and inside

What is the definition of the distal end of the esophagus (gastro-esophageal junction GEJ)?

In Western countries, the landmark is the upper end of the gastric longitudinal folds

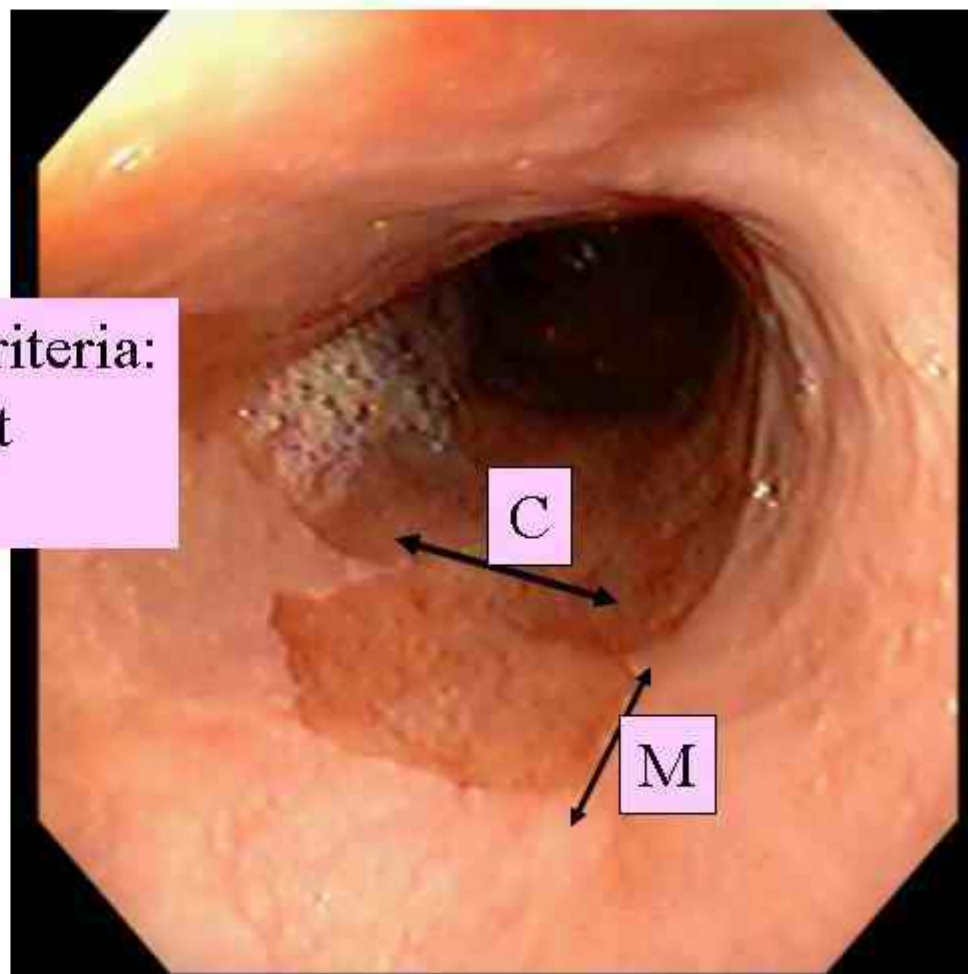




squamo-
columnar is in the esophagus

What is the definition of the distal end of the esophagus (gastro-esophageal junction GEJ)?

In Prague's C&M Barrett's criteria:
"C" for circumferential extent
"M" for maximal extent



DEFINITIONS

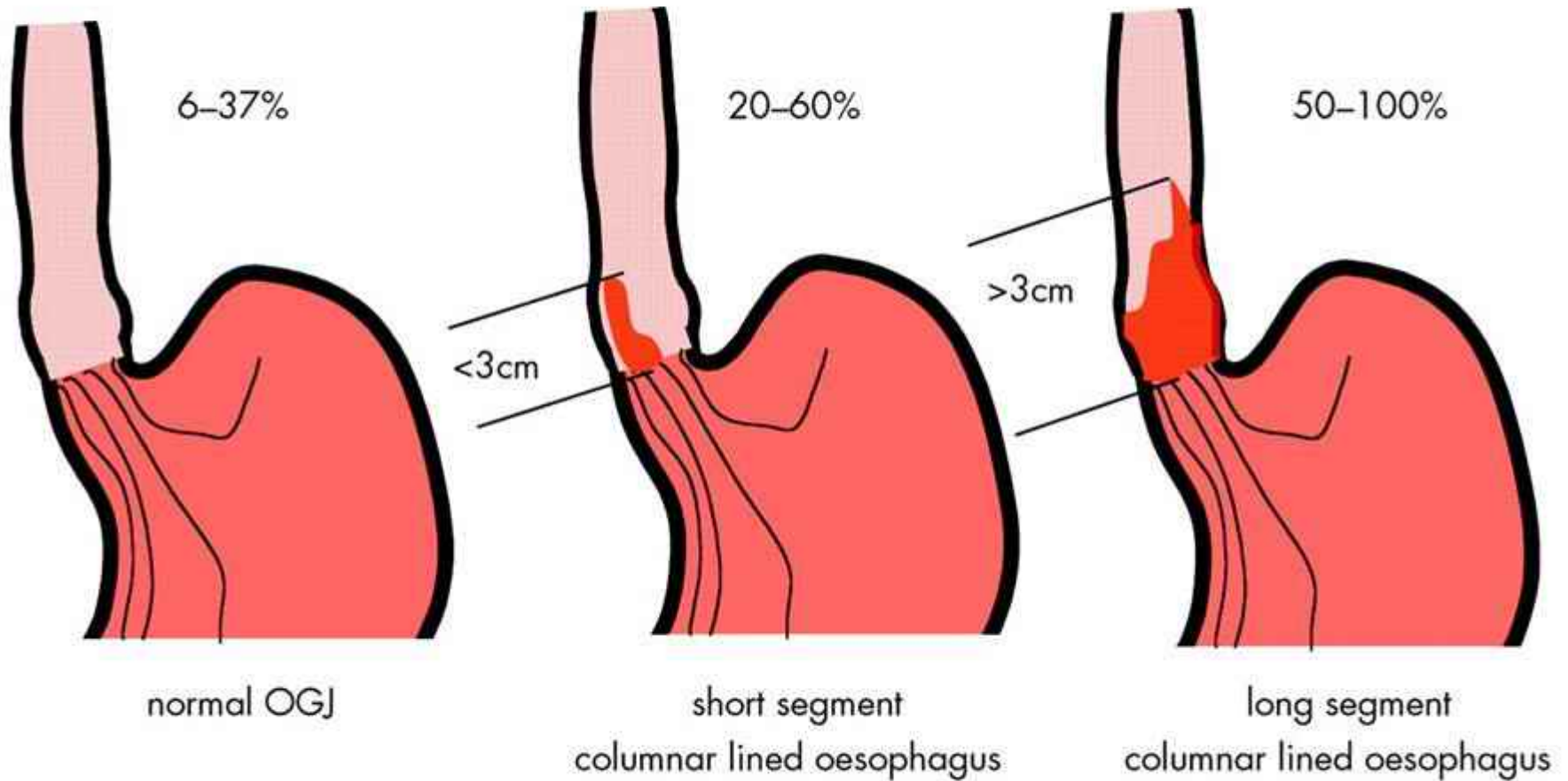
Columnar Lined Esophagus CLE

If you don't see goblets call it
Columnar Lined Esophagus
CLE

Replacement by glandular mucosa of any type.
Need to state whether goblet cells are present or
not.

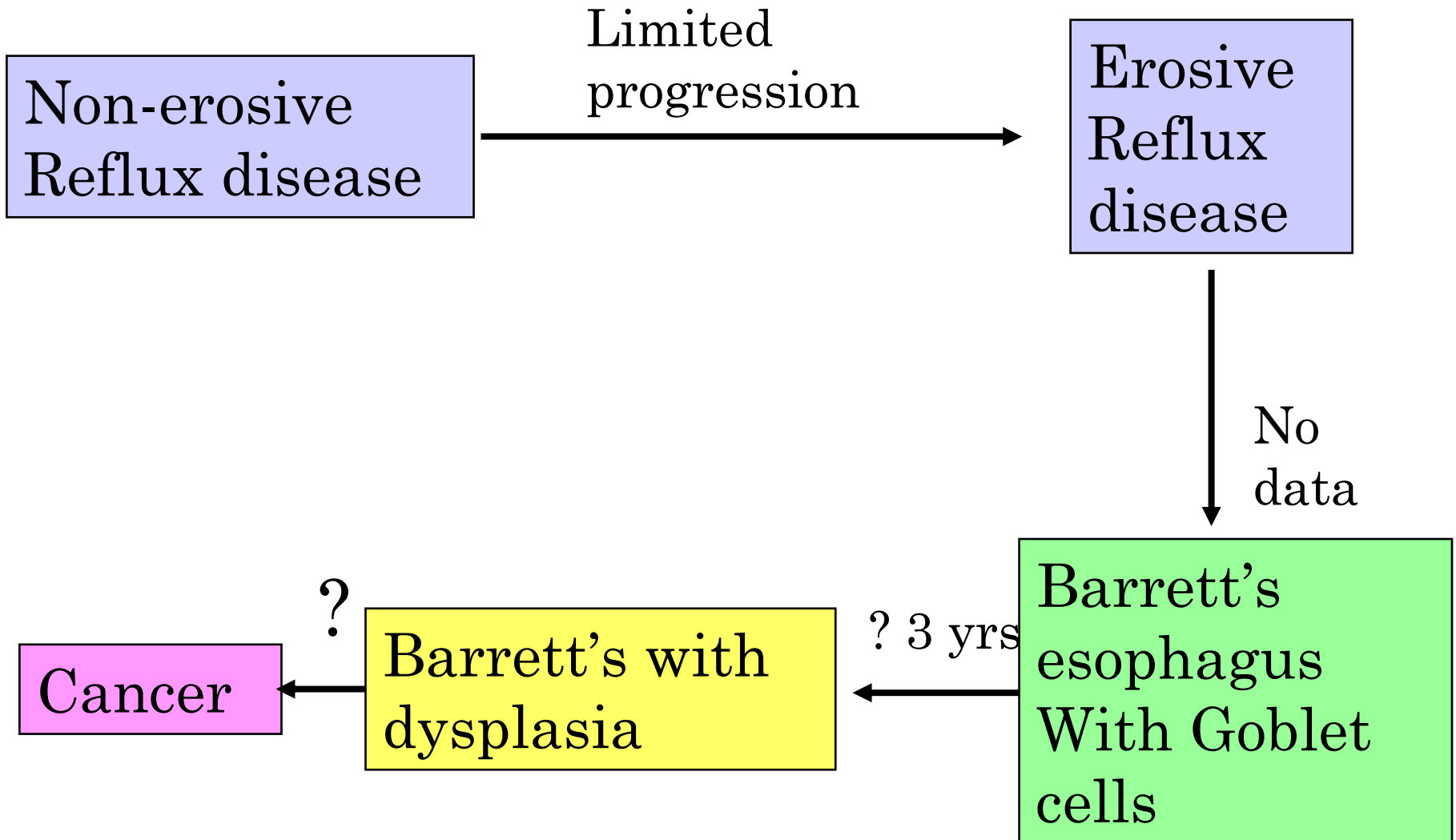
No goblets = implies no cancer risk)

Intestinal Metaplasia at the GEJ



Malfertheiner, P et al. Gut 2005;54:i13-20i

CANCER RISK POST BARRETT'S



PATHOLOGY ROLE

Non-erosive
Reflux disease

Limited
progression

Erosive
Reflux
disease

1. Diagnose GERD

No
data

4. Diagnose
cancer

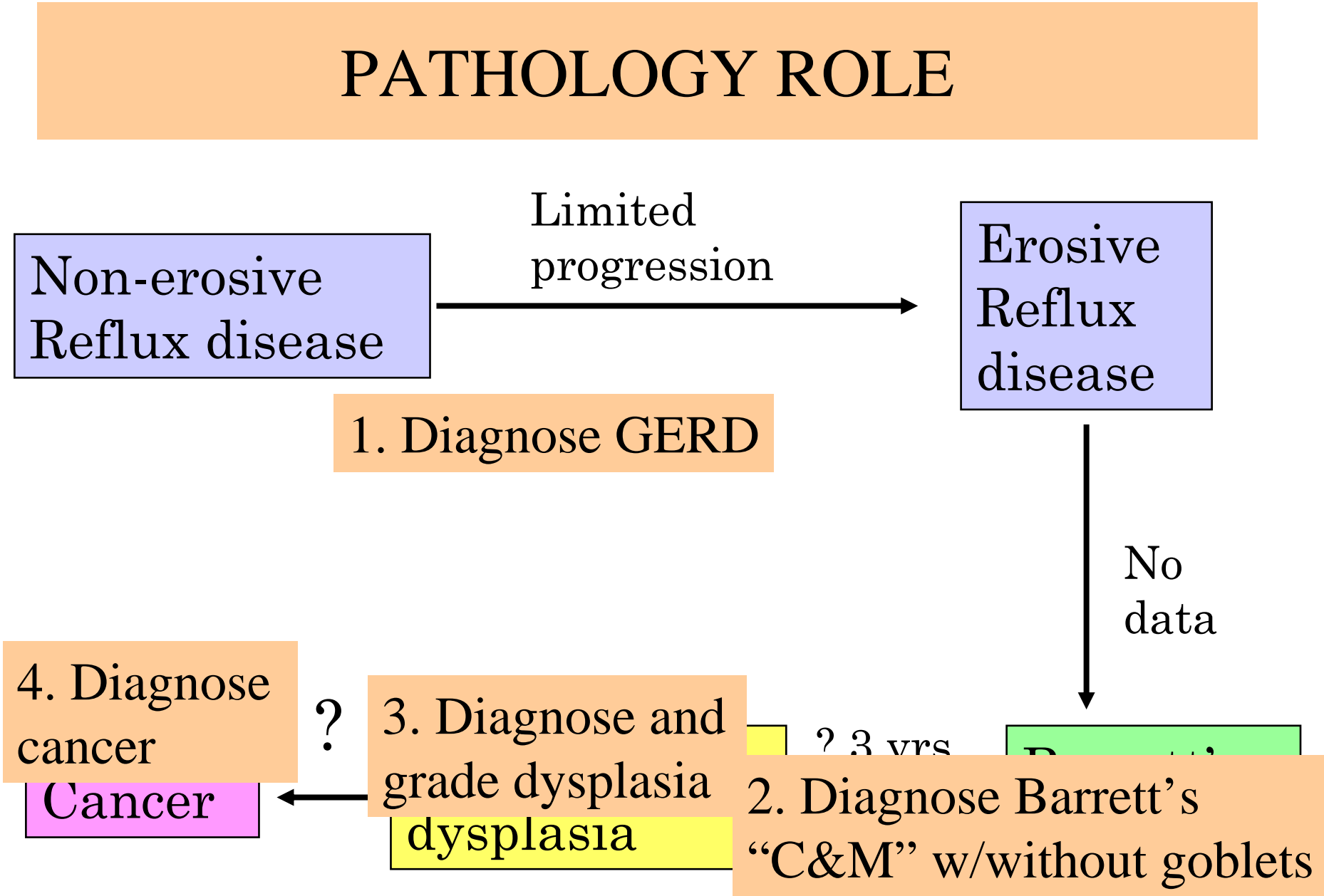
Cancer

?

