Reflux & Barrett's Oesophagus

Surveillance & Treatment

RAMSAY HEALTH CARE

Defining Barrett's Oesophagus

- Replacement of stratified squamous epithelium with intestinal metaplasia
- Importance of Barrett's oesophagus
  - Premalignant condition
    - Risk of oesophageal adenocarcinoma
  - Increasing incidence

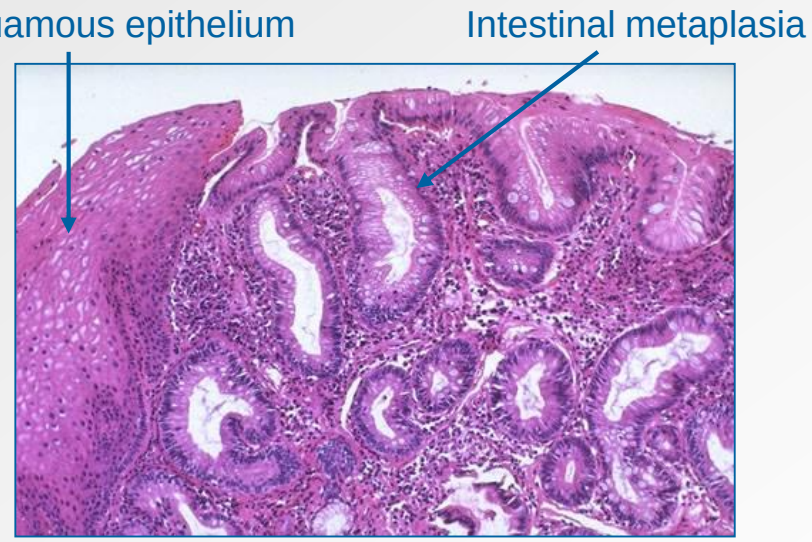


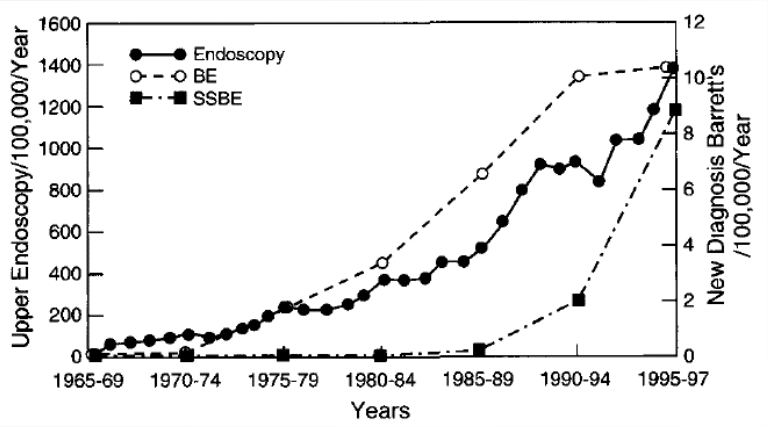
Table 1. Prevalence of BE and Prevalence of Gastroesophageal Reflux Symptoms and Esophagitis With BE or Without BE

	BE	LSBE	SSBE	No BE
No. of cases (%)	16 (1.6)	5 (0.5)	11 (1.1)	984 (98.4)
% with gastroesophageal reflux symptoms	56.3	80.0	45.5	39.7
% with esophagitis	25.0	60.0	9.1	15.4

NOTE. n = 1000.

(Ronkainen, *Gastro*, 2005)

Incidence of Barrett's



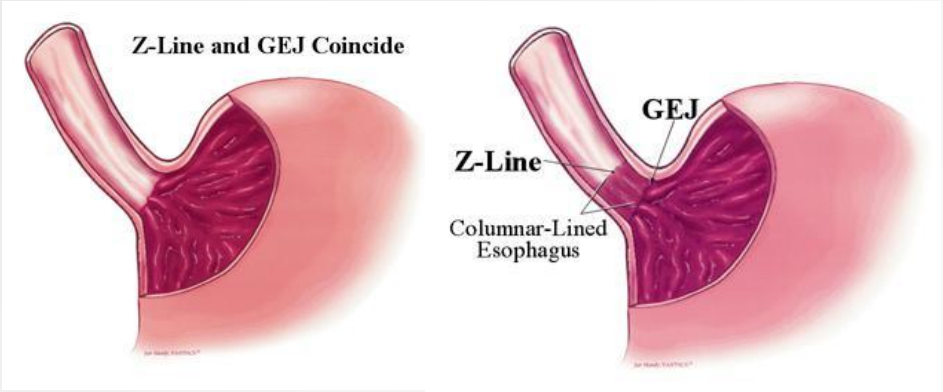
(Falk, *Gastro*, 2002)

Changing Definitions of Barrett's

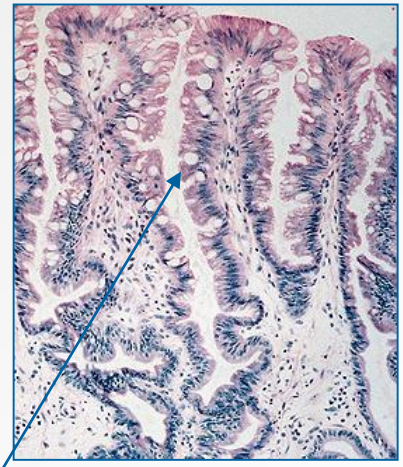
- Combined Endoscopic and Pathological
  - Endoscopy
    - Proximal migration of Z-line
  - Pathology
    - Intestinal metaplasia (US)
    - Columnar epithelium (UK)

(Sharma, *Gastro*, 2004)

(Playford, *Gut*, 2006)

