

Pathologie des Verdauungstraktes I.

*Ösophaguserkrankungen, Missbildungen, Divertikel,
Entzündungen, Tumoren*

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*250 Jahre EXZELLENZ
in medizinischer Lehre,
Forschung & Innovation
und Krankenversorgung*



VERY FEW KIDS DREAM OF
BEING A GASTRONAUT.



MISSBILDUNGEN

Gesichtsspalten: Stirn- und Oberkiefervorsatz verschmelzen sich miteinander nicht (Embryonalmonat 1.-2.)

Mundhöhle: entwickelt sich von zwei Gaumenleisten (oberer und unterer Teil)

Spalten des vorderen embryonalen Gaumens:

Lippenspalte - Hasenscharte - **Cheiloschisis**
häufig kombiniert mit anderen Spalten. OP ab 6. mo.

Kieferspalte - **Gnatoschisis**: Spaltung des Ober- und Unterkiefers. Immer in Kombination mit Lippenspalte



MISSBILDUNGEN

Spalten des hinteren embryonalen Gaumens:

Gaumenspalte - **Palatoschisis**: Spalte im harten Gaumen zwischen Mund- und Nasenhöhle.

Uvula bifida - doppeltes Zäpfchen

Spalten des vorderen UND hinteren embryonalen Gaumens

Lippen-Kiefer-Gaumenspalte - **Cheilognathopalatoschisis**-
WOLFSRACHEN





-Palatoschisis (cleft palate)

-Uvula bifida



ÖSOPHAGUS FEHLBILDUNGEN

Ösophagusatresie: nicht oder unzureichend angelegter Ösophagus

in 90 % der Fallen besteht gleichzeitig eine ösophagotracheale Fistel.

Komplikation: Polyhydramnion
(wegen intrauteriner Schluckstörung)

Dysphagia lusoria: abnormal angelegter Aortabogen o. arteria lusoria (atypische a. subcl.)

Kompression: Ösophagusstenose

Dysphagie: Schluckstörung



ÖSOPHAGUS - Fehlbildungen

Ösophagotracheafistel und Ösophagusatresie: häufige Fehlbildung der Neugeborenen, nicht getrennte Vorderdarmanlage

90 % der Falle Ösophagotracheafistel sind mit einem Blindsack des oberen Ösophagus kombiniert



MISSBILDUNGEN

Ösophagusatresie: in 90 % der Fällen besteht gleichzeitig eine ösophagotracheale Fistel. **Kompl.: Polyhydramnion**

Dysphagia lusoria: abnormal angelegter Aortabogen o.
Arteria lusoria (atypische a. subcl.)

Kompression: Ösophagusstenose

Dysphagie: Schluckstörung

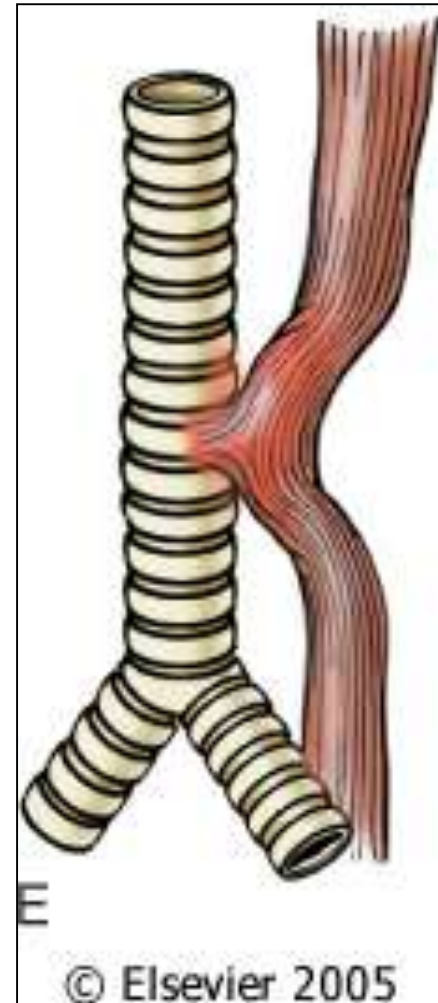
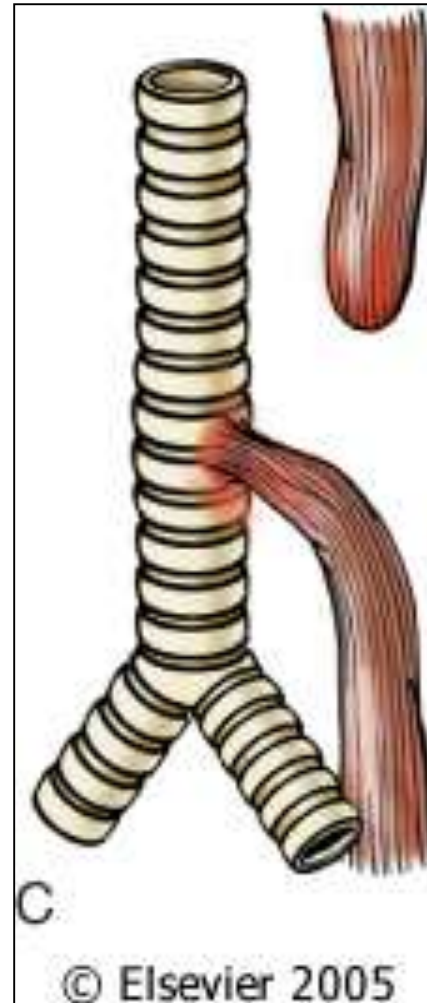
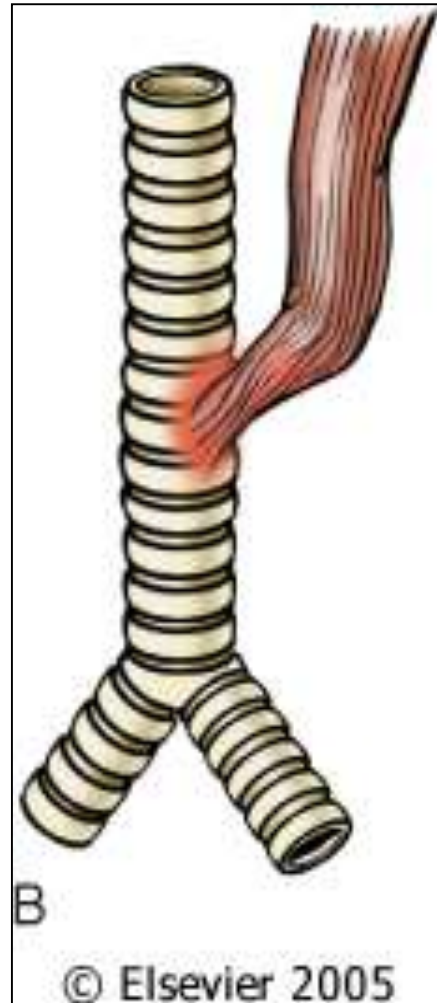
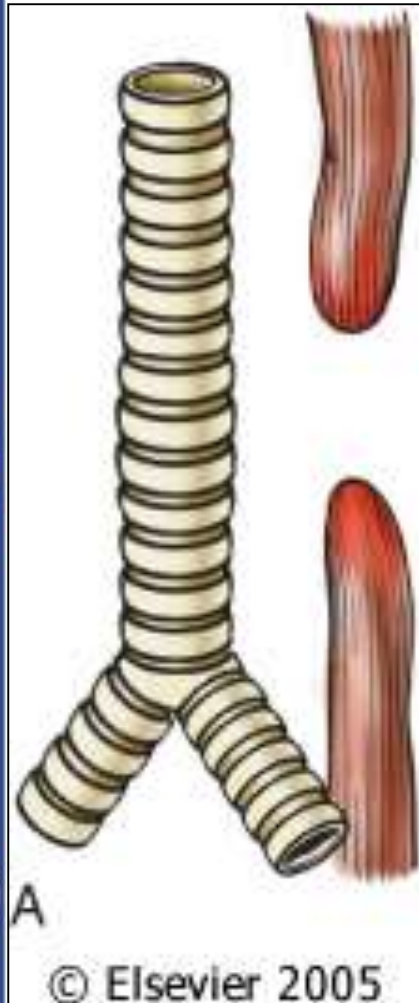
SPALTUNGEN:

Beeinflussung des Saug- und Schluckaktes,
Beeinträchtigung der Sprachenentwicklung !

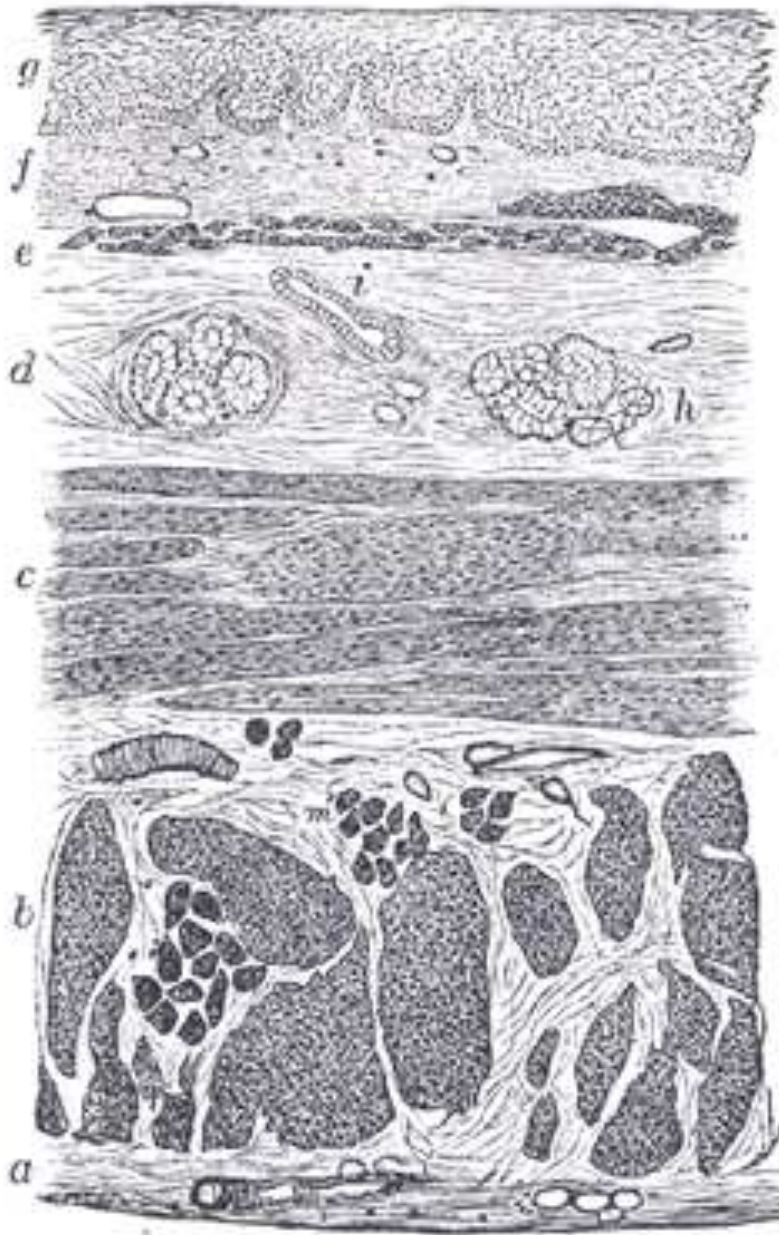
Gefahr der Aspiration - Pneumonie !



Esophagus Atresie und tracheoesophageale Fistel



Anatomie



Mukosa

Plattenepithel

Submukosa

Drüsen, Gefasse, Lymphgefasse
und Follikel, Venen !!!

Tunica musc propria

Adventitia

(keine Serosa)

ÖSOPHAGUS

Hiatushernien: Bauchhöhleninhalt ist in den Brustraum verlagert

Gleithernie: Kardia und Fundus, meist symptomlos

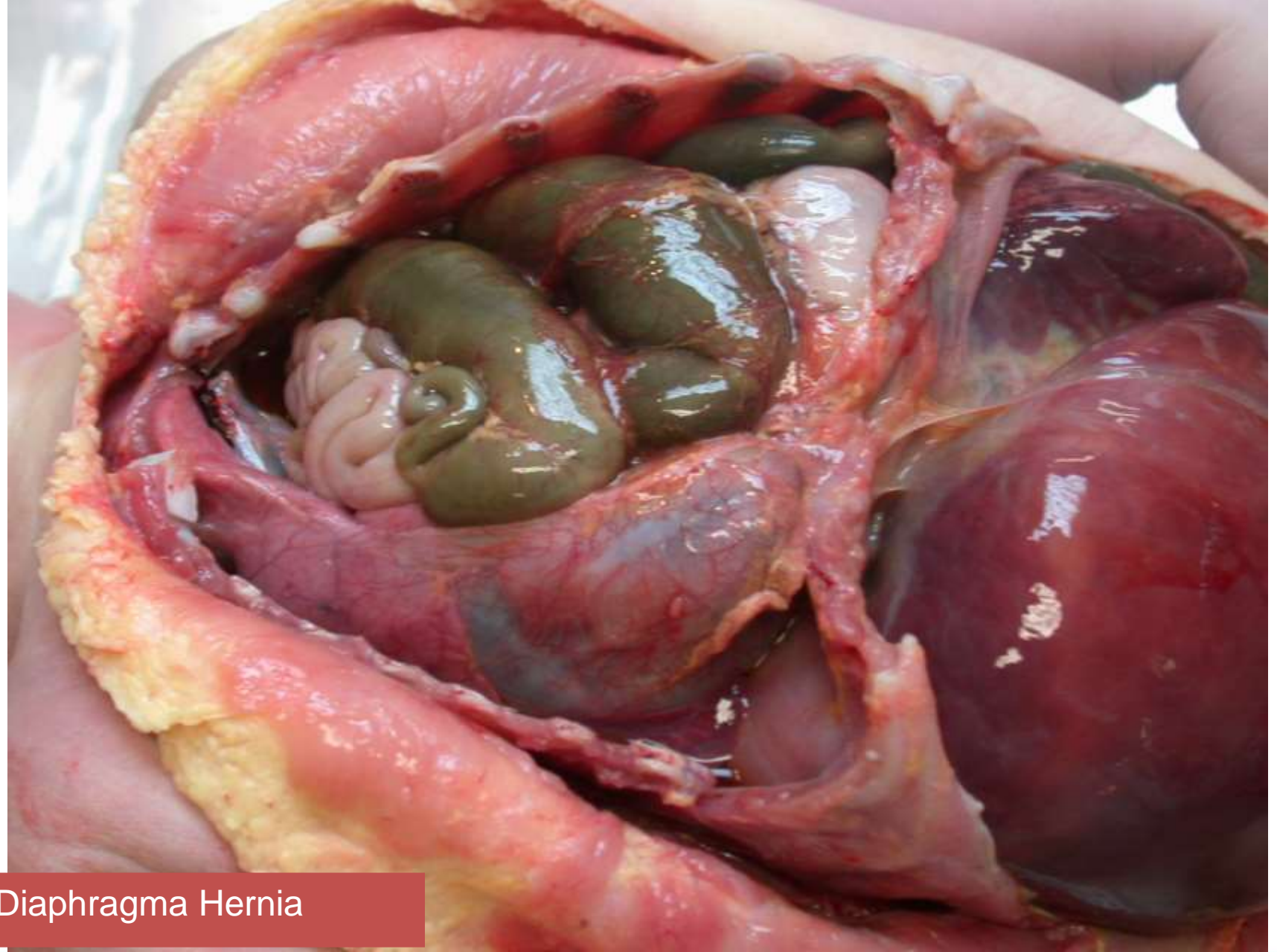
Paraösophageale Hernien: Lage der Kardia ist normal
Regurgitation, Sodbrennen

Varizen:

angeborene: Wandschwäche

erworben: bei portaler Hypertension, meist im unteren Drittel
des Ösophagus





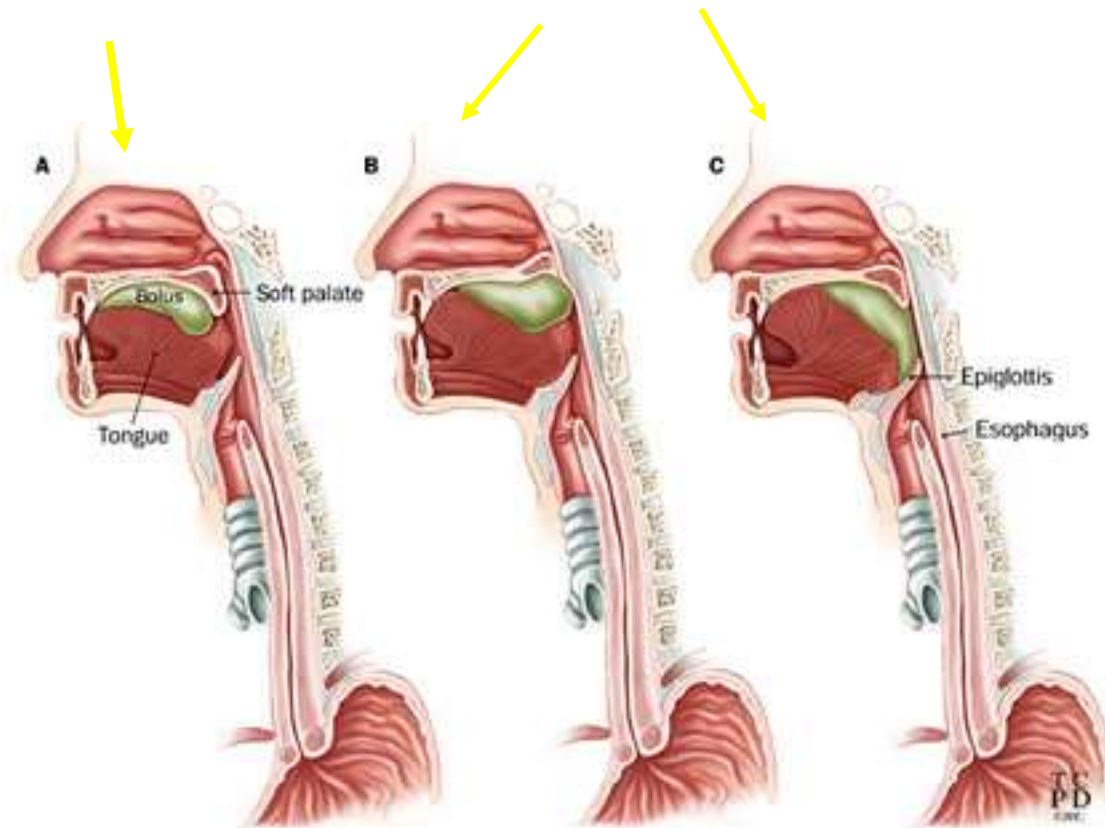
Diaphragma Hernia



Physiologie des Schluckes

Orale Phase

Pharyngeale Phase



Physiologie des Schluckes

Pharyngeale und ösophageale Phase:

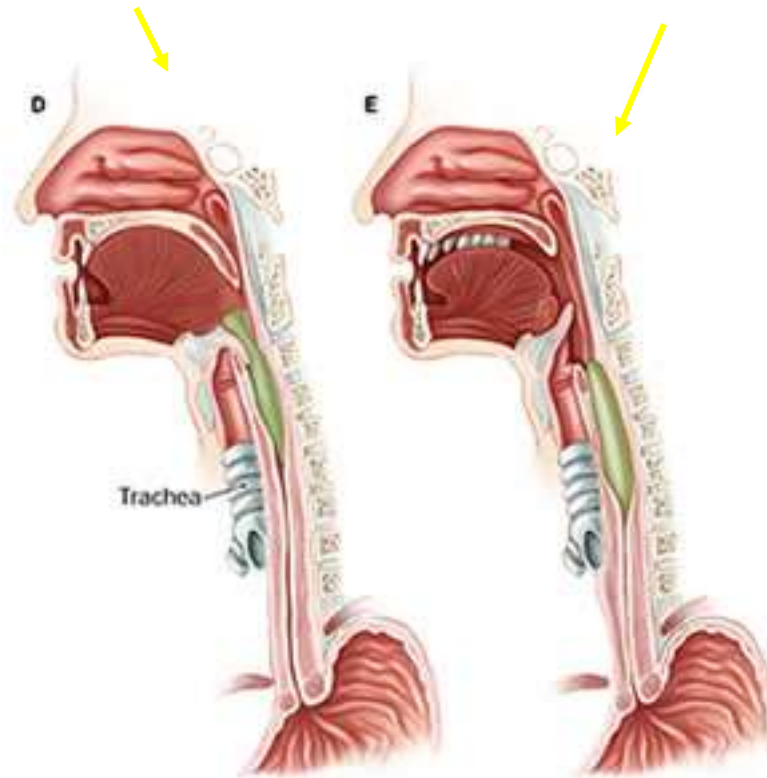
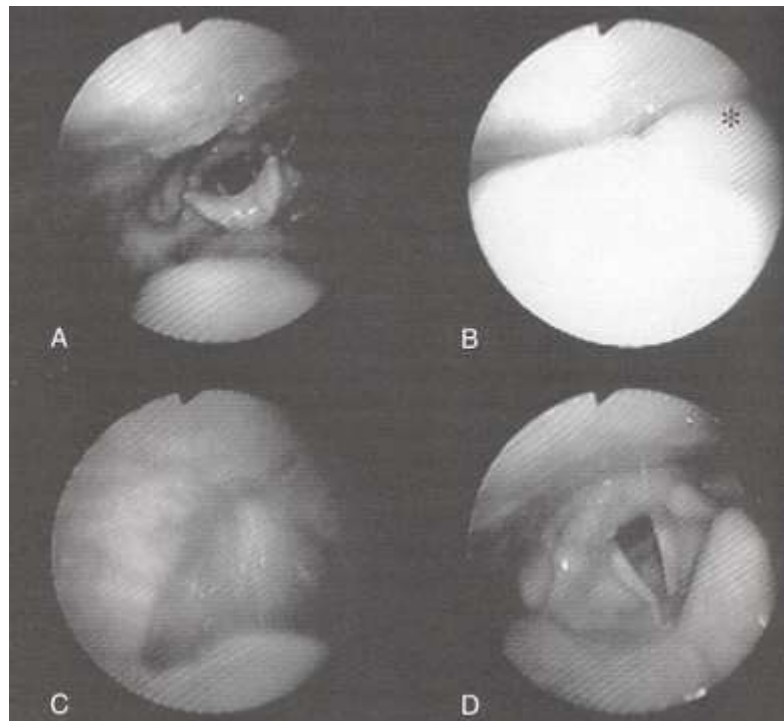


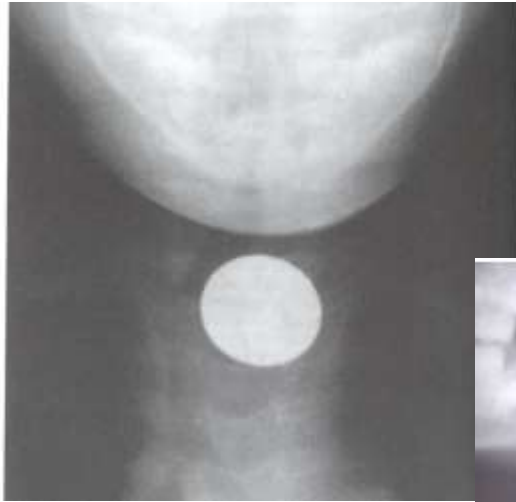
Figure 4 A-E. Pharyngeal phase of swallowing.

Fiberoptische Endoskopie

Bewertung der Schluckstörungen



Fremdkörper



ÖSOPHAGUS

Lichtungsveränderungen:

Achalasie: fehlende Öffnung des Kardiasphinkters
Speisenretention, Megaösophagus “Weinglassform”
Metaplasie, Karzinom, Perforation
in Südamerika: Achalasia ist eine Komplikation der Chagas
Krankheit (Myositiden - Trypanosoma cruzi).

Stenosen: angeboren o. verursacht bei Tumoren, Struma,
Sklerodermie. Es kann zu Megaösophagus kommen

Divertikel:

Varizen:



Cricopharyngeale Achalasie



Figure 16. Radiographic image of cricopharyngeal dysfunction.

Achalasia

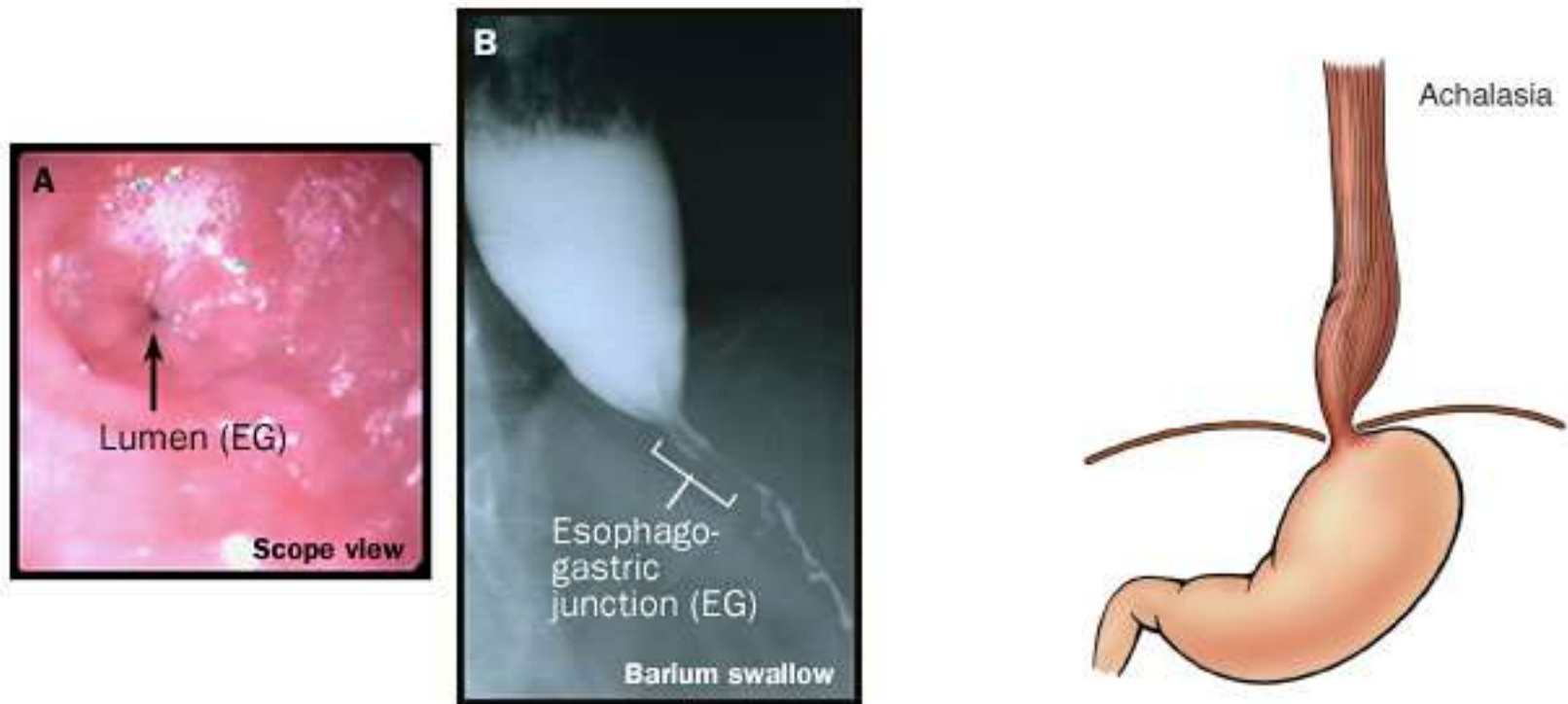


Figure 23. Endoscopic (A) and radiographic (B) findings in achalasia.

Strikturen / ätzende Schädigung bei Nahrungsaufnahme

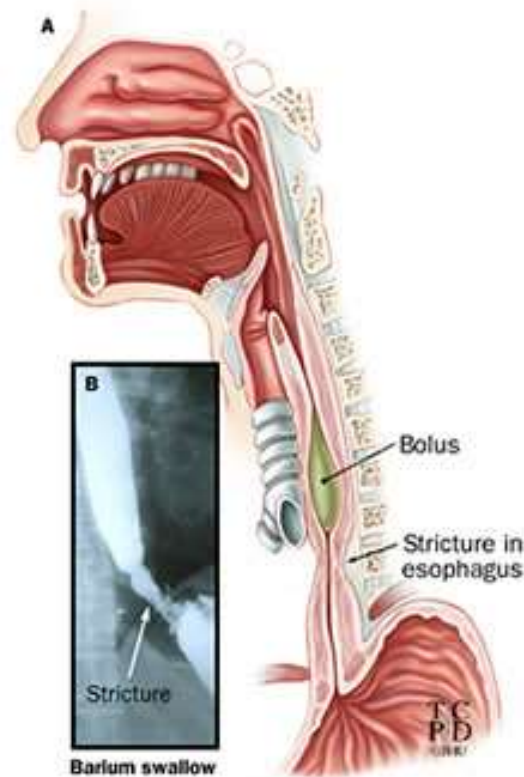


Figure 11. Esophageal stricture showing obstruction of food bolus with corresponding barium swallow.

diffuses Ösophagus Spasmus

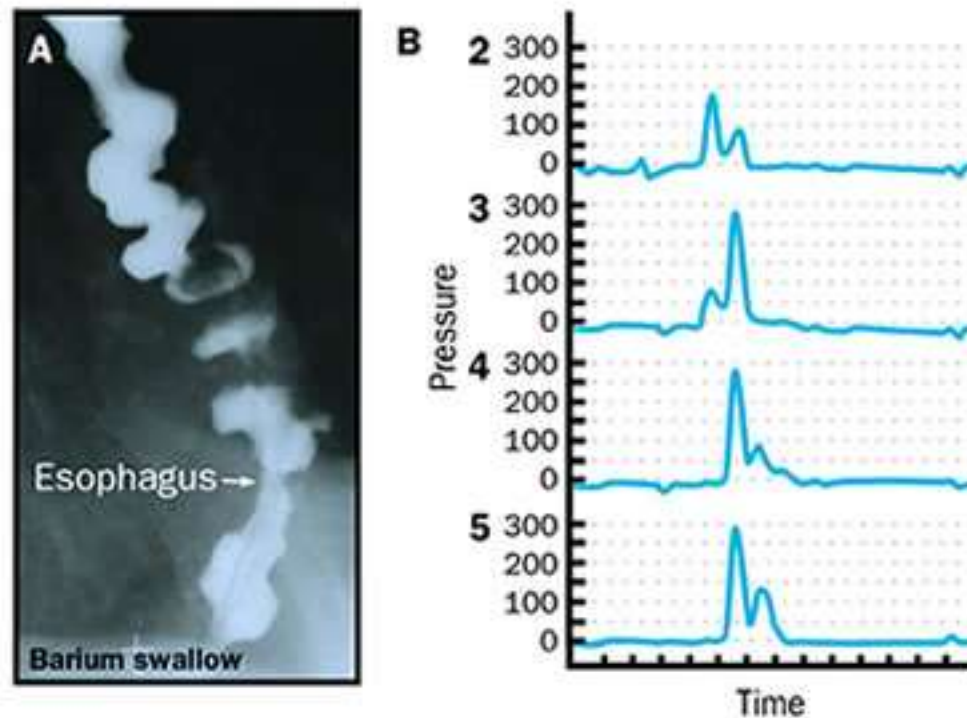


Figure 22. Barium swallow x-ray showing diffuse esophageal stricture (A) with corresponding manometric tracing (B).

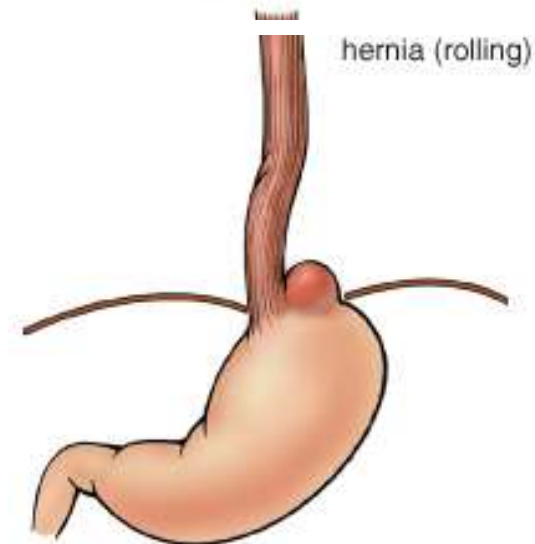
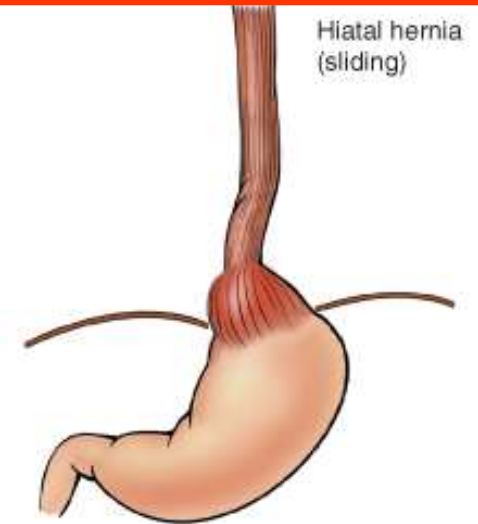
Motorische Dysfunktion assoziierte Lesionen

- **Hiatus Hernia**

- **Axial oder sliding** Hernia: 95% der Fälle
 - Protrusion des Magens über Zwerchfell
- **Paraesophageal oder „rolling“** Hernia: ein Teil des Magens entlang grosser Krümmung tritt in die Thorax ein.

SY: Sodbrennen, Regurgitation

Complications: assoziierte reflux Ösophagitis, Ulzeration, Blutung,
Perforation: Mediastinitis



Motorische Dysfunktion assoziierte Lesionen

Divertikel: angeborene o. erworbene Aussackungen

echte (alle Wandschichten) o. Pseudodivertikel (nur die Schleimhaut). Dysphagie, Hustenreiz, Regurgitation

Pulsionsdivertikel: angeborene o. erworbene Wandschwäche, beim erhöhten intraluminalen Druck:

Zenker Divertikel: 70 % aller Ösophagusdivertikel - Pseudodivertikel, im oberen Drittel

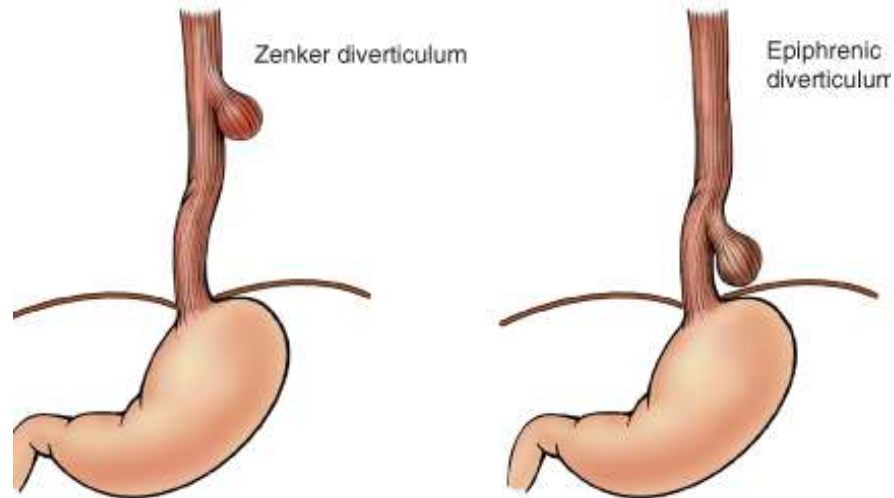
Das epiphrenische Divertikel: 10 % , Pseudodivertikel
Traktionsdivertikel: 20 %, meist symptomlos, Narbenzug parabronchial, in der Höhe von Bifurkation



Motorische Dysfunktion assoziierte Lesionen

Divertikel: Dilatation

- **echte-** (hat alle Wandschichten) Zenker Divertikulum (Pulsion-Kraniopharingeal),
 - Traktion
 - Epiphrenisch



- **falsche** - Mukosa/Submukosa: Pseudodivertikel (es hat nur die Schleimhaut:kein Muskelschicht)
- Komplikationen: Divertikulitis, Perforation, Ulzeration, Mediastinitis, Fistel

Zenker's Diverticulum

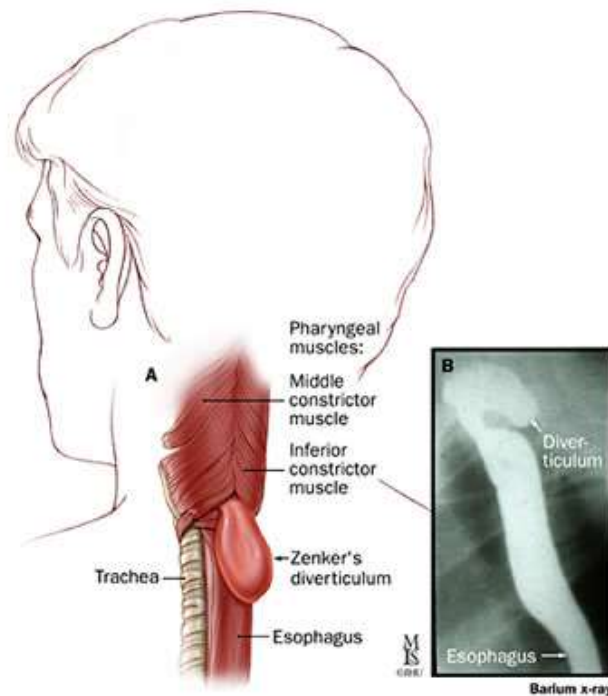
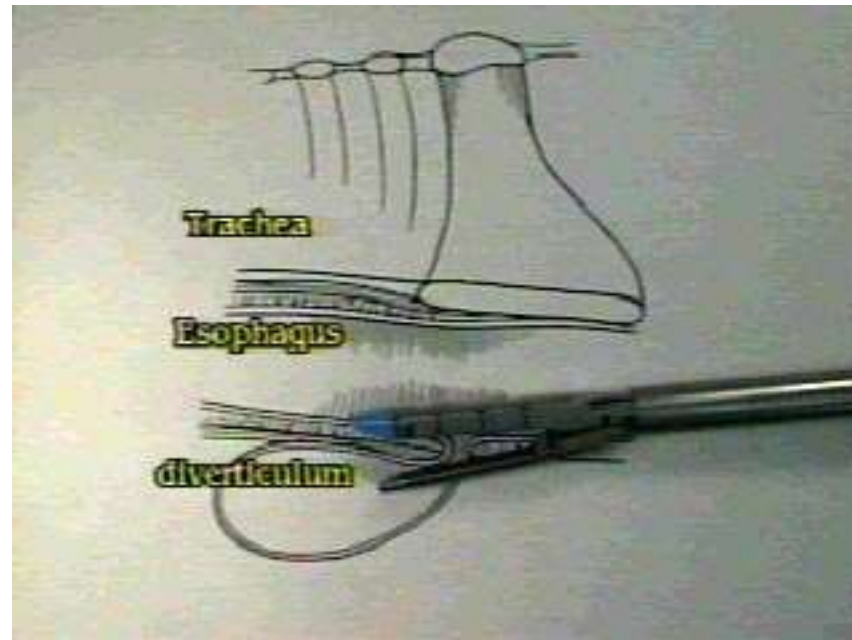
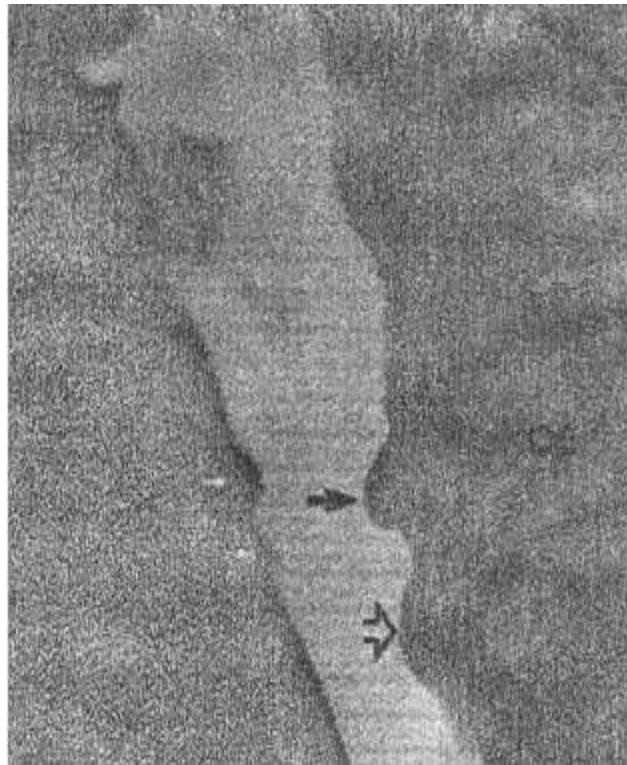


Figure 17. Zenker's diverticulum (A) with corresponding barium x-ray (B).