3. Diagnose and
grade dysplasia
dysplasia

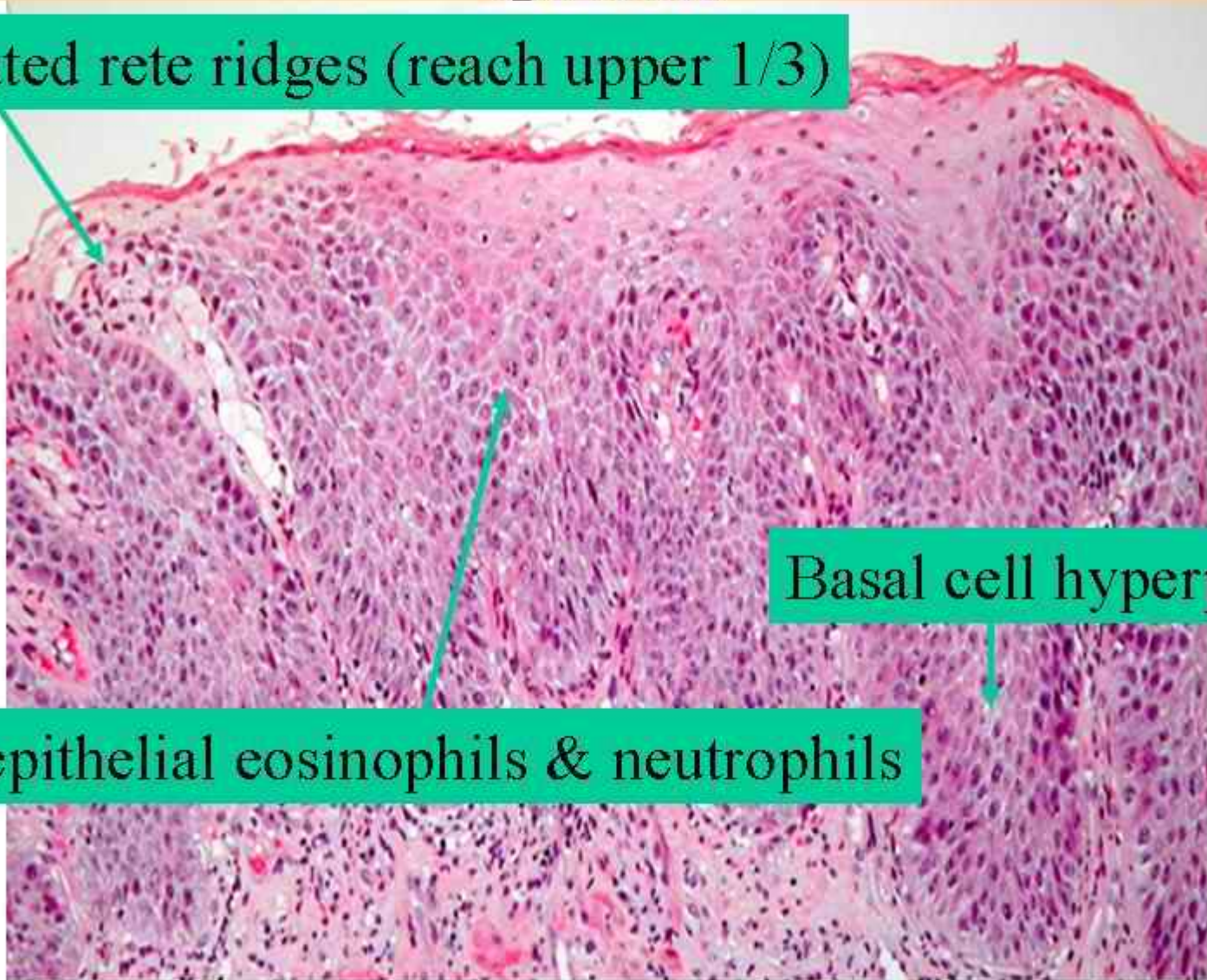
? 3 yrs

2. Diagnose Barrett's
"C&M" w/without goblets



CRITERIA USED TO DIAGNOSE GERD

Elevated rete ridges (reach upper 1/3)



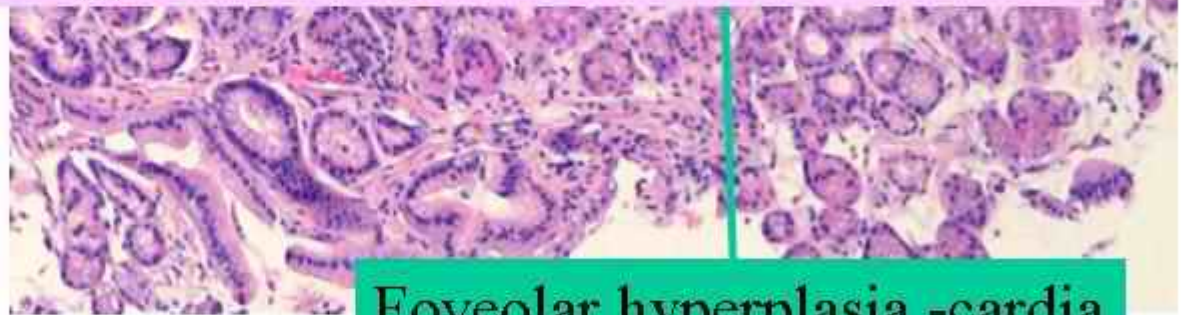
Basal cell hyperplasia

Intraepithelial eosinophils & neutrophils

ADDITIONAL CRITERIA USED TO DIAGNOSE GERD

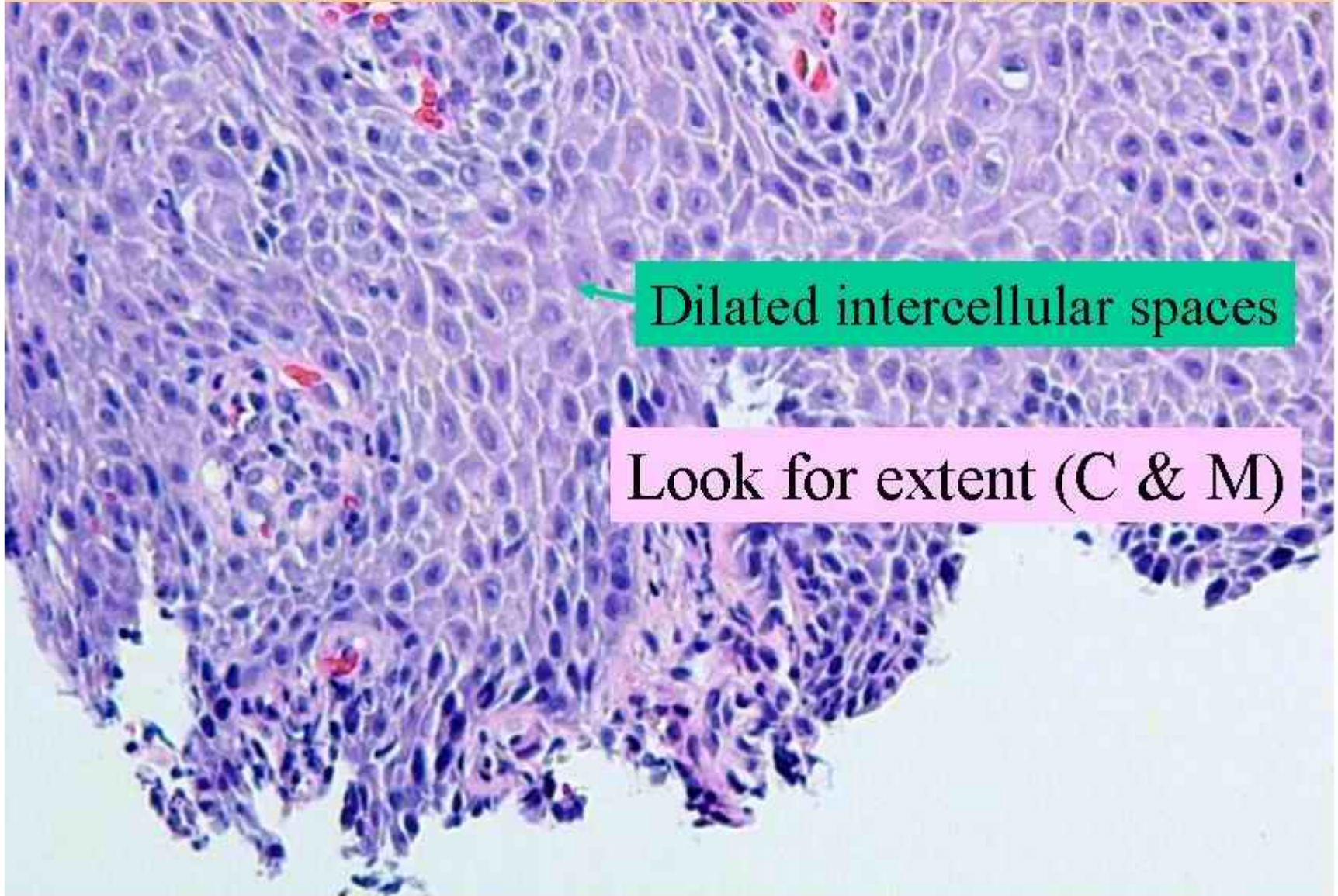


Differential is *H. pylori* gastritis in gastric cardia
Look for amount of acute and chronic inflammation
Best look in other gastric biopsies



Foveolar hyperplasia -cardia

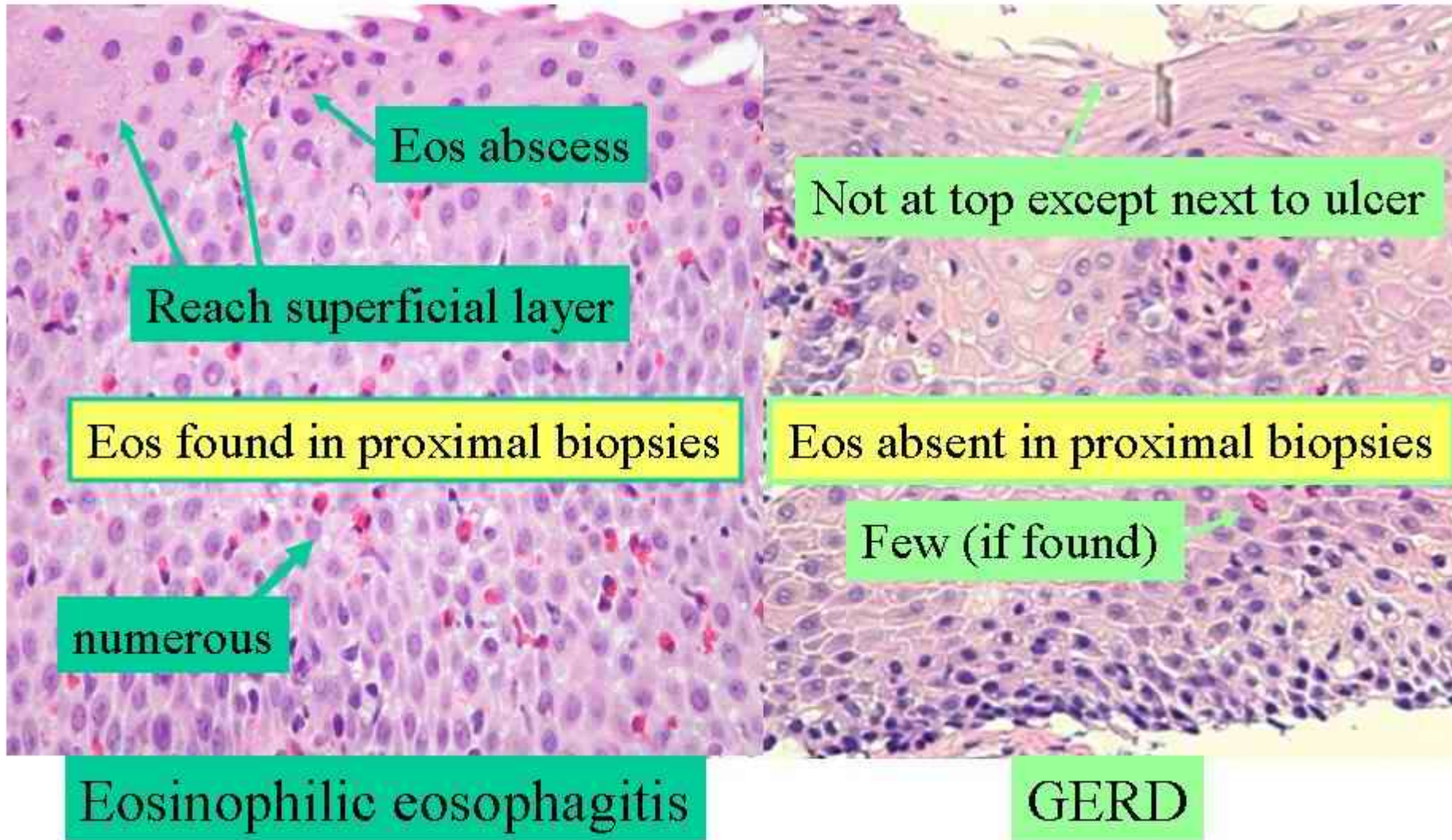
ADDITIONAL CRITERIA USED TO DIAGNOSE GERD



