Refractory GERD

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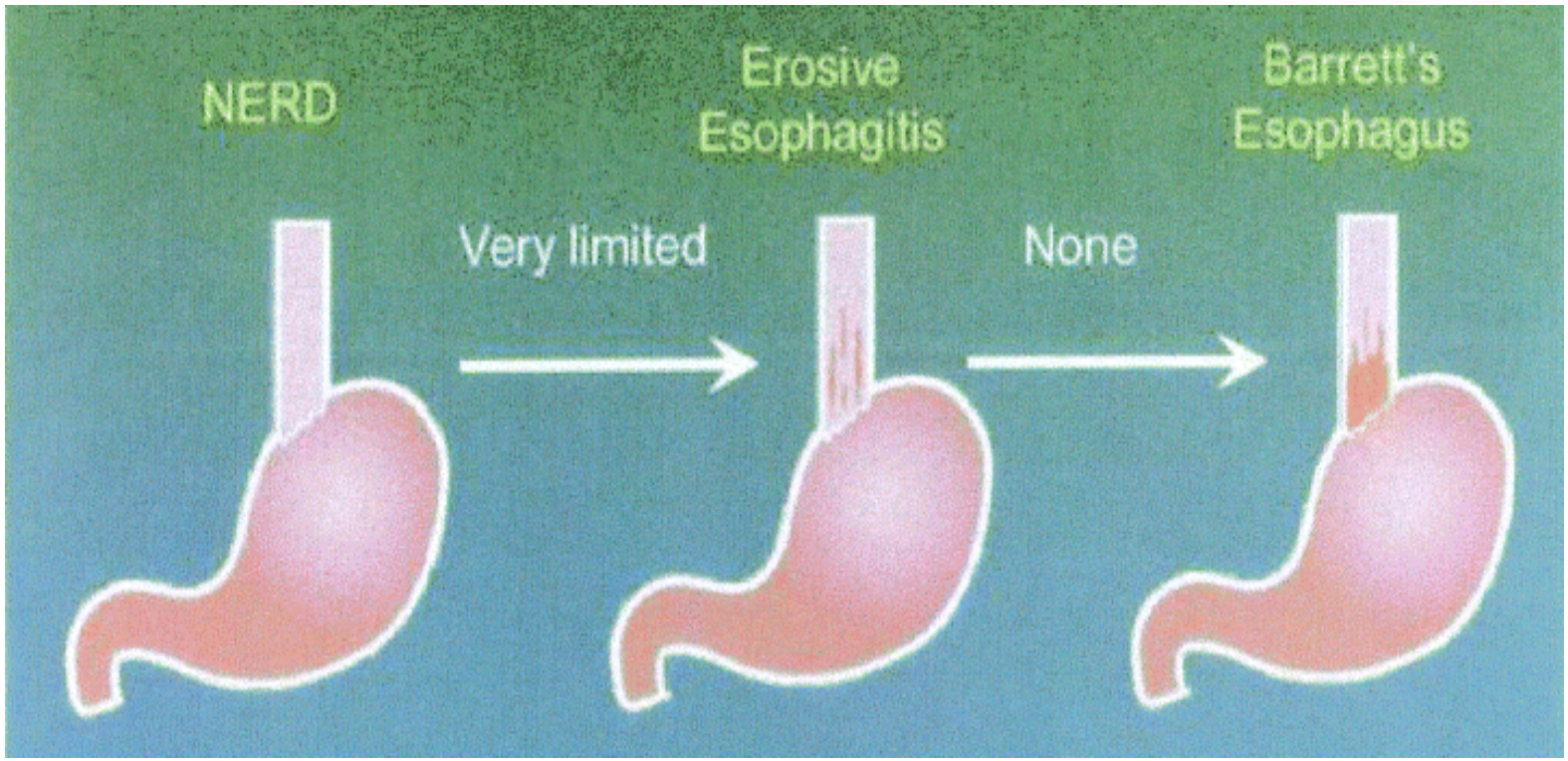
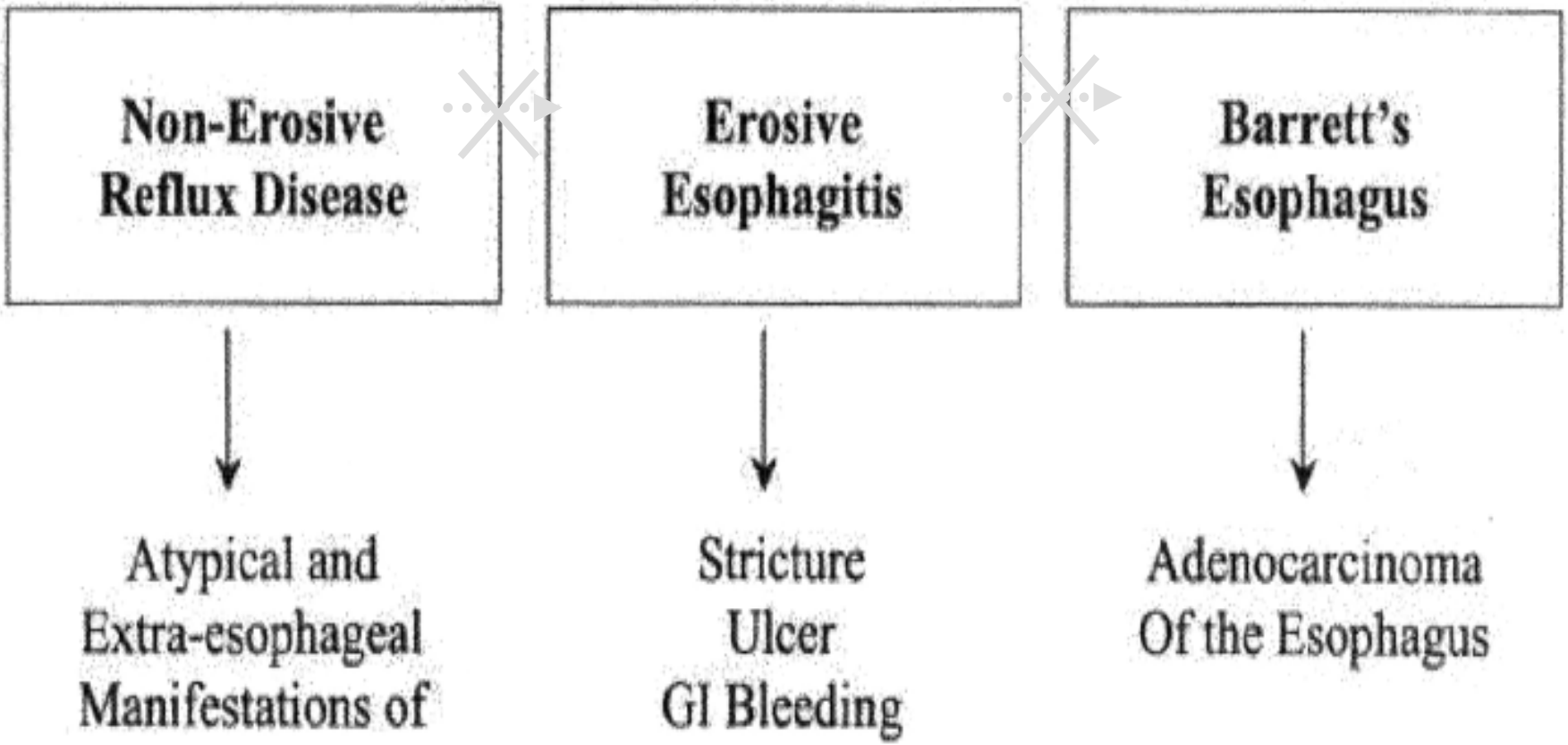
REFRACTORY GERD

