PREVALENCE OF GERD
Defined by Symptoms

- Up to 40% of adults
- 50% of GERD patients have complicated disease
- Chronic disease in most

Erosive GERD Presentations in Practice

Esophageal –Typical Symptoms

- **Heartburn (nighttime/daytime)**
- **Extraesophageal regurgitation**

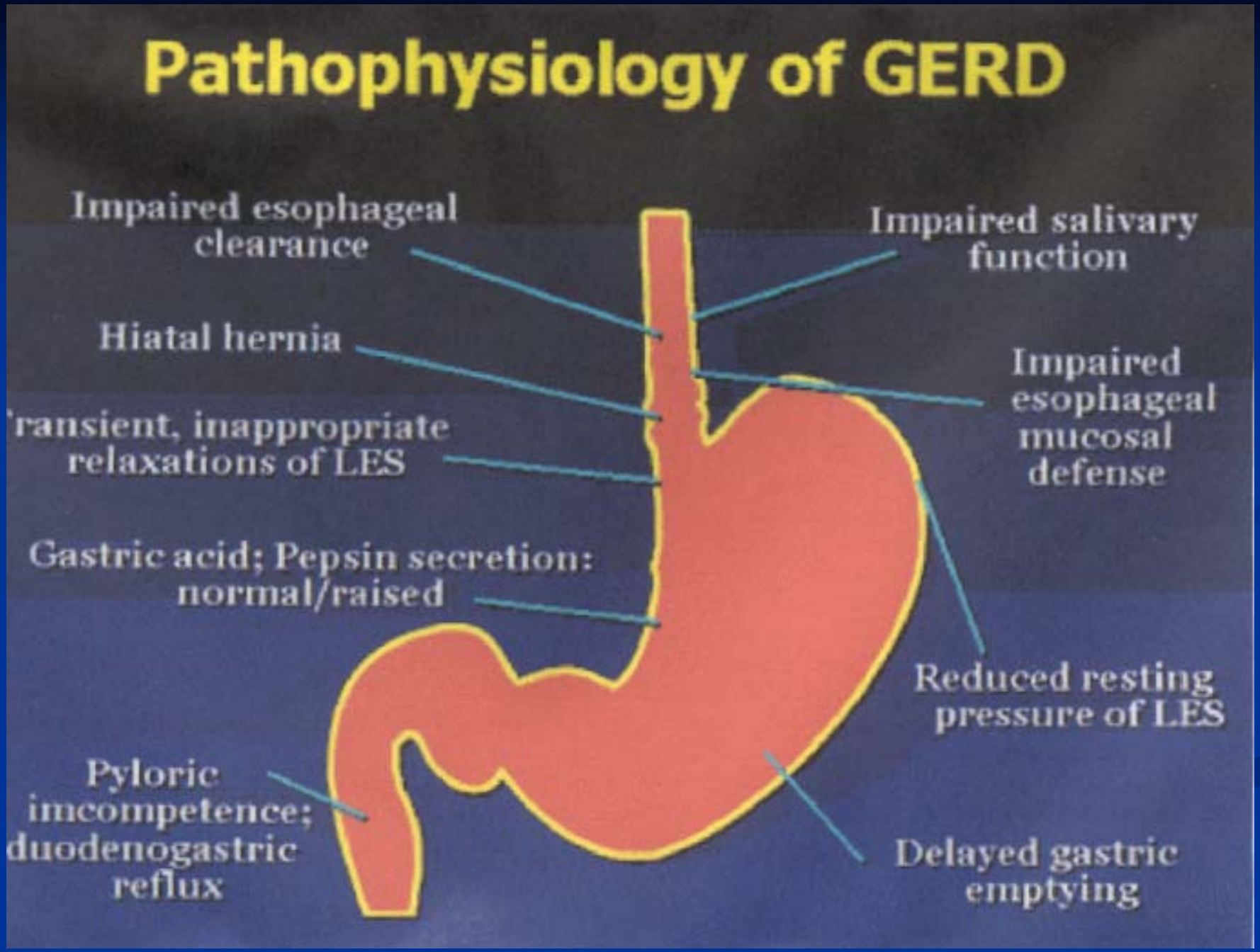
Extraesophageal – Atypical Symptoms

- **Dysphagia**
- **Bleeding (including occult)**
- **Noncardiac chest pains**
- **Hoarseness**
- **Cough, wheezing**
- **Asthma-like symptoms**

Untreated Complications

- **Peptic stricture**
- **Barrett's esophagus**
- **Esophageal adenocarcinoma**

Goyal, R.K., *Harrison's Principles of Internal Medicine*.14th ed. 1998:1588-1596. Beers, M.H., et al. *Merck Manual of Diagnosis and Therapy.* 17th ed.1999:232. Garnett, W.R. et al. *Pharmacotherapy.*1997:17:938-958. Kahrilas, P.J., *JAMA*. 1996:276:983-988.


Pathophysiology of GERD
Impaired esophageal clearance
Impaired salivary function
Hiatal hernia
Impaired esophageal mucosal defense
ransient, inappropriate relaxations of LES
Gastric acid; Pepsin secretion: normal/raised
Reduced resting pressure of LES
Pyloric imcompetence; duodenogastric reflux
Delayed gastric emptying

Gastroesophageal Reflux

Damage correlates with duration of reflux exposure

AND

Caustic potential of refluxed material

Mechanism of Reflux

- Transient decrease in LES with normal baseline
  - Truly hypotensive sphincter
    - Hiatal hernia