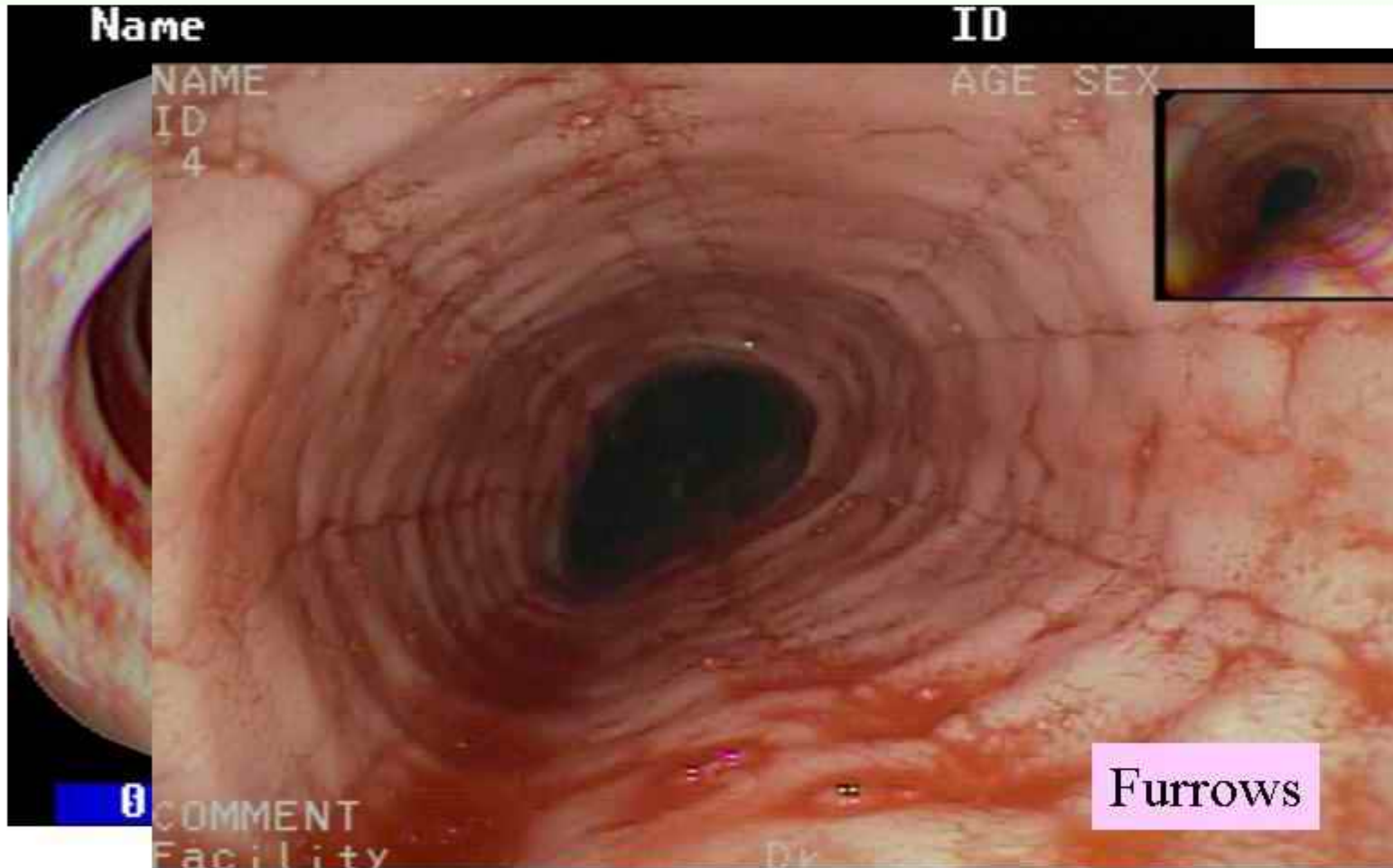
Dilated intercellular spaces

Look for extent (C & M)

Intra epithelial EOSINOPHILS (GERD vs. Eosinophilic Esophagitis)



Eosinophilic Eosophagitis



Role of Histology in the Diagnosis of GERD

The sensitivity of histologic changes in reflux esophagitis is only 50% to 65%.

The objective diagnosis of GERD should be based on pH monitoring & endoscopic changes (not histology) specially in non-erosive disease.

Histology is only needed to exclude Barrett's esophagus and related malignancy.

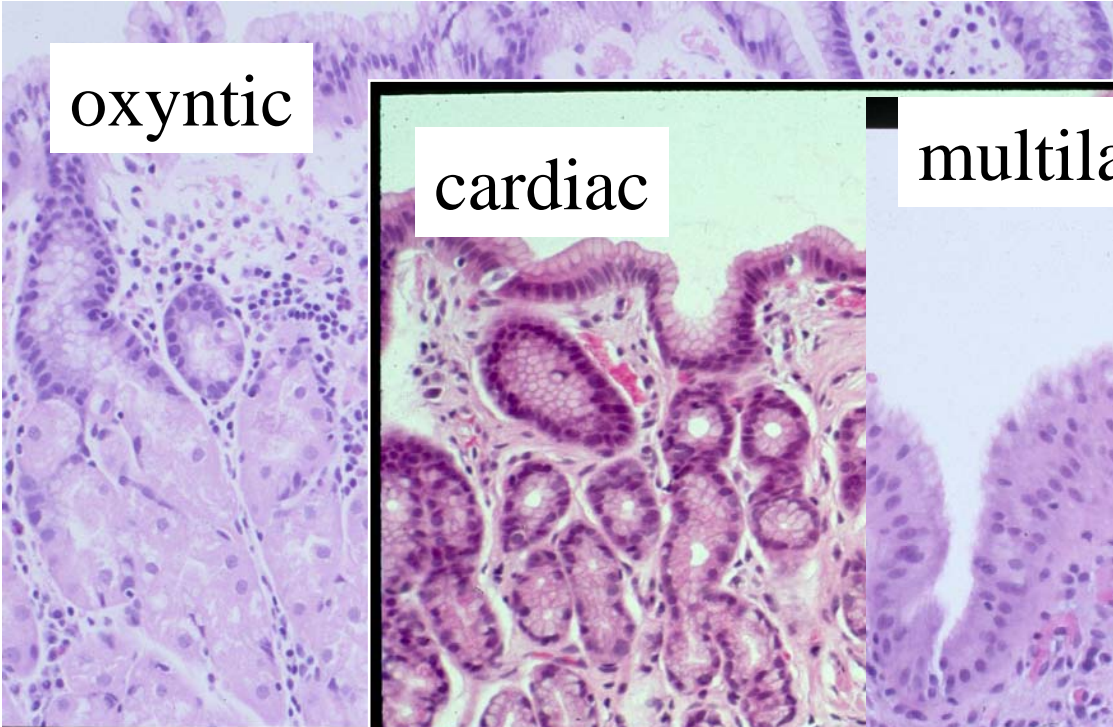
Problems in the biopsy diagnosis of Barrett's Esophagus

1. Definition
2. Is the diagnosis of BE/CLE endoscopic or pathologic?
3. Can we distinguish SSBE from IM in native cardia?

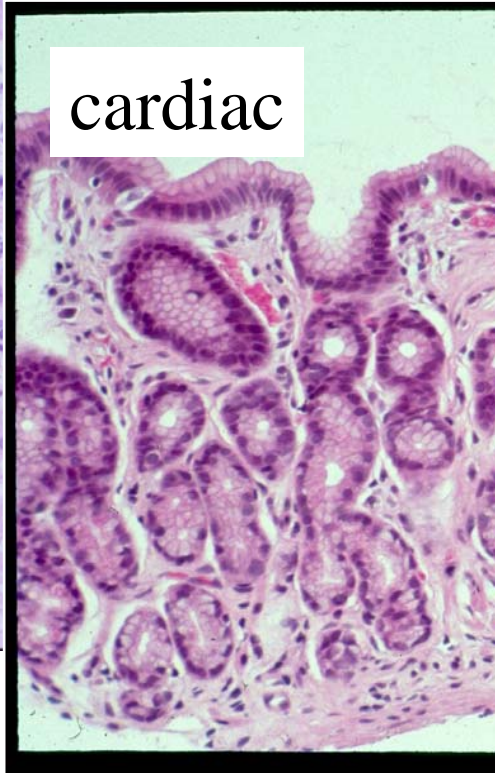
Types of epithelium in Columnar Lined Esophagus (CLE)

(No goblet cells- implies no malignant risk)

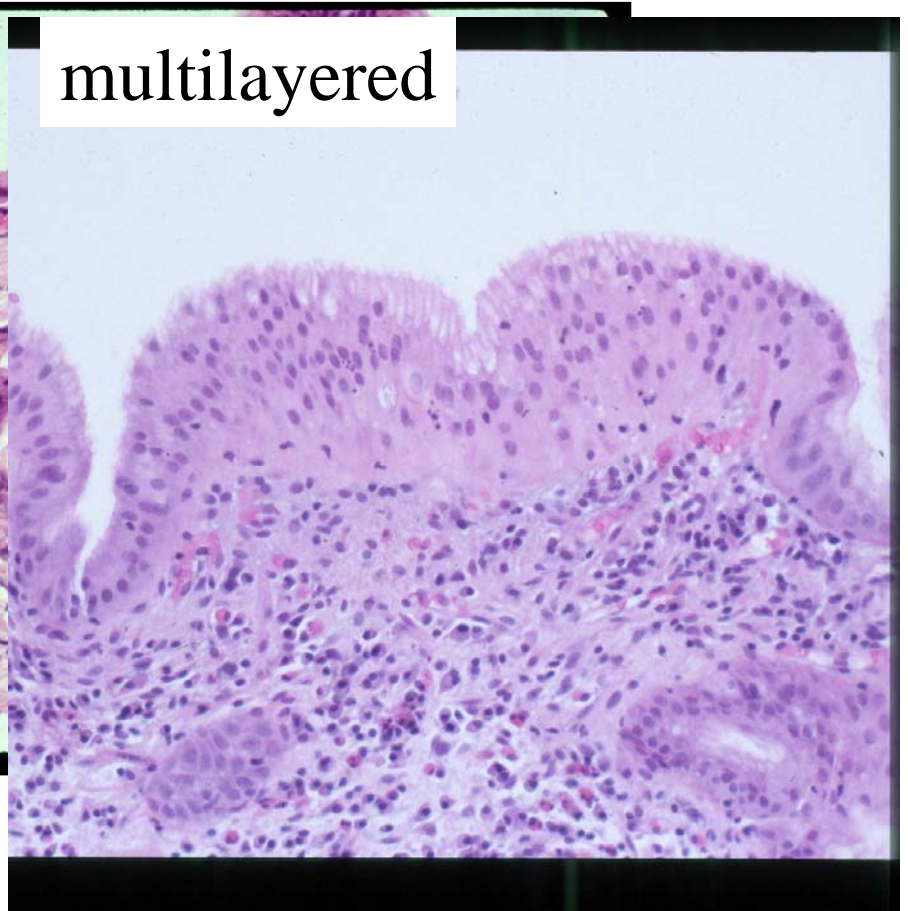
oxyntic



cardiac



multilayered



Implied: no cancer risk

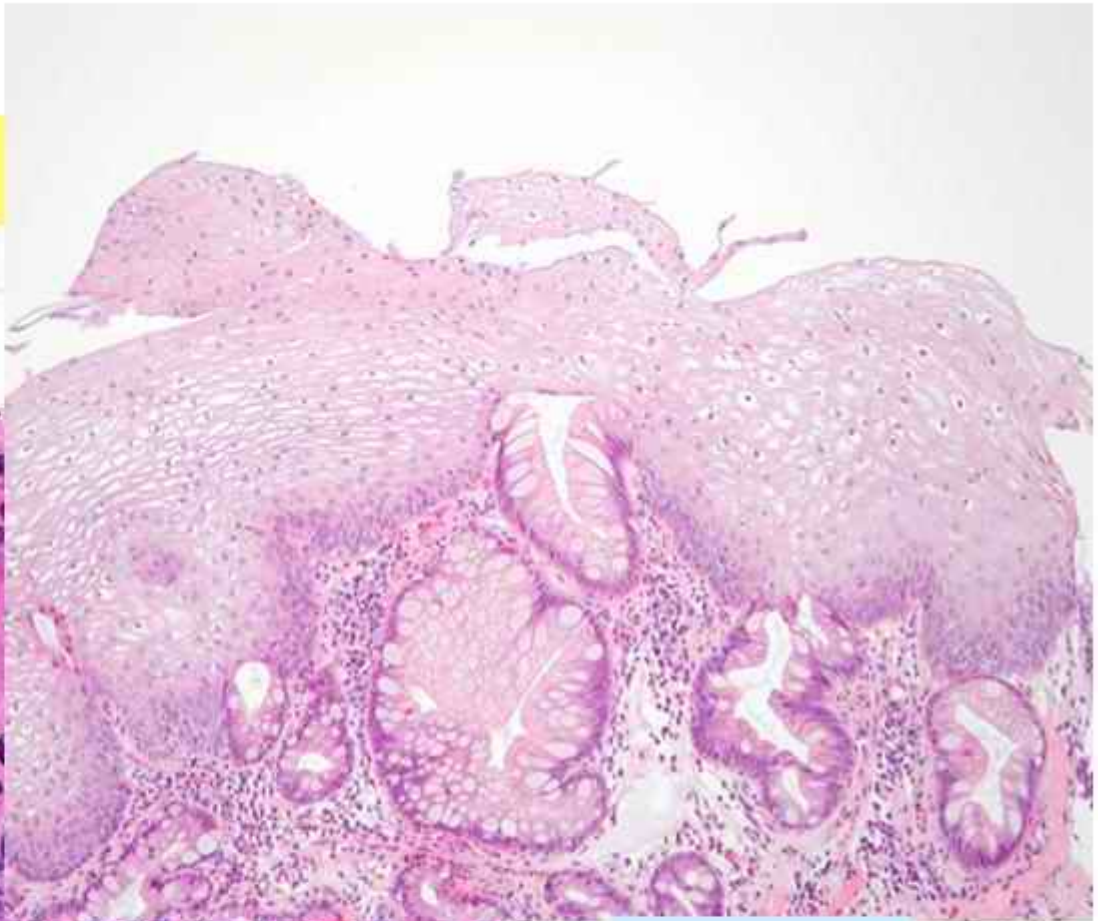
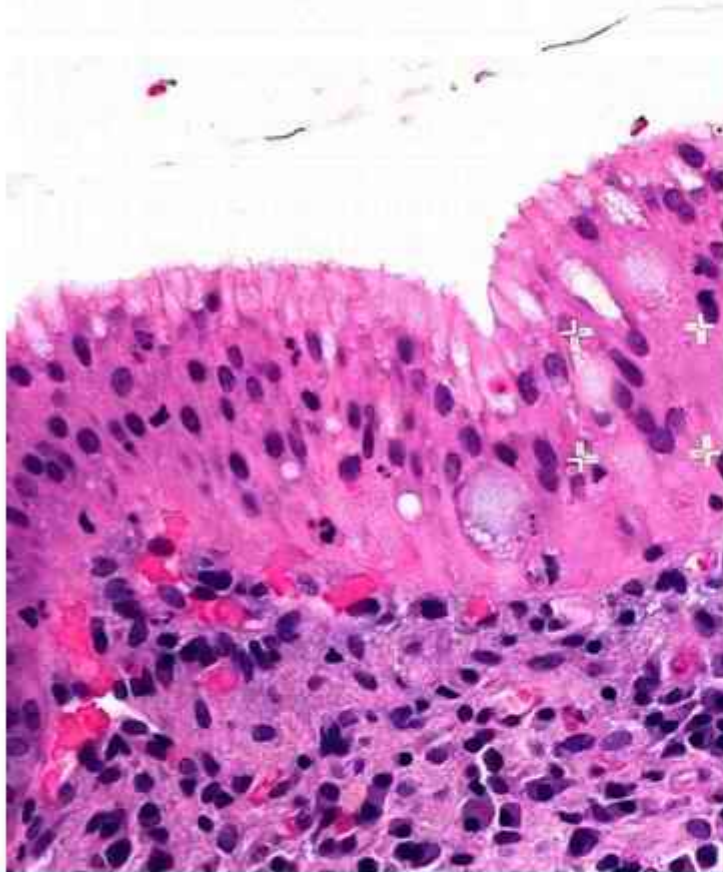
DEFINITIONS: Barrett's Esophagus

Replacement by glandular mucosa with goblet cells/intestinalized mucosa with an appropriate endoscopic appearance

Goblets = implies a cancer risk

You need histology (goblet cells) and an appropriate endoscopic appearance for a diagnosis of Barrett's esophagus