Zenker's Diverticulum



Zervikale Rippe Krankheit



ÖSOPHAGITIS

Refluxösophagitis: durch eine Kardiainsuffizienz, Rückfluss der Magensaft

physiologischer Reflux versus Refluxkrankheit
(gehaufter Reflux) versus Refluxösophagitis
(Refluxkrankheit mit erkennbaren Epitheldefekten)

Barrett Syndrom: metaplastischer Ersatz des distalen Ösophagusepithel: Kardia Typ, Fundus Typ mit Belegzellen, Intestinaler Typ mit Becherzellen

Soorösophagitis: *Candida albicans*



Untere Ösophagus Sphinkter

- Normalerweise es verhindert die saurige den Rückfluss des Mageninhaltes
- Es relaxiert die Ernährung durchzulassen
- Es haltet einen Druck von 15-30 mmHg auf.



Untere osophageale Sphincter
<http://www.becomehealthynow.com/article/bodydigestive/727/>

GERD

↪ Symptomen

- ↳ Sodbrennen
- ↳ Regurgitation
- ↳ Nausea

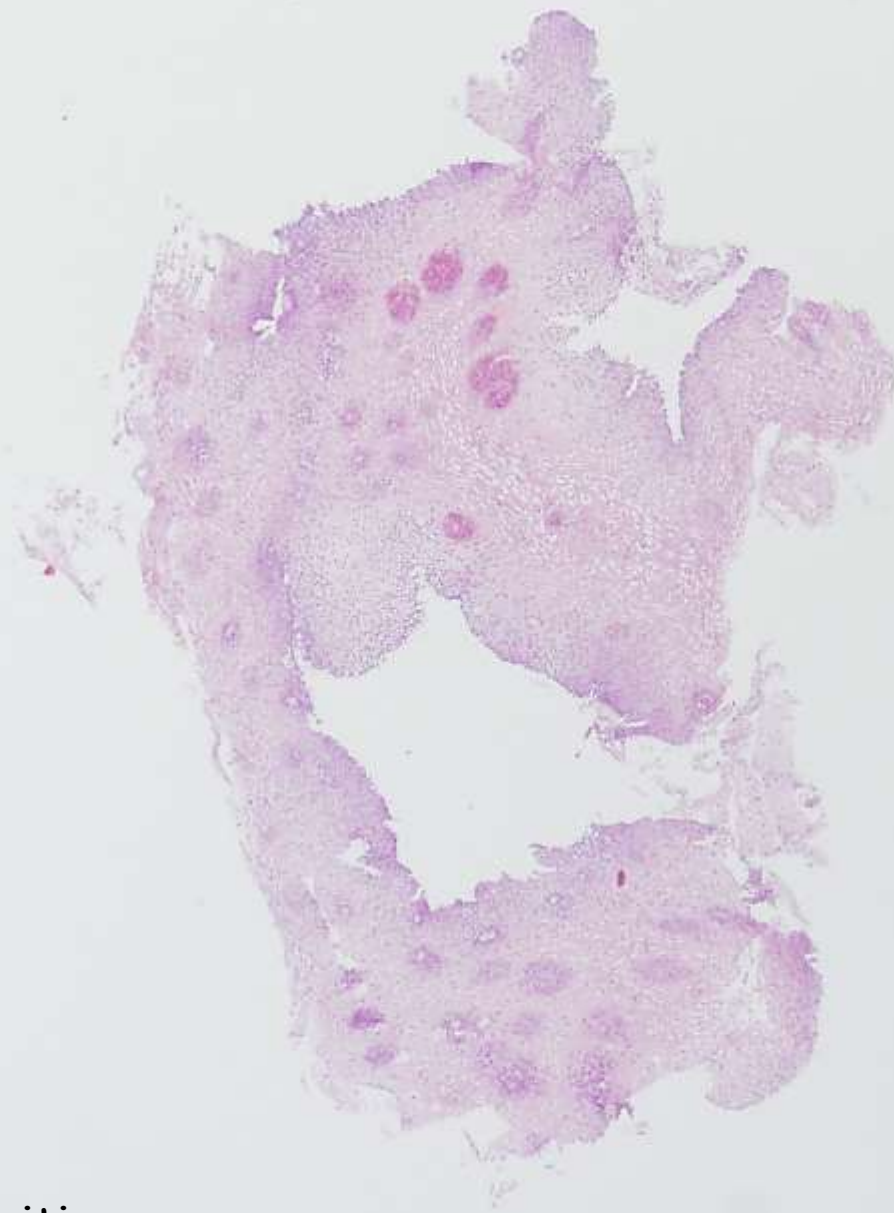
↪ Reflux

- ↳ LES ist zu schwach
- ↳ mangelnde
Schlussfähigkeit – es
bleibt geöffnet



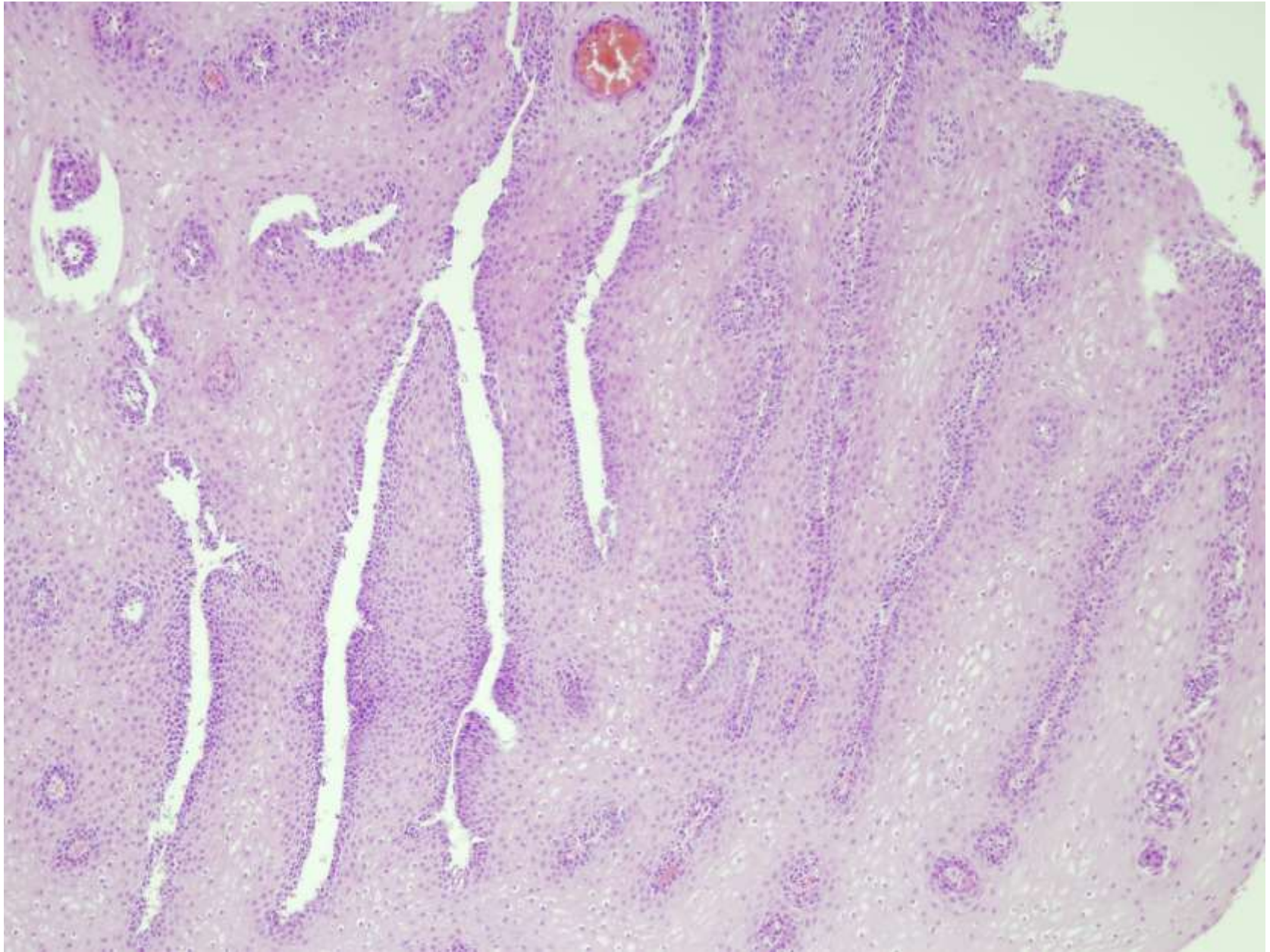
LES mit GERD

(Jackson Gastroenterology, 2004)



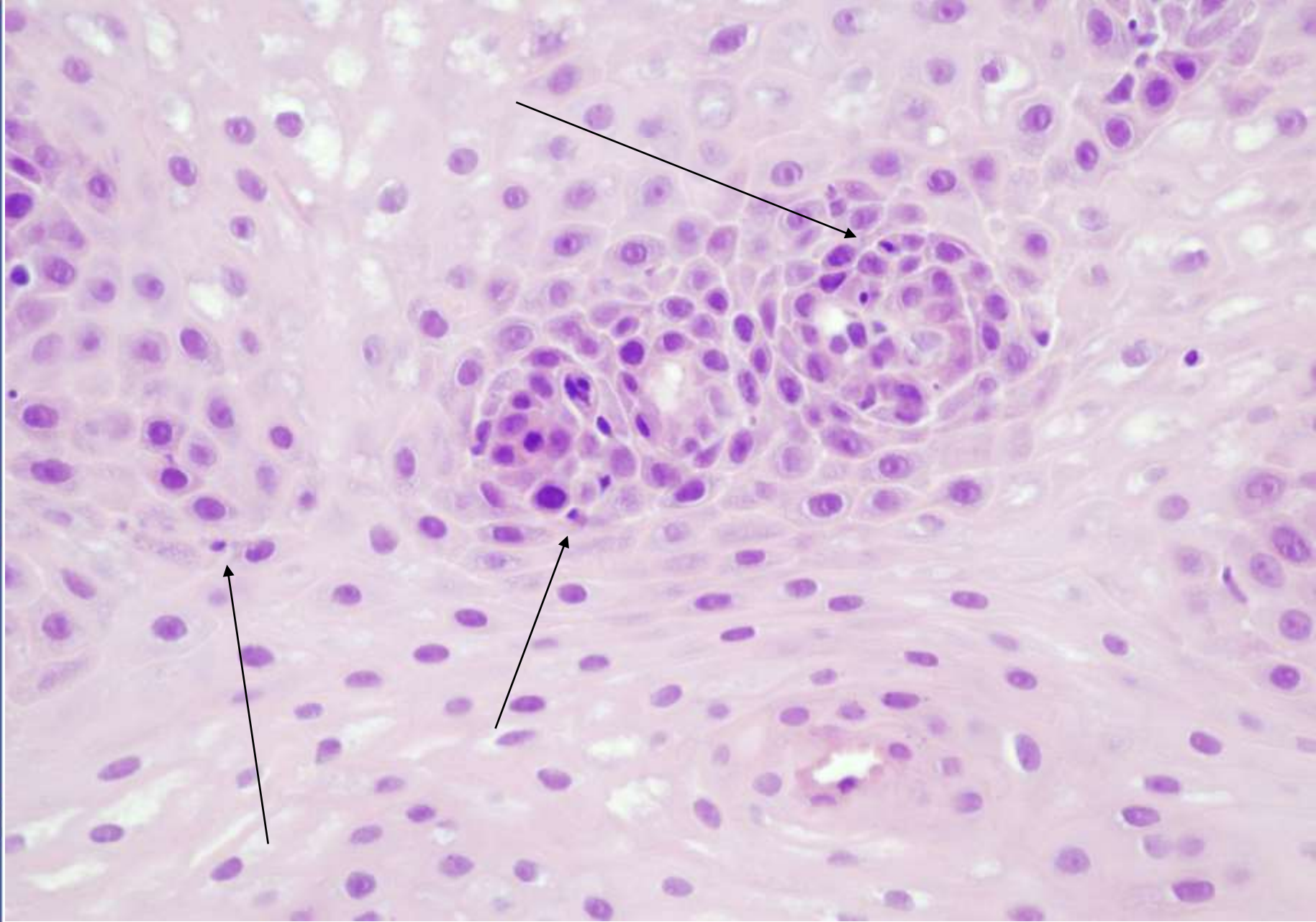
Reflux esophagitis





<http://report.semmelweis.hu/linkattendance.php?attendance=22357EY3SCNLL8FS>

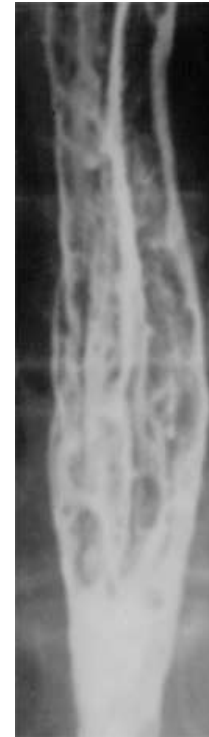




Luft Kontrast Barium Esophageogram



Normal



fungöse Plaquen



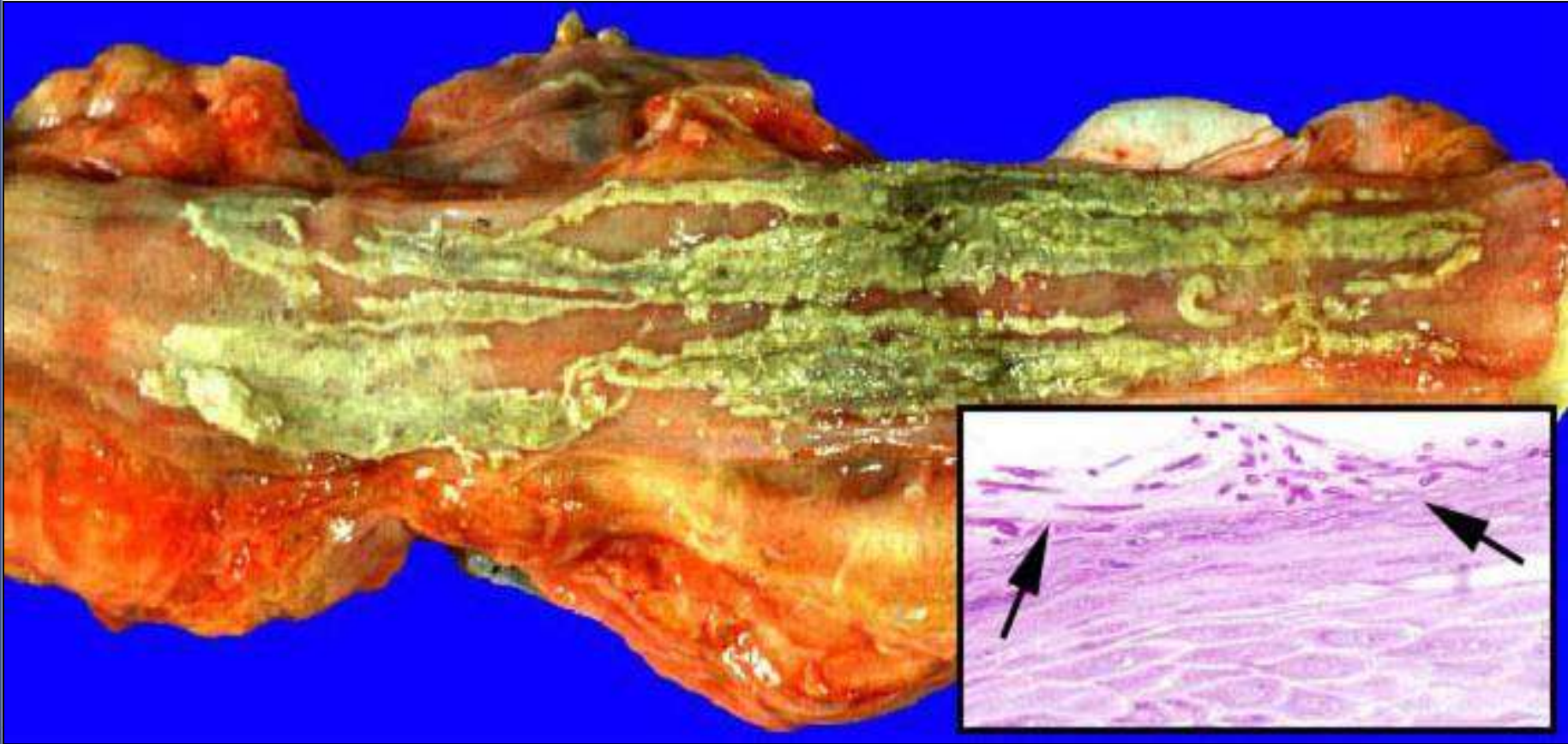


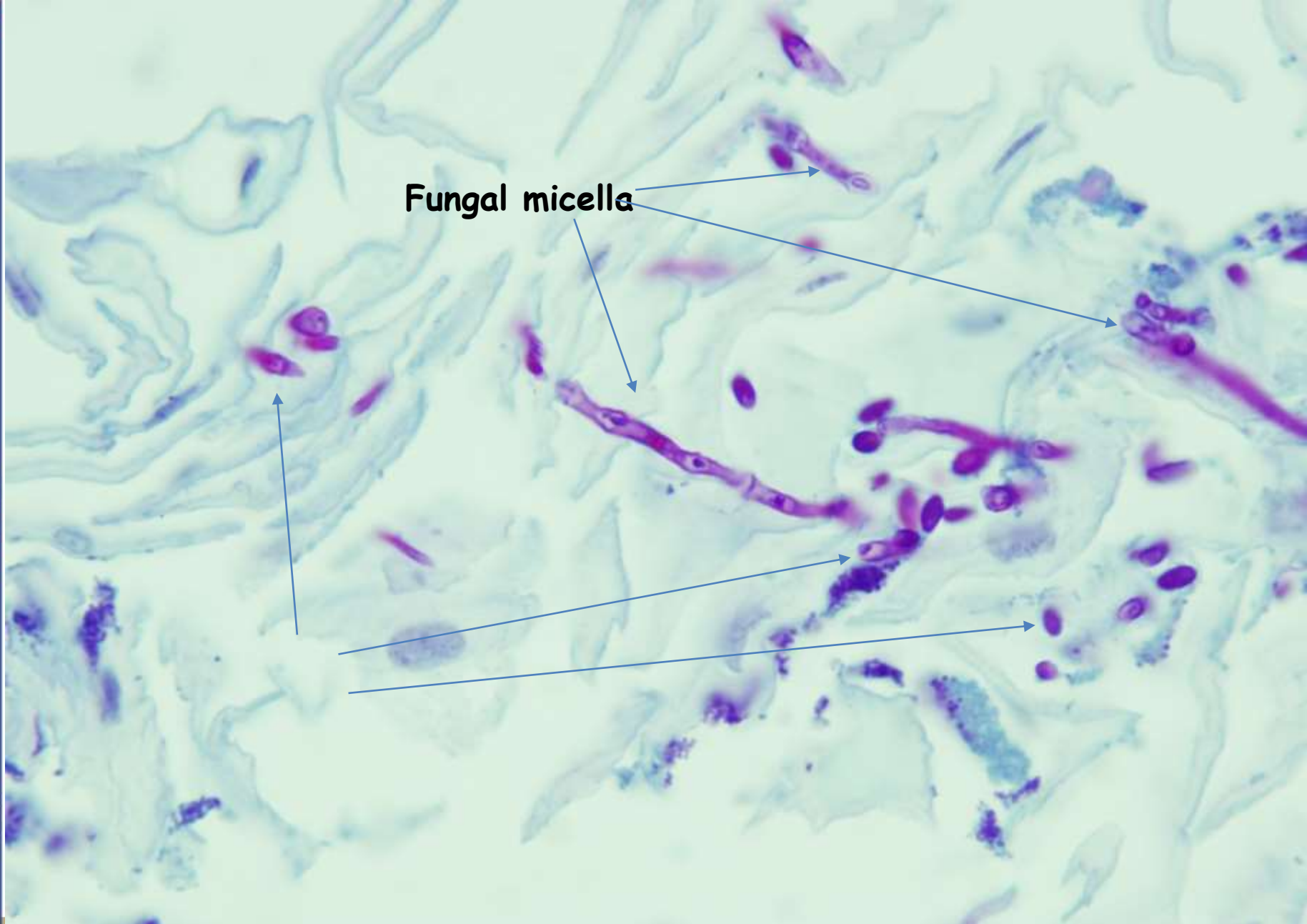
Infektive Esophagitiden

↪ **Candidiasis:** Antibiotika,
Immunsuppression

↪ **Herpes simplex und CMV:** Ulzera mit
intranukleare Inklusionen







Fungal micella



Motorische Dysfunktion assoziierte Lesionen

Mallory-Weiss Syndrom:

longitudinale Einrisse in der Schleimhaut

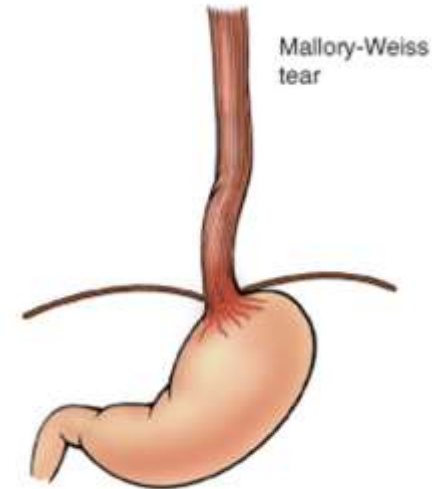
Ursache: Alkoholismus, chronisches Erbrechen

Hiatus Hernia, Reflux.