Protection from Reflux

- Protection from reflux afforded by esophageal acid clearance

  Prolongation of clearance time occurs in 50% of GERD patients

THE GERD SPECTRUM

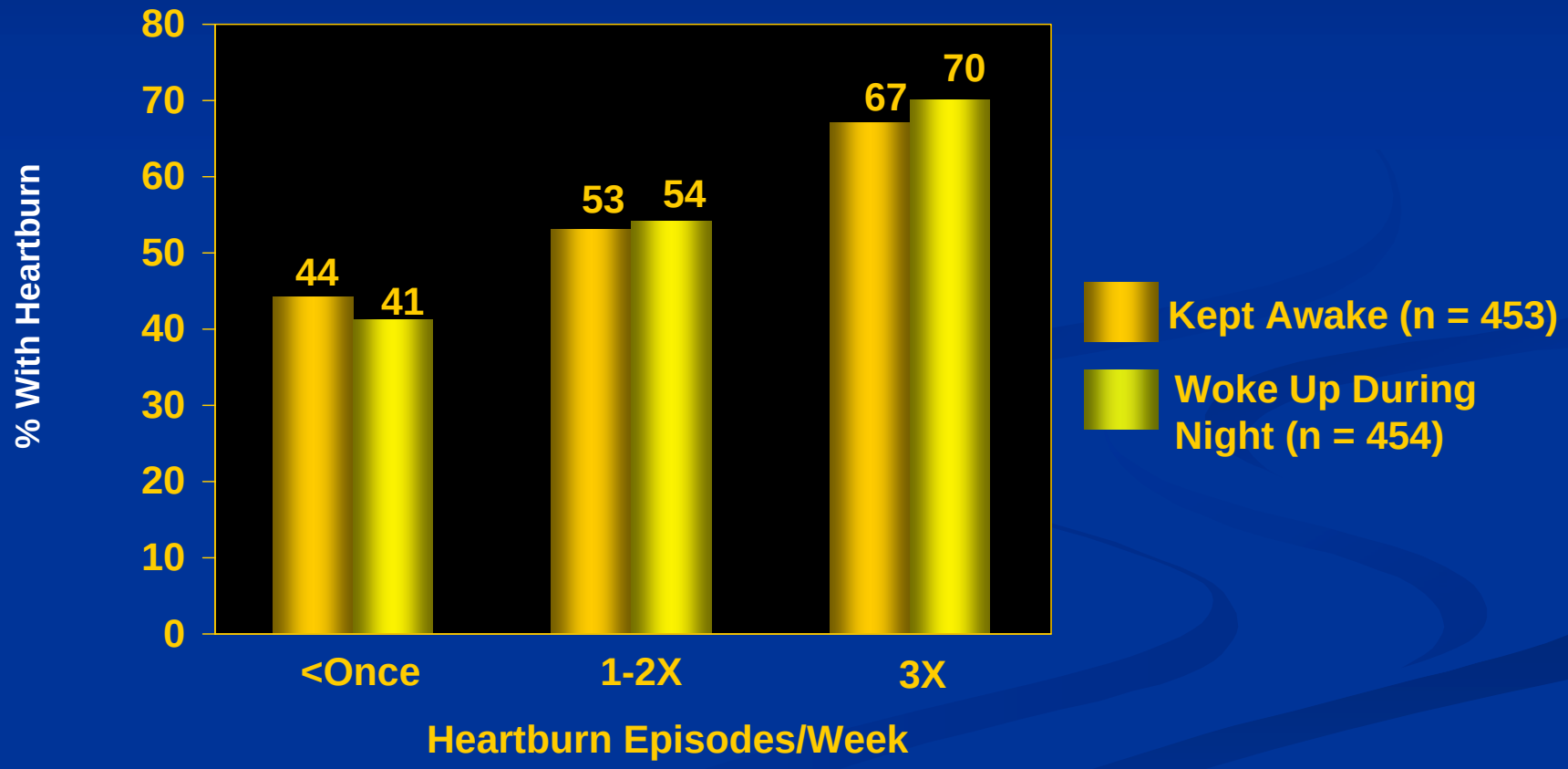
Typical Manifestations (Heartburn/Regurgitation)	Atypical Manifestations*	Complications
With Erosive Esophagitis Without Esophagitis*	Angina-like Pain Asthma/Cough Laryngitis	Ulceration Stricture Metaplasia (Barrett's)

* Requires Abnormal pH-metry

Clinical Manifestations

- Heartburn
- Regurgitation
- Chronic Coughing

Impact of heartburn during sleep



The Gallup Organization. May 2000:26-27.