(implies a cancer risk)



Barrett's

Multilayered epithelium with goblet cells

Intestinal Metaplasia: is it cardia? Or is it Barrett's

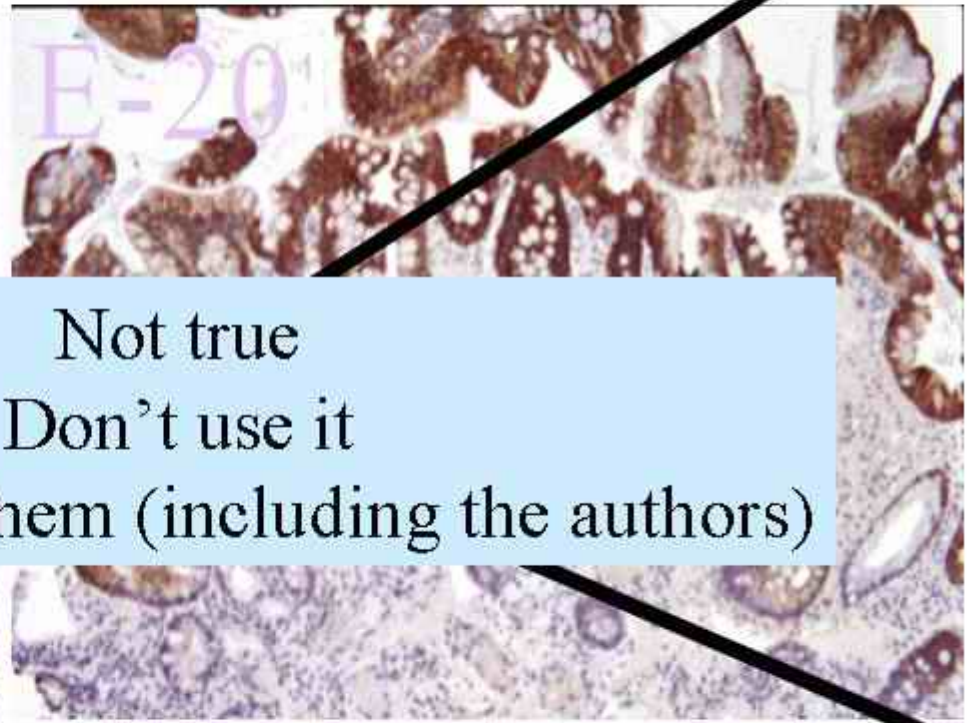


Cardia



Short segment Barrett's

CYTOKERATIN 7/20 PROFILE IN BARRETT'S



Not true
Don't use it
No body uses them (including the authors)

CK 7 Diffuse

CK 20 Superficial band like

Ormsby et al Hum Pathol 1999; 30:288-294

Intestinal Metaplasia: is it cardia? Or is it Barrett's What are your options?

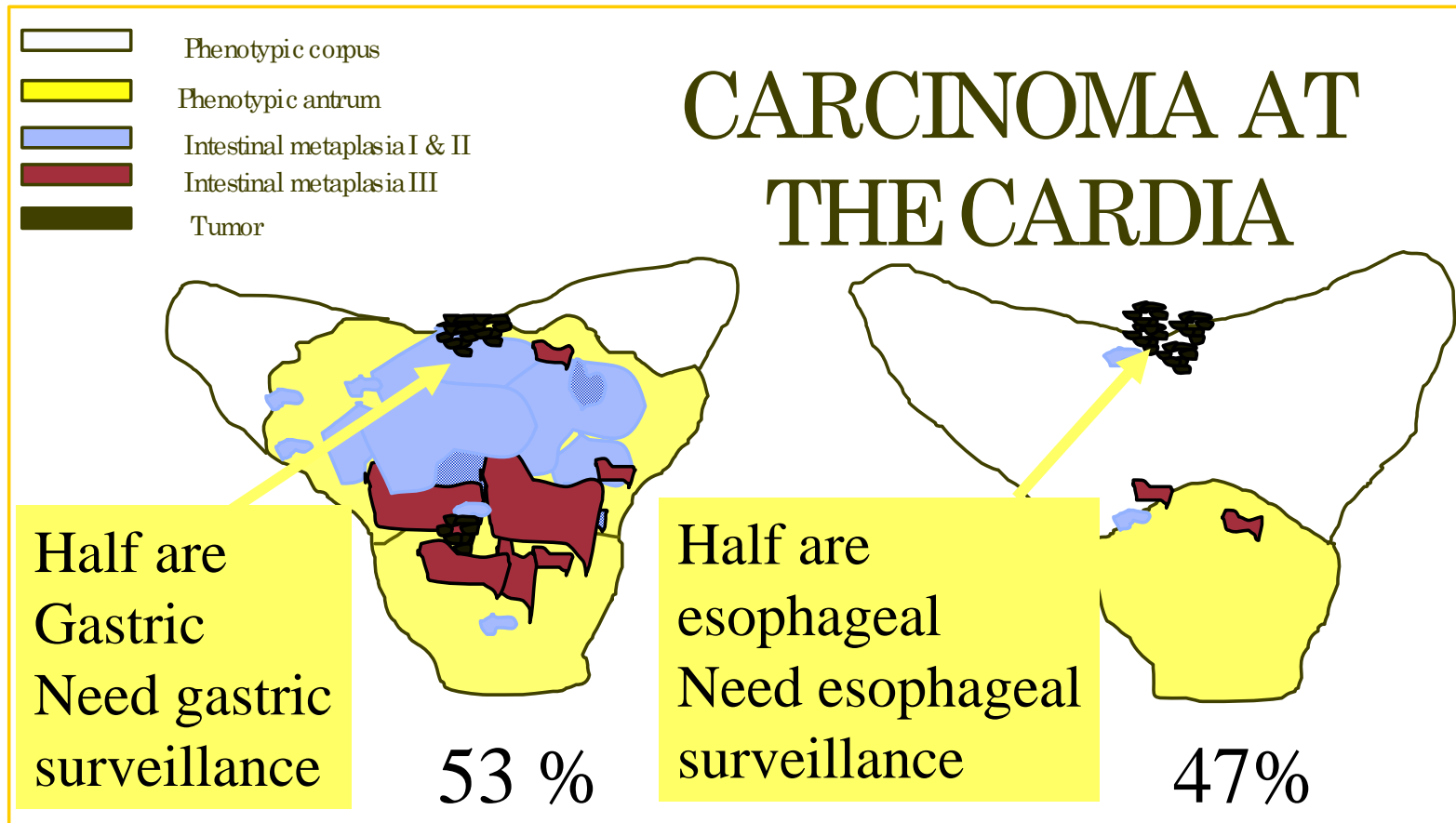
Issue a diagnosis of:

Columnar Lined epithelium with no goblet cells

Columnar Lined Epithelium with goblet cells

Let the gastroenterologist decide
whether it is metaplasia of the
gastric cardia or distal end of
esophagus (Barrett's)

What are the Possible Sources of GEJ Cancer?



El-Zimaity et al 2005

Either way you need to screen

- If intestinal metaplasia is from SS or LS Barrett's patients needs to be screened for dysplasia and cancer post Barrett's.
- If intestinal metaplasia is from the gastric cardia patient need to be screened for gastric atrophy and possible development of gastric dysplasia and cancer.

Is it intestinal metaplasia of the gastric cardia or Barrett's metaplasia?

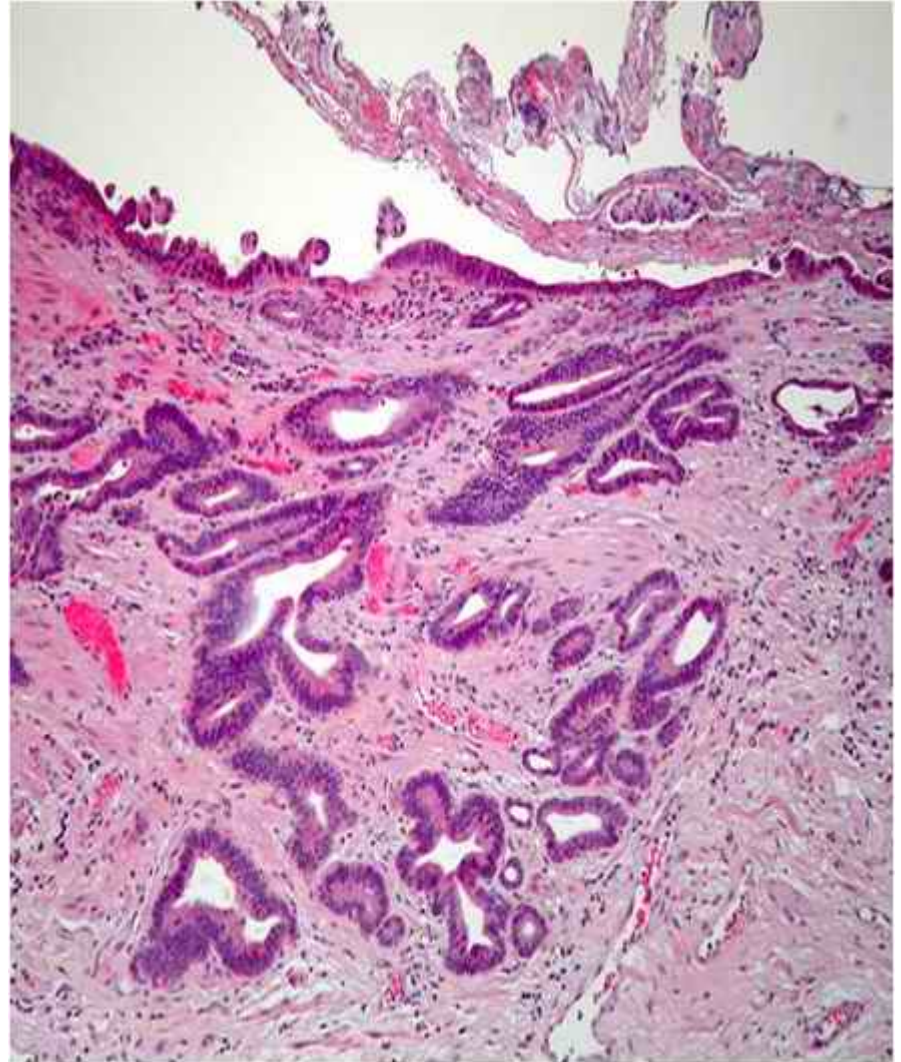
- Biopsy the stomach.
- In Barrett's: stomach is healthy
- In metaplasia post gastritis (cardia), the stomach has a lot of *H. pylori* associated changes.

Is there Dysplasia?

1. Architectural pattern
2. Nuclear Pattern
3. Surface maturation

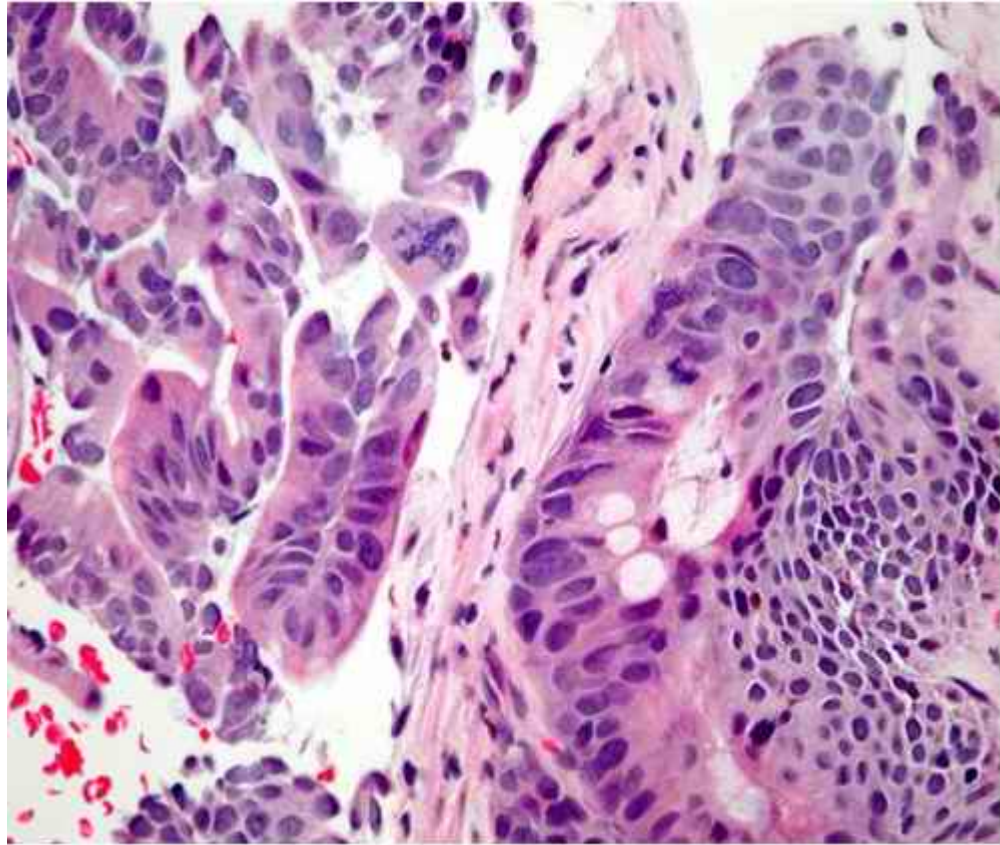
LOW GRADE DYSPLASIA

- Preserved crypt architecture
- Nuclei are enlarged, but don't reach apical surface
- Loss of surface maturation