Symptome: Blutung, Hematemesis, Melaena

Boerhave Syndrom: spontane Ösophagusruptur

Wegen Laceration oder Erbrechen



Saure-Ösophagitis: Koagulationsnekrose

Lauge Ösophagitis: Kolliquationsnekrose

Tumoren: meist Plattenepithelkarzinom, ulzerierend, polypös oder diffus infiltrierend

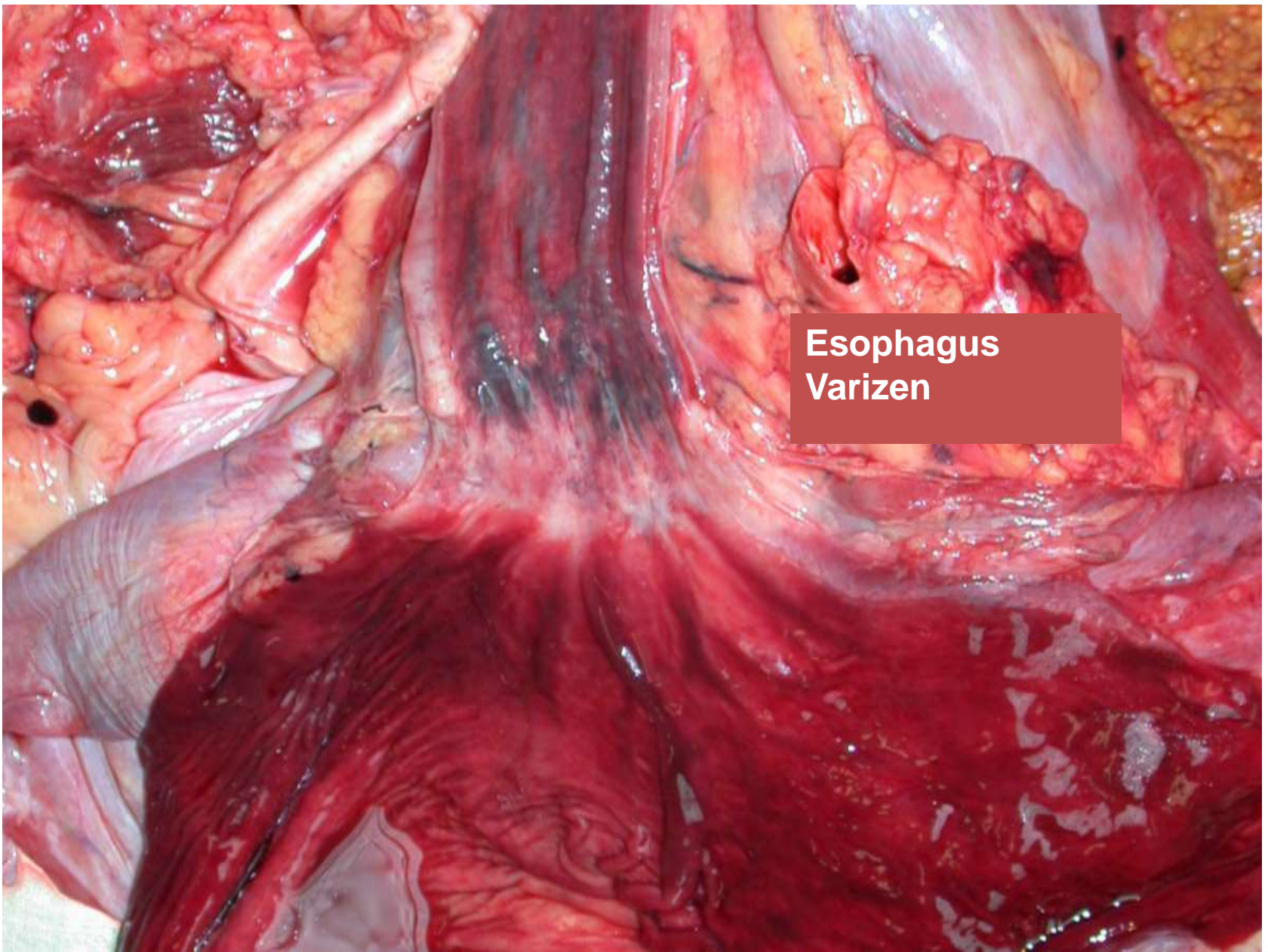
Retrosternalen Schmerz, Regurgitation



Esophagus Varizen

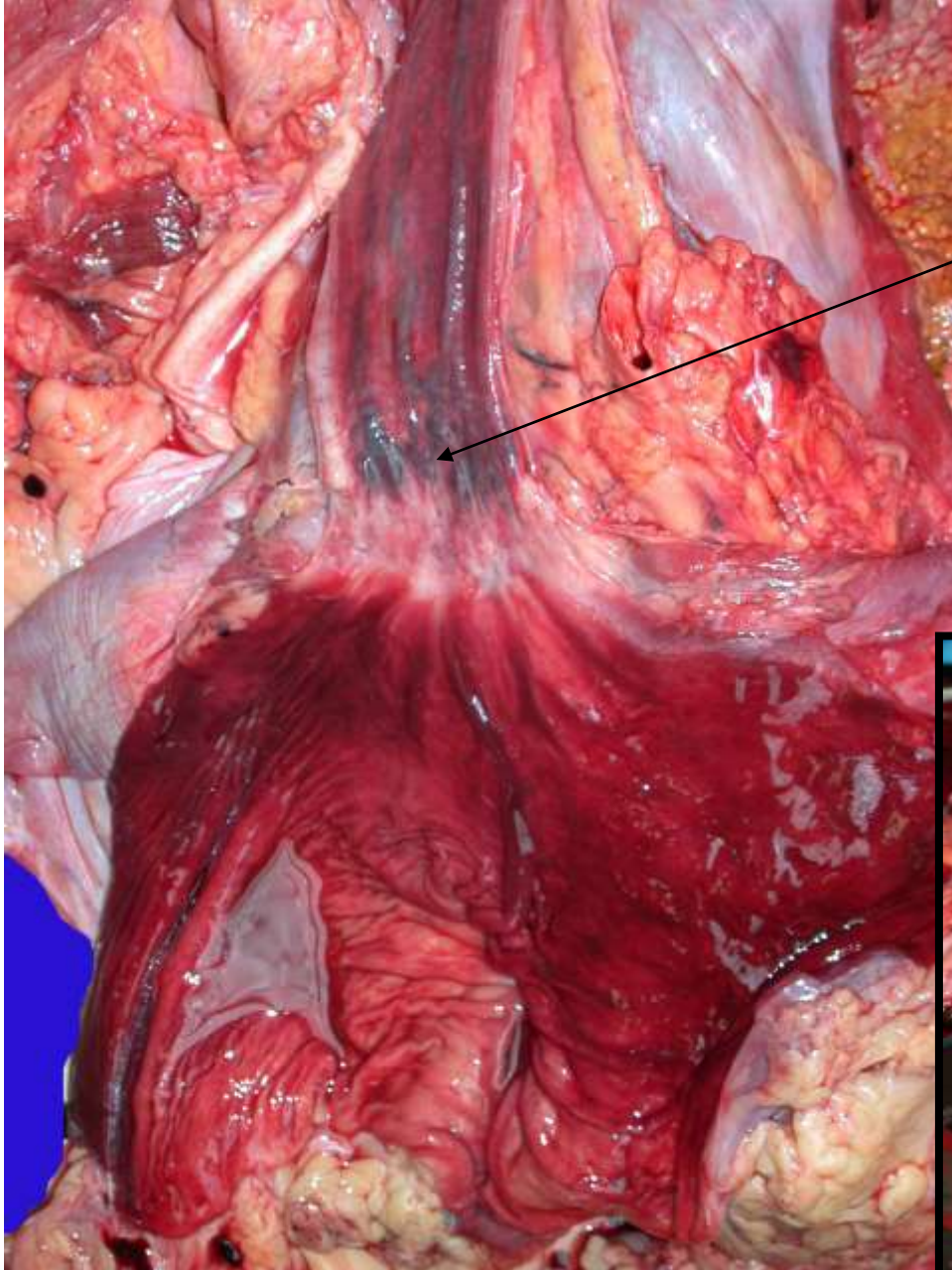
- ↪ In portaler Hypertension
- ↪ Zirrhose (Alkoholismus)
- ↪ ~ Ruptur → massive Hematemesis
- Blutbrechen
- ↪ Therapie:
 - ↳ Ballon Tamponade und Sklerotherapie





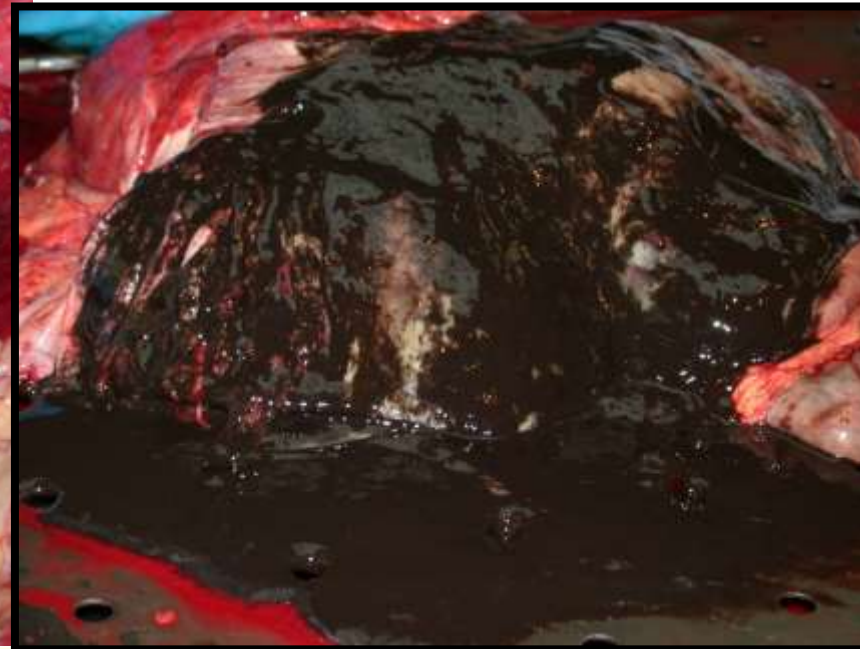
**Esophagus
Varizen**

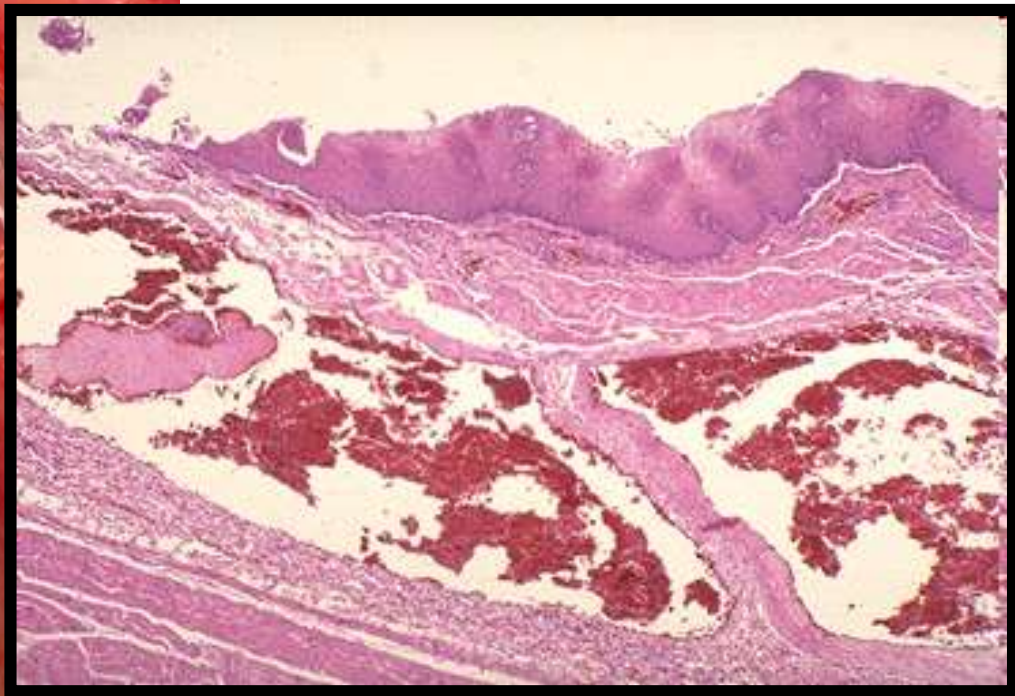




Varizen

Blutung







SURGERY

Vol. 41

JUNE, 1956

No. 6

THE LOWER ESOPHAGUS LINED BY COLUMNAR EPITHELIUM
N. R. BARRETT, LONDON, ENGLAND

...esophagus lined with **columnar epithelium** (rather than the usual squamous epithelium) due to a congenitally shortened esophagus leading to a tubular portion of stomach being trapped in the chest.

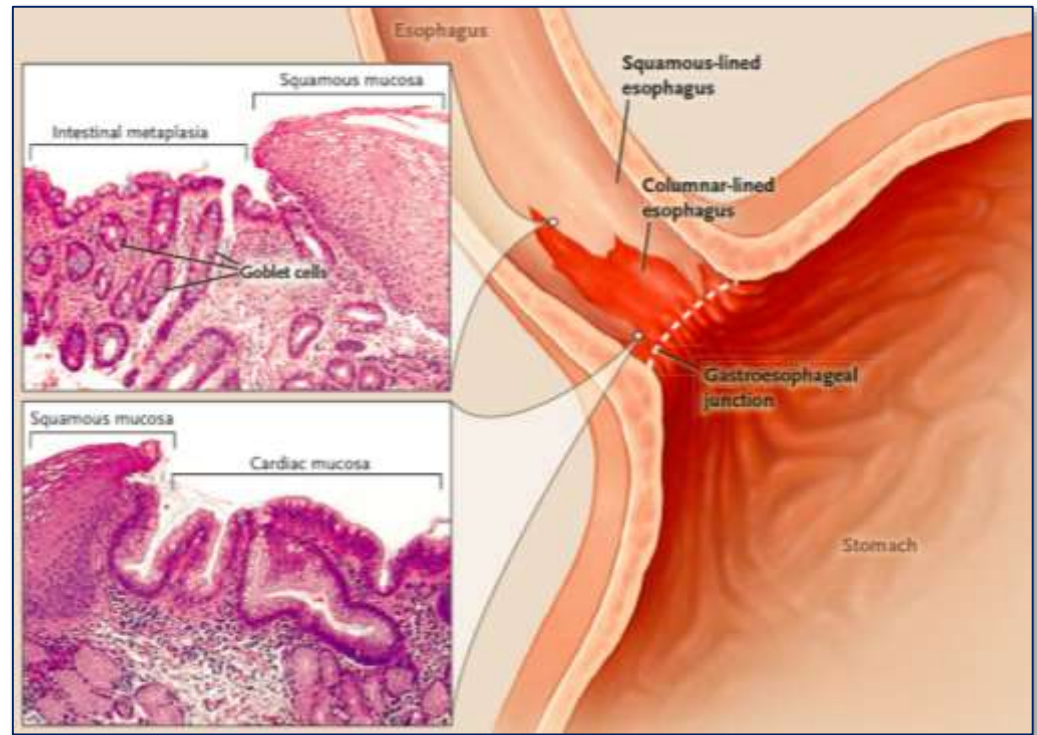
Barrett NR – Br J Surg 1950; Barrett NR – Surgery 1956



BE diagnosis



Spechler SJ & Souza RF
NEJM 2014



The ingredients for a correct diagnosis of BE

1. **endoscopic** evidence that columnar mucosa extends above the gastroesophageal junction and lines the distal esophagus
2. **biopsy** confirming the presence of columnar intestinal metaplasia

3. Definition of Barrett's esophagus (BE)

In **Japan** (Japan Esophageal Society) and the **UK** (British Society of Gastroenterology), BE is defined simply as metaplastic CLE that is recognizable macroscopically.

i.e.; **Barrett's esophagus = CLE**

In **Germany** and the **USA**, however, BE is defined as the metaplastic replacement of any length of the esophageal epithelium that can be recognized at endoscopy and that is confirmed by biopsy of the tubular esophagus to show intestinal metaplasia, excluding intestinal metaplasia of the gastric cardia.