Role of Endoscopy

Alarm symptoms

Dysphagia

Odynophagia

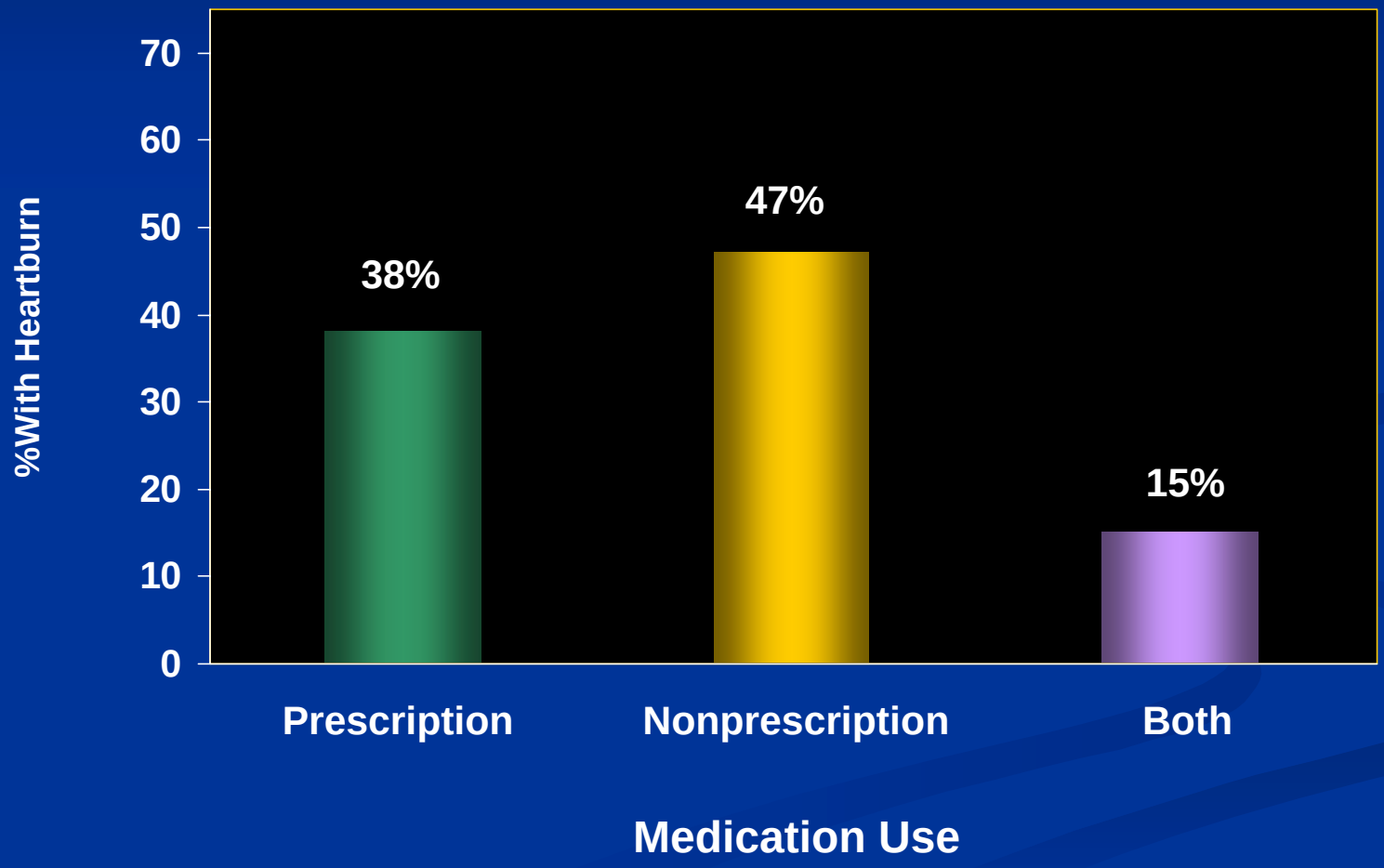
Bleeding

Chest pain

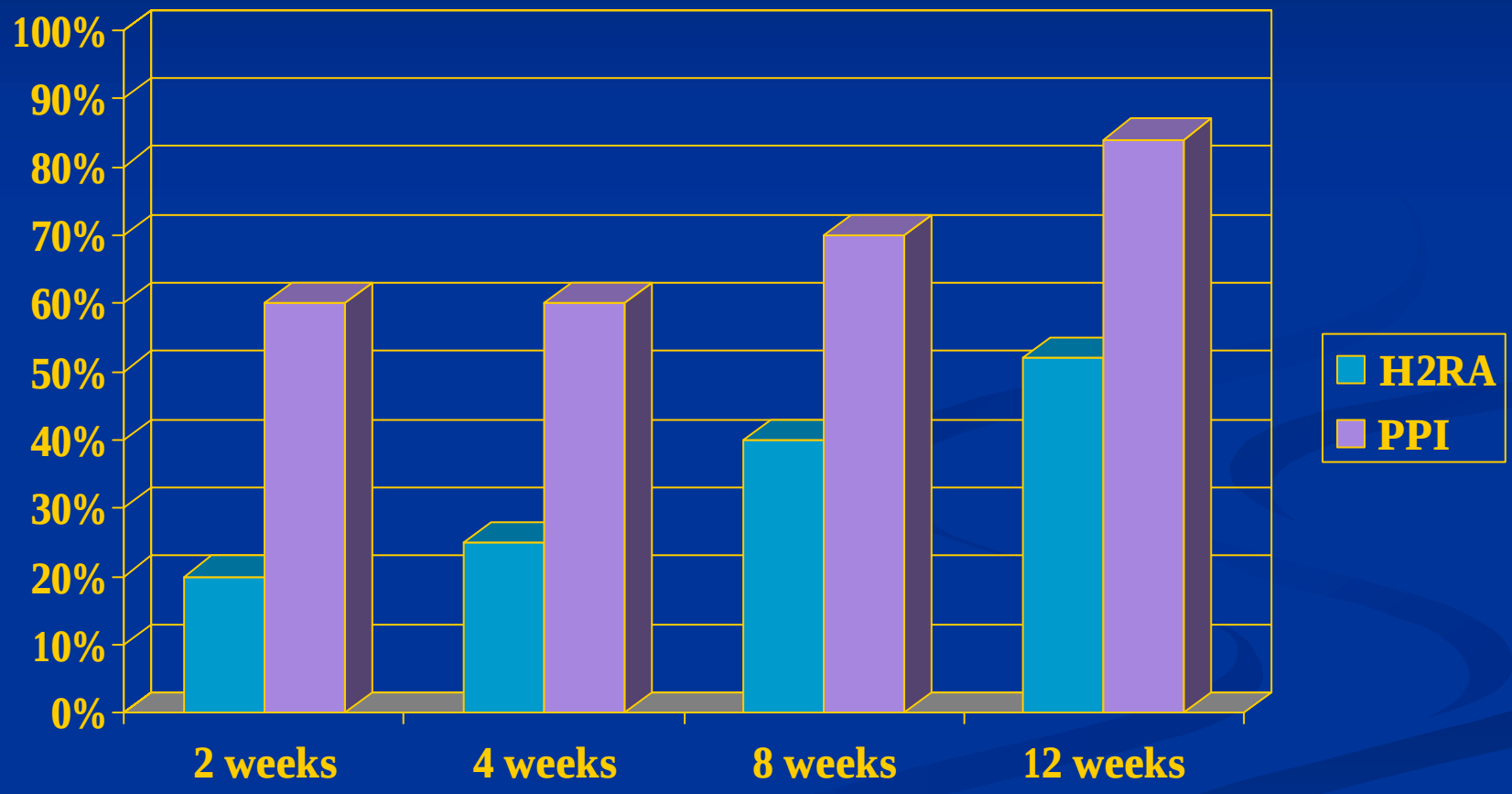
Supraesophageal symptoms

Use of Medication for Heartburn

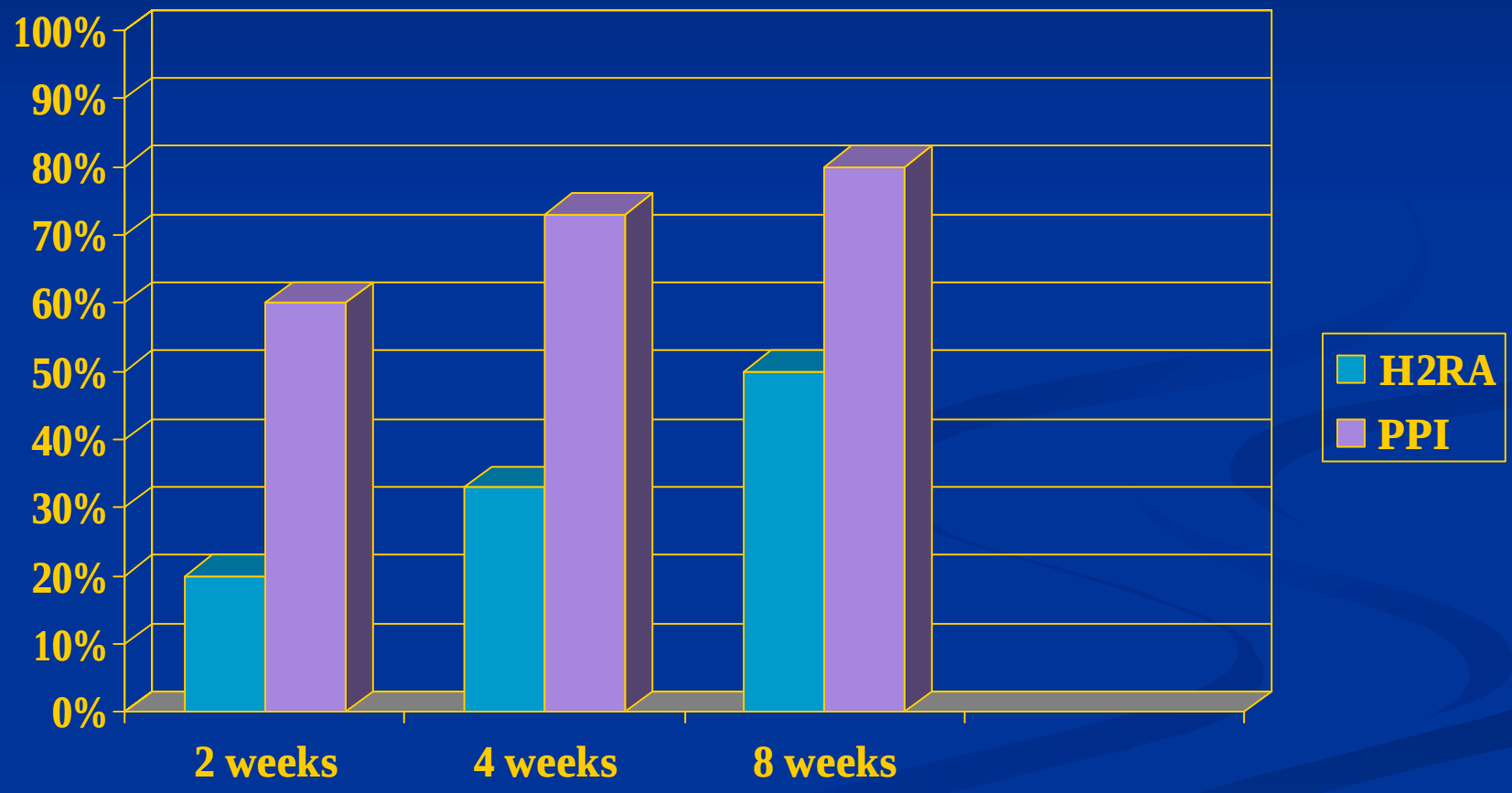
(n = 1,000)