- Patients with GERD not responding to once daily PPI
- These therapy resistant patients have become the new face of clinical practice
- 10-40% of GERD pts fail to respond to symptomatically (partially or completely) to standard PPI dosing.
- During 1997-2004: an increase of 50% in bid dosing of PPI w/ GERD

GERD—A Spectrum of Disease?

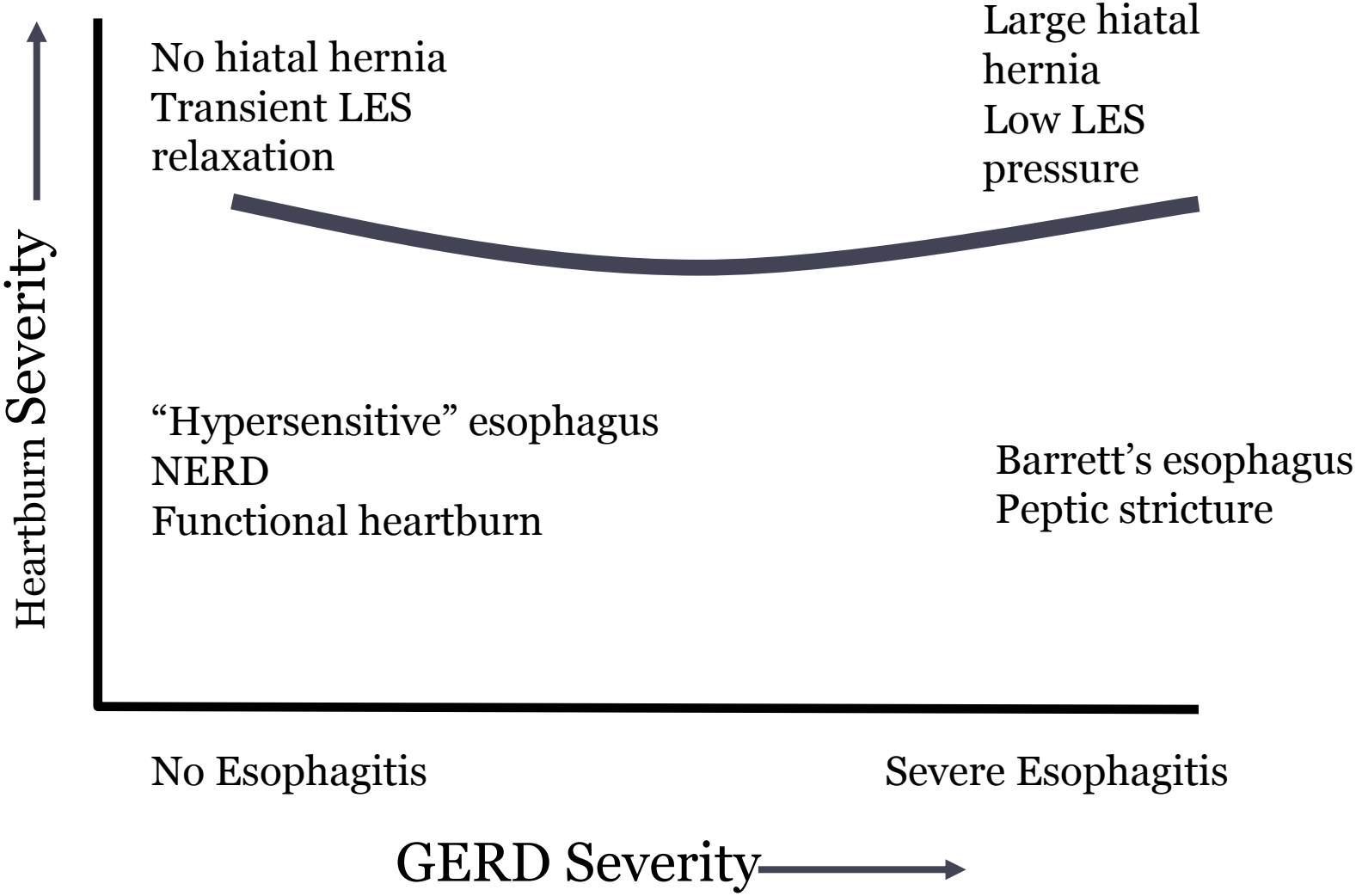


New Conceptual Model for GERD



Fass R et AL. Am J Gastroenterol 2002;97:1901-9.