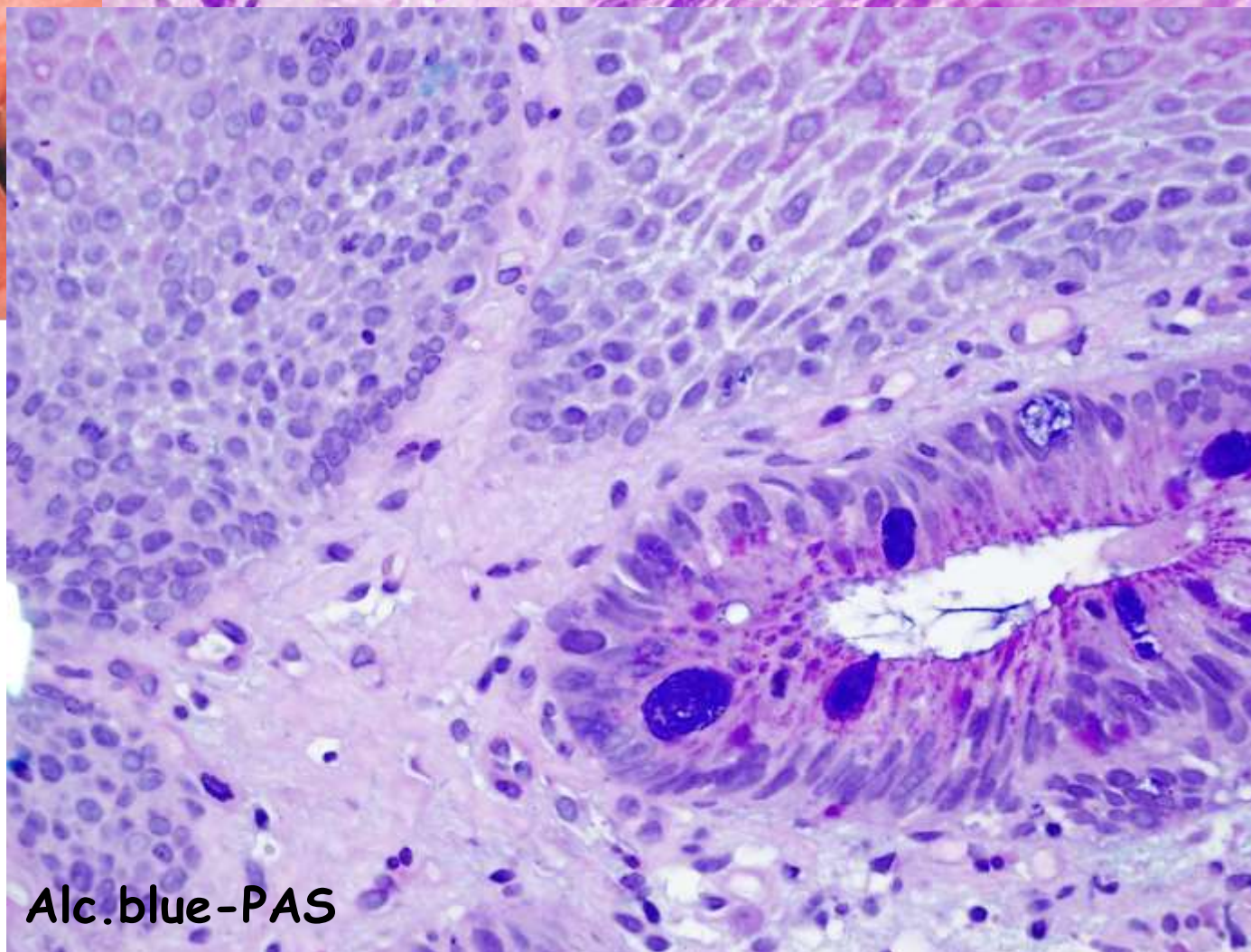
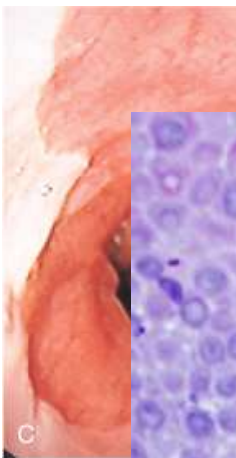
i.e.; **Barrett's esophagus = CLE + goblet cells**

Playford RJ: New British Society of Gastroenterology guidelines for the diagnosis and management of Barrett's oesophagus. Gut 2006;55:442

The Practice Parameter Committee of the American Colleges of Gastroenterology: Sampliner RE, et al. Am J Gastroenterol 2002;97:1998

Official Journal
of the Japan
Esophageal
Society



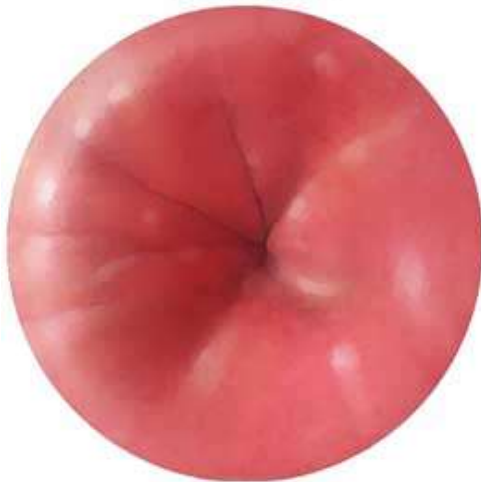


Alc.blue-PAS

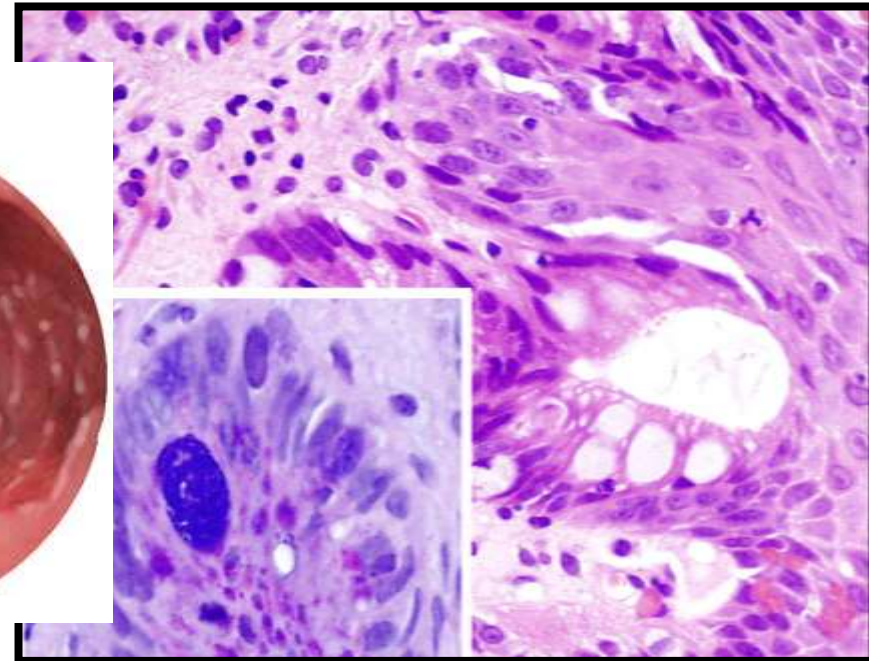


Barrett Ösophagus

Normal lower
esophagus

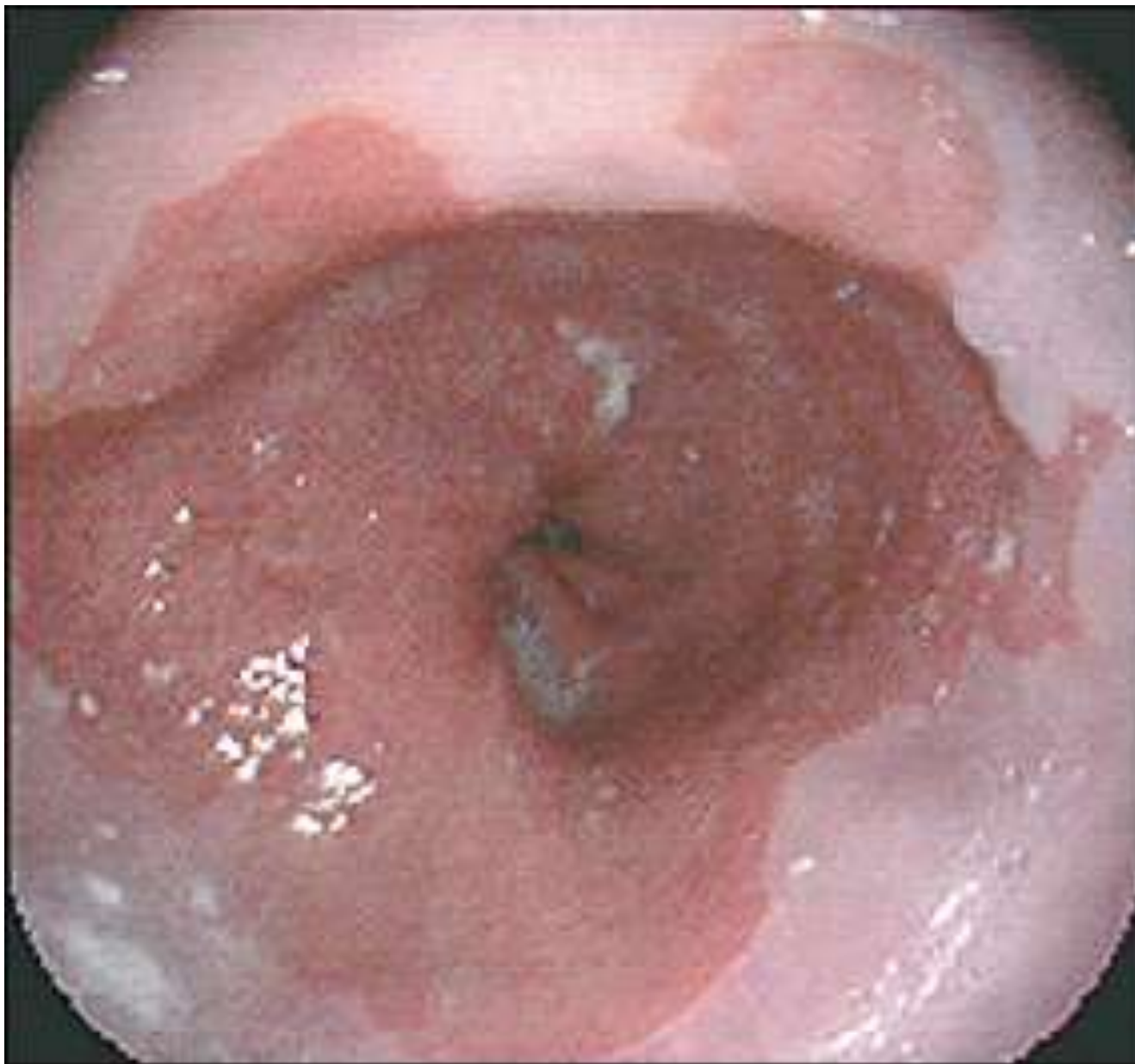


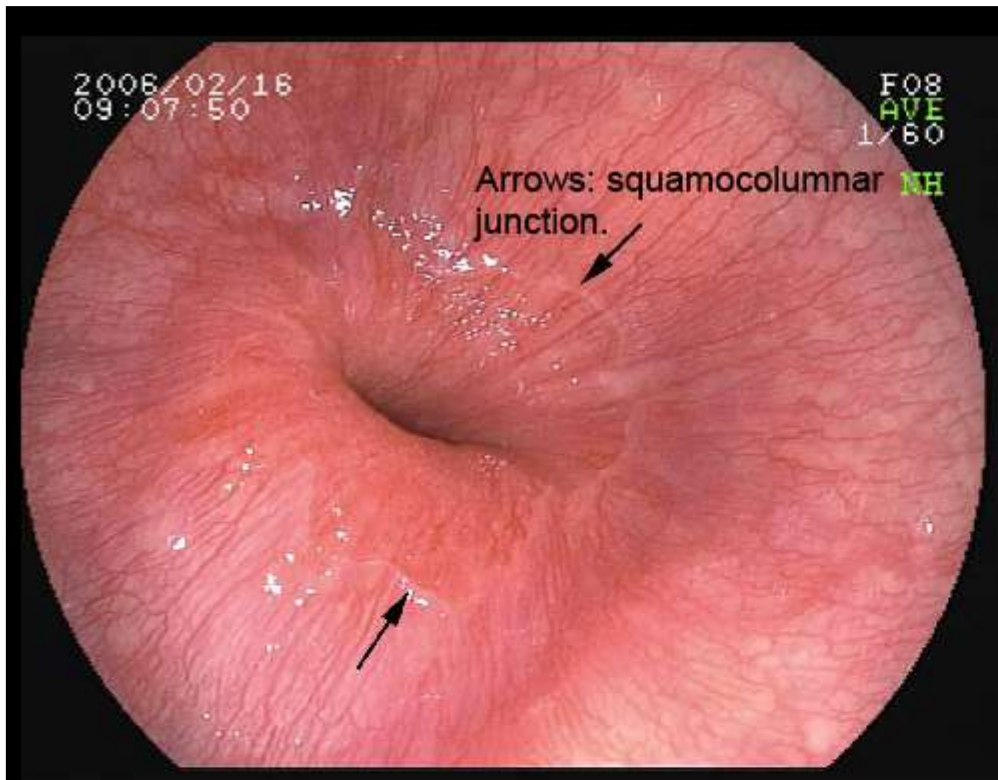
Barrett's
mucosa



www.mayoclinic.org/barretts-esophagus/images/...







Palisade longitudinal vessels in the columnar-lined esophagus (CLE).

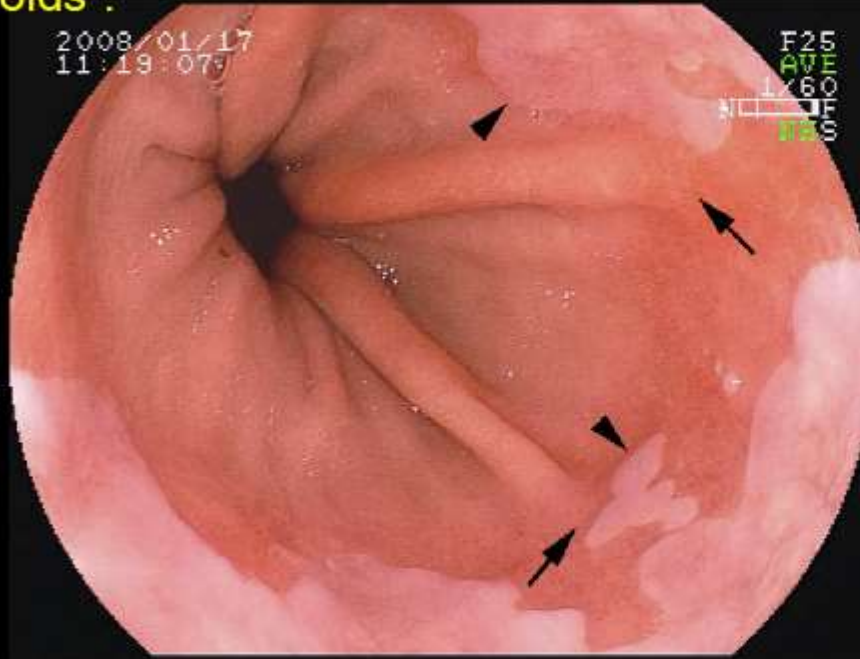
Palisade vessels are seen in both the squamous-lined and columnar-lined esophagus. In this case, a diagnosis of CLE can be made by endoscopy alone.

Palisade vessels are always seen within the esophagus (De Carvalho. Acta Anat 1966, Hoshihara et al. Gastroenterol Endosc 1986). These vessels are observed in the lower esophageal sphincter. The EGJ is defined endoscopically in Japan as the lower limit of the palisade vessels (by the Japan Esophageal Society 2000, Takubo et al. Esophagus 2003, Arch Pathol Lab Med 2005).

Takubo et al 2009



In Western countries, the definition of the EGJ is the “upper limit of gastric folds”.



Sharma P, Dent J, Armstrong D, Berman JJ, Gossner L, Hoshihara Y, Jankowski JA, Janghard O, Lundell T, Tytgat GN, Vieth M. Gastroenterology 2006;131: 1392-9

Endoscopic appearance of the upper end of the gastric mucosal folds at the EGJ in a patient with Barrett's esophagus.

The upper limit shows considerable up and down movement, depending on the volume of air in the esophagus.

When a small volume of air is present in the esophagus, the upper end of the mucosal folds (arrows) extends up to or beyond the level of the lower end (arrowheads) of the squamous epithelium.



BARRETT'S CASCADE

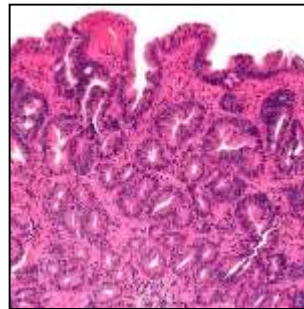
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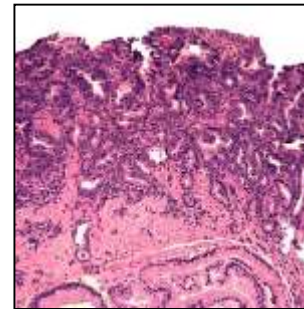
BM



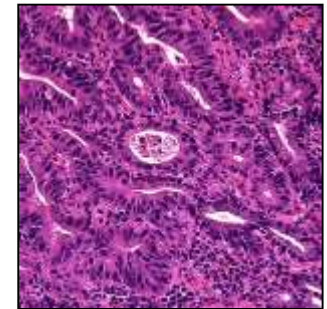
LG-IEN



HG-IEN



BAc



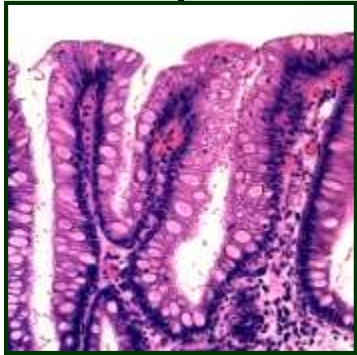
Length of Barrett's esophagus and cancer risk: Implications from a population based study

H Pohl, O Pech, H Arash, M Stolte, H Manner, A May, K Kraywinkel, A Sonnenberg, C Ell

AMONG PATIENTS WITH NEWLY DIAGNOSED T₁ BARRETT-CANCER

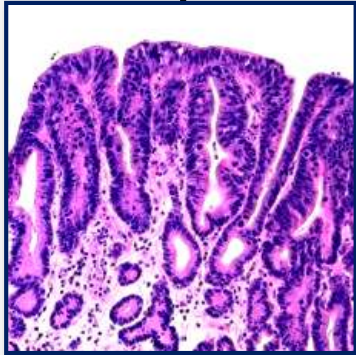
%	BM Length at recruitment	Annual Transition to Barrett-Cancer	Patients who would need to undergo EGDS to find one BC/year
20%	ULTRA-SHORT	0.01 %	12,365
24%	SHORT	0.03 %	3,440
56%	LONG	0.22 %	450

Endoscopic surveillance



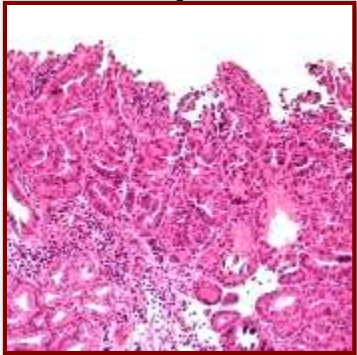
No dysplasia

Endoscopy every 3-5 yr



LGD

Endoscopy every 6-12 mo or eradication therapy



HGD

Endoscopic eradication therapy

...the clinical impact

Spechler SJ & Souza RF - NEJM 2014; De Jonge PJF, et al – Gut 2014



Native epithelium



Metaplastic changes

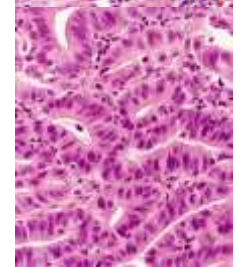
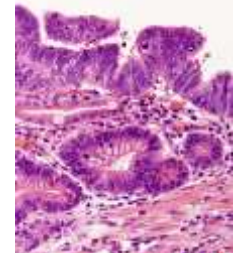
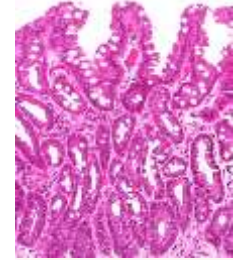
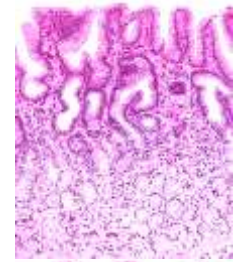
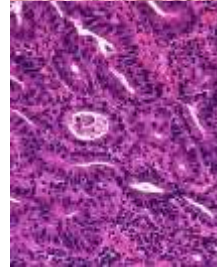
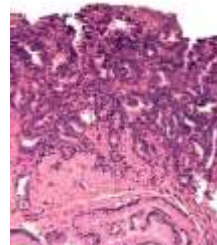