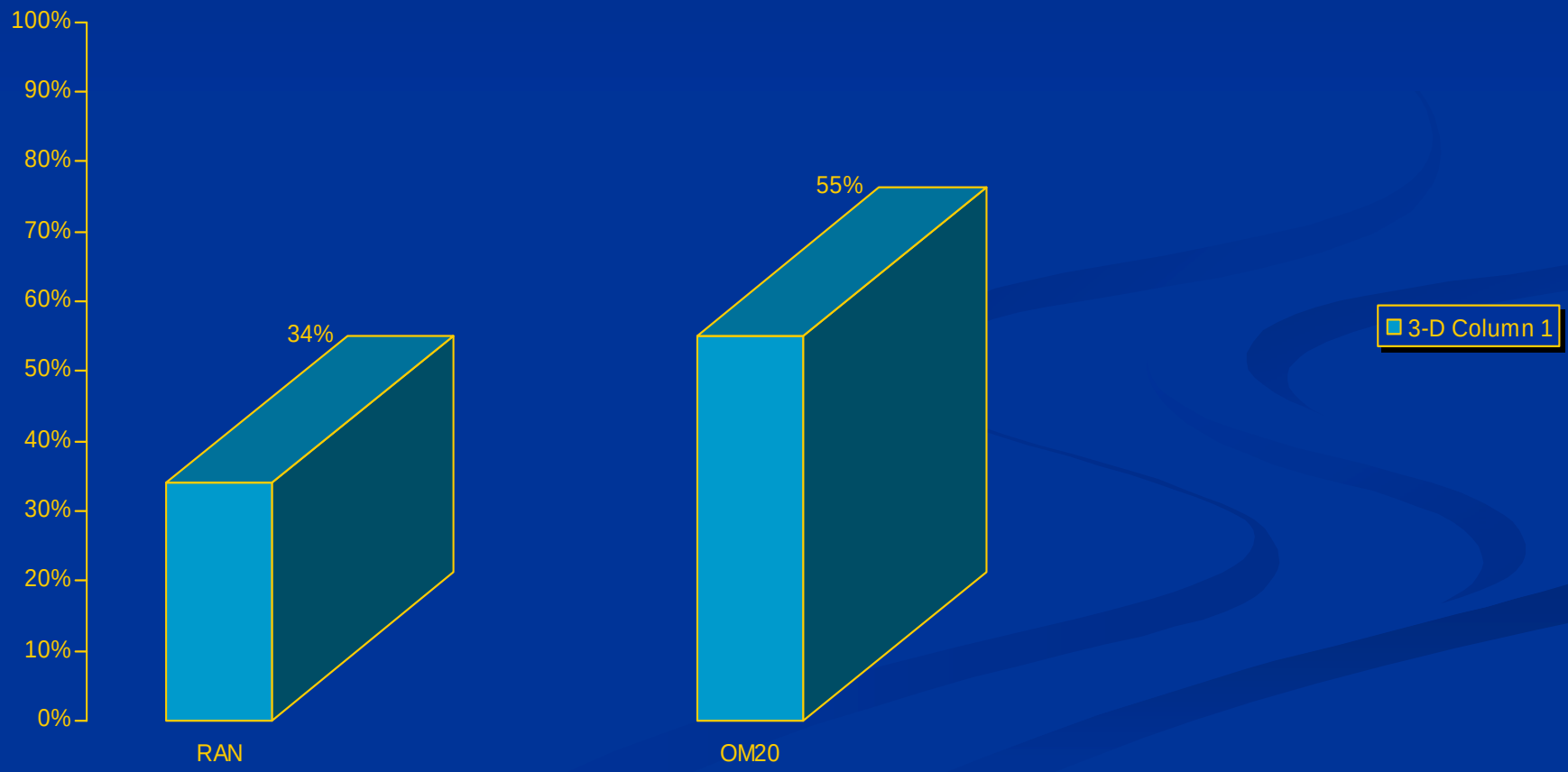
Healing of Erosive Esophagitis



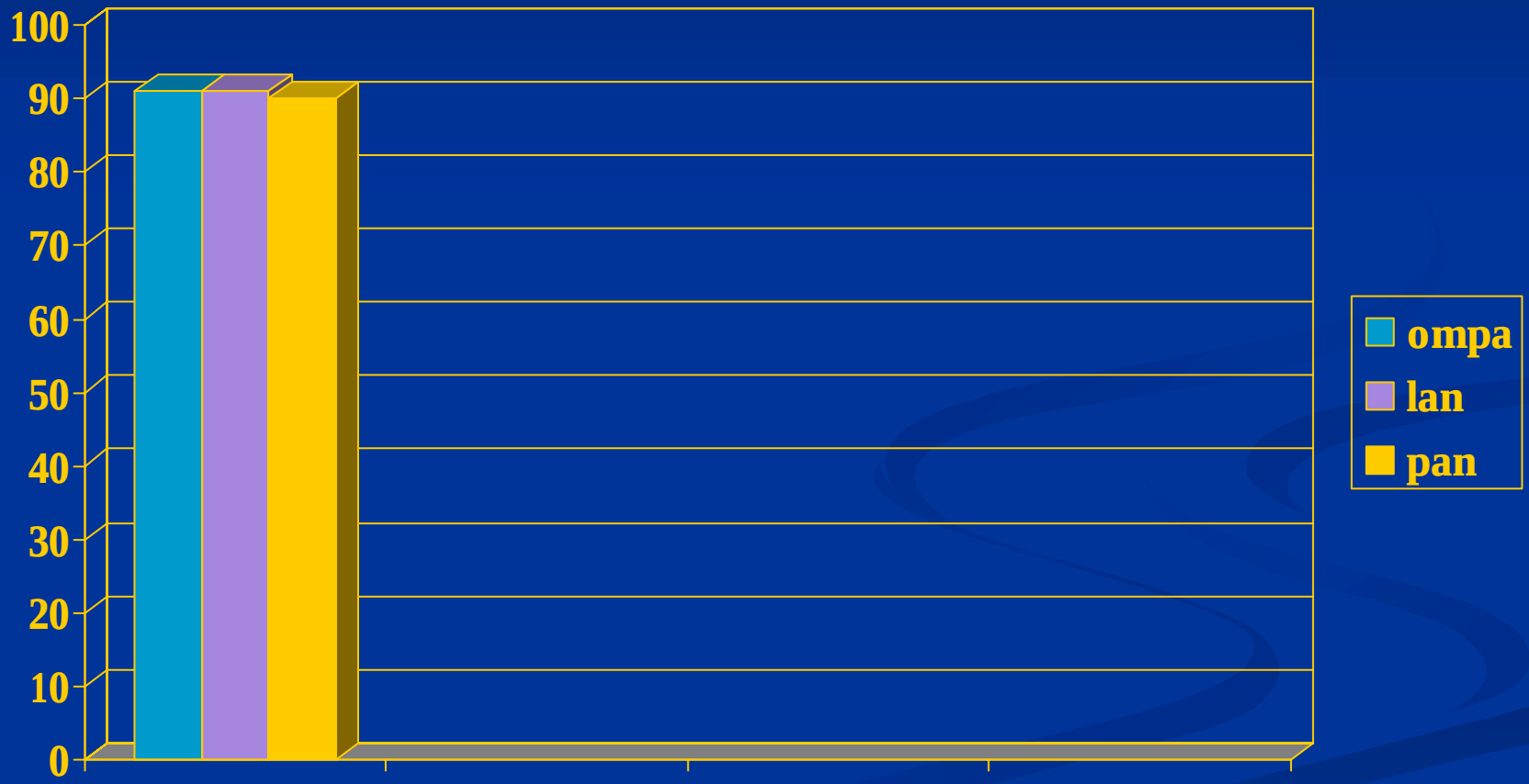
Relief of Heartburn

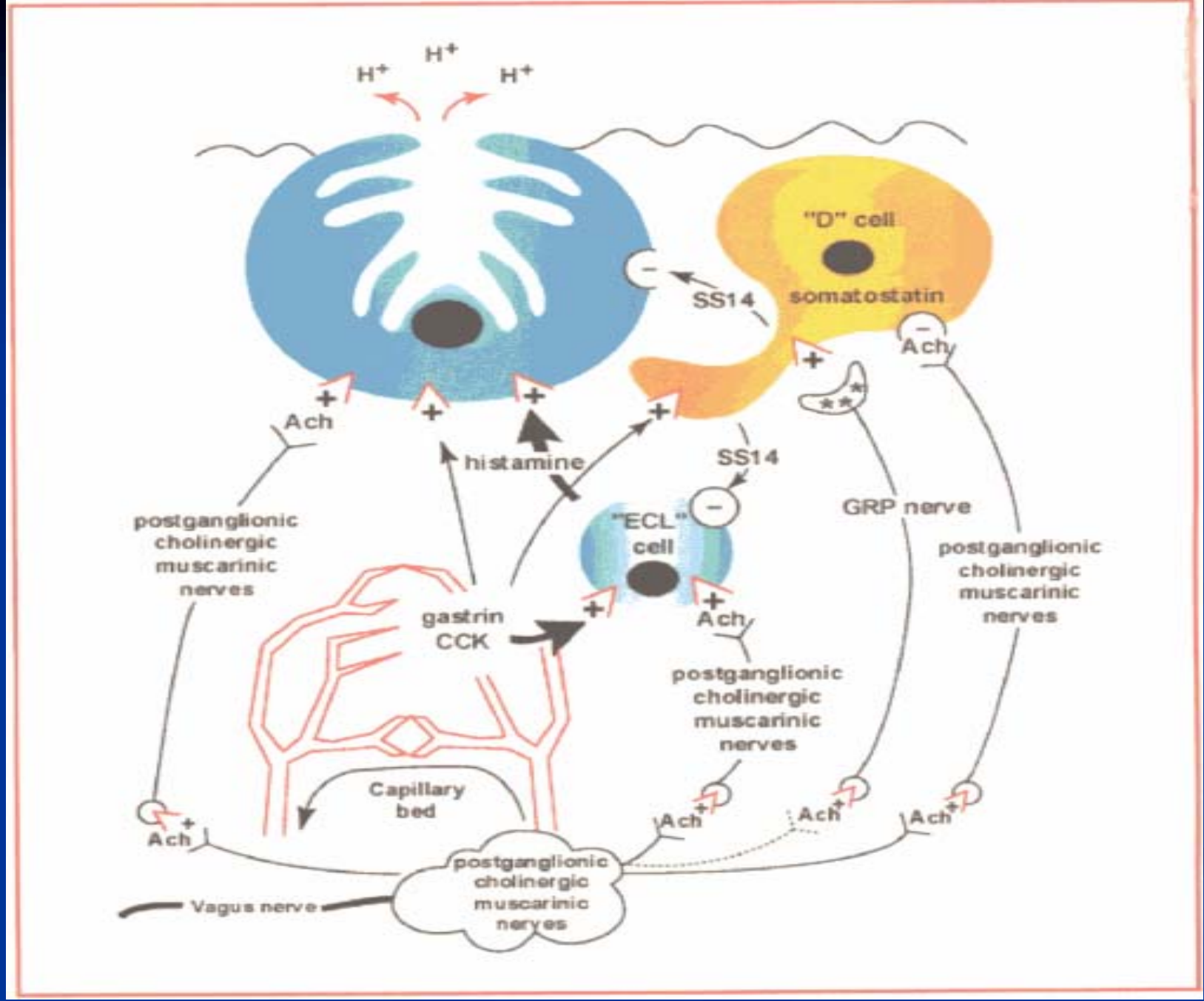


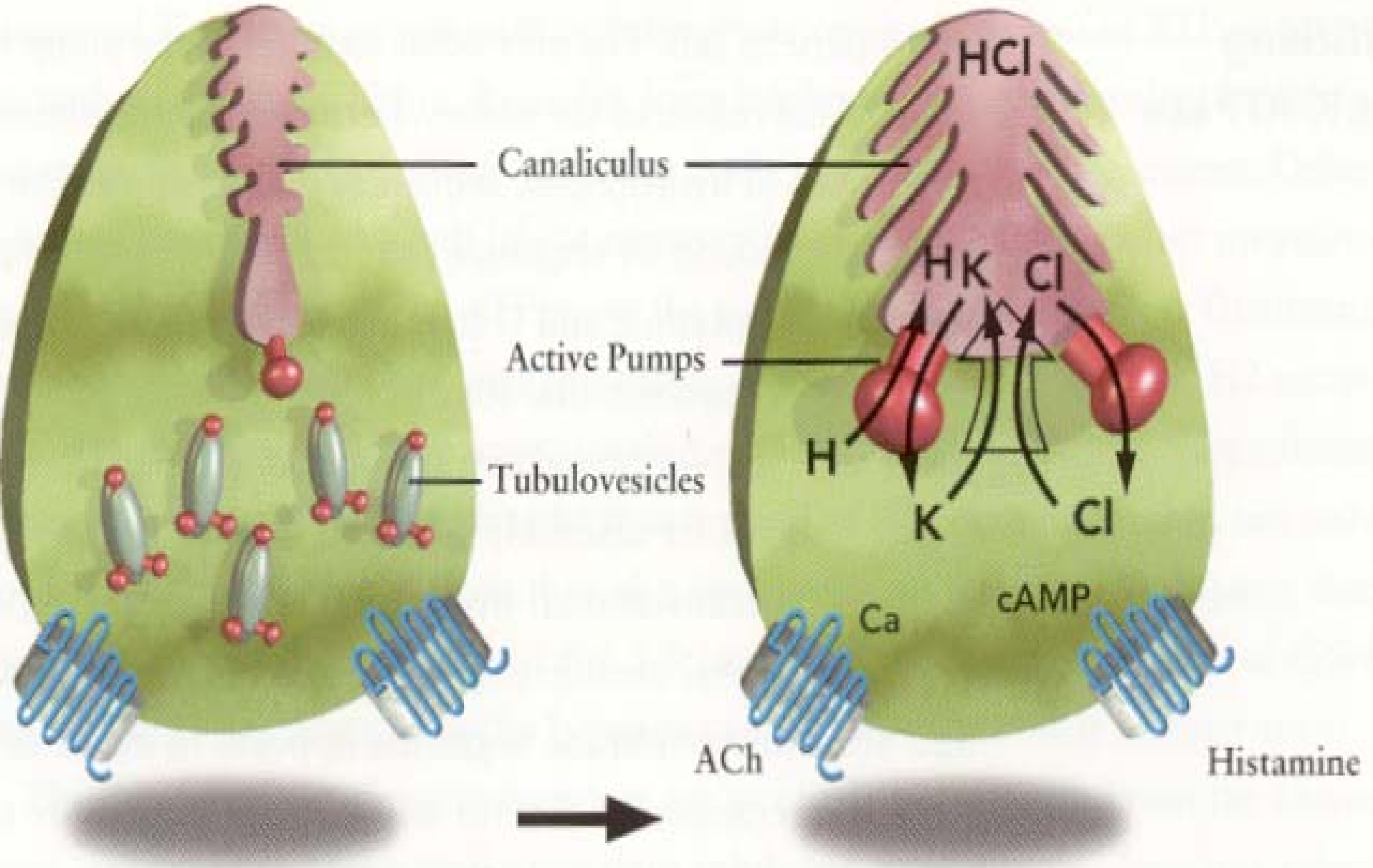
PPI v. H2RA in Maintaining Remission



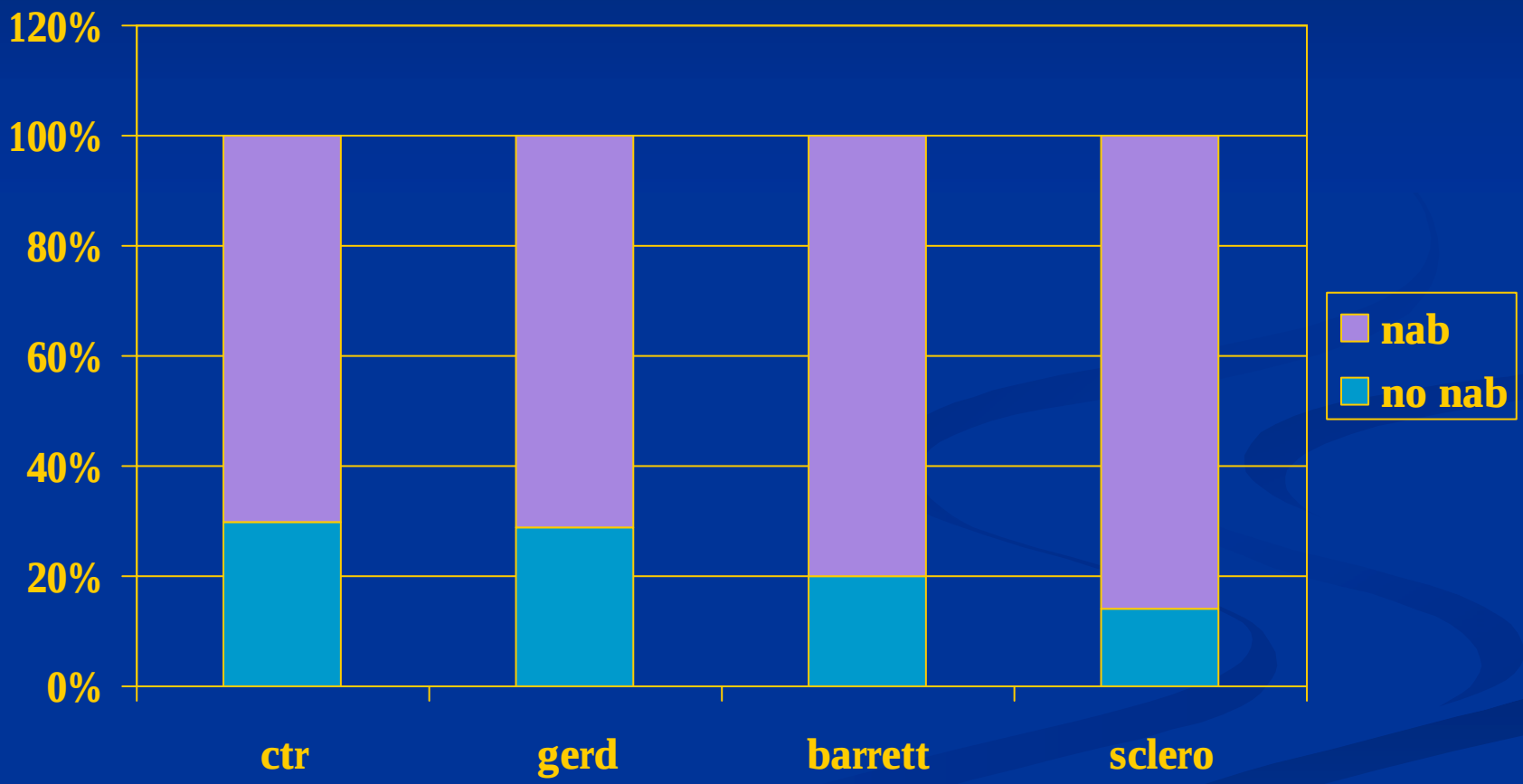