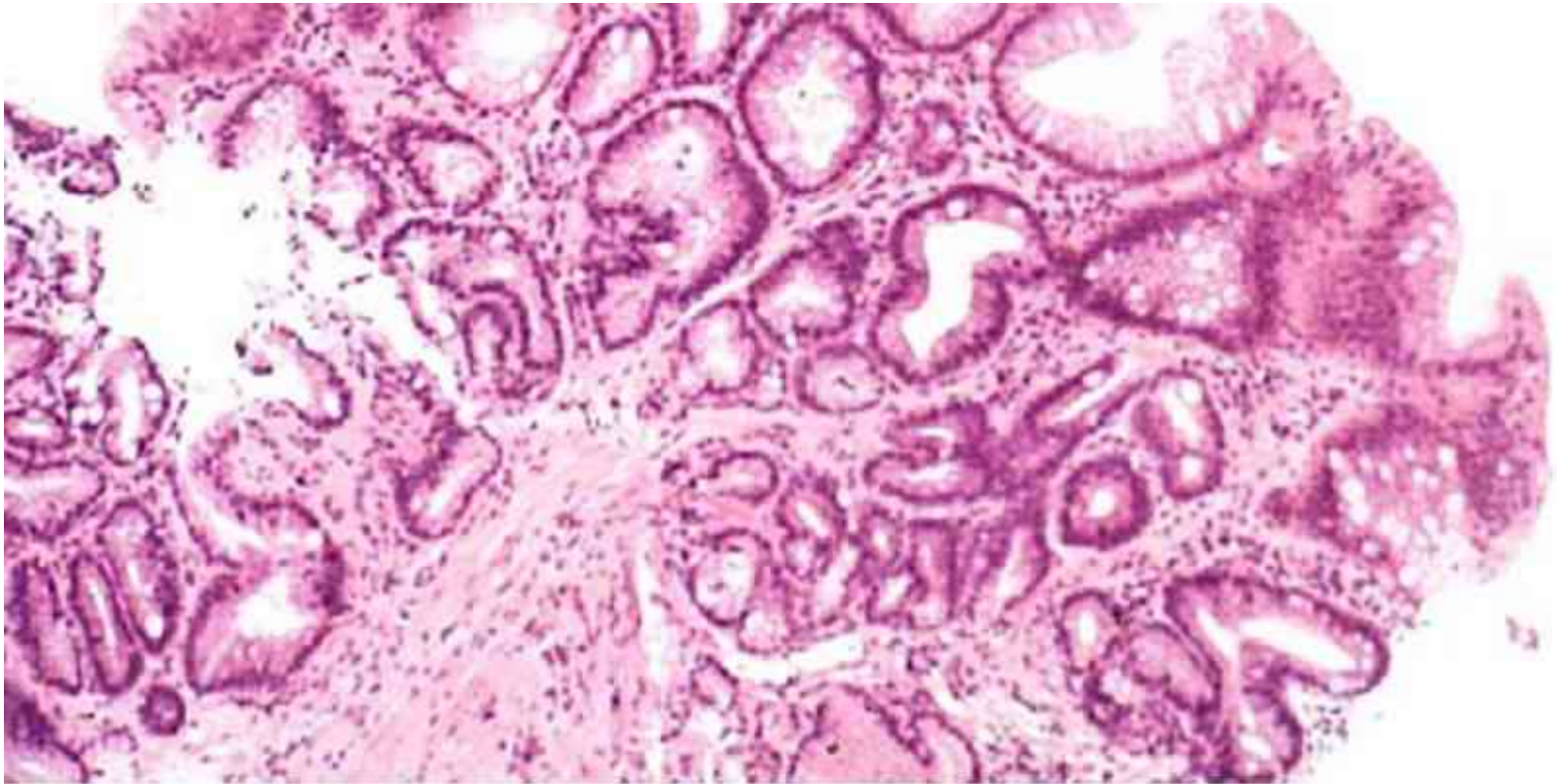


- Architectural distortion (with branching, lateral budding or cribriform pattern)
- Nuclear abnormalities as in low-grade dysplasia but there is bigger variation among the nuclei; stratified nuclei reaches luminal surface; loss of polarity.
- Loss of surface maturation.

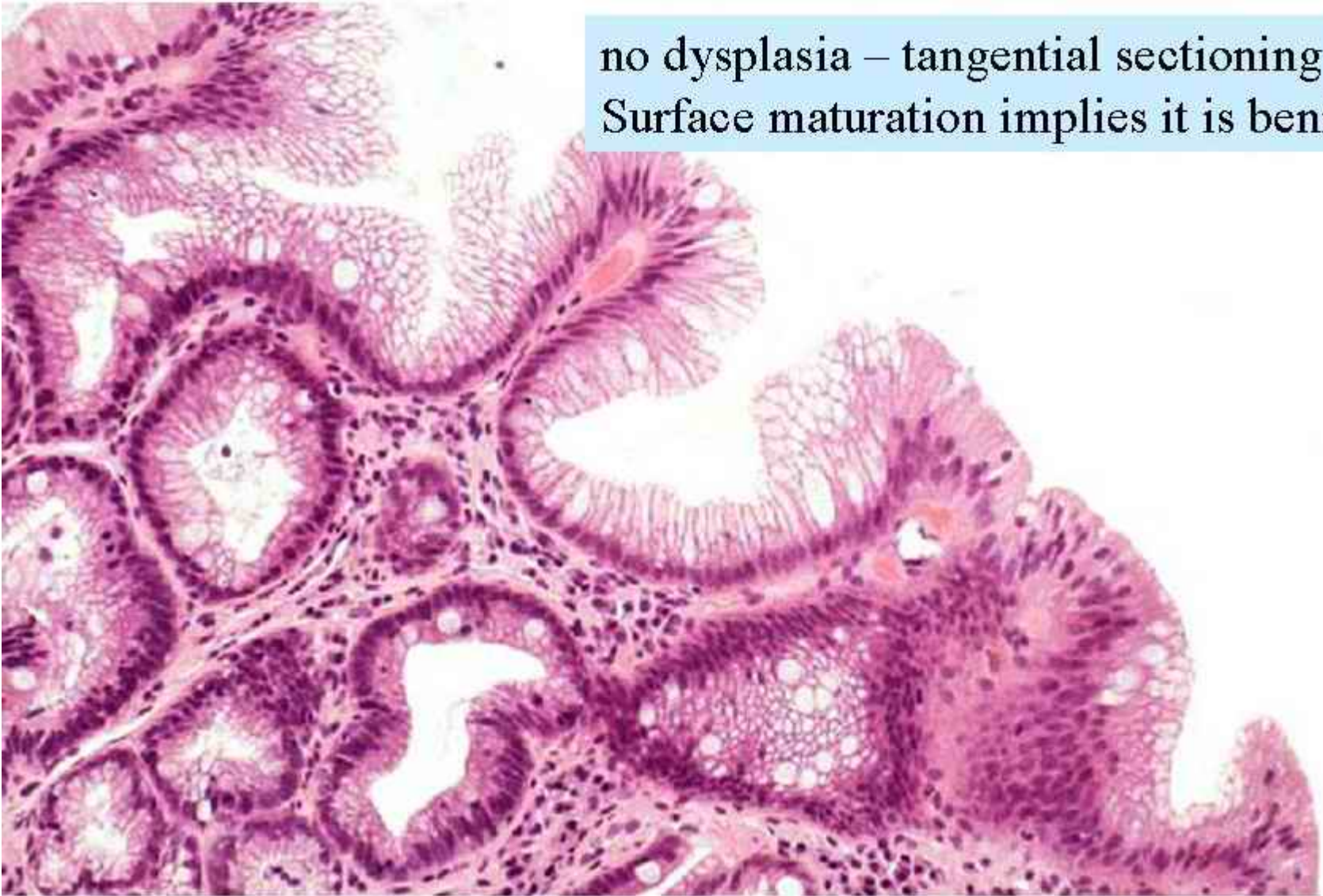
High grade dysplasia



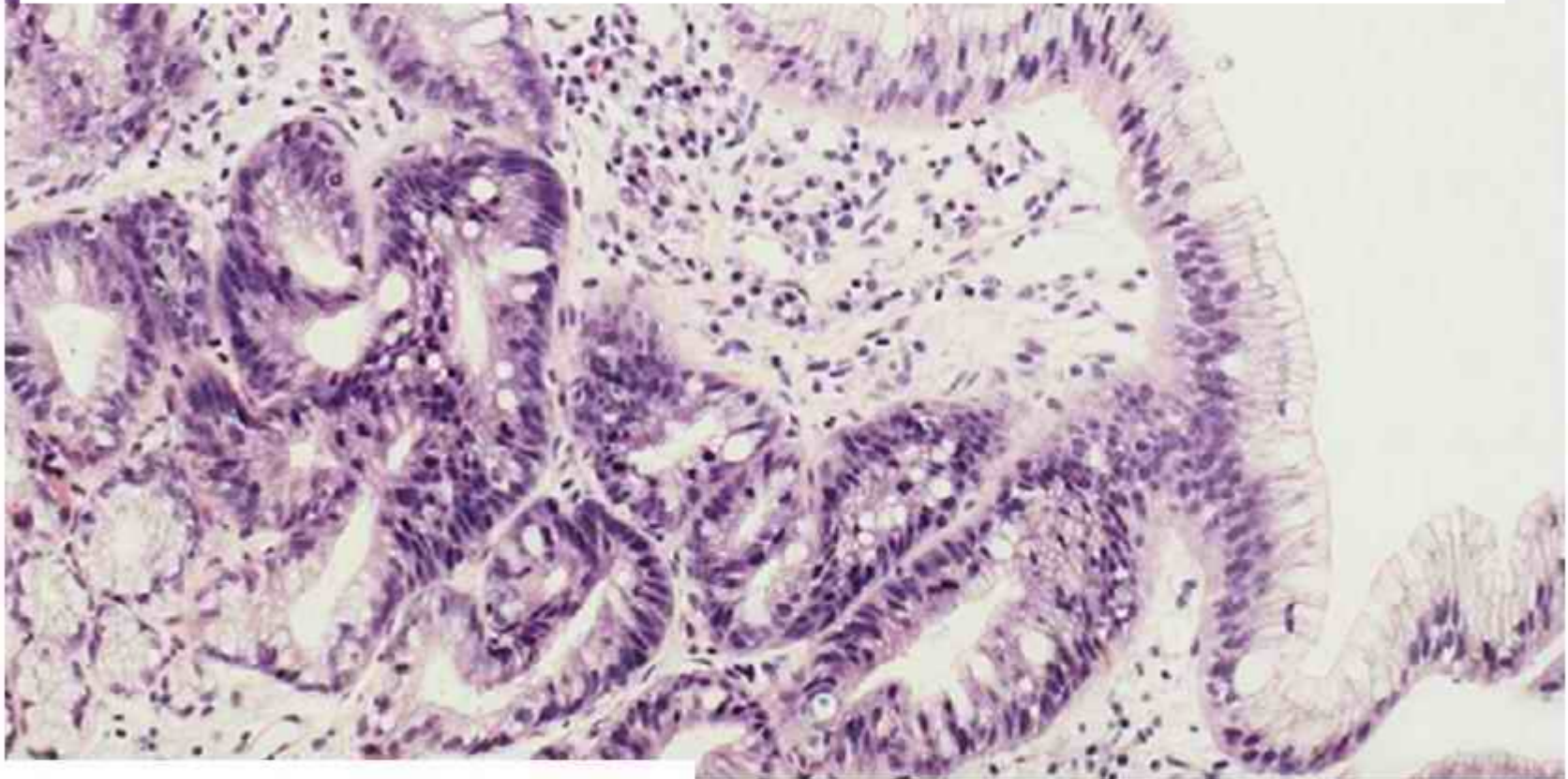
1. Architectural pattern = normal
2. Nuclear Pattern = basal ? Nuclear maturation
3. Surface maturation = present



