THE CORRELATIONS BETWEEN DYSPEPSIA, PEPTIC ULCER AND HELICOBACTER PYLORI

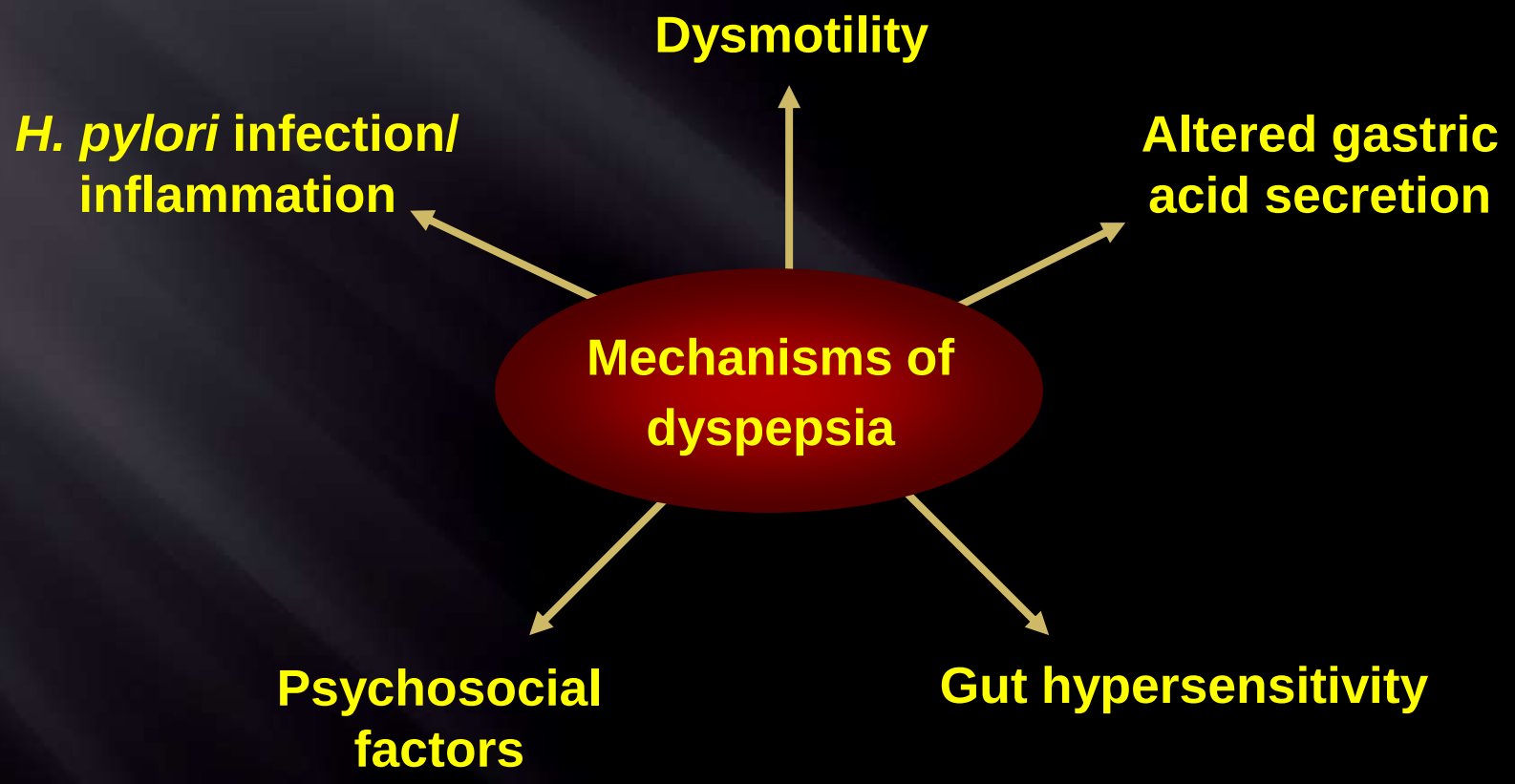
Erwin Budi Cahyono

DYSPEPSIA

- DEFINITION :