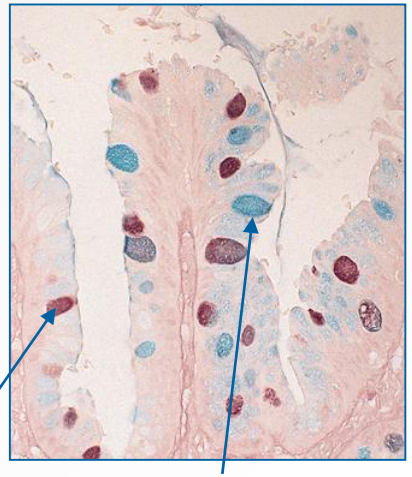


IM – Barrett's



Goblet cells

Barrett's diamine stain

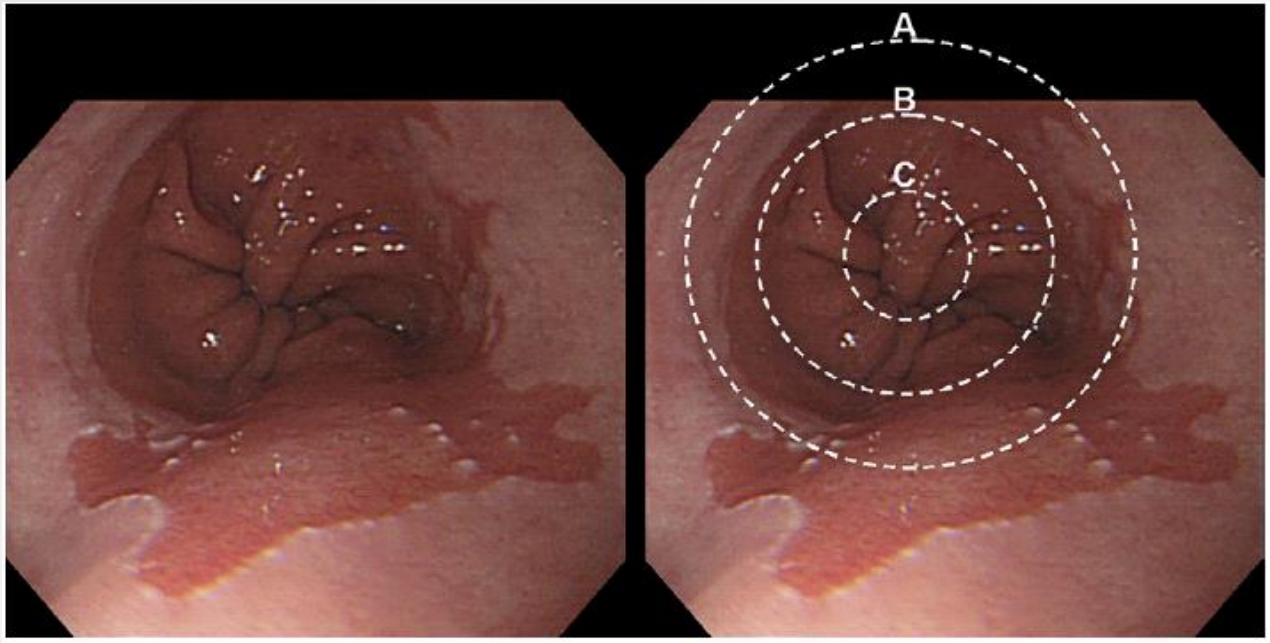


Sulfated mucin

Non-sulfated mucin

Challenges in Diagnosis

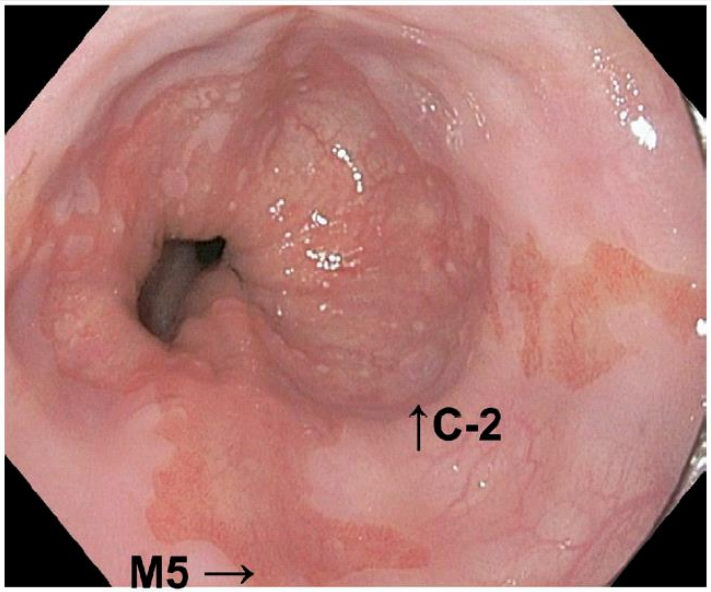
- Endoscopic landmarks
  - Where does oesophagus end and stomach begin?
    - Gastric folds best landmark to begin measure

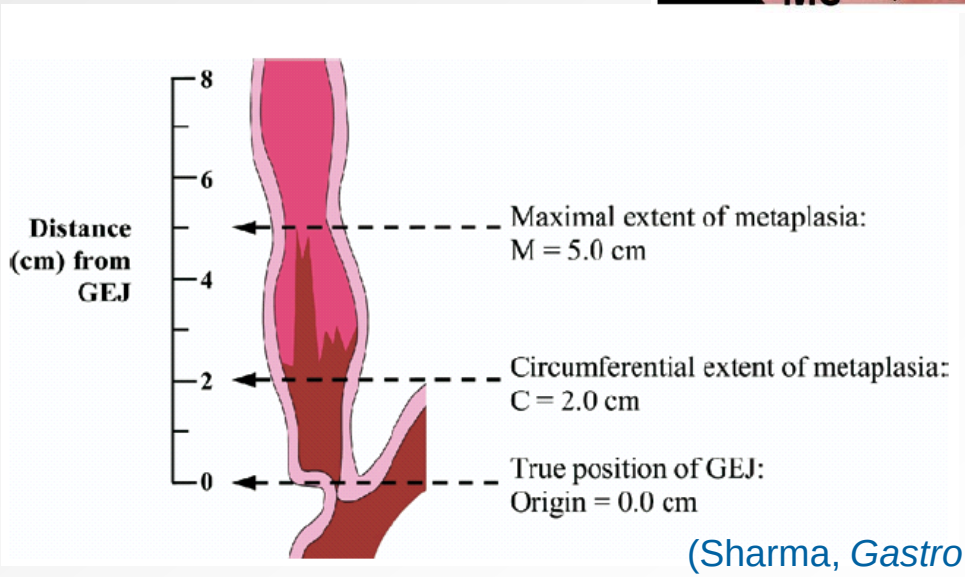


(Amano, *Gastrointestinal Endo*, 2005)

Challenges in Diagnosis

- How long is my Barrett's?
  - Measurement from GOJ
  - Prague criteria
    - Measure maximal extent of IM
    - Measure circumferential IM
  - Length is one factor that determines risk for OA

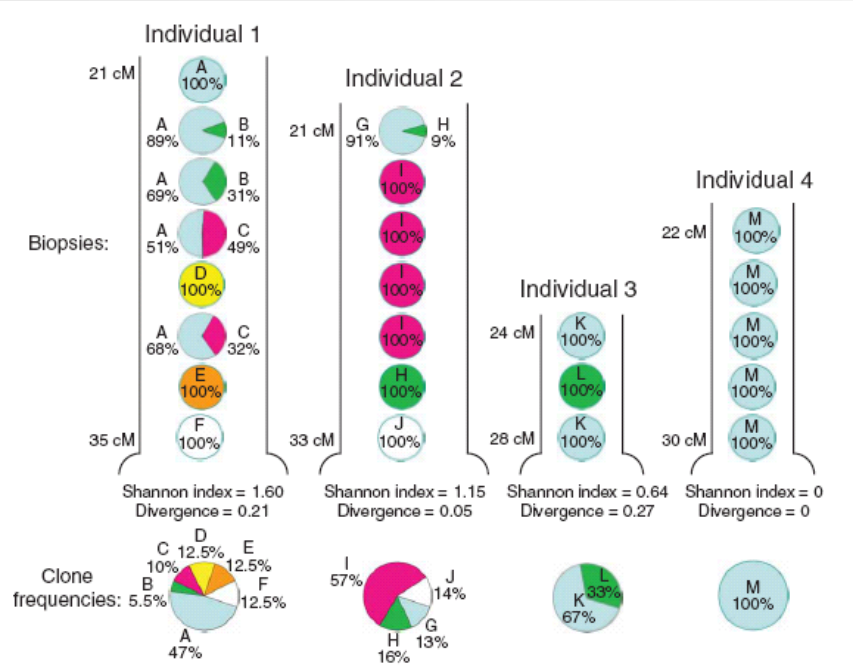




(Sharma, *Gastro*, 2006)

Risk Factors for Progression to Adenocarcinoma

- Risk of OA related to:
  - Length of BE
  - Degree of dysplasia
  - Number of molecular clones in length of BE
  - Complexity of clones



Predictor	Range	RR (95% c.i.)	*P* value
Segment length (per cm)	1–19	1.16 (1.08–1.24)	<0.001
Number of clones (per clone)	1–9	1.68 (1.47–1.91)	<0.001
Number of LOH clones (per clone)	1–9	1.99 (1.71–2.32)	<0.001
Clones per sample (per 0.1)	0.1–1.0	1.18 (1.04–1.34)	0.012
LOH clones per sample (per 0.1)	0.08–1.0	1.18 (1.04–1.34)	0.008
Shannon diversity index (per 1.0)	0.0–2.10	8.46 (4.59–15.6)	<0.001
Shannon LOH diversity index (per 1.0)	0.0–2.05	11.0 (5.80–21.0)	<0.001
Mean pairwise divergence (per 0.1)	0.00–0.54	1.96 (1.54–2.50)	<0.001
Mean pairwise divergence by LOH (per 0.1)	0.00–0.54	2.15 (1.67–2.77)	<0.001

(Maley, *Nat Gen*, 2006)