no dysplasia – tangential sectioning
Surface maturation implies it is benign

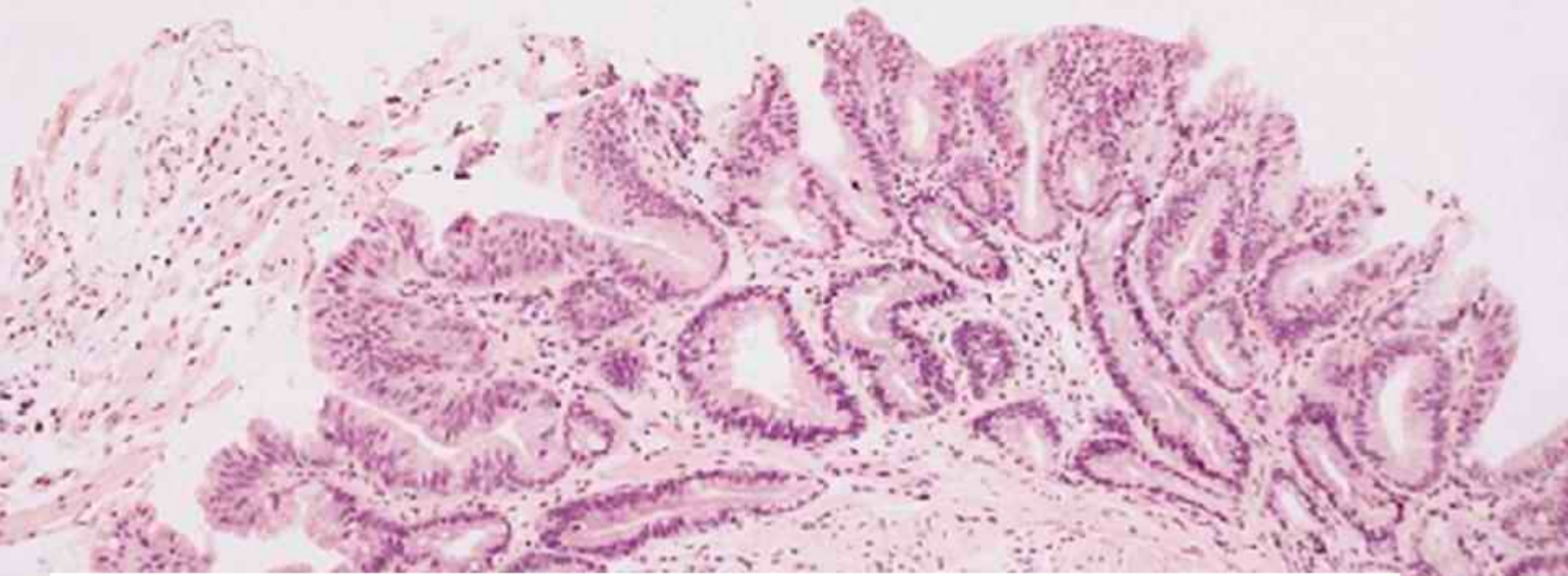


1. Architectural pattern = mild distortion
2. Nuclear Pattern = basal
3. Surface maturation = present/?

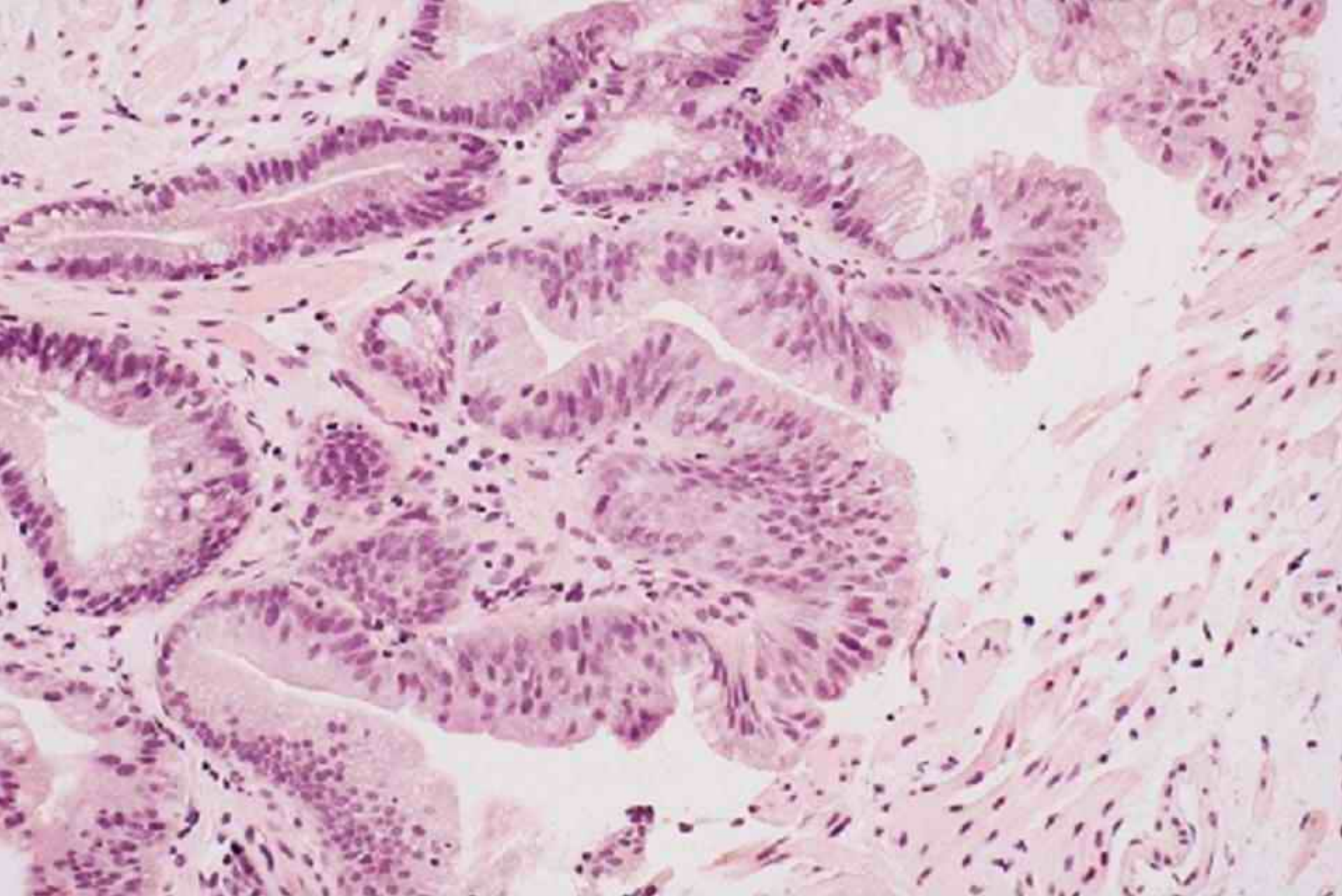


Indefinite for dysplasia

HUM PATHOL 32:368-378

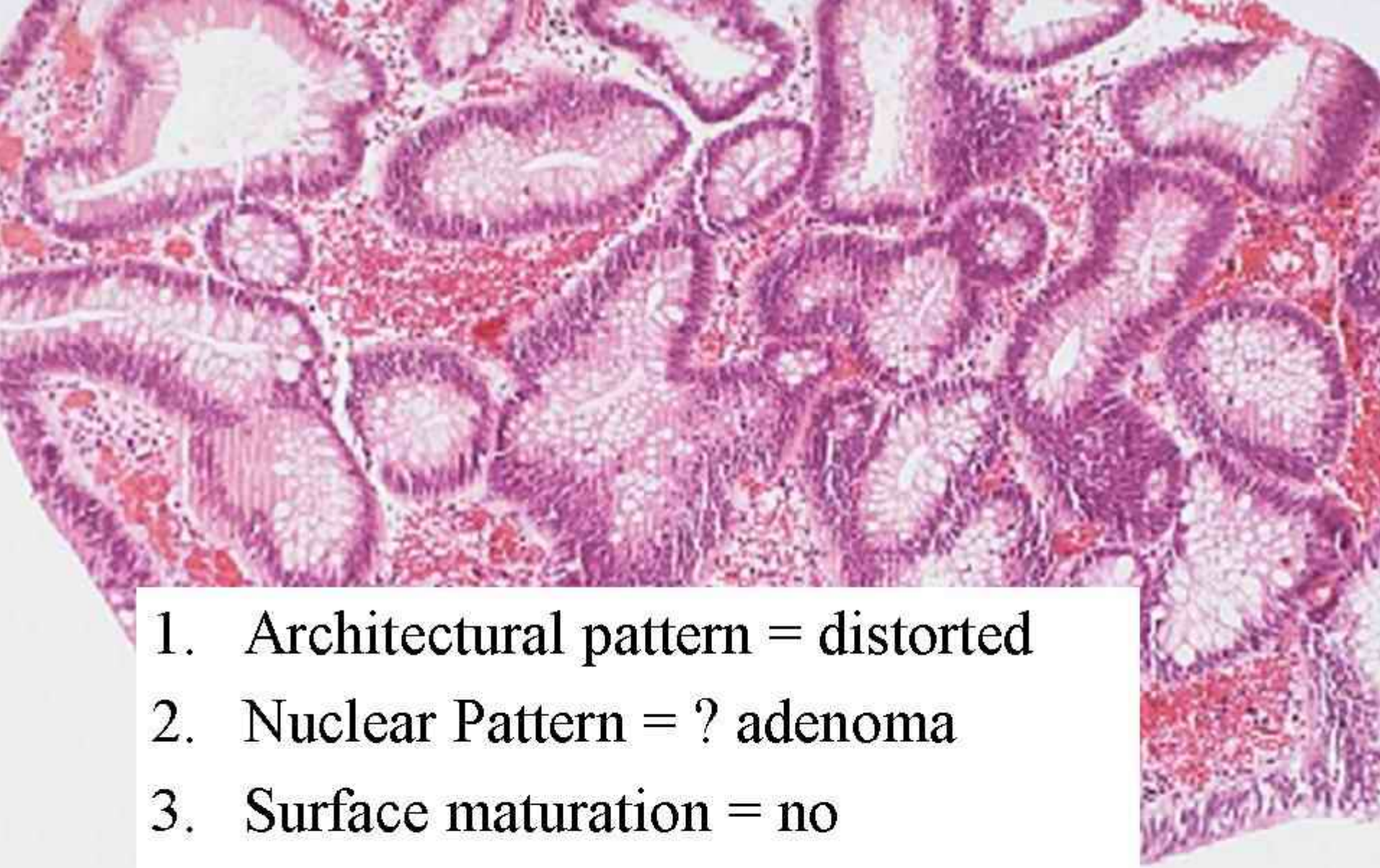


1. Architectural pattern = mild distortion
2. Nuclear Pattern = basal
3. Surface maturation = ????



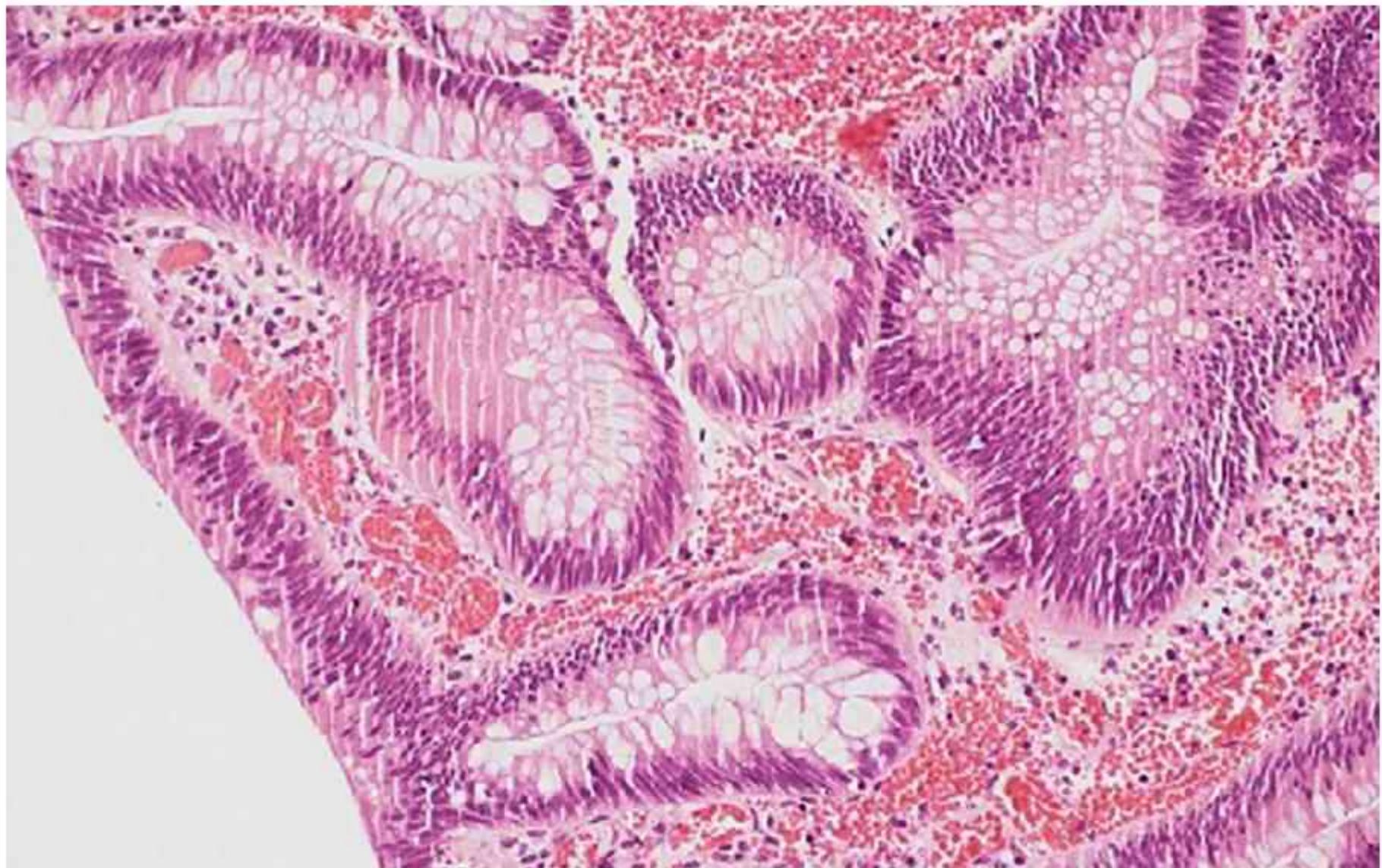
HUMPATH

Low-Grade Dysplasia (lack of surface maturation)



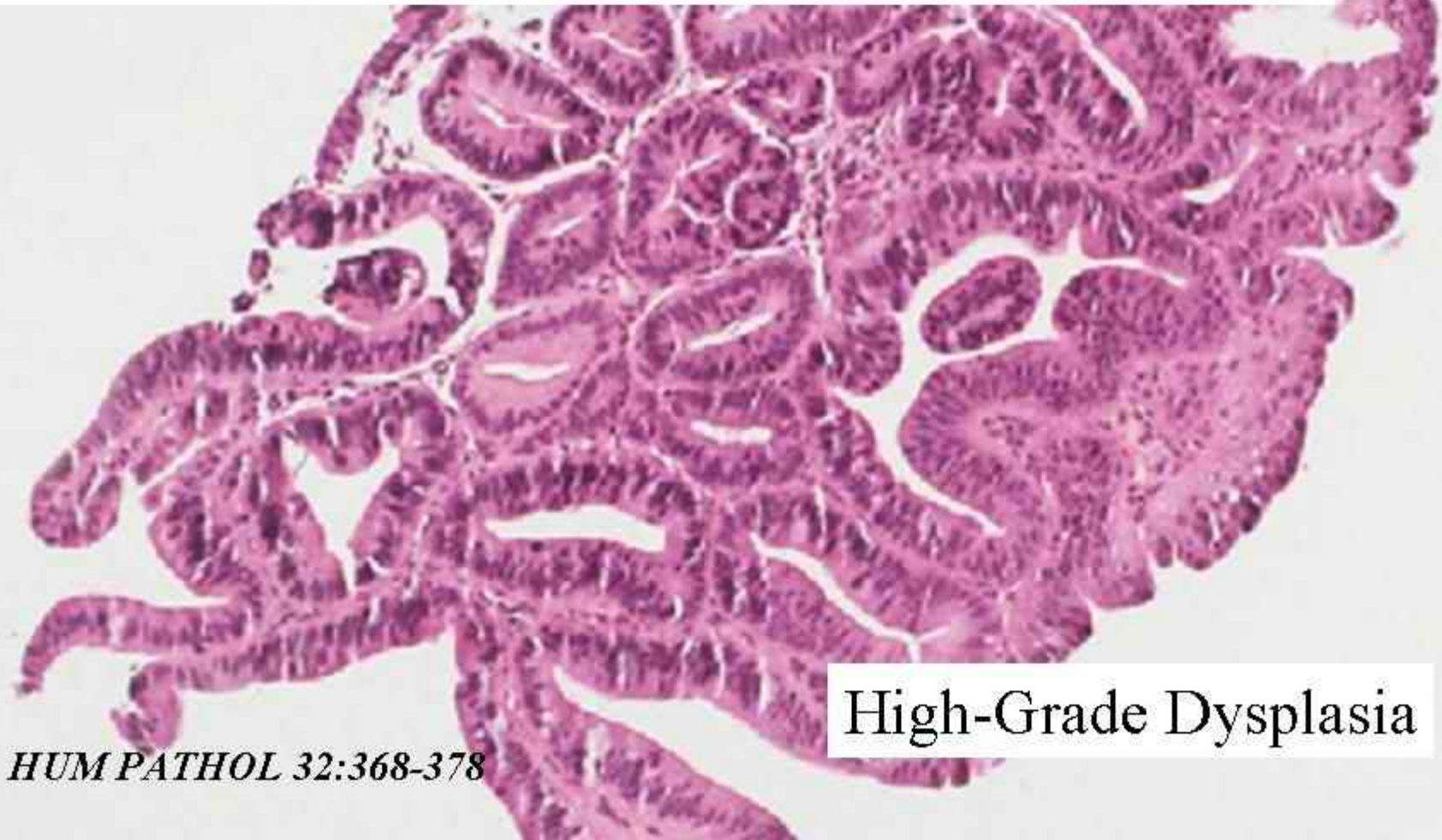
1. Architectural pattern = distorted
2. Nuclear Pattern = ? adenoma
3. Surface maturation = no

Low-Grade Dysplasia (resembles tubular adenoma)