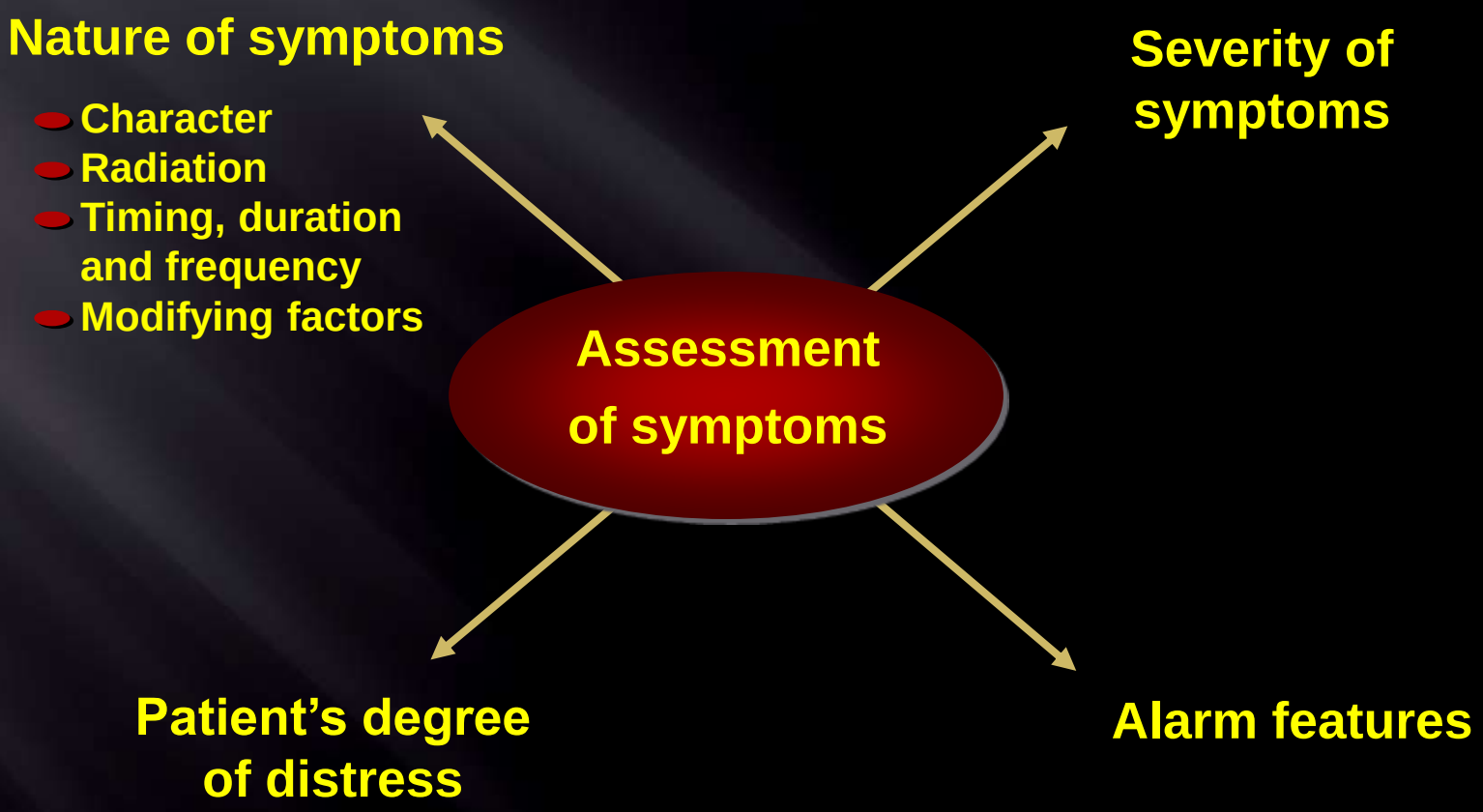
  Symptoms like pain or nausea in epigastrium accompanied by disgust, vomit, bloat, easy to full, fullness or nitre, which is suspected come from the abnormality of upper gastro-intestinal tractus.

Dyspepsia: pathogenic mechanisms



Witteman & Tytgat, *Netherlands J Med* 1995; **46**: 205–11.
Talley *et al*., *BMJ* 2001; **323**:1294–7.
Tack *et al*., *Curr Gastroenterol Rep* 2001; **3**: 503–8.

Dyspepsia: symptom assessment



Paré, *Can J Gastroenterol* 1999; **13**: 647–54.

Classification

- *acute dyspepsia (new onset dyspepsia)*
  - Suddenly Sigh with the quality of sigh which is usually more tremendous with a longer response to the medication.
- *chronic dyspepsia*
  - Sigh which is sometimes disappear, sometimes appear, more than two weeks. The sigh is not as tremendous as acute dyspepsia with a quick response to the medication.

Ethiology

- **Organic Dyspepsia :**
  - There is an organ abnormality as ulcer gastro-duodenal, gastro esofageal reflux and gastric carcinoma (Talley, 1998)

Functional Dyspepsia

- A common term which is given to the patient as : abdominal pain or nausea on the upper of stomach which is repeatedly happen more than three months, and at least a long of that time 25% symptoms of dyspepsia appear and no evidence organic disease which is responsible to that symptoms clinically, biochemistrically, endoscopy and ultrasonografy (Talley *et al*, 1991). But, patient with gastritis and duodenitis non erosif is included in this term (Hu & Kren, 1998)