Healing of Erosive GERD



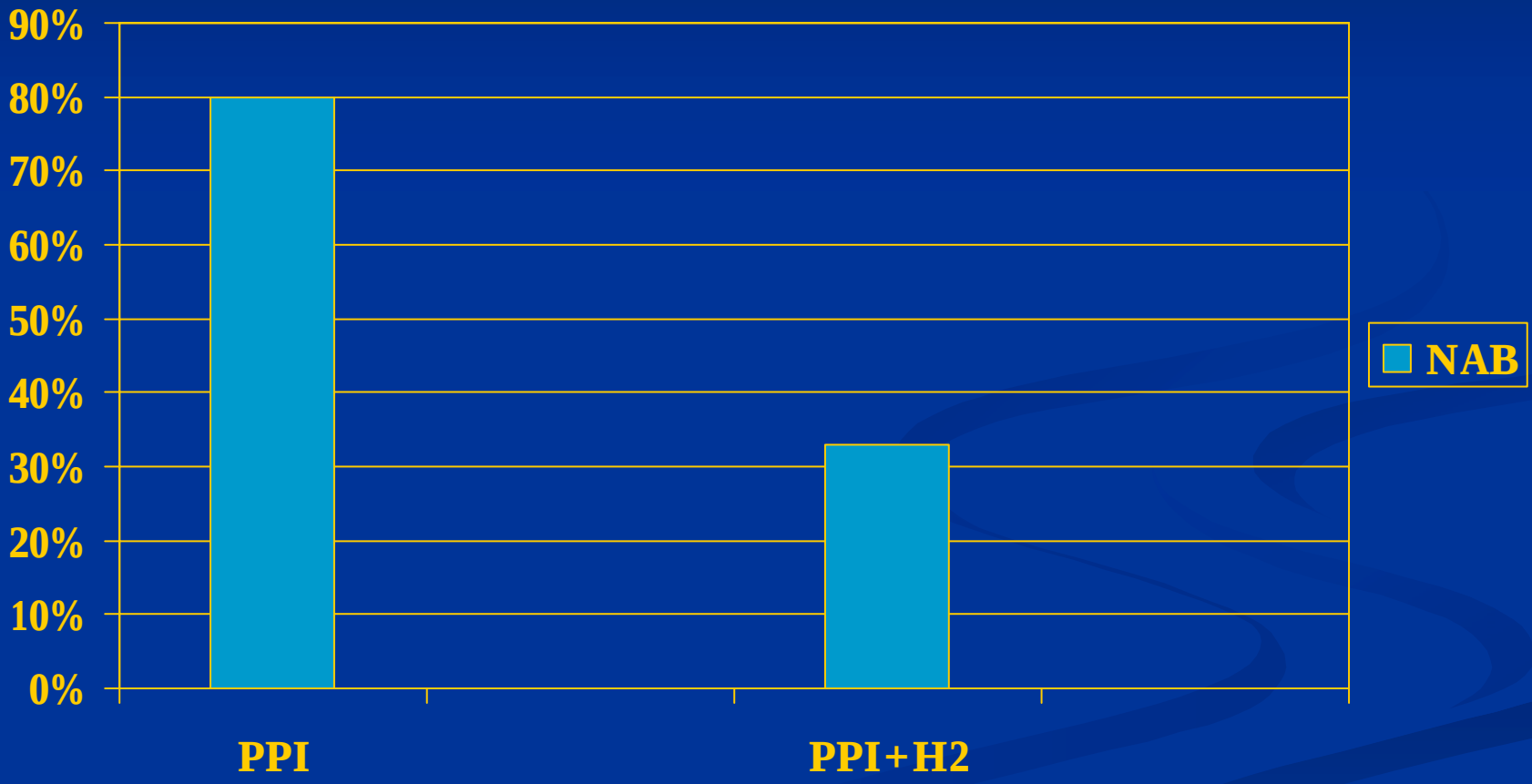

H+
H+
H+
"D" cell
somatostatin
SS14
Ach
Ach
histamine
SS14
GRP nerve
postganglionic
cholinergic
muscarinic
nerves
"ECL"
cell
gastrin
CCK
Ach
postganglionic
cholinergic
muscarinic
nerves
postganglionic
cholinergic
muscarinic
nerves