Molecular Model of Progression to Adenocarcinoma

Model of Barrett's progression

Normal squamous mucosa

GORD

Glandular epithelium

Low grade dysplasia

10-28% over 5yrs

High grade dysplasia

16-59% over 5yrs

Risk of cancer

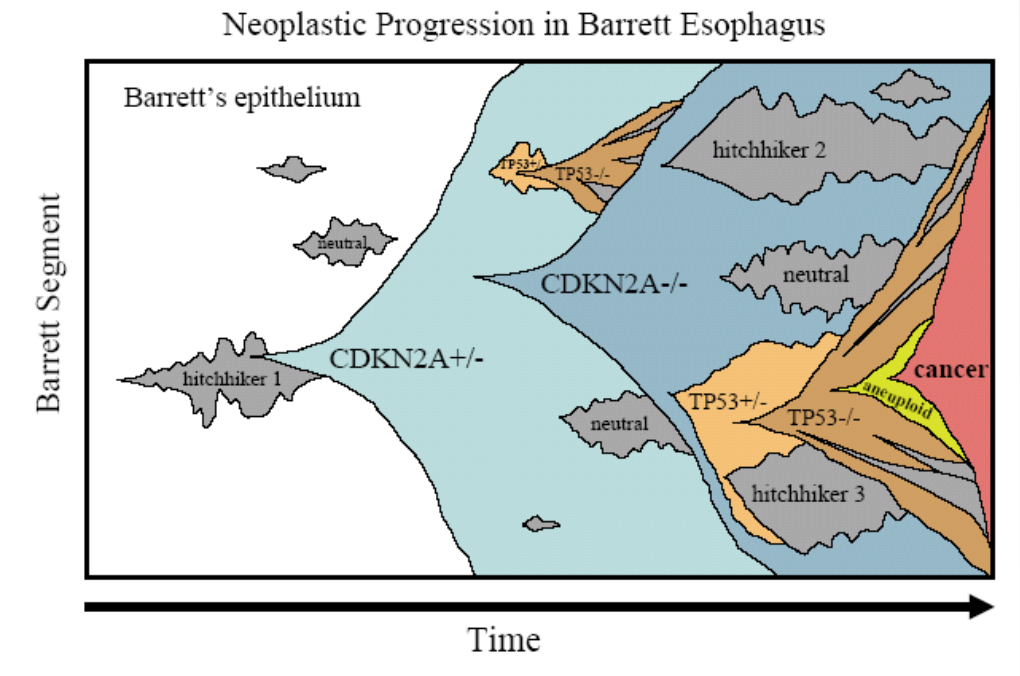
Adenocarcinoma

(Schnell, *Gastro*, 2001)

(Reid, *Am J Gastro*, 2000)

(Skacel, *Am J Gastro*, 2000)