Heartburn Severity May Not Correlate with Disease Severity in GERD



Causes

- Most of GERD pts not responding to PPI originate from NERD and Functional Heartburn (FH)- 70%.
- Erosive Esophagitis accounts for 30-40% of the GERD population (~56% response rate with daily PPI)

Causes- Refractory GERD w/Esophagitis

- Pill induced esophagitis
- Autoimmune Skin diseases
  - Epidermolysis bullosa acquisita, pemphigus vulgaris, lichen planus (endo: erythema,blistering of mucosa, whitish nod, prox stricture disease)
- Acid Hypersecretion
  - ZE tx to ↓ gastric acid sec to <10mEq/h
  - Rapid metabolizers of PPI
- Eosinophilic Esophagitis

Causes- Refractory Gerd w/o Esophagitis

- Nocturnal gastric acid breakthrough (NAB)
- Nonacid gastroesophageal reflux
- Missed gastroesophageal reflux
- Functional Heartburn
- Wrong diagnosis

- Investigators believe that only GERD pts with partial or lack of response to bid PPI should be considered PPI failures. (others say daily is enough)

CAUSES: Compliance

- In a study of 100 pts w/ persistent GERD only 46% were dosed optimally.
- Of those suboptimally: 39% consumed PPI >60 min before meal, 30% after meals, 28% at bedtime, 4% prn symptoms
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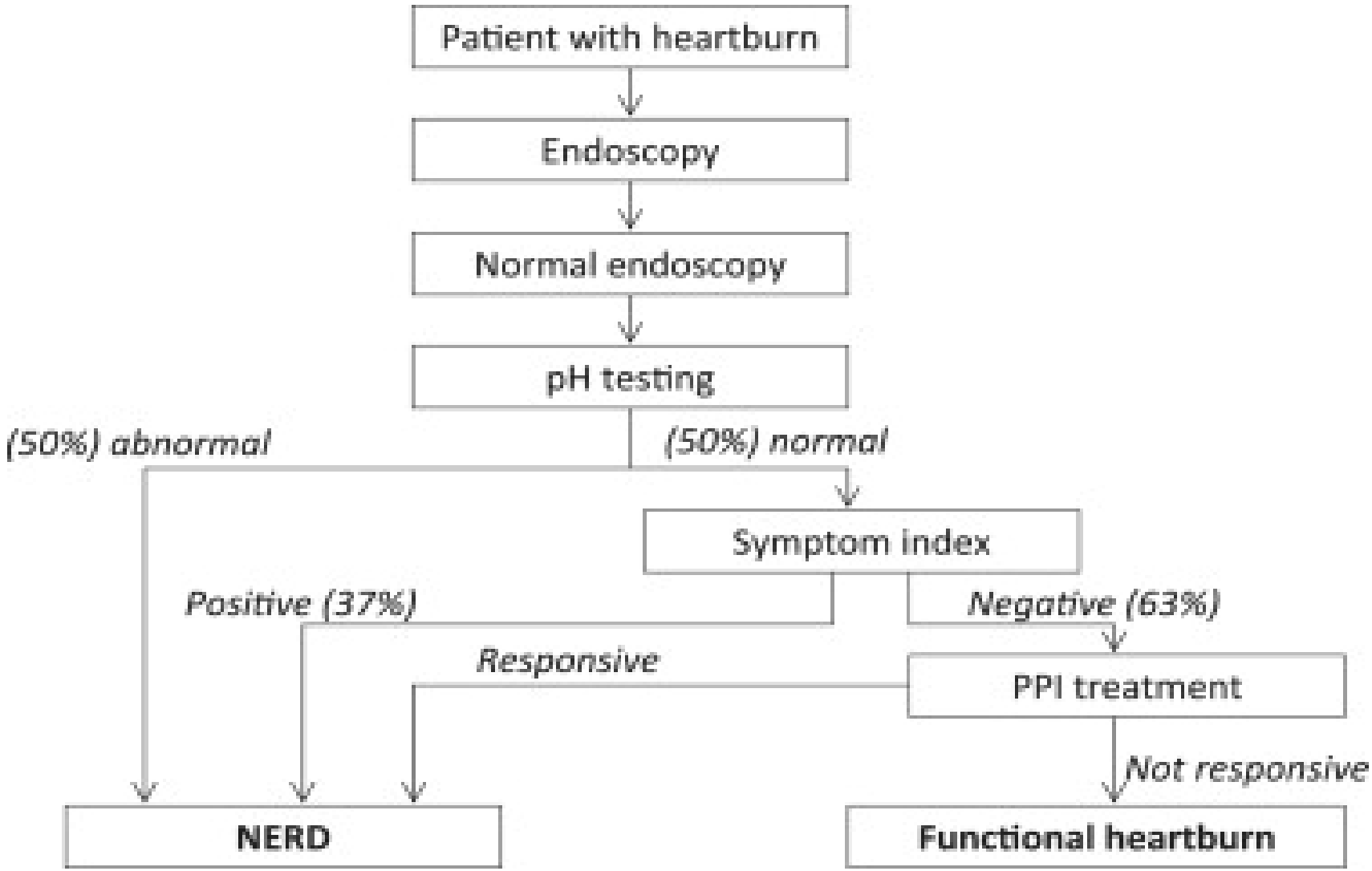
CAUSES: weakly acidic/alkaline reflux