Dysplastic lesions



Adenocarcinoma

Multi-step cascades



**OESOPHAGUS
BARRETT**

**STOMACH
CORREA**



Gut

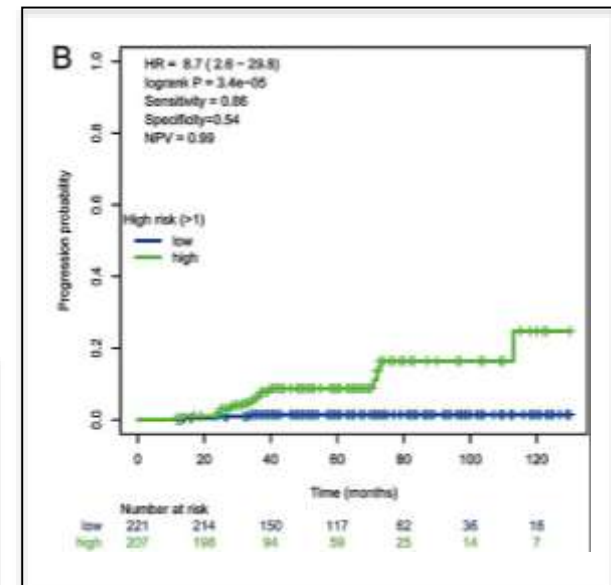
2015

Derivation of genetic biomarkers for cancer risk stratification in Barrett's oesophagus: a prospective cohort study

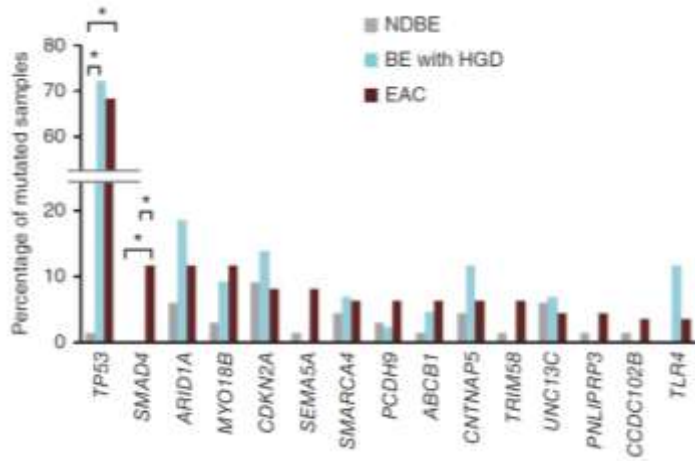
Margriet R Timmer, *et al*

***P16* loss, *MYC* gain, and aneuploidy** (centromeric probes for CEP7/CEP17, as surrogate marker for DNA ploidy change) measured by FISH (brush cytology) **is an independent predictor of progression in non-dysplastic BE.**

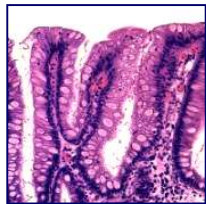
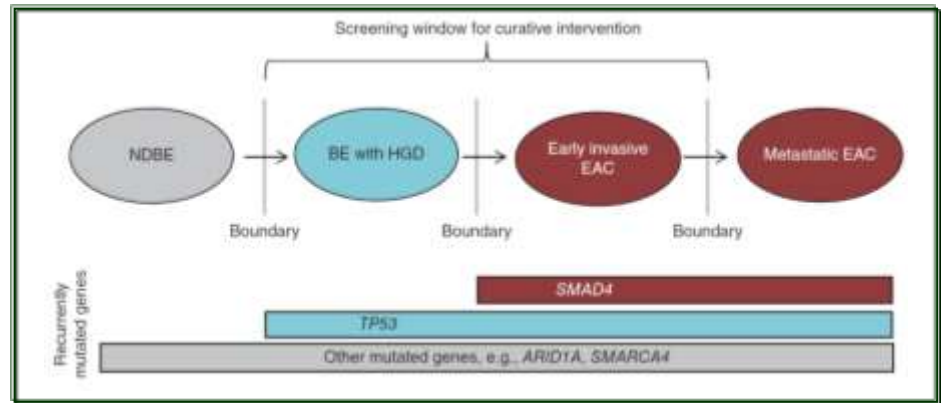
A prediction model including this Abnormal Marker Count is advantageous over a clinical model using only age and BE length for long-term risk stratification.



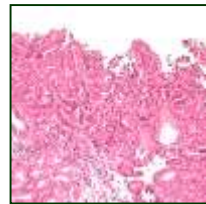
Ordering of mutations in preinvasive disease stages of esophageal carcinogenesis.



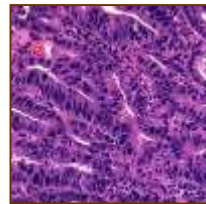
Only *TP53* and *SMAD4* mutations occurred in a stage-specific manner, confined to HGD and EAC, respectively.



n= 66



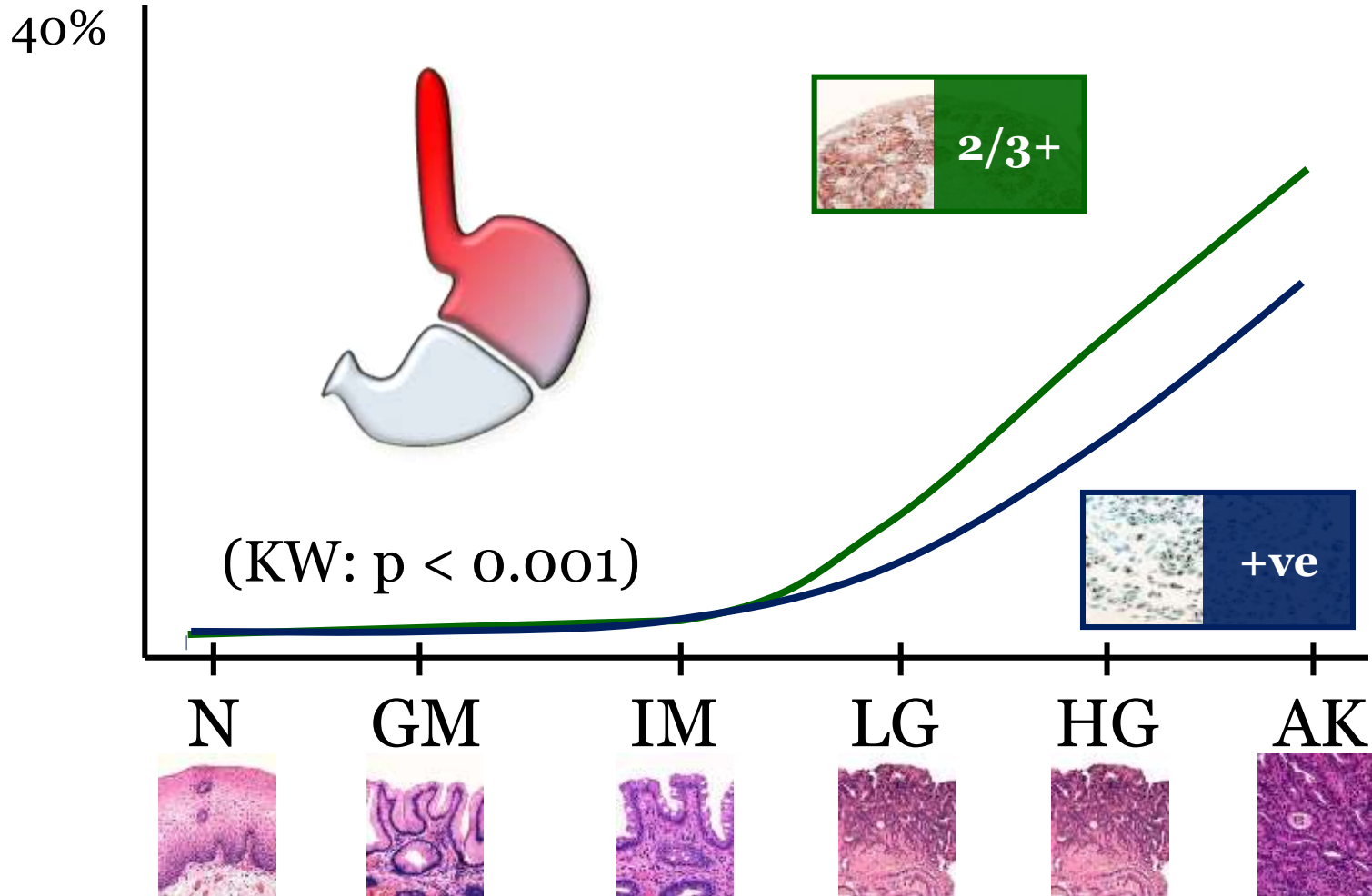
n= 43



n= 112

Weaver JM, et al – Nat Genet 2014

HER2 is overexpressed and amplified in dysplastic lesions



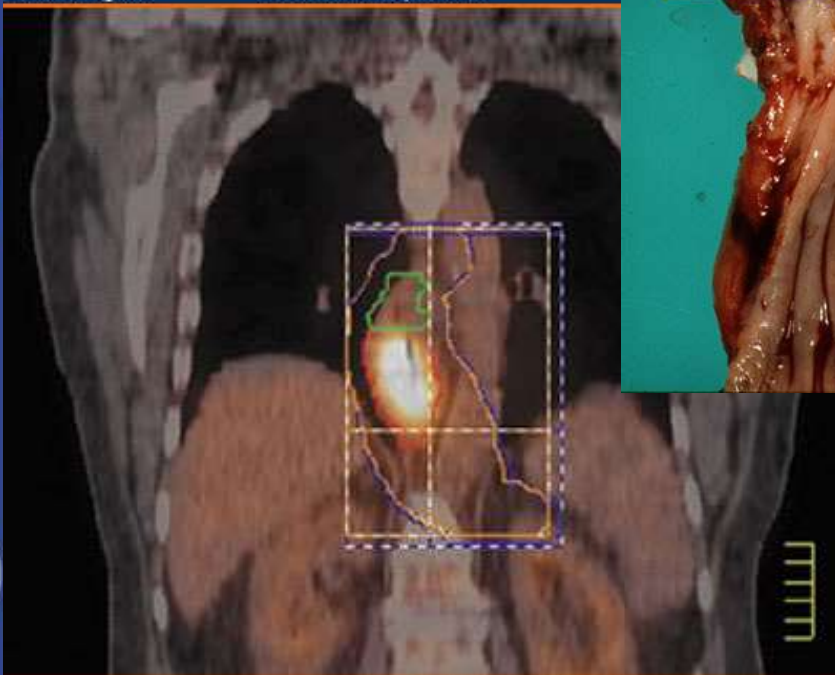
Fassan M, Rugge M et al - *Histopathology* 2012



TUMOREN des Ösophagus

Medscape®

www.medscape.com



Source: Appl Radiol © 2004 Anderson Publishing, Ltd.

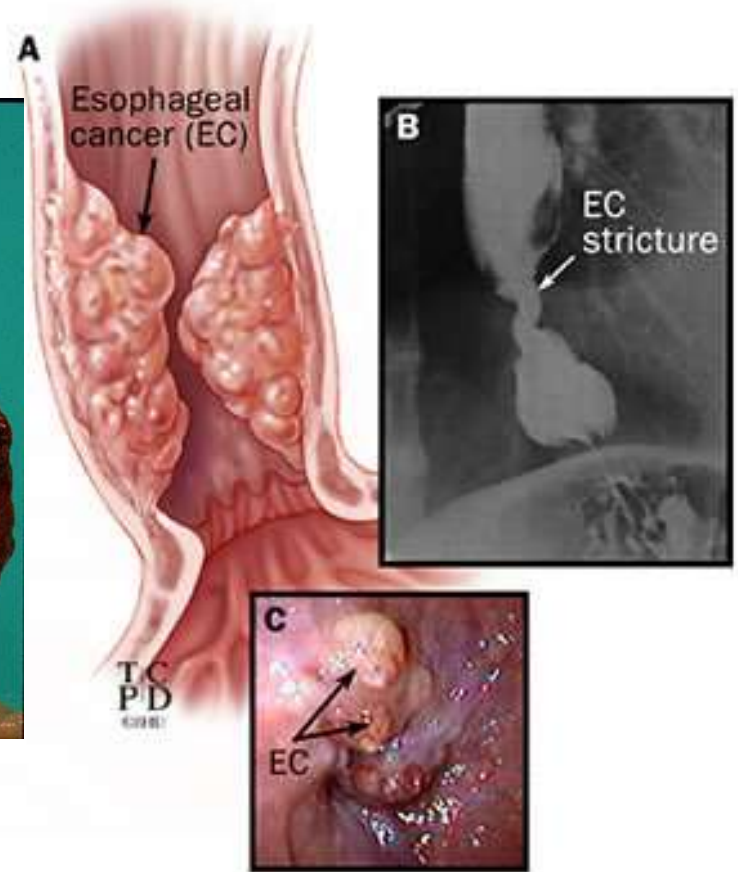
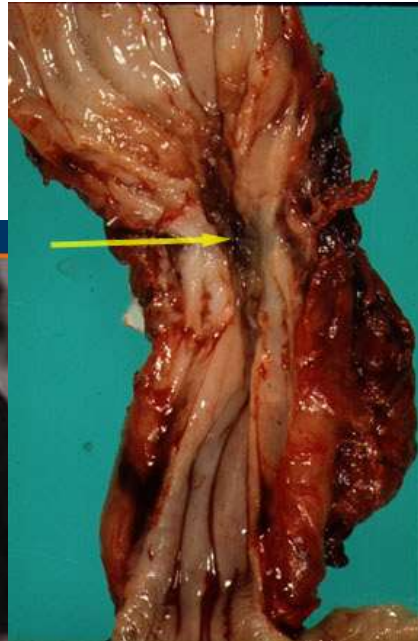


Figure 21. Esophageal cancer (A) with corresponding barium swallow x-ray (B) and endoscopic view (C).



Neoplasien

↪ Gutartige Tumoren:

↳ Leiomyom

↳ Lipom

↳ Fibrom

↳ Plattenepithel -Papillom

↳ Kondylom

↳ Inflammatorisches Polyp



Bösartige Tumoren

↪ Plattenepithelkarzinom

↪ Adenokarzinom



Plattenepithelkarzinom

↪ Über 50 Jahre, geographische Unterschiede

↪ männlicher Predominanz

↪ **Etiologie:**

↪ **Diat:** (Vitamin A, C Defizienz, hohes nitrit Gehalt des Wassers, Fungus infizierte Ernährung)

↪ **Lebensstyl** (heisses Getranek und Essen, **Alkohol**, smoking)

↪ **Ösophagus Krankheiten** (langfristige Ösophagitis, Achalasia),

↪ **Genetische Pradisposition**



↪ 20% obere Drittel, 50% Mittelteil, 30% untere Drittel

↪ **Makroskopie:**

- Exophytisch
- Exkavation ulzeriert)
- Flach

↪ **Micr:** meistens mittelmässig oder gut differenziert
→ Varianten: Verrukös, basaloid, „spindle cell”