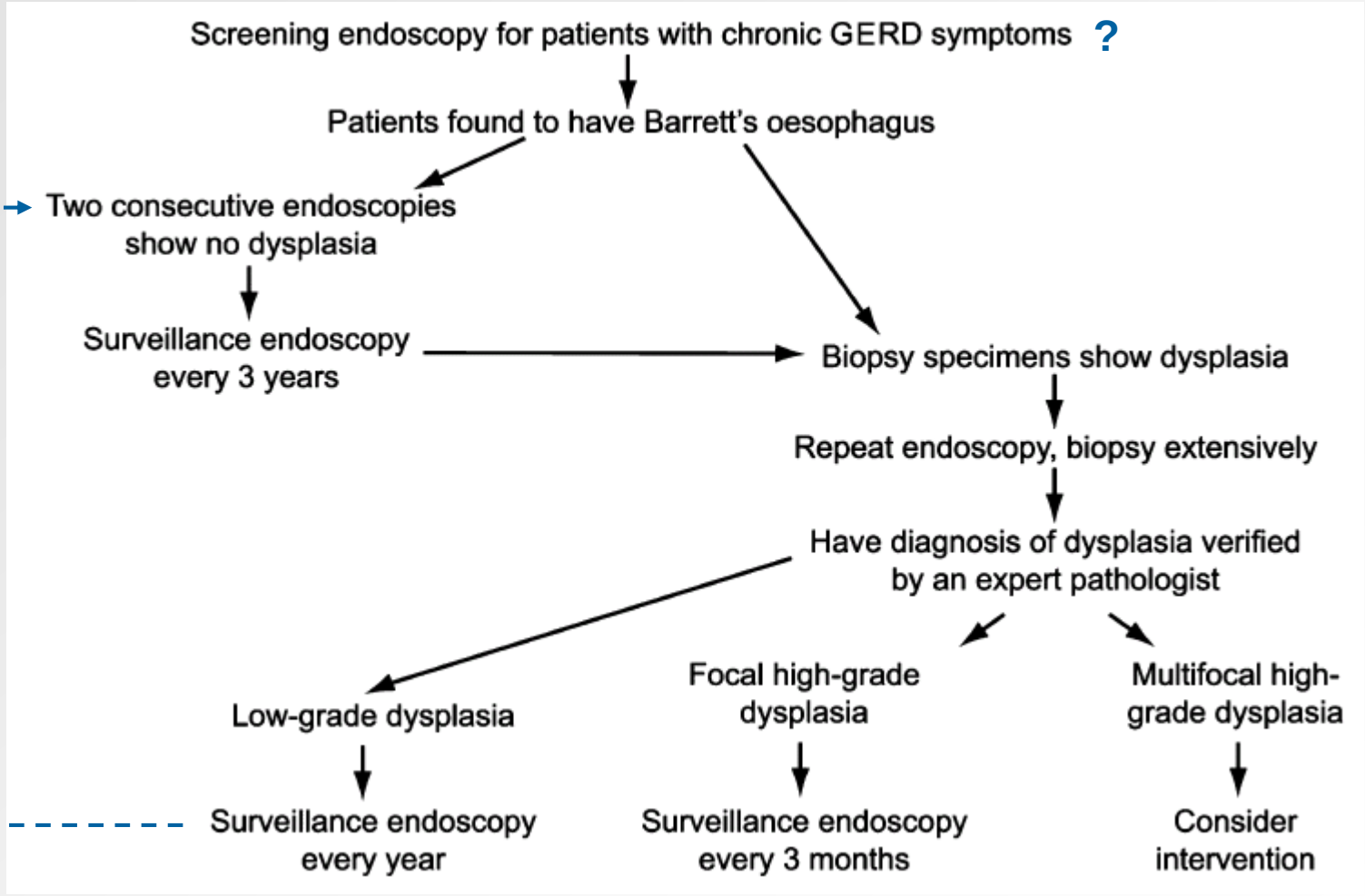
Clonal evolution theory of progression



Screening & Surveillance of Barrett's

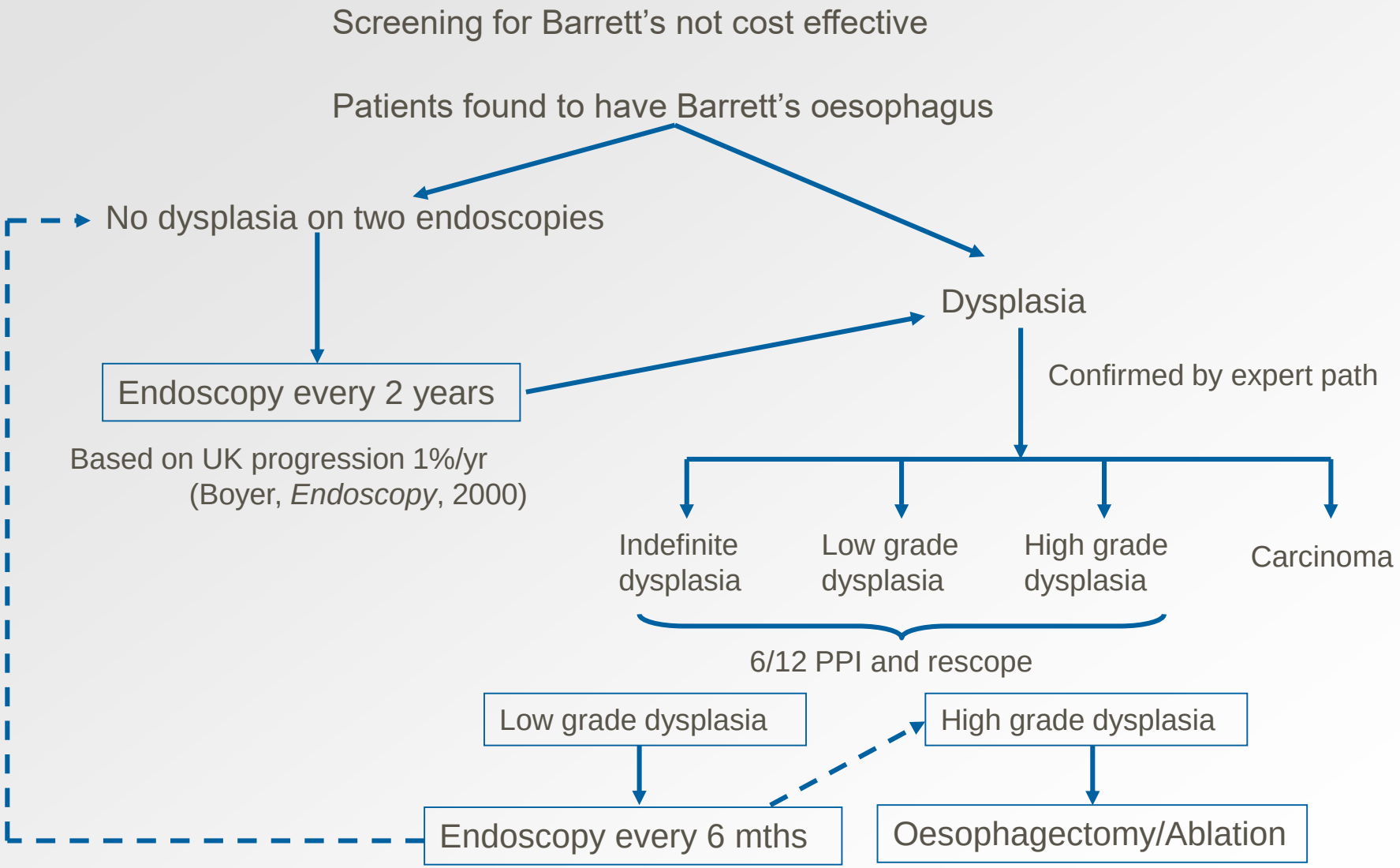
- Screening
  - Not cost effective to screen population endoscopically
  - Cannot screen GORD patients because 40% of BE is silent
- Surveillance
  - American College of Gastroenterology and British Society of Gastroenterology have guidelines but no Australian guidelines
  - Established Barrett's needs to be managed
    - Incremental risk of progression based on degree of dysplasia

Current Strategy for BE Surveillance in USA



(Spechler, *Alim Pharm Ther*, 2004)

BSG Guidelines for Barrett's Surveillance



www.bsg.org.uk

Management of Dysplasia

- Few studies have examined eradication of Barrett's
  - Prohibitive cost
- Low grade dysplasia has increased risk of progression
  - Management options
    - Surveillance
    - Ablation
- High grade dysplasia has ~40% risk of OA
  - Management options
    - Surgery
    - Ablation

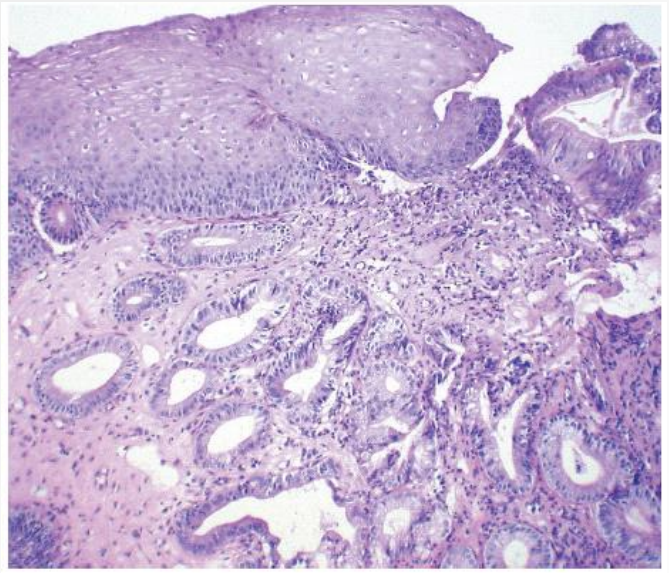
Ablative Technologies

- Thermal and Photothermal
  - Electrocoagulation (MPEC)
  - APC (Argon Plasma Coagulation)
  - Nd-YAG laser
  - Photodynamic therapy (PDT)
    - Use oral photosensitizer (5-ALA)
    - 530nm light
- Radiofrequency Ablation
- Mucosal resection
  - EMR (Endoscopic mucosal resection)
  - Mucosectomy?

(Sharma, *Gut*, 2006)

Complications of Ablation

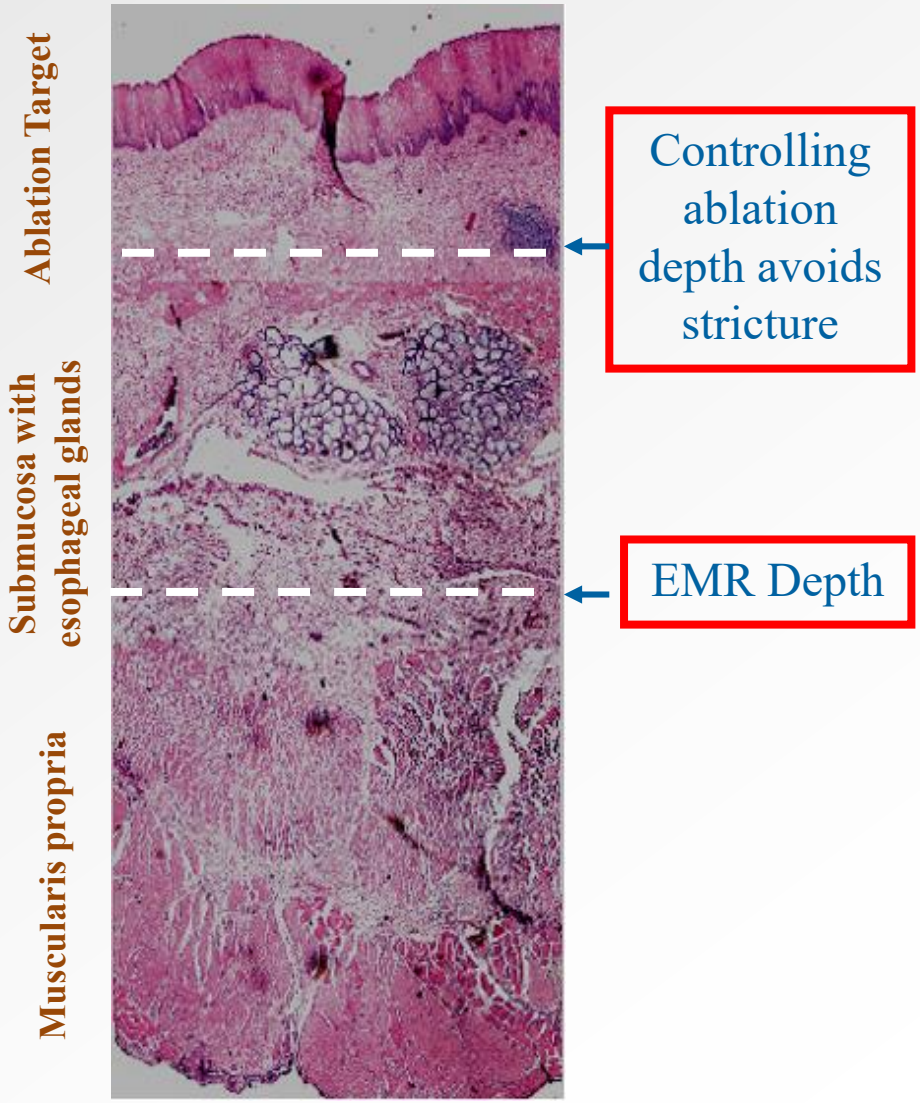
- Stricture 10-50%
- Chest pain 30-50%
- Dysphagia <20%
- Odynophagia 30-60%
- Photosensitivity in PDT
- Subsquamous Barrett's
  - 5-90%
  - Progression rate to OA unknown