- This mechanism is poorly understood but distension of the esophagus and/or esophageal hypersensitivity are the possible culprit.


Patient with heartburn
Endoscopy
Normal endoscopy
pH testing
(50%) abnormal
(50%) normal
Symptom index
Positive (37%)
Negative (63%)
Responsive
PPI treatment
Not responsive
NERD
Functional heartburn

Diagnostic Tests

- These are utilized to identify residual reflux (acidic, non-acidic, or bile), anatomical and histological abnormalities of the UGI tract and functional heartburn.

- 1) **EGD:** The value is low in refractory GERD pts

>>Rare cases could show: ZE, pill-induced esophagitis, achalasia, eosinophilic esophagitis, gastroparesis.

>>DIS (dilated intracellular spaced) seen by EM can confirm reflux as the culprit.

Diagnostic Tests

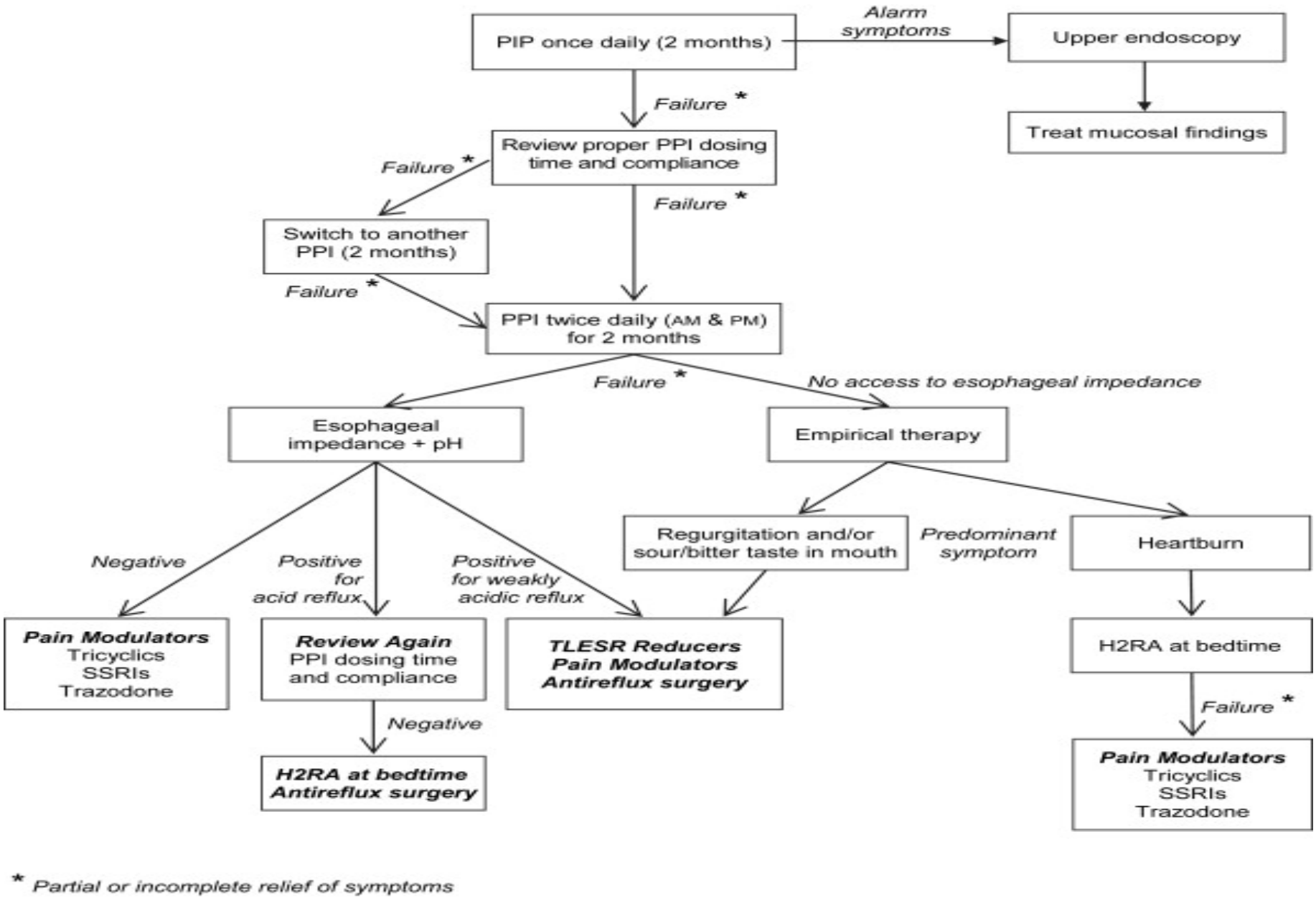
- 2) **Ambulatory 24-h esophageal pH monitoring**
- Allows for quantification of esophageal acid exposure and the relationship b/n symptoms and acid exposure.
- May test on or off PPI therapy
- In one study with refractory GERD, 31% and 4% with daily and BID PPI had abnormal pH test. Also another showed 32% and 16% respectively.

Diagnostic Tests

- 3) **Impedance-pH monitoring** allows for the detection of most reflux events and distinguishes b/n acidic, weakly acidic, and weakly alkaline reflux.
- Studies have shown that typical or atypical GERD symptoms while on PPI may be d/t non acid reflux.