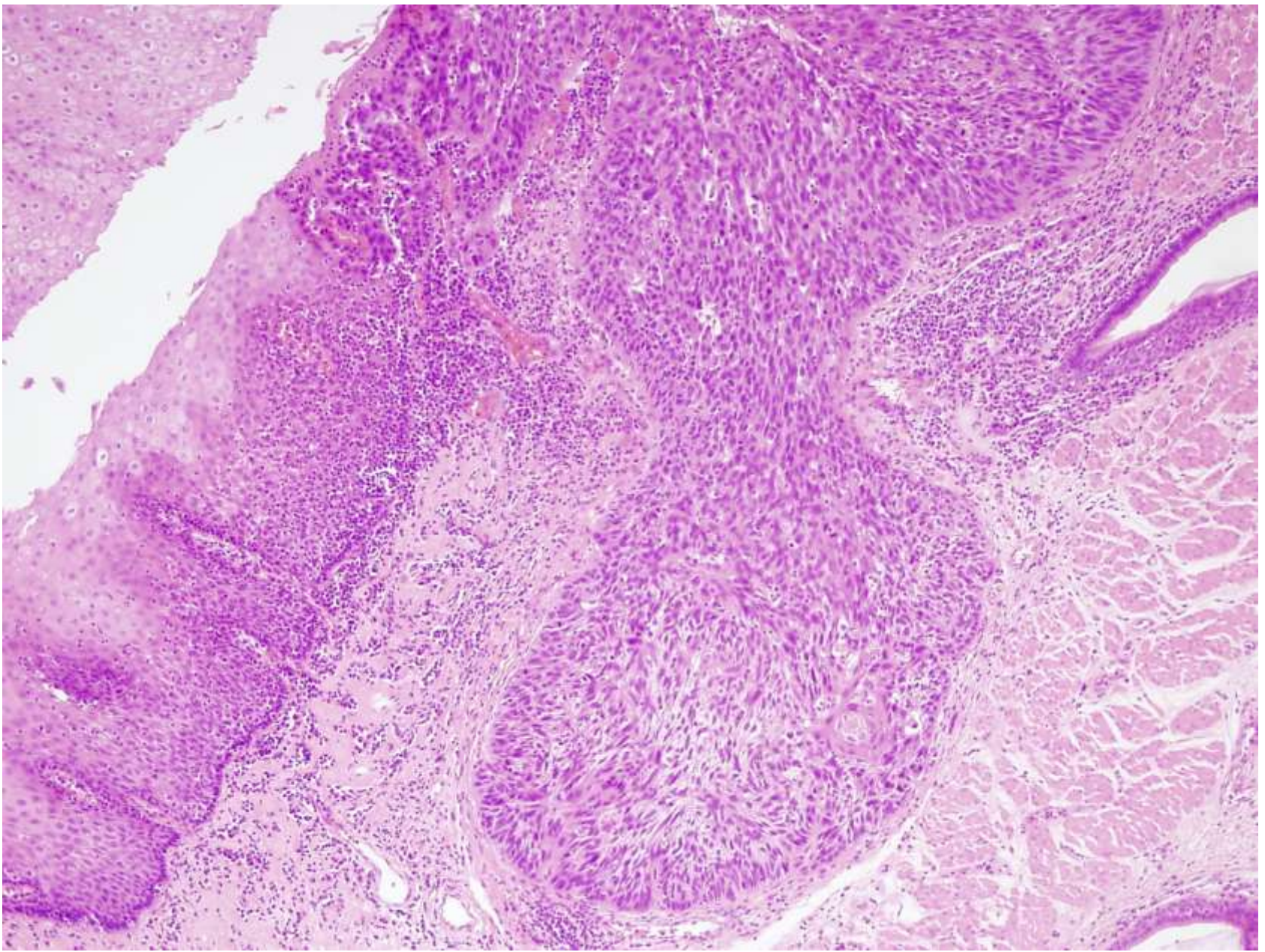
↪ **Metastasen:**

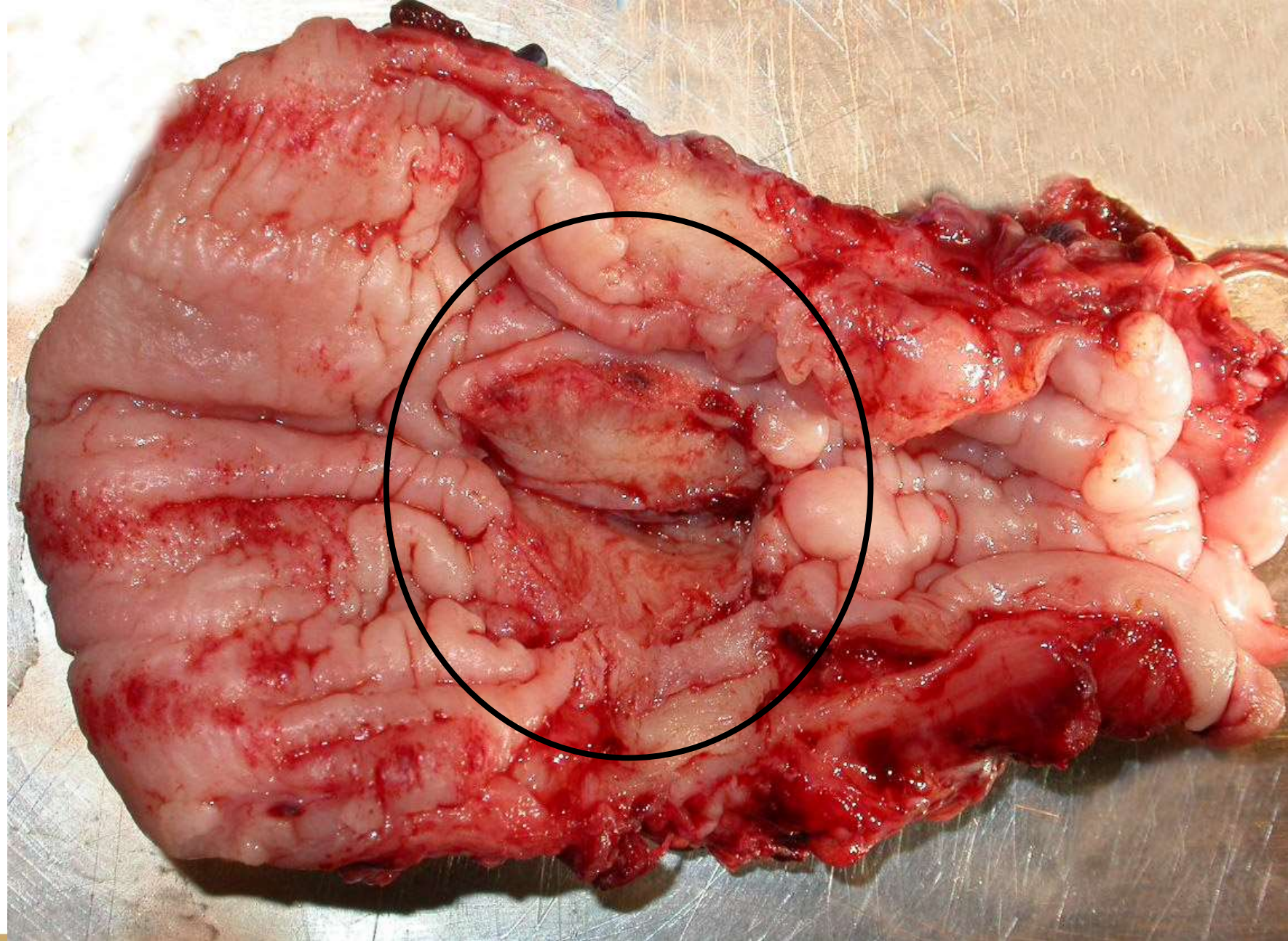
- Regionale Lymphknoten

↪ **Lokale Extension:**

↪ zu Mediastinum, Beatmungstrakt, Aortenwand



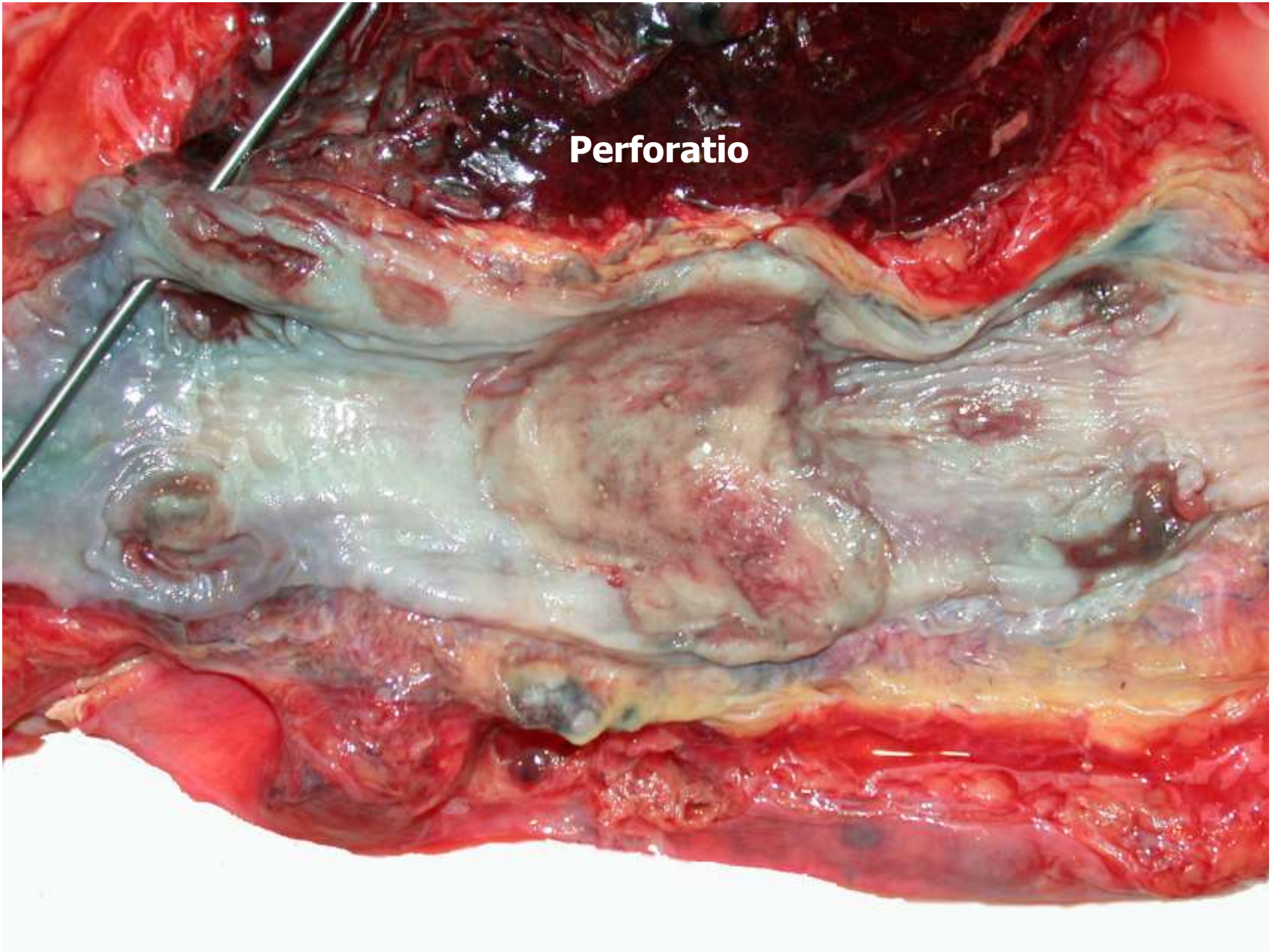






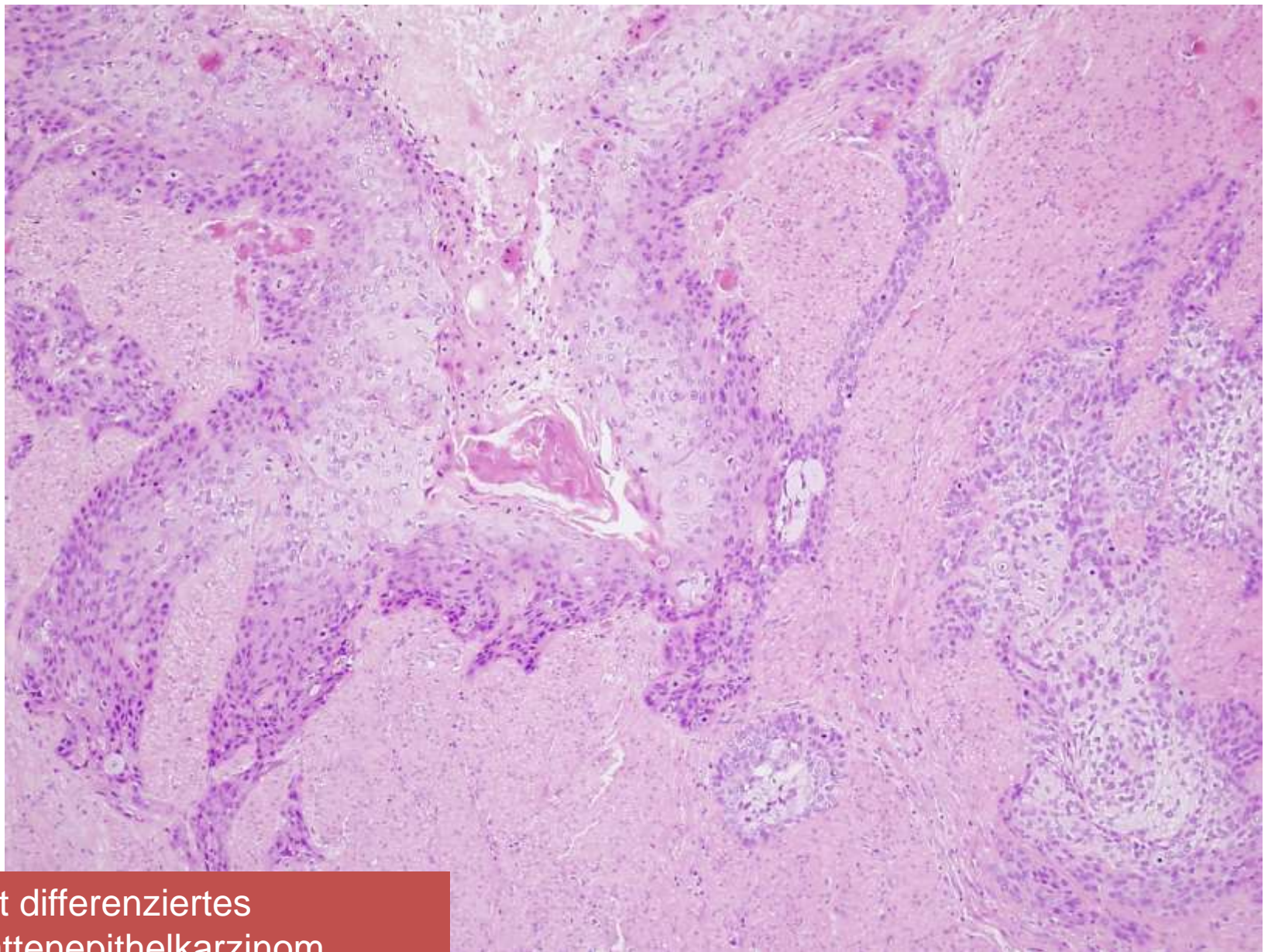
Perforation





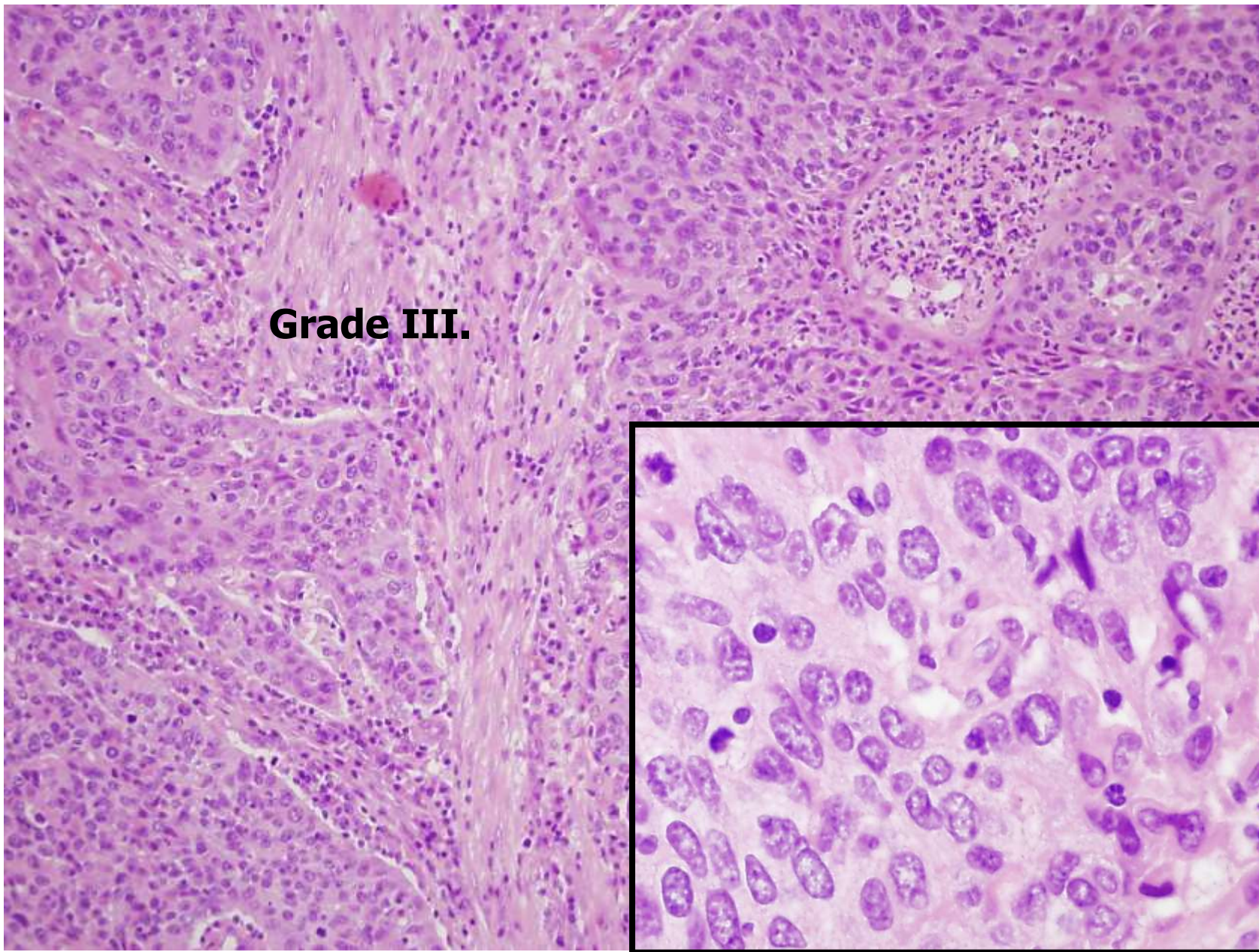
Perforatio





Gut differenziertes
Plattenepithelkarzinom





Grade III.

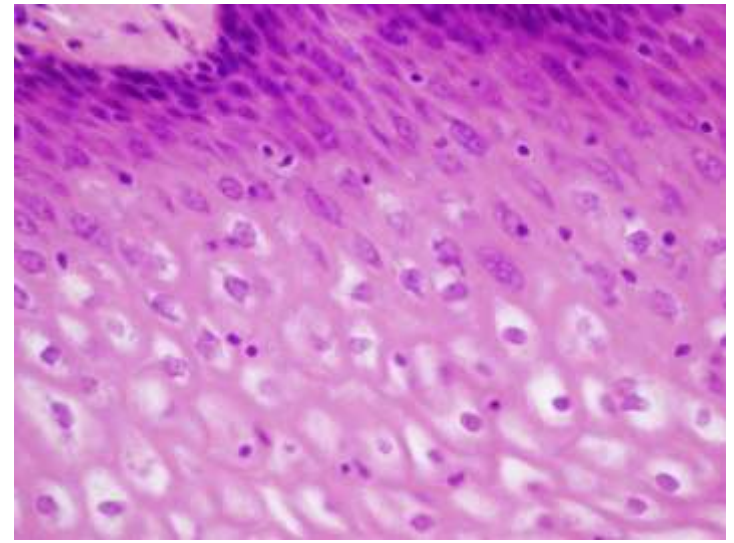
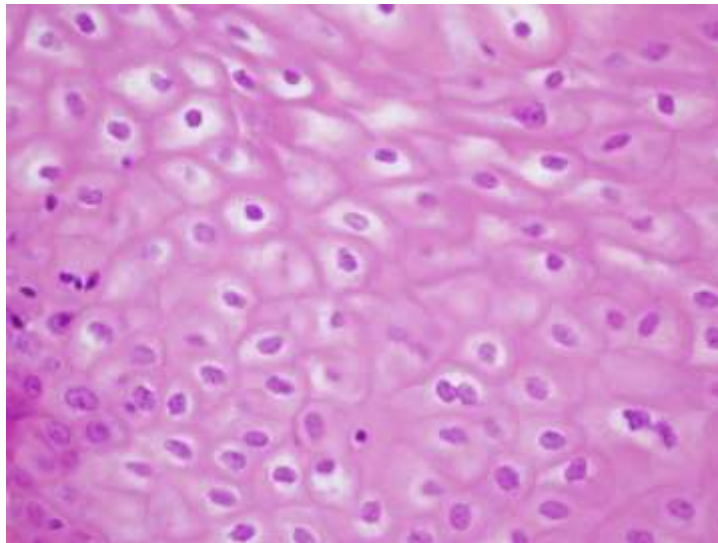


Evaluation of the prevalence of human papillomavirus and Epstein-Barr virus in esophageal squamous cell carcinomas

Die Rolle der HPV und EBV Viren in der Karzinogenese.

Tumoren der Ösophagus Plattenepithel Karzinom Patienten were in 56% HPV +, die Mehrheit der Falle: HPV18. In Kontroll Fallen HPV kam nur in 22% vor, elő HPV, die Mehrheit der Falle: HPV18. EBV war in Tumoren und in nicht tumorösen Fallen nicht nachweisbar.

