Barrett’s Esophagus

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Norman Barrett (1950) described the esophagus as:

“that part of the foregut, distal to the cricopharyngeal sphincter, which is lined by squamous epithelium”

- Columnar lining due to congenital shortening
- Tubular portion of stomach “trapped in the chest”

Allison/Johnstone (1953) & Lortat–Jacob (1957)

- Columnar epithelium-lined esophagus
- Ulcers in this area: “Barrett’s ulcers”
- Ultimately named “Barrett’s esophagus”
Definition

- Change in distal esophageal epithelium
- Any length
- Recognized as columnar mucosa on EGD
- Confirmation of intestinal metaplasia
- Multiple biopsies
- Pre-malignant lesion for adenocarcinoma

Variants

- Gastric fundus: resembles stomach epithelium
- Junctional: resembles cardiac epithelium
- Intestinal: glandular epithelium characterized by the goblet cell
Anatomical landmarks

- **Squamocolumnar junction**
  - Juxtaposition of pale squamous epithelium and red columnar epithelium
  - Z-line

- **Gastroesophageal junction**
  - Esophagus ends and Stomach begins
  - Most proximal part of the gastric folds

- When Z-line above GE junction = Barrett’s
Metaplastic process at GE junction
  ◦ Squamous to columnar conversion
  ◦ Exposure to exceed acid
  ◦ Prolapse of esophageal mucosa into gastric milieu
  ◦ Inflammatory changes
  ◦ Loss of muscle function
  ◦ Mechanically defective sphincter
  ◦ Free reflux w/ higher degrees of mucosal injury
  ◦ Acid and Bile reflux
Pathogenesis

- Chronic GERD = Barrett’s in 5% to 15% pts
- Unclear:
  - Severe esophagitis w/o BE
  - Relative symptoms with severe dysplasia
- Genetic predisposition?
- Barrett’s gene remains elusive
- Hereditary pattern:
  - BE occurs in family groups more often
  - Low penetrance (no 1st degree relative correlation)

Barrett’s progression

Normal Lining  Barrett’s Esophagus with low-grade dysplasia  with high-grade dysplasia  Invasive carcinoma
Intestinal metaplasia
- Goblet cells = mucous producing cells
- Alcian blue stain differentiates from normal stomach tissue
Dysplasia

- 15 to 25% if low-grade dysplasia included
- 5 to 10% if only high-grade dysplasia
- Histologic examination
- 4 categories:
  - No dysplasia
  - Indefinite
  - Low grade dysplasia
  - High grade dysplasia
- Non-dysplastic:
  - 5 to 10% per year progress to dysplasia

1. Reid et al. Gastroenterology 102:1212, 1992
High Grade Dysplasia

- Advanced neoplasia confined to epithelium
- Limited by basement membrane
- Not found in lamina propria
- No regression
- Precursor and marker for invasive cancer
- Dx: Esophagoscopy and biopsy

Histopathologic Interpretation:
- Establishing presence of dysplasia
- Grading dysplastic changes
- Distinguishing HGD from invasive cancer
Reid et al: 5yr probability of cancer
- 59% if HGD on initial EGD
- 31% if HGD on surveillance EGD

Buttar et al: 3yr probability of cancer
- 56% if multifocal HGD (> 5 crypts)
- 14% if focal HGD (< crypts)

Cleveland Clinic: Esophagectomy for HGD
- Invasive cancer present in 45% pts final pathology

Adenocarcinoma

- Incidence \(\uparrow\) 300\% to 500\% last 40 yrs
- 40\% in asymptomatic patients (no GERD)
- Unpredictable “Barrett’s lifetime”
  - Cancer risk as function of duration of Barrett’s

Annual incidence of malignant transformation

0.5\% to 1.0\%
OR
125 x greater than gen. population
Adenocarcinoma
Remains controversial
- Inability to predict BE prior to endoscopy
- Invasiveness & expense of EGD
- Increasing asymptomatic population
- Not enough evidence for recommendation
- Prevention of a very rare malignancy
  - \( \approx 7,000 \) EAC cases in US 2004
  - 40% asymptomatic
  - Age of onset > 70yrs
- High chance of missed lesions on EGD
Proposed predictors:
- Male gender
- Age > 40 yrs
- Obesity
- Heartburn
- Long duration GERD (> 13 yrs)

Early recognition warrants early surveillance

Life expectancy of EAC pts:
- Longer if dx by screening EGD rather than at onset of symptoms

Not yet recommended
Treatment

- Non-dysplastic & Low grade dysplasia
  - Highly effective Medical & Surgical Rx
- Medical = Proton Pump Inhibitors
  - 1st line agents for esophagitis
  - Reduced incidence of dysplasia
- Surgical = Antireflux surgery
  - Nissen, Dor, Toupet Fundoplications
  - Long term relief of symptoms
  - Regression of dysplasia and intestinal metaplasia
  - Prevention of HGD and adenocarcinoma
Hofstetter et al:
- 85 pts w/BE at 5 yrs after surgery
- 80% asymptomatic and 20% recurrence of reflux
- 81% normal post-op 24hr pH monitoring

DeMeester et al:
- 37 pts with 73% loss of intestinal metaplasia

Gurski et al:
- 77 surgical pts & 14 medical pts
- Low grade dysplasia regression: 36.8% and 7%
- Low grade to non-dysplastic: 68%
- Eight pts progressed (all with long segment BE)
- Median time of biopsy proved regression: 18.5 months