- One study showed that refractory GERD pt on PPI bid- 68% of heartburn episodes were d/t weakly acid reflux.
- Doing study on PPI has more value and improves diagnostic yield by 15-20% resulting in better symptom correlation than pH testing alone.

Diagnostic Tests

- 4) Bilitec testing is the refluxate marker for bile reflux. Duodenogastro-esophageal reflux.



* Partial or incomplete relief of symptoms

Treatment

- 1) **Assuring compliance and adequate dosing time** should be the first management before any other intervention.
- 2) **Lifestyle modification**: wt loss and elevation of bed are effective in improving GERD.
- 3) **H2 blockers**: early studies showed that bed time use ↓ the # of nocturnal acid breakthrough

Treatment

- 4) **PPI**: These are the most efficacious. Doubling dose of PPI has become the standard if pt fails daily dose.
- 5) **Transient lower esophageal sphincter relaxation reducers**: baclofen reduces DGER and weakly acid reflux. (CNS related S/E's)
- 6) **Antireflux surgery**: refractory GERD is the MC indication for this (88%). Usually most typical pre-op s/s are regurgitation and heartburn with good 1 yr satisfaction rates 87%

Treatment

- 7) Acupuncture
- 8) Psychological Tx- treatment of anxiety and depression

Significance of Intragastric pH >4 in GERD

- Pepsin is inactive at pH >4
- Most bile acids and pancreatic enzymes inactive at pH >4
- Esophageal mucosa injury is rare at pH >4

Hunt. *Arch Intern Med*. 1999;159:649-657.
Smith et al. *Gastroenterology*. 1989;96:683-689.