Capillary
bed
Ach
Ach
Ach
Ach
postganglionic
cholinergic
muscarinic
nerves
Vagus nerve


Canaliculus
Active Pumps
Tubulovesicles
HCl
HK Cl
H
K
Cl
cAMP
Ca
ACh
Histamine

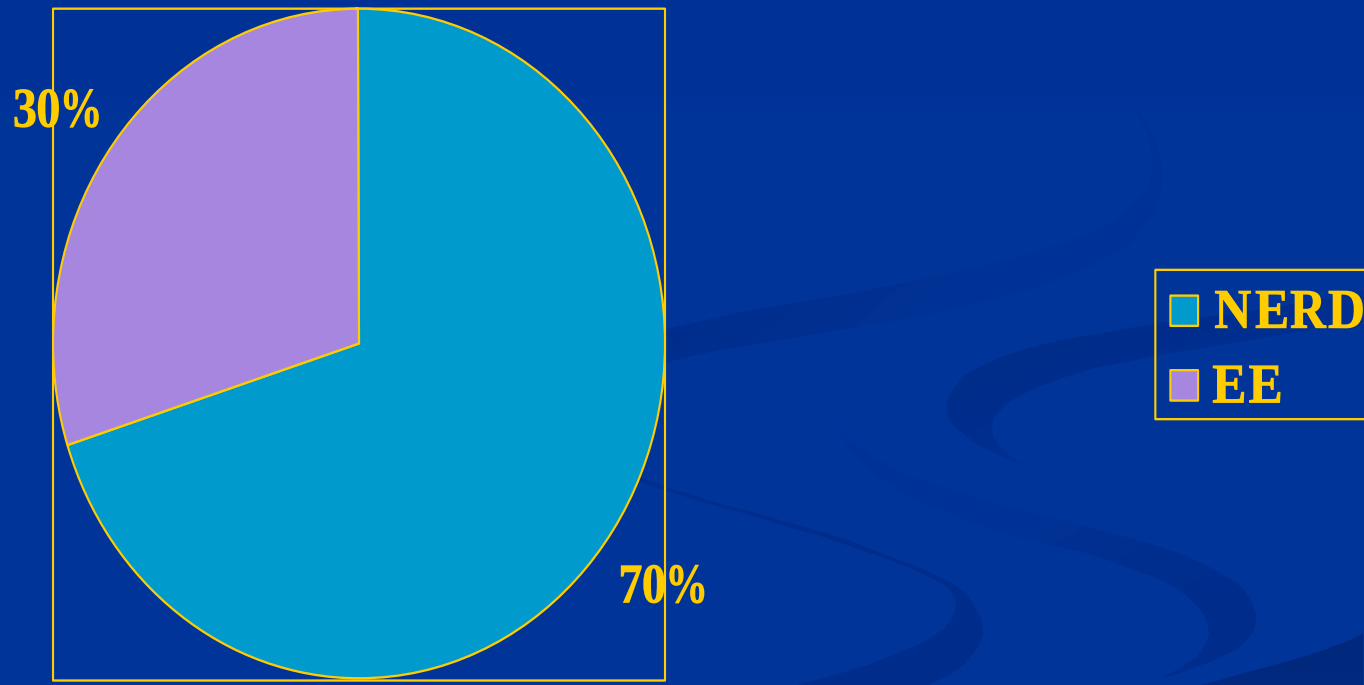
Nocturnal Acid Breakthrough



NAB in GERD



Nonerosive Reflux Disease



NERD v. EE

Heartburn severity is similar

Response to Rx is 10–30% less

Rarely have typical complications but rather atypical complications/symptoms

24 hr esophageal pH studies normal in 50%

Heartburn and Normal Endoscopy

- Abnormal acid exposure
- Functional heartburn
- Hypersensitive v. not acid reflux