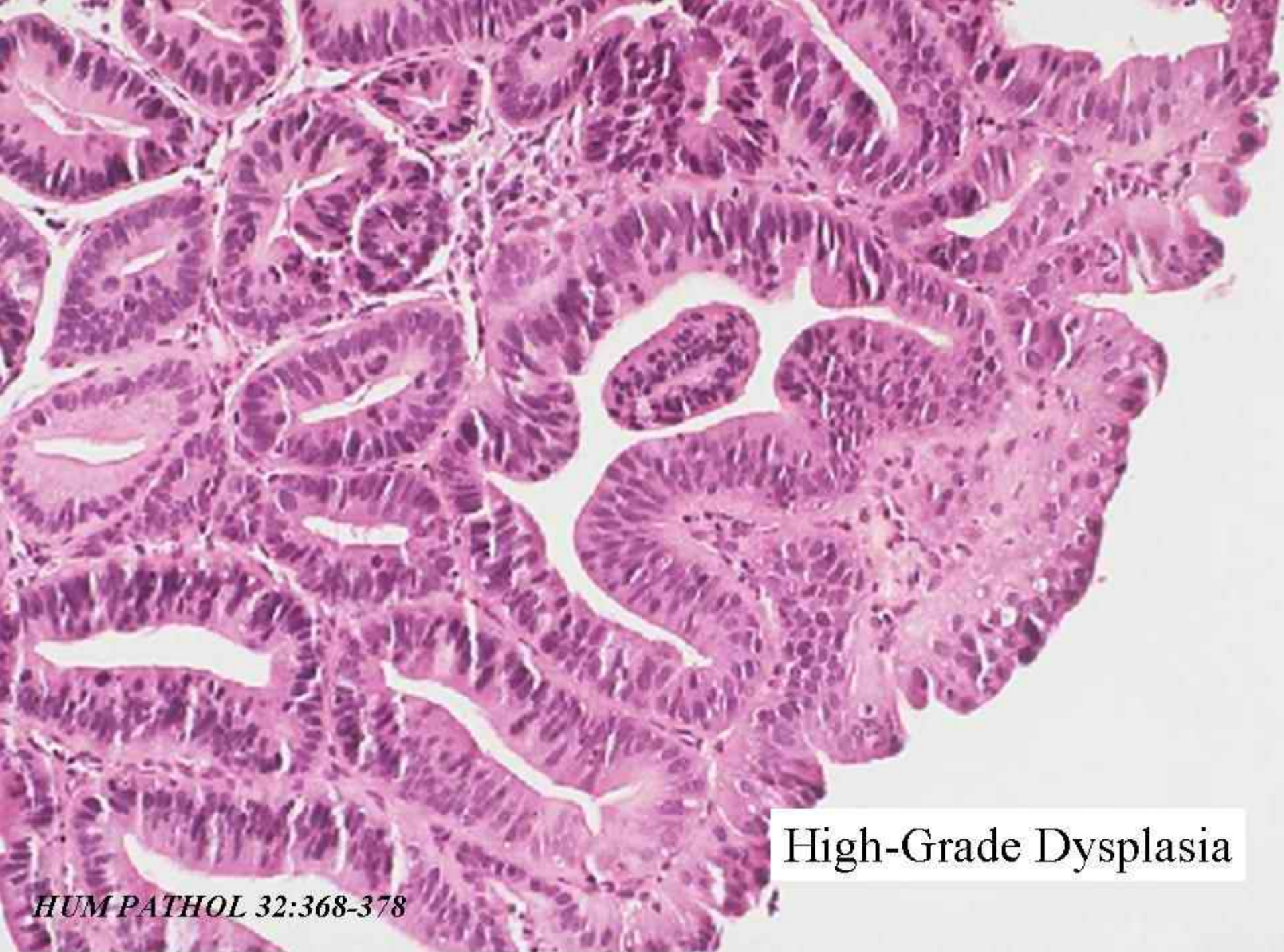


Low-Grade Dysplasia (resembles tubular adenoma)

1. Architectural pattern = complex
2. Nuclear Pattern = prominent atypia
3. Surface maturation = negative

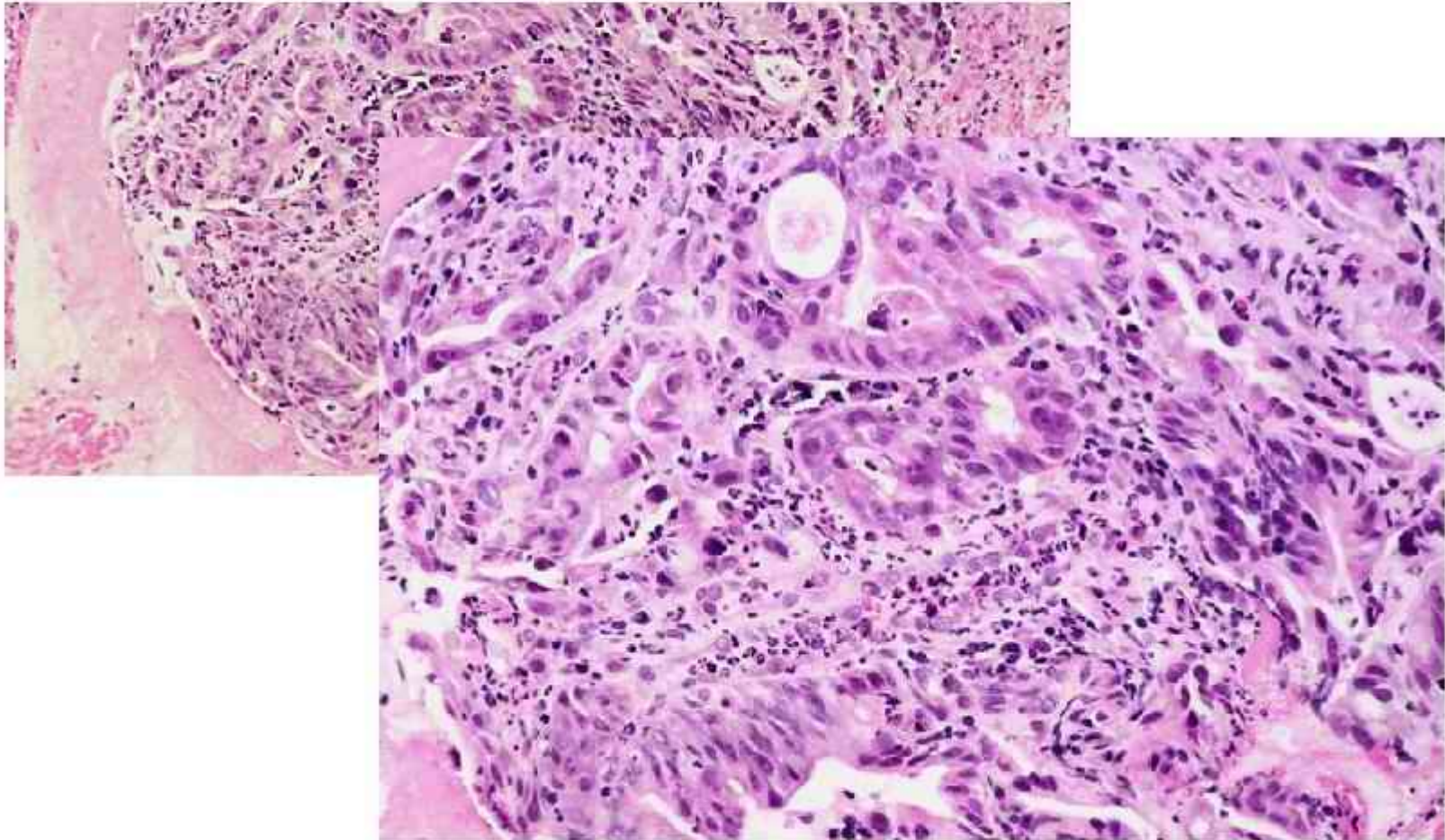


High-Grade Dysplasia

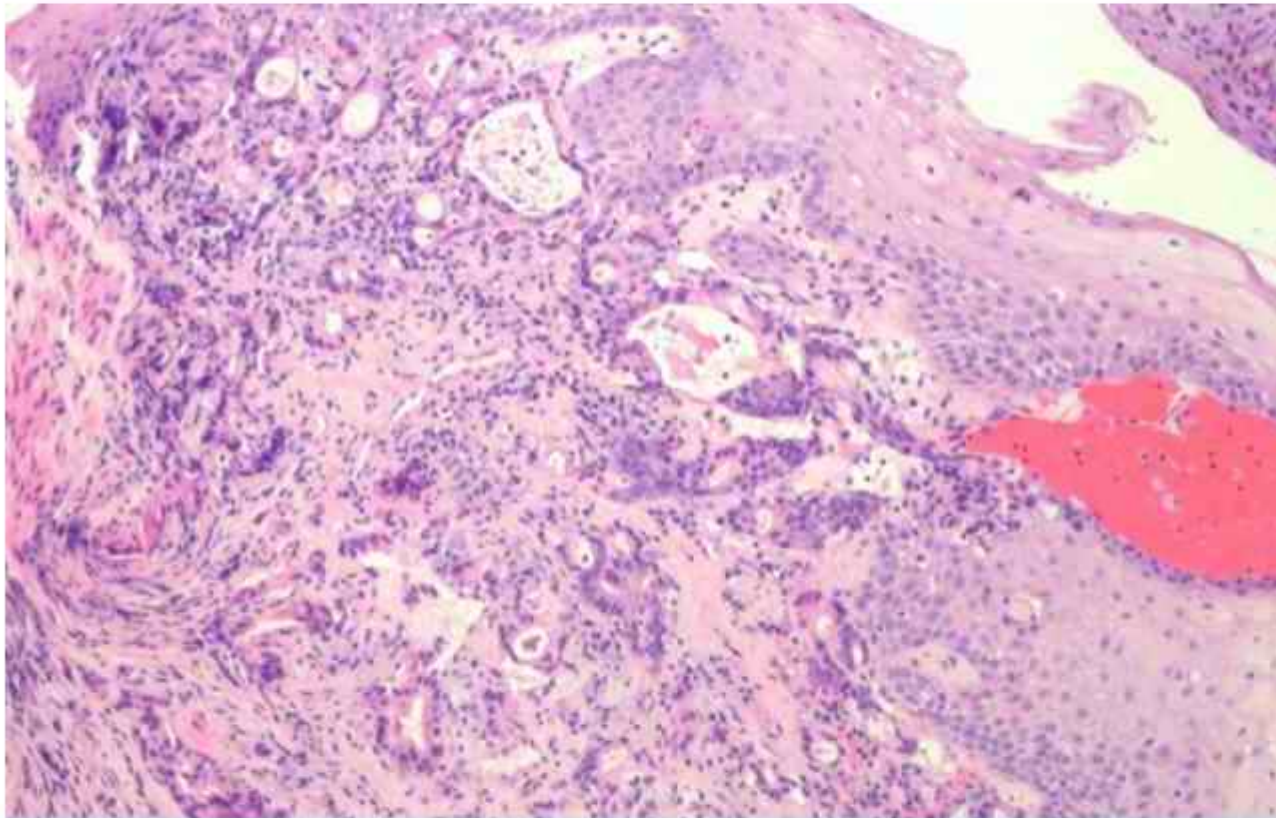


High-Grade Dysplasia

Intramucosal Carcinoma: syncytial arrangements of cells and complex glandular budding is believed to reflect early invasion (before desmoplasia becomes well-developed).



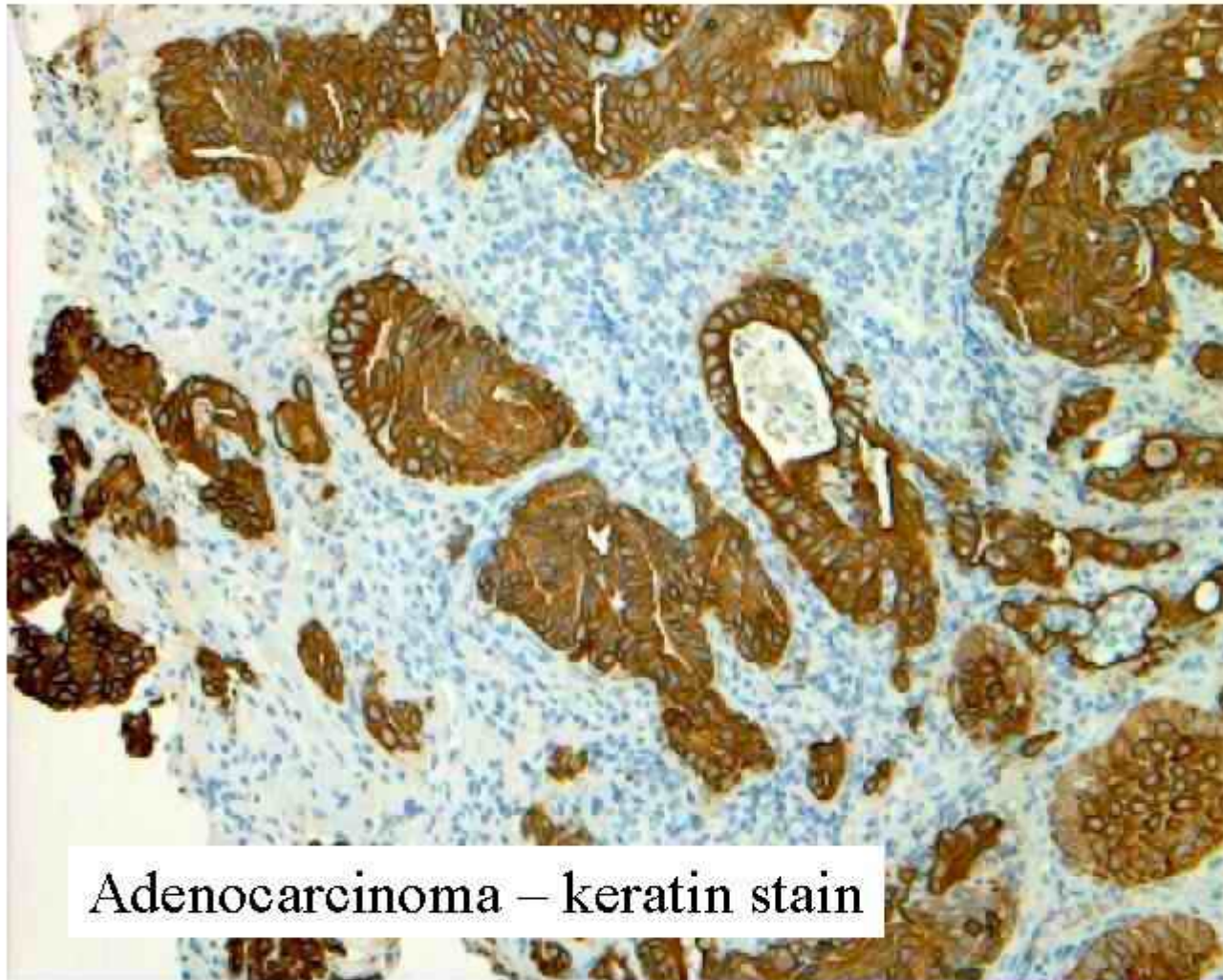
ADENOCARCINOMA IN BARRETT'S ESOPHAGUS



Invasive (deep lesions) are usually easy to diagnose

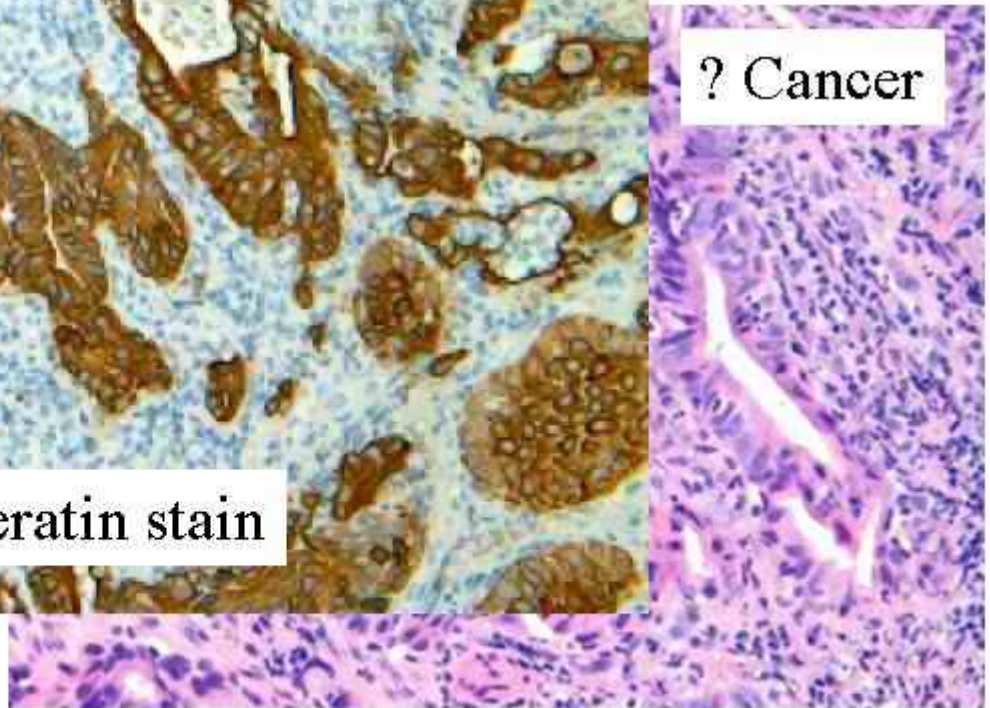
AdenoCa





Adenocarcinoma – keratin stain

? Cancer



What is the Interobserver variation between pathologists?

substantial

There is considerable interobserver variation in interpretation even among experts. This is most marked in the differential between no dysplasia, indefinite vs. low grade dysplasia.