Regression is dependent on length of BE segment and time of f/u after surgery
LOTUS multicenter randomized trial
- Medical vs Surgical Rx of GERD pts with Barrett’s
- 554 patients with GERD
- 60 pts with BE (28 to PPI, 32 to LARS)
- 4 pts with treatment failure
- Esophageal pH better controlled after LARS
- No difference in post-operative complications
- Similar level of symptomatic reflux control

Success of LARS is similar in pts w or w/o BE
Nissen Fundoplication

Collis–Belsey procedure
Schnell et al:

Endoscopic surveillance q3 months for 1st year, q6 months 2nd year, yearly thereafter

Mean follow up 7.3 years

Only 16% cohort developed cancer
1,550 Barrett's patients
7,000 EGDs
46,000 Barrett's specimens read by the same pathologist

“Intensive endoscopic surveillance with biopsies—rather than immediate esophagectomy—is the management of choice for patients with flat HGD and no cancer”

“Surgical resection of the esophagus should be reserved only for those patients in whom cancer has been documented”
**Surveillance**

<table>
<thead>
<tr>
<th>Dysplasia</th>
<th>Documentation</th>
<th>Follow-up</th>
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<tbody>
<tr>
<td>None</td>
<td>• Two EGD w/bx in 1 yr</td>
<td>• Endoscopy q 3 yrs</td>
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<tr>
<td>Low Grade</td>
<td>• Highest grade</td>
<td>• 1 yr interval until no dysplasia x 2</td>
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<td></td>
<td>• Bx within 6 months</td>
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<tr>
<td></td>
<td>• Expert pathologist</td>
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<tr>
<td>High Grade</td>
<td>• Mucosal irregularity</td>
<td>• Endoscopic resection</td>
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<tr>
<td></td>
<td>• Repeat EGD w/bx within 3 months</td>
<td>• q 3 month EGD surveillance or intervention based on results and patient</td>
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<td>• Expert pathologist</td>
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Endoscopic Mucosal Resection
- Less invasive than esophagectomy
- Saline lift, snare removal, band technique
- Determines depth of invasion of visible lesion
- Endoscopic excision of lesions up to 1.5cm

Ell et al:
- 98% survival at 5 yrs
- Highly selected pts with early EAC
- Well diff. intramucosal tumors w/o lymph invasion
- Short-segment Barrett’s esophagus

Treatment of HGD

- Endoscopic ablation:
  - Electrocoagulation
  - Laser
  - Argon–beam coagulation
  - Radiofrequency ablation
  - Photodynamic therapy (PDT)

- PDT
  - Porfimer sodium
  - Light of specific wavelength (630 nm)
  - Intracellular reaction leads to cell death
  - Strictures
  - Residual buried Barrett’s dysplasia and cancer
Remains the standard of care for HGD
High volume centers = low mortality
Minimally invasive approach
  - Vagal-sparing esophagectomy
  - No vagotomy or pyloroplasty
95% cancer survival at 5 years
Early cancers confined to mucosa
  - No need for extensive lymphadenectomy

Surgical survival

Described by Akiyama et al in Japan

- Reduced morbidity
  - Dumping syndrome
  - Diarrhea
  - Weight loss

- Stripping
- Invagination of muscle
- Colon interposition

Das et al: 742 pts
- 99 pts (13.4%) treated w/EMR
- 643 (86.6%) pts treated w/esophagectomy
- Stage 0 and Stage 1 esophageal cancer
- Follow up for 56 and 59 m respectively
- No statistical significance in 5 yr survival
- Most EMR pts were stage 0
- Esophagectomy pts were stage 1

Barrett’s esophagus is as much a surgical as it is a medical disease.

Early detection is key to success in management.

Surveillance even after anti-reflux therapy is of utmost importance.

With new endoscopic advances; careful selection of patients for treatment approach.

Goal is: Keep Cancer Away
A 58 y.o. male with history of GERD undergoes EGD with biopsy results of high grade dysplasia. What’s the next step in management of this patient?

a. Esophagectomy
b. Medical trial with PPI’s
c. Endoscopic Mucosal Resection
d. Repeat EGD and biopsy in 3 months

Answer: d
Intestinal metaplasia is differentiated from gastric metaplasia by presence of:

a. Parietal cells  
b. G cells  
c. Goblet cells  
d. Columnar epithelium

Answer: c
Which of the following statements about Barrett’s is NOT true?

a. 40% of patients are asymptomatic
b. Treatment is directed based on degree of dysplasia
c. If dysplastic segment < 3cm, no intervention is necessary
d. Severe esophagitis can mask areas with intestinal metaplasia
e. 0.5% to 1.0% pts/yr progress to adenocarcinoma

Answer: c
Which of the following statements about Barrett’s is NOT true?

a. Most pts who develop carcinoma in Barrett’s are men aged 55 to 60
b. Pts with high grade dysplasia should undergo esophagectomy
c. Endoscopic surveillance effectively reduces the stage at presentation to stage 2 or lower
d. Barrett’s occurs in 10% to 15% of pts with GERD
e. Low-grade dysplasia should be treated with an antireflux procedure as well as antacids

Answer: e
Keep spinning him, Nurse Wilson. Keep spinning him! On three, let go!
One... two...