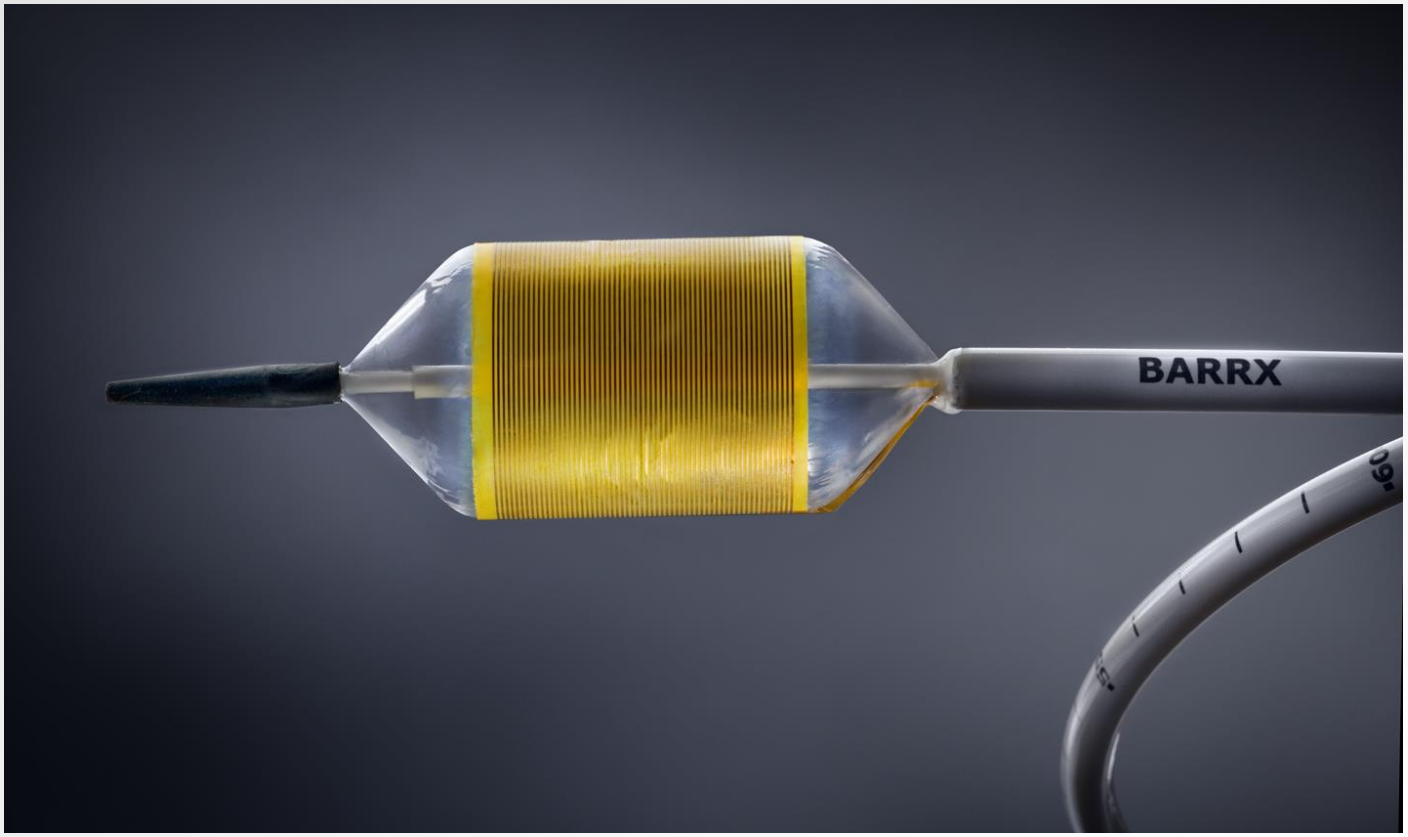
Subsquamous Barrett's

A Promising Ablative Technique

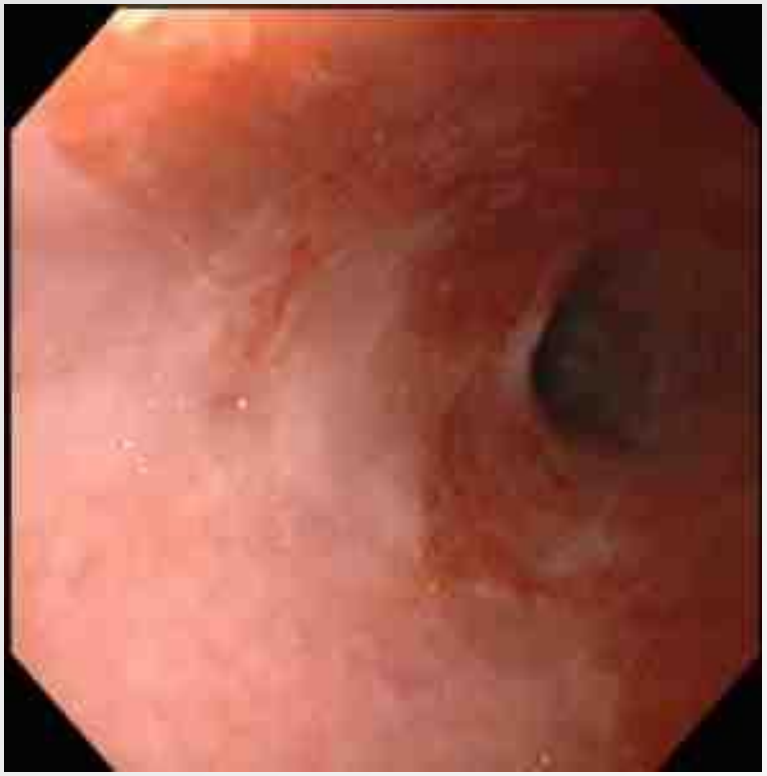
- Radiofrequency ablation
  - Another form of thermal injury
  - Controlled release of energy better control of ablative depth
  - HALO^{360} and HALO^{90} devices



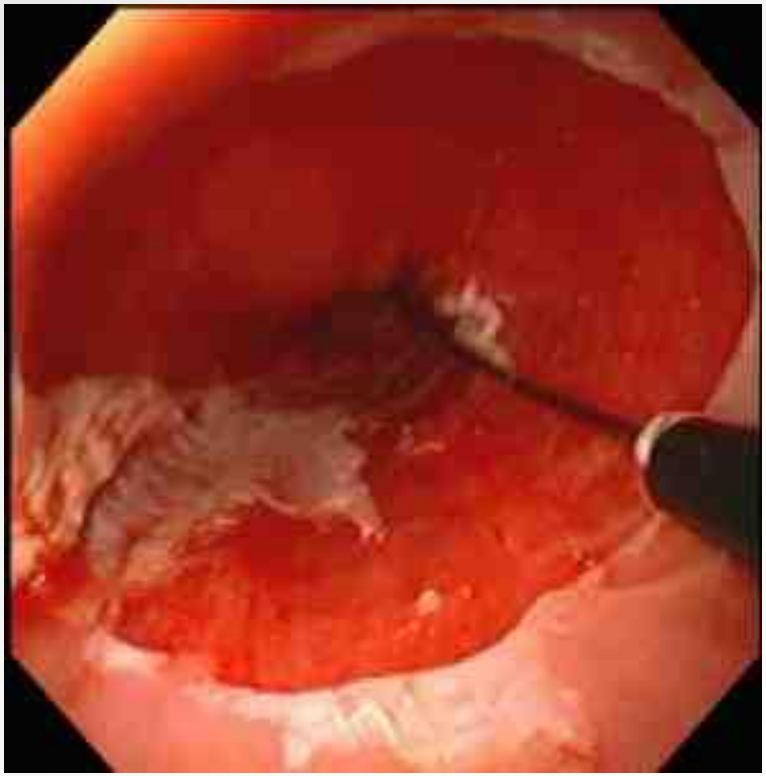
HALO^{360} Ablation Catheter



Endoscopic Appearance



Baseline, 4 cm IM



Immediate Slough

Complete Response after HALO^{360}

Conclusions

- Barrett's oesophagus = premalignant condition
- Risk factors for progression to OA
  - Length of Barrett's oesophagus
  - Clonal diversity of Barrett's oesophagus
  - Smoking