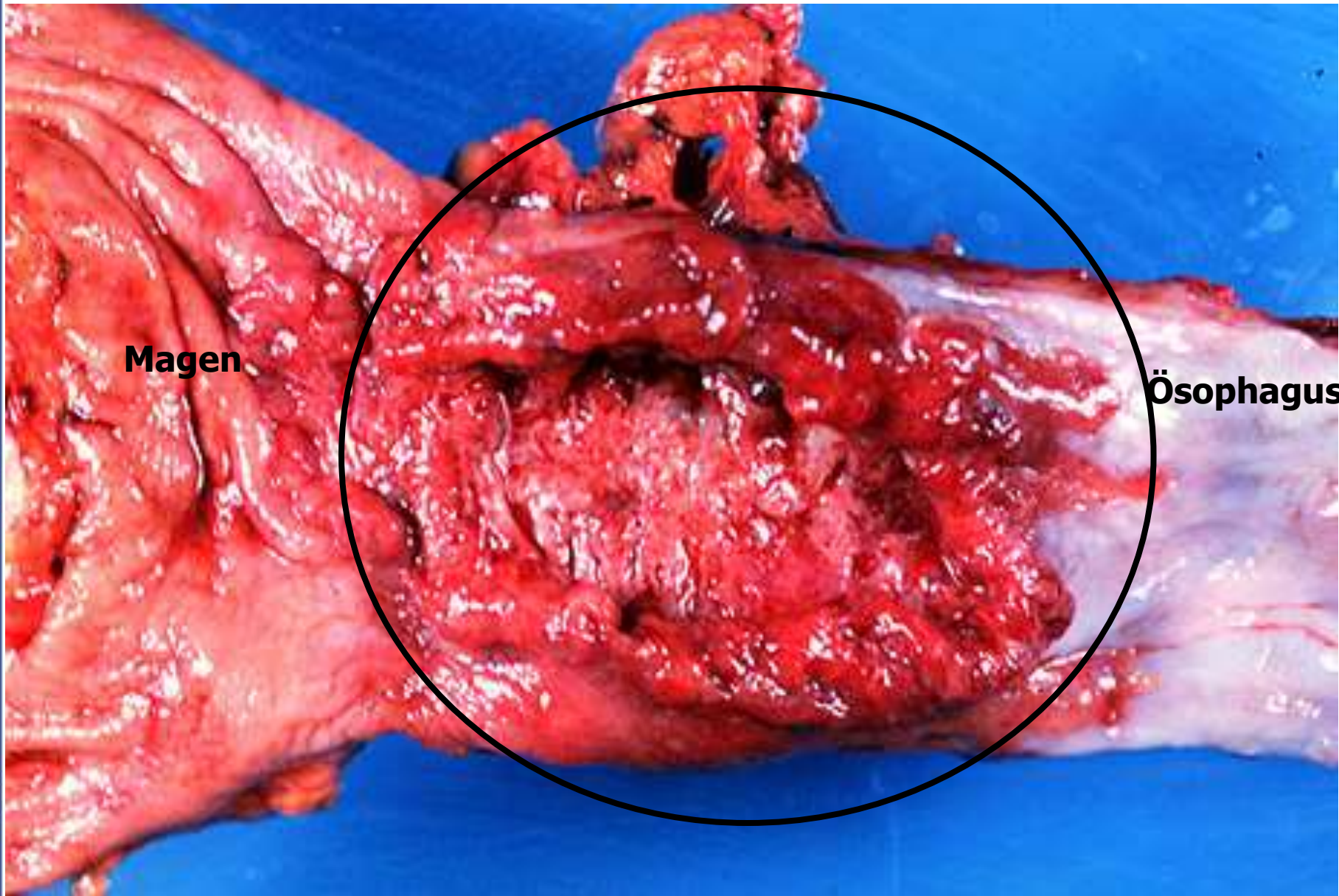
HPV könnte in der Entwicklung der Ösophaguskarzinomen **eine wichtige Rolle spielen.**



Adenokarzinom

- ↪ Barrett Ösophagus assoziiert
- ↪ Distale Ösophagus, männliches Pradominanz
- ↪ Symptomen:
 - ↳ Schluckstörungen (schwer zu schlucken), Blutung, Erbrechen, Pein, Gewichtsverlust
- ↪ **Gross:**
 - ↳ Flache Flecken, manchmal grosse nodulare Masse
- ↪ **Mikr:**
 - ↳ intestinal Typ Adenokarzinom (meistens)
- ↪ **schlechte Prognose**



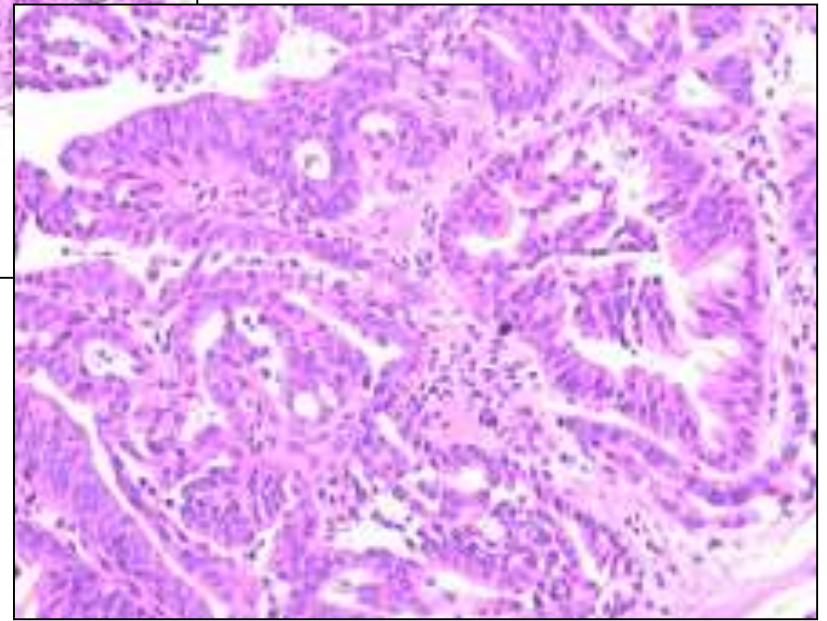
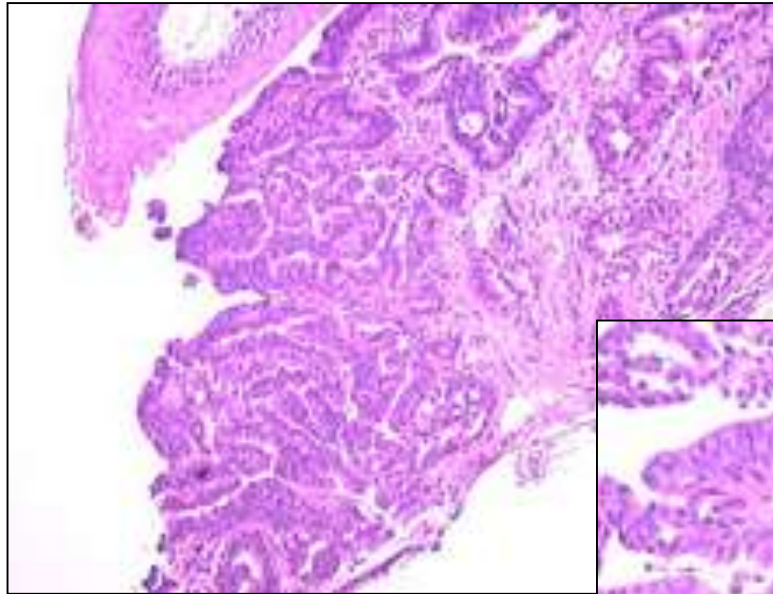


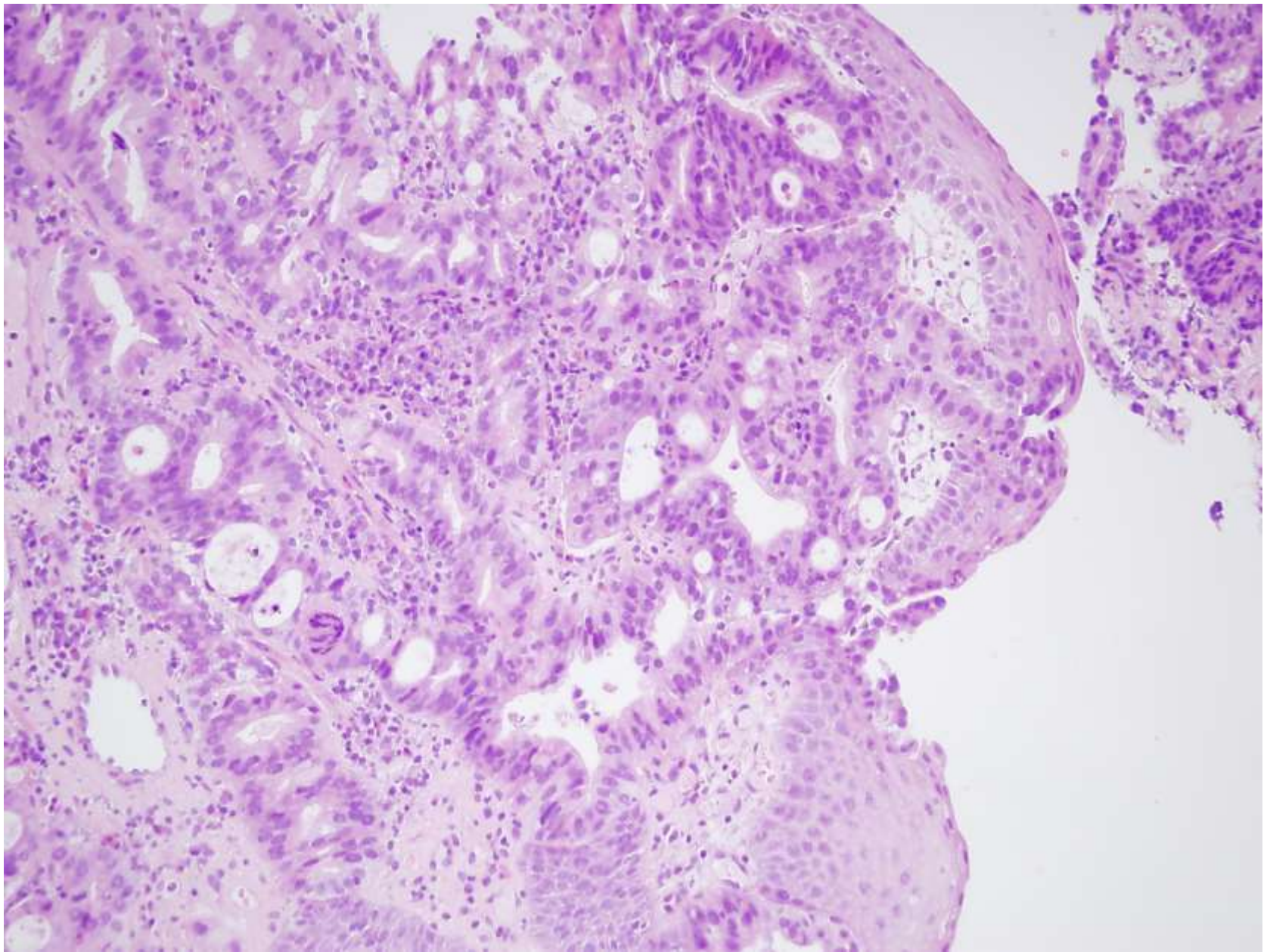
Magen

Ösophagus



Adenokarzinom







Adenokarzinom

This histological slide shows a cross-section of tissue. The upper portion is a dense, pink-stained mass of tumor cells, labeled as adenocarcinoma. Below this, there is a layer of columnar epithelium with a serrated surface, labeled as Barrett's metaplasia. The underlying tissue appears to be normal gastric mucosa with its characteristic pits and glands.

Barrett Metaplasie



TNM classification

T1 Lamina propria, submucosa, „frühes“

T2 Muscularis propria

T3 Adventitia

T4 surrounding tissues

N1 Regionale Lymphknoten

M1 ferne Metastasen



TNM

Primary tumor (T)

TX: Primary tumor cannot be assessed

T0: No evidence of primary tumor

Tis: Carcinoma in situ

T1: Tumor invades lamina propria or submucosa

T2: Tumor invades muscularis propria

T3: Tumor invades adventitia

T4: Tumor invades adjacent structures

Regional lymph nodes (N)

NX: Regional lymph nodes cannot be assessed

N0: No regional lymph node metastasis

N1: Regional lymph node metastasis

Distant metastasis (M)

MX: Distant metastasis cannot be assessed

M0: No distant metastasis

M1: Distant metastasis

Tumors of the lower thoracic esophagus:

M1a: Metastasis in celiac lymph nodes

M1b: Other distant metastasis

Tumors of the midthoracic esophagus:

M1a: Not applicable

M1b: Nonregional lymph nodes and/or other distant metastasis

Tumors of the upper thoracic esophagus:

M1a: Metastasis in cervical nodes

M1b: Other distant metastasis



Surg Clin North Am 2005;85:555-567

AJCC stage groupings

Stage 0

Tis, N0, M0

Stage I

T1, N0, M0

Stage IIA

T2, N0, M0

T3, N0, M0

Stage IIB

T1, N1, M0

T2, N1, M0

Stage III

T3, N1, M0

T4, any N, M0

Stage IV

Any T, any N, M1

Stage IVA

Any T, any N, M1a

Stage IVB

Any T, any N, M1b



Br J Surg 2004;91:1586-1591 OA Khan, C Alexiou, I Soomro et al.
Pathological determinants of survival in node negative esophageal cancer

219 N0 Plattenepithelkarzinom oder Adenokarzinom Ösophagustumoren,

Untersuchte Faktoren: Alter, Geschlecht, Histologie, Resektionsoberfläche, Stadium, Grade, vaskuläre und perineuralische Invasion, Barrett Metaplasie – Überleben.

Ein parametrische und mehrparametrische Analyse:

Schlechte Prognose war mit höheren T Stadium, mit Adenokarzinom Diagnose und niedrige Differentiation (höheres Grade)

TNM allein kann die Prognose nicht pünktlich voraussagen.



World J Surgery 2005;29:39-45 Ch Mariette, L Finzi, G Piessen et al.
Esophageal carcinoma: Prognostic differences between squamous cell carcinoma and adenocarcinoma

742 kurative OP in 20 Jahren.

624 Plattenepithelkarzinom und 118 Adenokarzinom Falle.

Adenokarz. Patienten waren älter, mit mehr fortgeschrittenen Fällen, mit regionalen metastatischen Lymphknoten, mit mehreren Rezidiven.

5 Jahre Überleben nach R0 Resektion in Plattenepithelkarzinom Patienten war 46%, sofern in Adenokarzinom Patienten 45%.

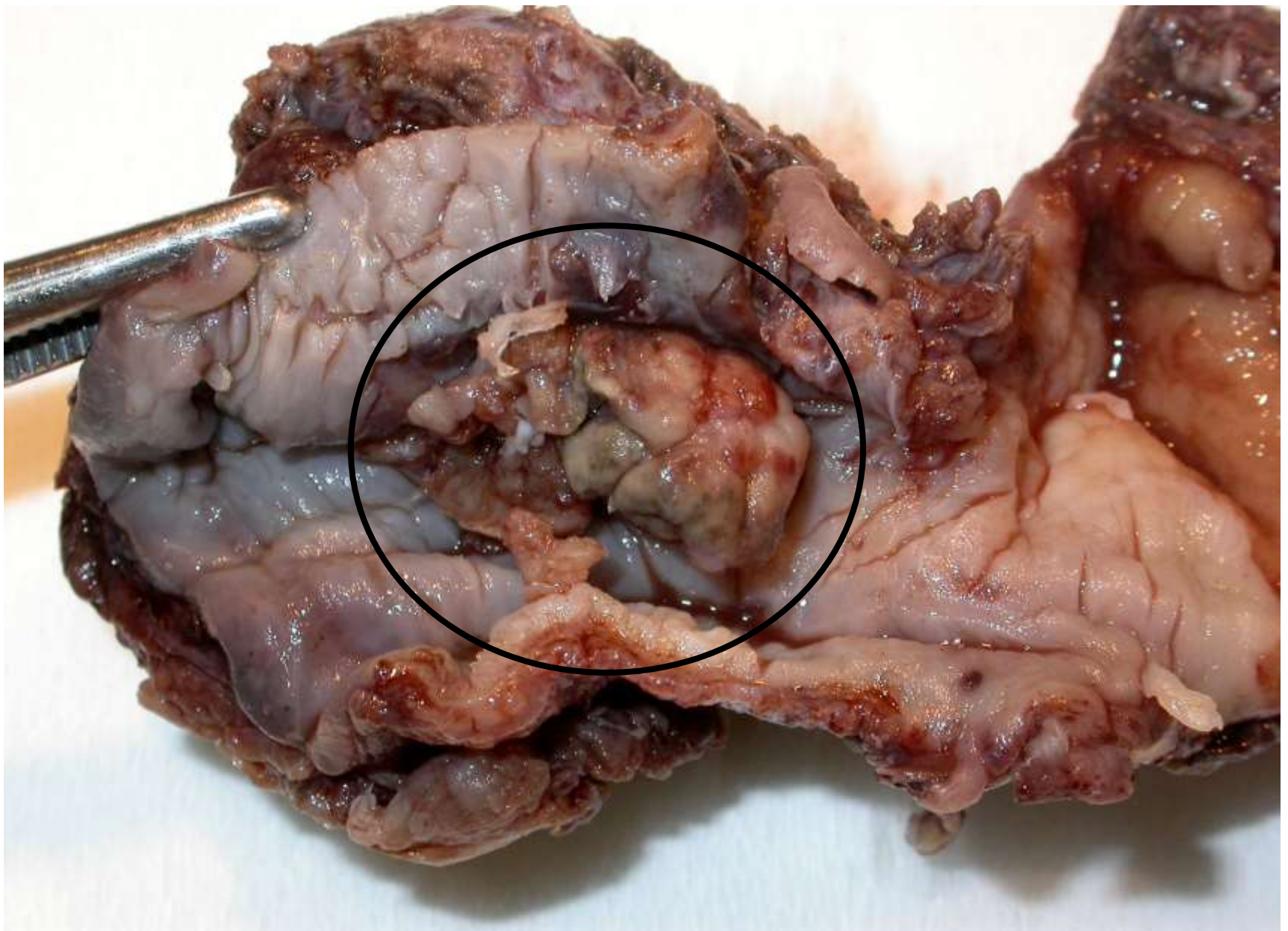
5 Jahre Überleben der T1 N0 oder Stadium I Adenokarzinom Patienten war in Adenokarzinom Patienten signifikant besser.



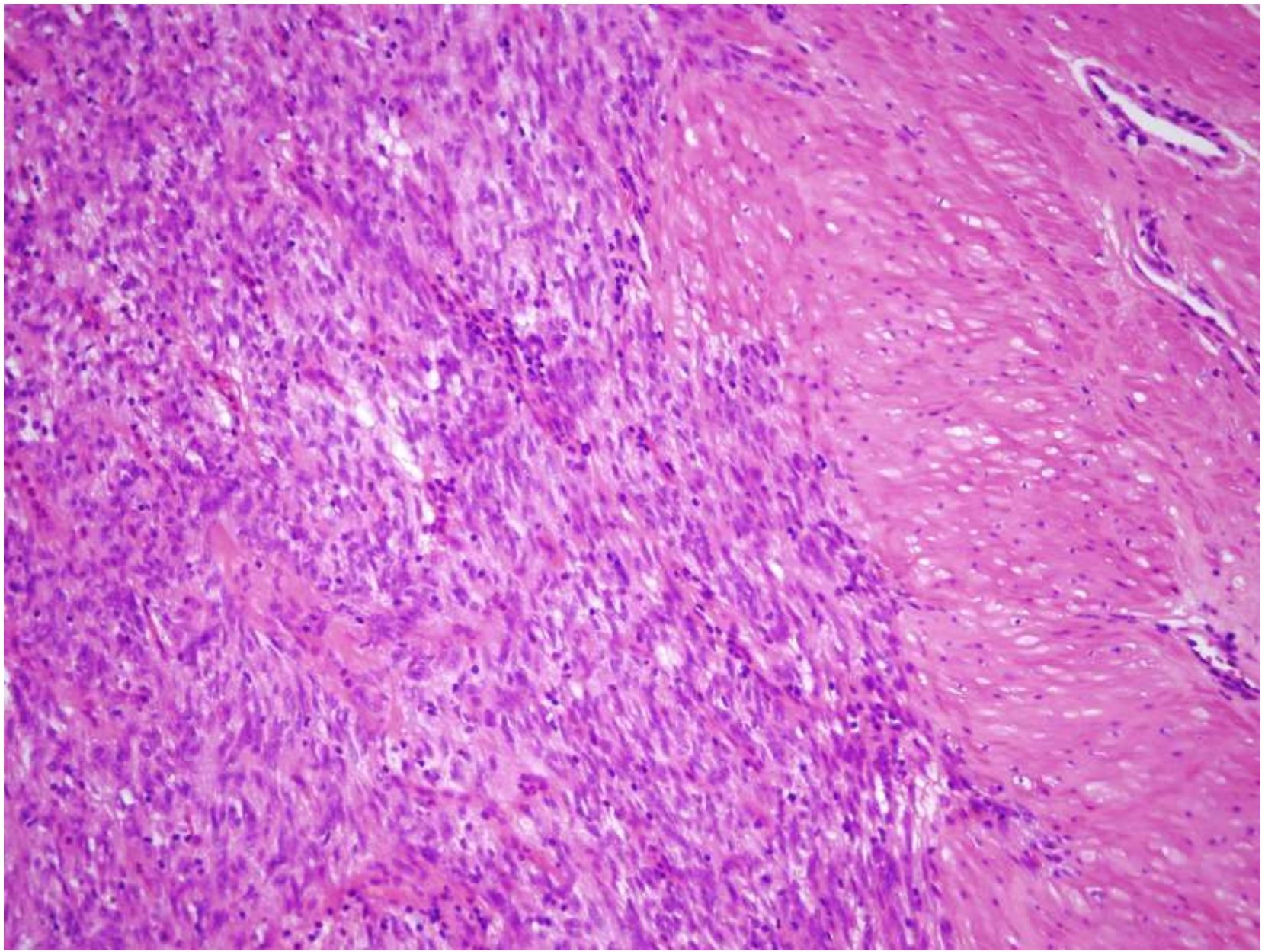
GIST

Gastrointestinal stromal tumor









**Danke für
Ihre Aufmerksamkeit !!!**