GERD and the OLDER Patient

- Frequency

- Factors that influence
  - LES pressures
  - Acid clearing time
  - Hiatal hernia

WARNING

- Older patient less likely to report heartburn
- More likely to have dysphagia, chest pain, or vomiting

Severity of symptoms does not correlate with the degree of esophagitis therefore lower threshold to do endoscopy

Barrett's Esophagus

- Columnar epithelium replaces the squamous epithelium in the distal esophagus when reflux disease damages the mucosa and healing occurs through a metaplastic process. This columnar epithelium is a form of intestinal metaplasis that is prone to develop adenocarcinoma.

Treatment

- Symptom Relief
  - PPIs
- Complications
  - Erosions, ulcers, strictures
  - Progession of metaplasia
- Effective acid suppression one step forward
  - Mucosal ablation may be key

Treatment of Reflux in Barrett's

- Rationale

Exposure to esophageal acid activates protein kinase pathways that increase proliferation and decrease apoptosis.

Markers of proliferation were reduced in esophageal biopsies when acid was normalized by PPI.

? Screen GERD for Barrett's ?

- EGD in GERD
- 3 to 5% have long segment
- 10 to 15% have short segment

- Who to screen ?
- White males > 50 with Gerd > 5 yrs.

Dysplasia

- HGD associated with cancer 30-40%

- ACG Recommendation
- No dysplasia q 3 yr
  Low grade q 6 mo. x 2
- No progression then q 1 yr.

Surveillance

- Treat aggressively prior to bx's
  - HGD get 2nd opinion
- Surgery v. survey q 3 mo.

Surveillance Initial Dx

patients	19	58
stage 0-1	58 %	17 %
5-yr. survival	62 %	20 %

Barrett's and Surgery

- 10 studies with 408 patients
- 86% Segment unchanged
- Equal numbers regressed/progressed

Mucosal Ablation

Photodynamic therapy (PDT)

100 patients

Barrett's undetectable in 43

Eradication HGD 88%

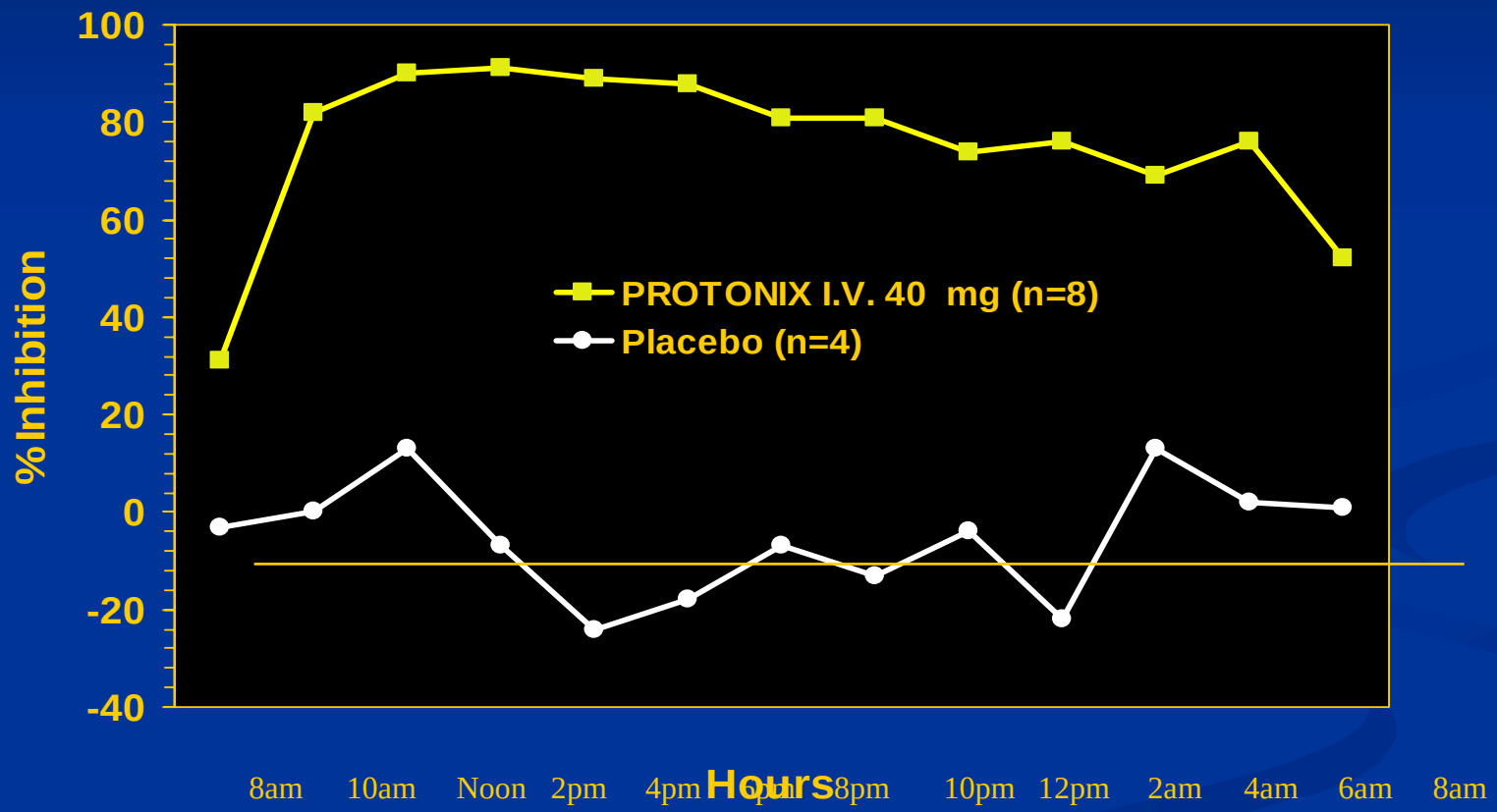
Eradication LGD 92%

Ablative Therapy

Endoscopic mucosal resection

(EMR)

Protonix 40 mg I.V. vs. Placebo



*pentagastrin stimulated

Data on file, Wyeth-Ayerst Laboratories. Study 100-US.
Pisegna JR et al. *Am J Gastroenterol*. 1999;94:2874-2880.