- Screening to find Barrett's oesophagus not cost effective
- Surveillance programs have altered to reflect local incidence rates
- Ablation technologies are improving but not yet advocated for non-dysplastic Barrett's oesophagus

Treatment for Barrett's oesophagus (Review)

Rees JRE, Lao-Sirieix P, Wong A, Fitzgerald RC

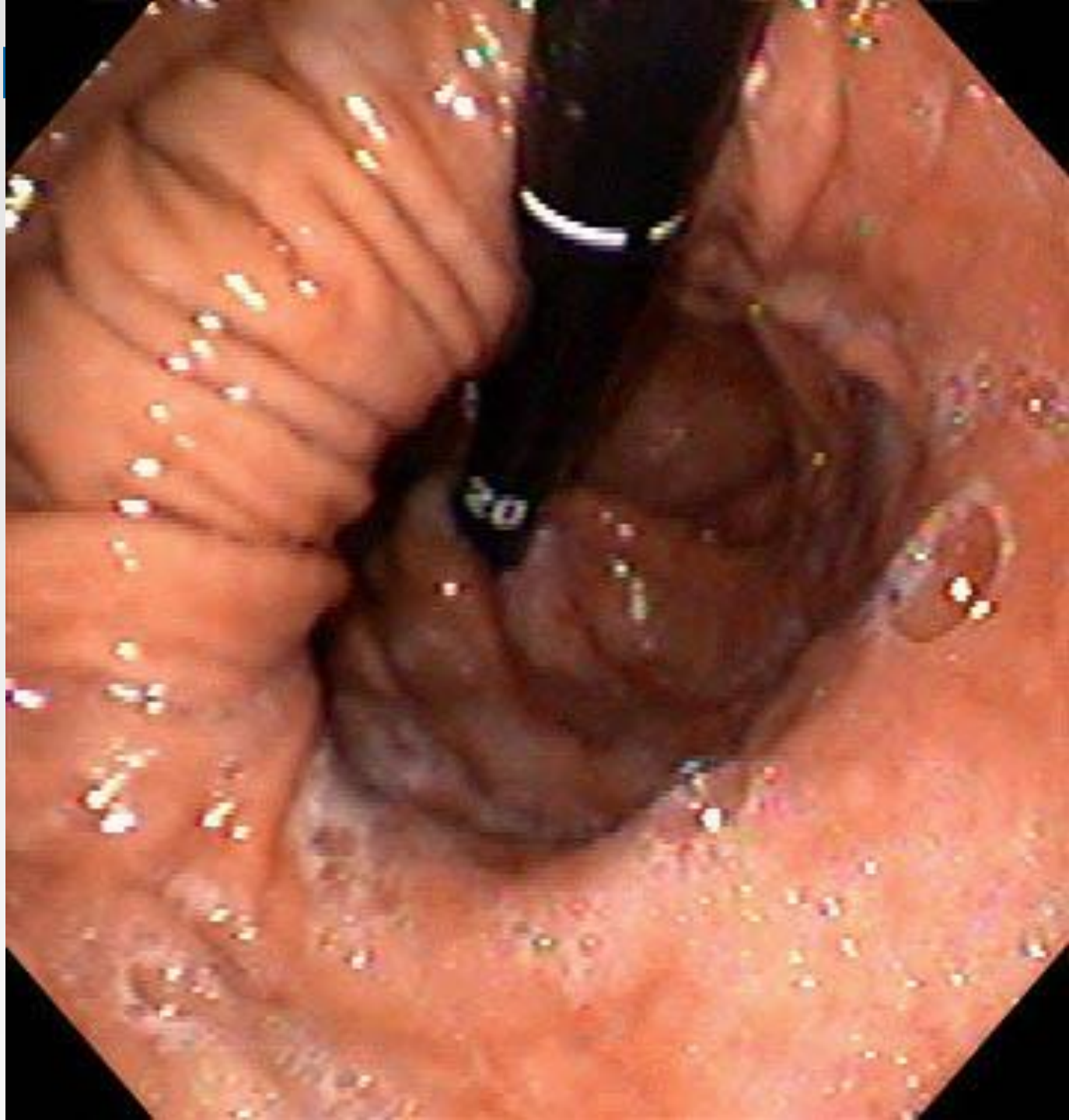
This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2011, Issue 7

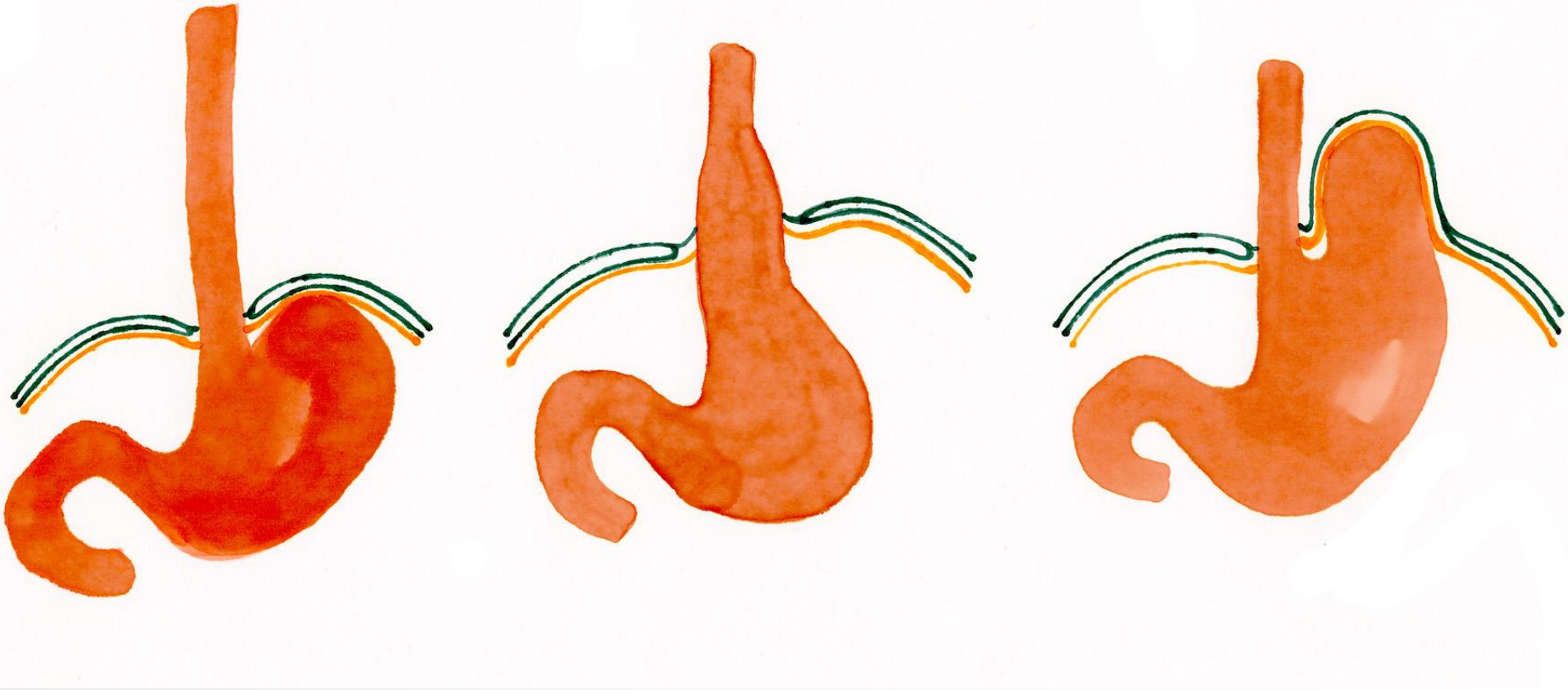
http://www.thecochranelibrary.com

Treatment for Barrett's oesophagus (Review)