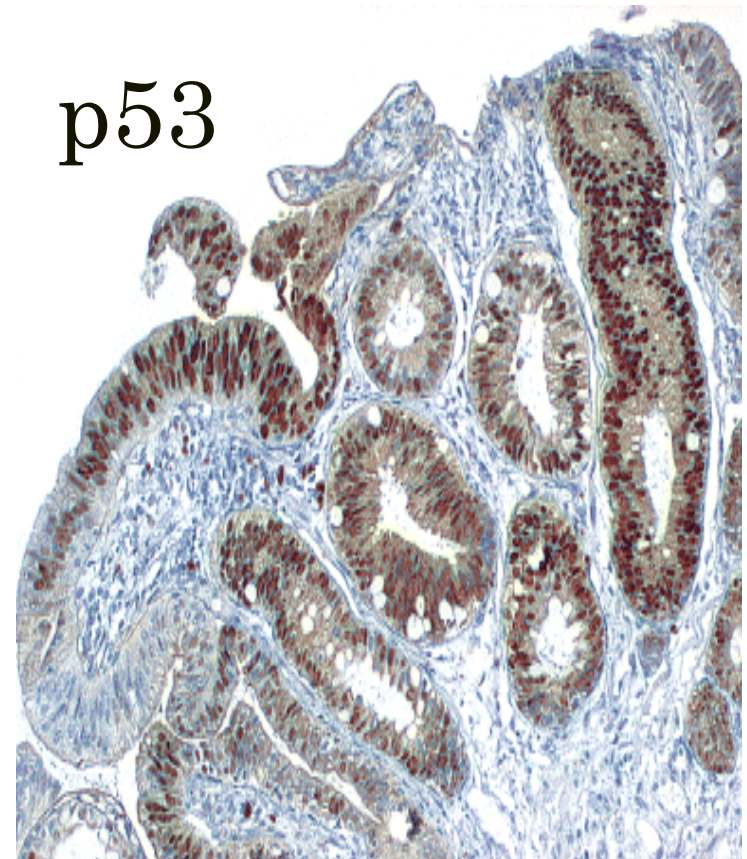
Less subjective markers are needed.

Role of Biomarkers in Diagnosing Dysplasia in Barrett's

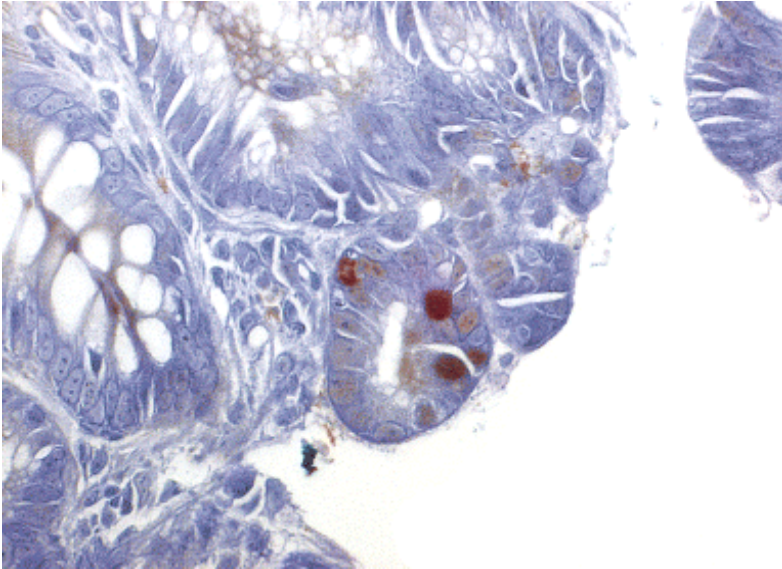
1. P53
2. Racemase

p53 in Diagnosing Dysplasia in Barrett's

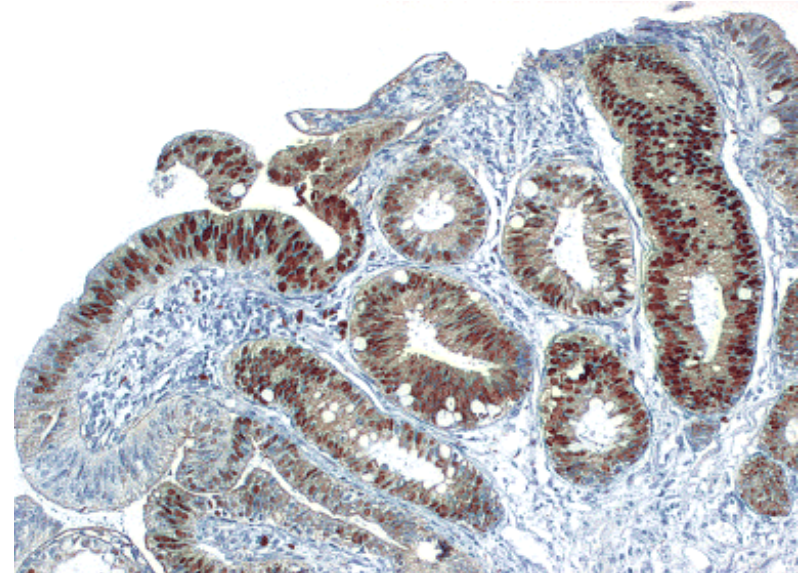
Though controversial, alterations in p53 expression can facilitate the interpretation of an epithelial abnormality.



What is a positive stain for p53



Sporadic nuclear staining should be considered negative (-).



Nuclear staining in continuity indicates clonal expansion of mutated cells (+).

p53 Role in Diagnosing Barrett's





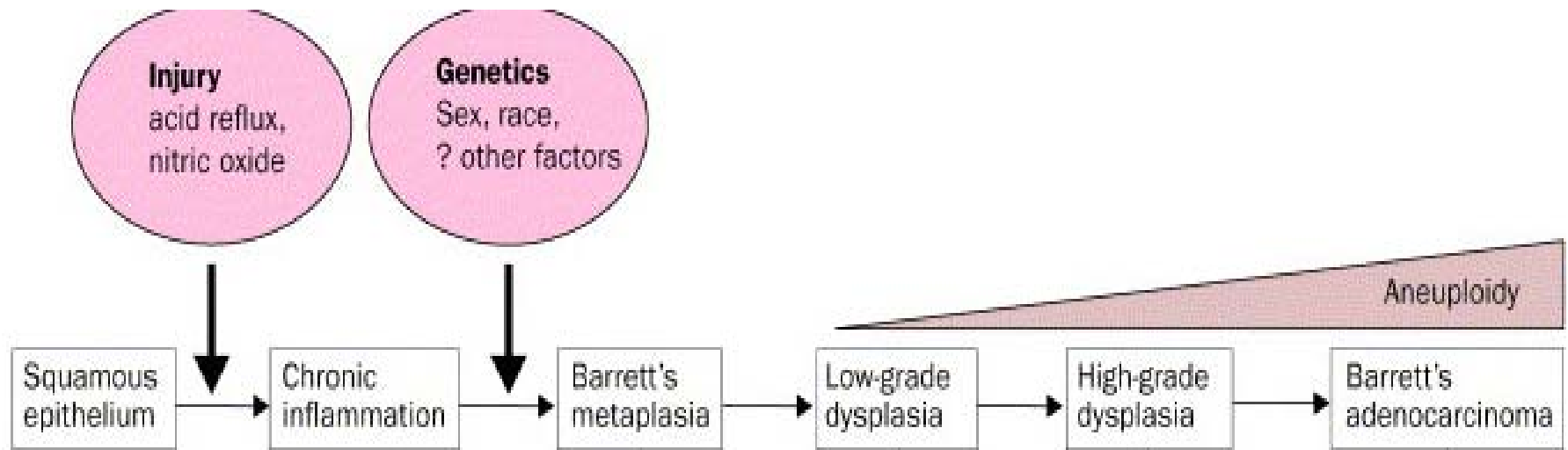
Non dysplastic	Low grade dysplasia	High grade dysplasia	Carcinoma
1.4 % (0-10%) 	30% (0-60%) 	68% (50-100%) 	72% (45-100%) 

Table shows gradual increase in p53 expression
as dysplasia increases.

Why is p53 use controversial?

Because of the considerable overlap in expression between and within categories.

SUGGESTED USE FOR p53 IN BARRETT'S



If histopathology suggests dysplasia, and is p53 (+) specimen is more likely to be dysplastic; if it is dysplastic it is more likely to progress to cancer if p53 (+).

Racemase

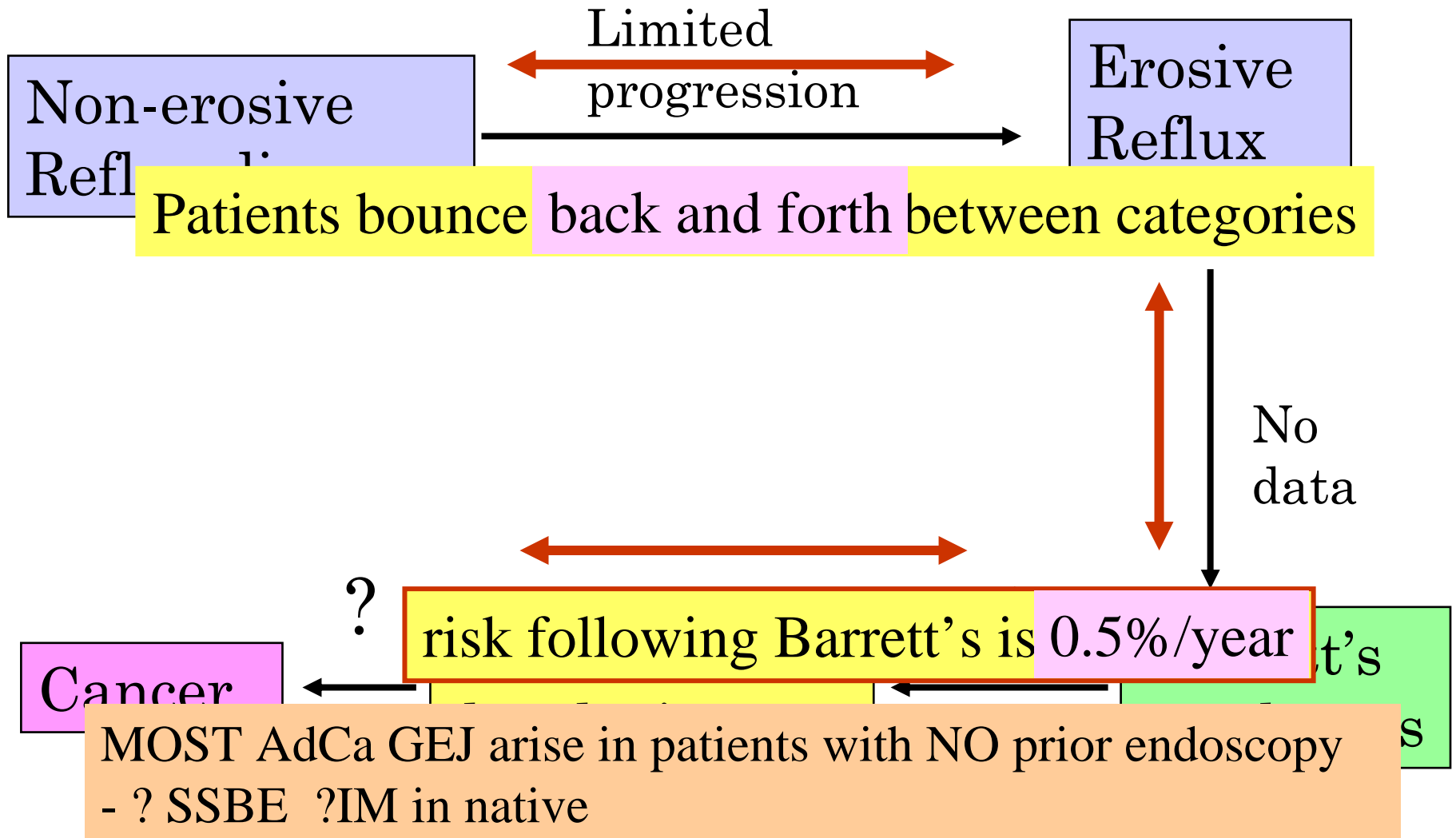
Is AMACR expression a marker for neoplastic progression?

- AMACR stands for alpha-methylacyl-coenzyme A racemase
- Two studies indicate specificity for Barrett's esophagus. **The jury is still out. More studies are needed.**
- Third study indicates lack of reliability.

Observer variation in the diagnosis of superficial oesophageal adenocarcinoma

Even experienced gastrointestinal pathologists frequently disagree on a diagnosis of high grade dysplasia versus intramucosal adenocarcinoma.

CANCER RISK POST BARRETT'S



Proposed Classification of Intestinal Metaplasia at GEJ

Term	Length	Cancer risk	Surveillance
LSBE	> 3 cm	Yes	Yes
SSBE	< 3 cm	Yes	Yes
Gastric cardia IM		Unclear	has gastric cancer risk ? No risk for GEJ

The diagnosis and reporting of Barrett's esophagus

- Main differential with GERD is Eosinophilic esophagitis. History, endoscopic appearance and proximal biopsies will help differential.
- Barrett's is columnar lined esophagus. Call it columnar lined in absence of goblets. Call it Barrett's metaplasia if you see goblets.
- Use architecture, nuclear features, and surface maturation to diagnose low grade dysplasia and high grade dysplasia.
- In doubt, P53 expression can facilitate interpretation but can only be used in conjunction with histopathology.

Considering the mortality with esophagectomy and substantial interobserver variability in diagnosing dysplasia and intramucosal carcinoma, endoscopic mucosal resection should be the preferred treatment.