Rees JRE, Lao-Sirieix P, Wong A, Fitzgerald RC

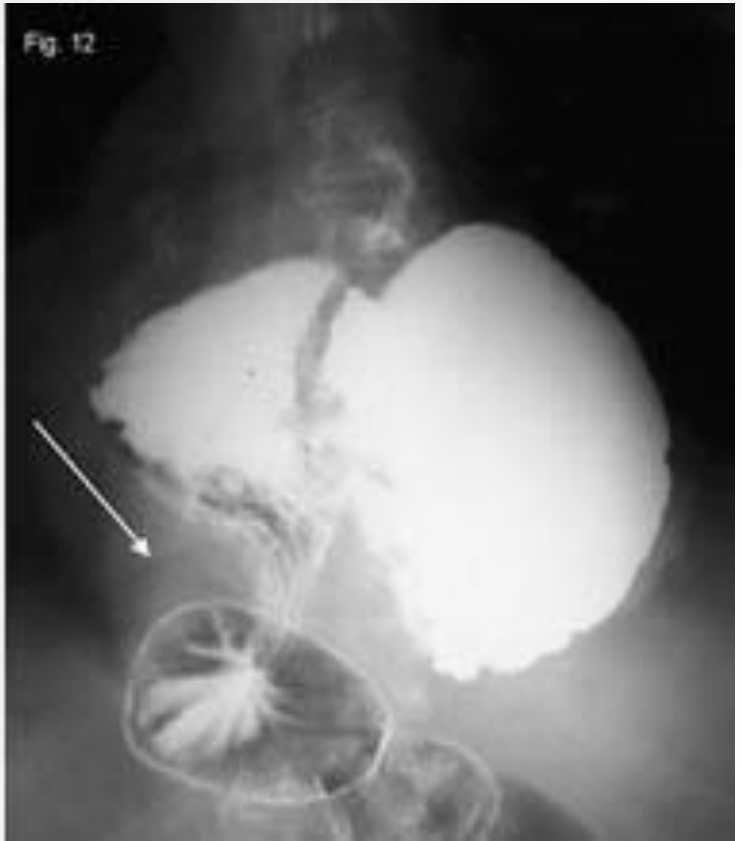
- Medical & surgical treatments
  - Improve symptoms
  - Induce regression of Barrett's segment
  - Do not induce significant eradication of Barrett's
  - Prospective evidence for prevention/eradication of dysplasia with surgery
  - Not known if reduction in cancer risk





When?

- All patients considered for repair unless comorbidities
- Symptoms main indication to operate
- Potential for incarceration & strangulation



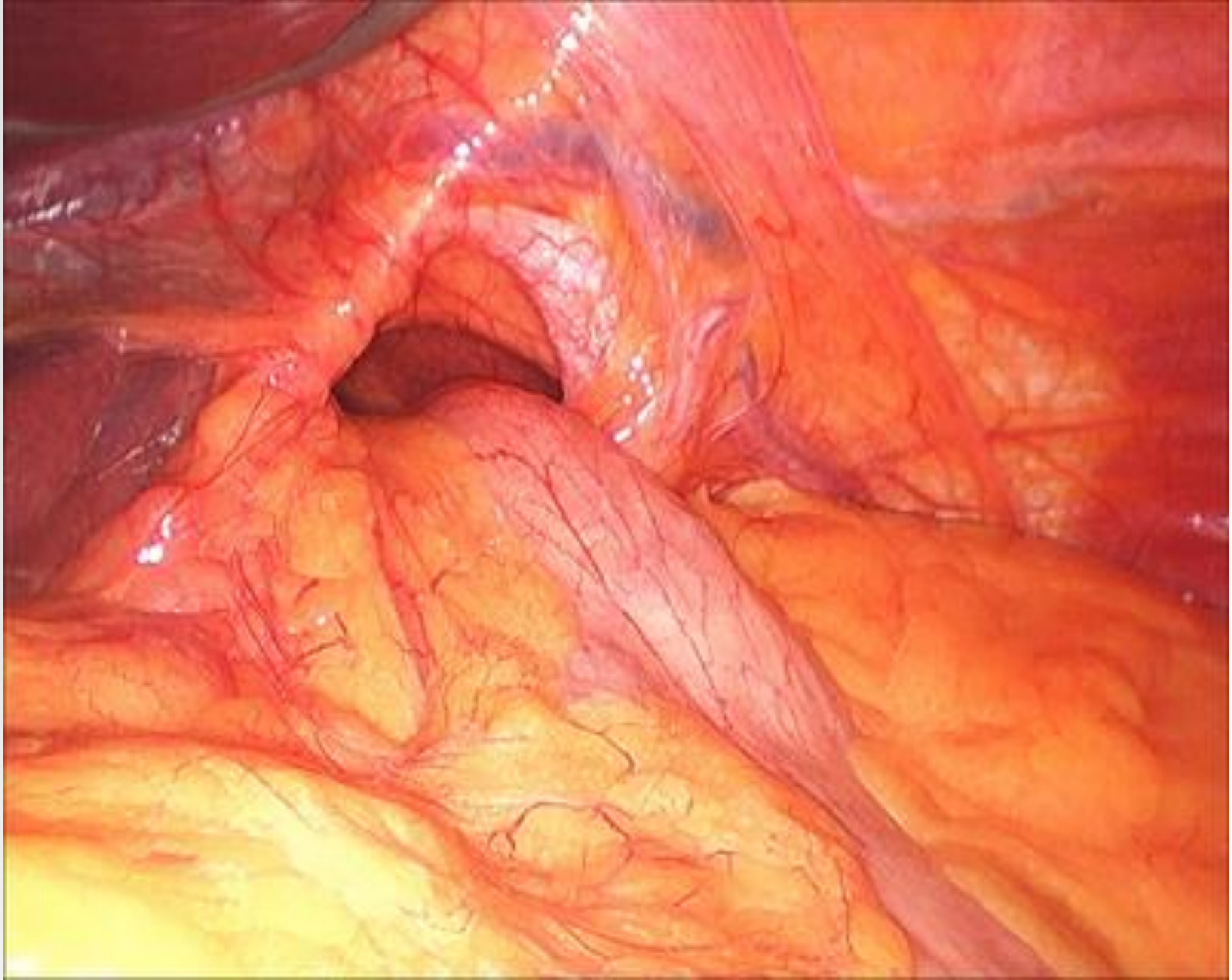
When?

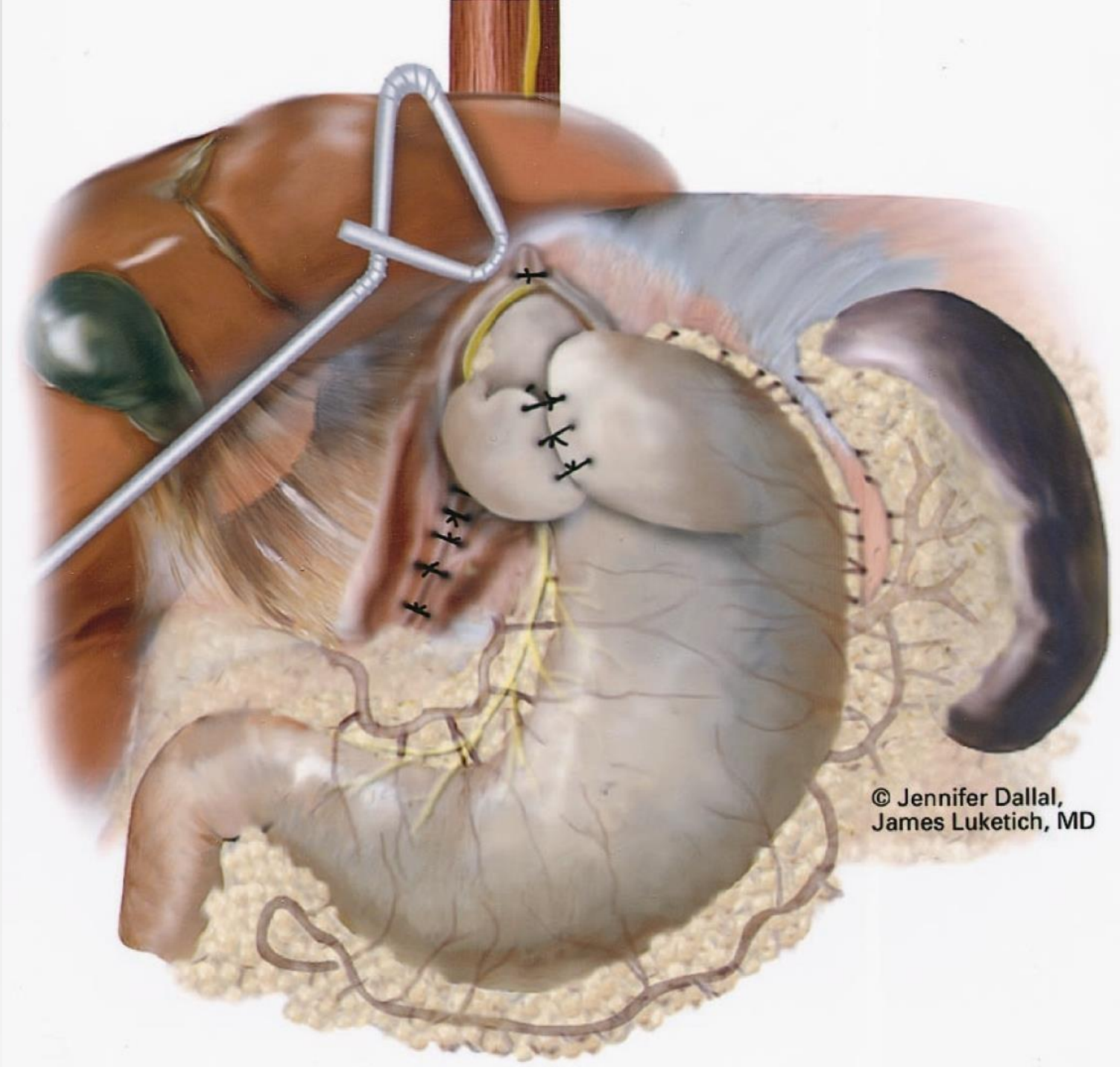
- Skinner & Belsey
  - Study in 1967
  - 21 patients with paraoesophageal hernia
  - Followed conservatively for 5 years
  - 6 patients (29%) died from complications of HH
- Allen et al.
  - 23 patients with paraoesophageal hernia
  - Refused operative repair
  - Median follow-up of 78 months
  - 4 patients (17%) had progressive symptoms
  - 1 patient (4%) died of aspiration pneumonia

When?

- Stylopoulos et al.
  - Population-based decision analysis model
  - Asymptomatic or minimally symptomatic paraoesophageal hernias
  - Emergency surgery required in only 1.2%
  - Operative mortality of emergency surgery 5.4%

- Watchful waiting if elderly & minimally symptomatic

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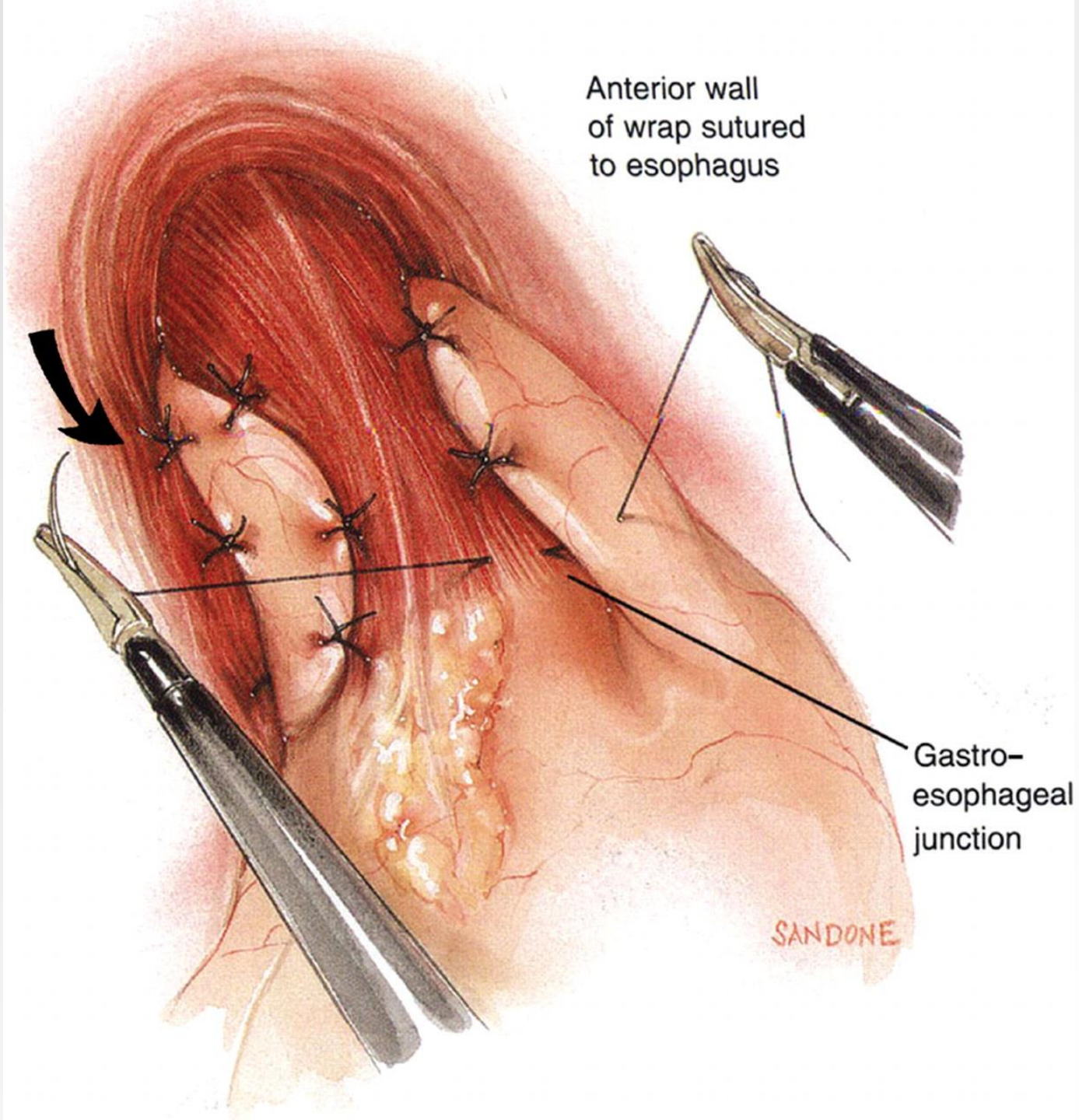
Anterior wall
of wrap sutured
to esophagus
Gastro–
esophageal
junction
SANDONE