Rome III Diagnostic Criteria for Functional Dyspepsia

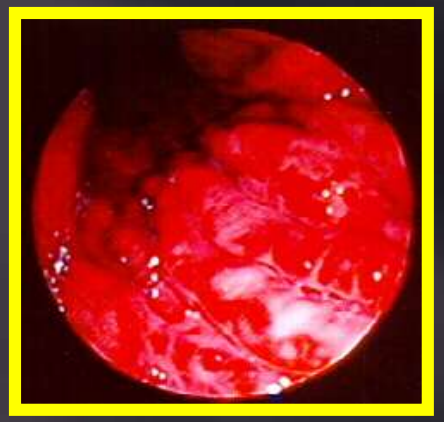
Functional Dyspepsia
At least 3 months, with onset at least 6 months previously, of 1 or more of the following: • Bothersome postprandial fullness • Early satiation • Epigastric pain • Epigastric burning And •No evidence of structural disease (including at upper endoscopy) that is likely to explain the symptoms

Rome III Diagnostic Criteria for Epigastric Pain Syndrome

Epigastric Pain Syndrome
At least 3 months, with onset at least 6 months previously, with ALL of the following: Pain and burning that is: • intermittent • localized to the epigastrium of at least moderate severity, at least once per week, • and NOT: generalized or localized to other abdominal or chest regions 2. relieved by defecation or flatulence 3. fulfilling criteria for gallbladder or sphincter of Oddi disorders

Rome III Diagnostic Criteria for Postprandial Distress Syndrome

Postprandial Distress Syndrome
At least 3 months, with onset at least 6 months previously, of 1 or more of the following: • Bothersome postprandial fullness 1. occurring after ordinary-sized meals 2. at least several times a week • Early satiation 1. that prevents finishing a regular meal 2. and occurs at least several times a week



GASTRITIS

- Peradangan mukosa lambung (Dx PA)
- Gastroskopi: eritema, edema, erosiva
- Klinik: keluhan dispepsia

- Sering dijumpai dalam klinik:
  - Gastritis antrum, Gastritis erosiva,
  - Gastritis hemoragika, Gastritis atropik,

- Penyebab:
  - infeksi Helicobacter pylori, OAINS,
  - refluks empedu, obat lain, stress, alkohol

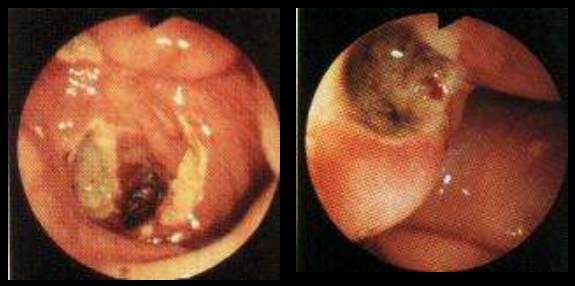
ULKUS PEPTIK

- **Ulkus Peptik**
  - **Kerusakan (luka) mukosa, besar (≥ 5mm) dan dalam (≥ submukosa), sifat jinak**
  - **Gastroskopi: bentuk ulkus**
  - **Klinik: keluhan dispepsia**

- **Pembagian berdasarkan lokasi kelainan:**
  - **Ulkus Esofagus**
  - **Ulkus Gaster**
  - **Ulkus Duodenum**

Diagnosis

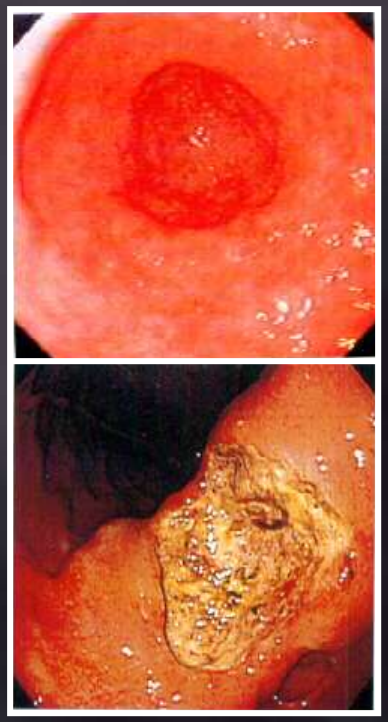
1. **Keluhan / gejala**
   - ** Sindroma Dispepsia*
   - ** Komplikasi: muntah, muntah/berak darah, nyeri hebat.*
2. **Tanda fisik**
   - ** Tidak jelas, nyeri tekan uluhati (hebat – komplikasi)*
3. **Radiologi (foto seri SCBA)**
   - ** Kontras tunggal akurasi rendah, sebaiknya kontras ganda*
   - ** Gastritis (edema, hipersekresi), Ulkus (niche/ kawah ulkus)*
4. **Gastroskopi**
   - ** Diagnosis utama, akurasi >95%,*
   - ** Dx. endoskopi, biopsi (PA, CLO, dll.)*

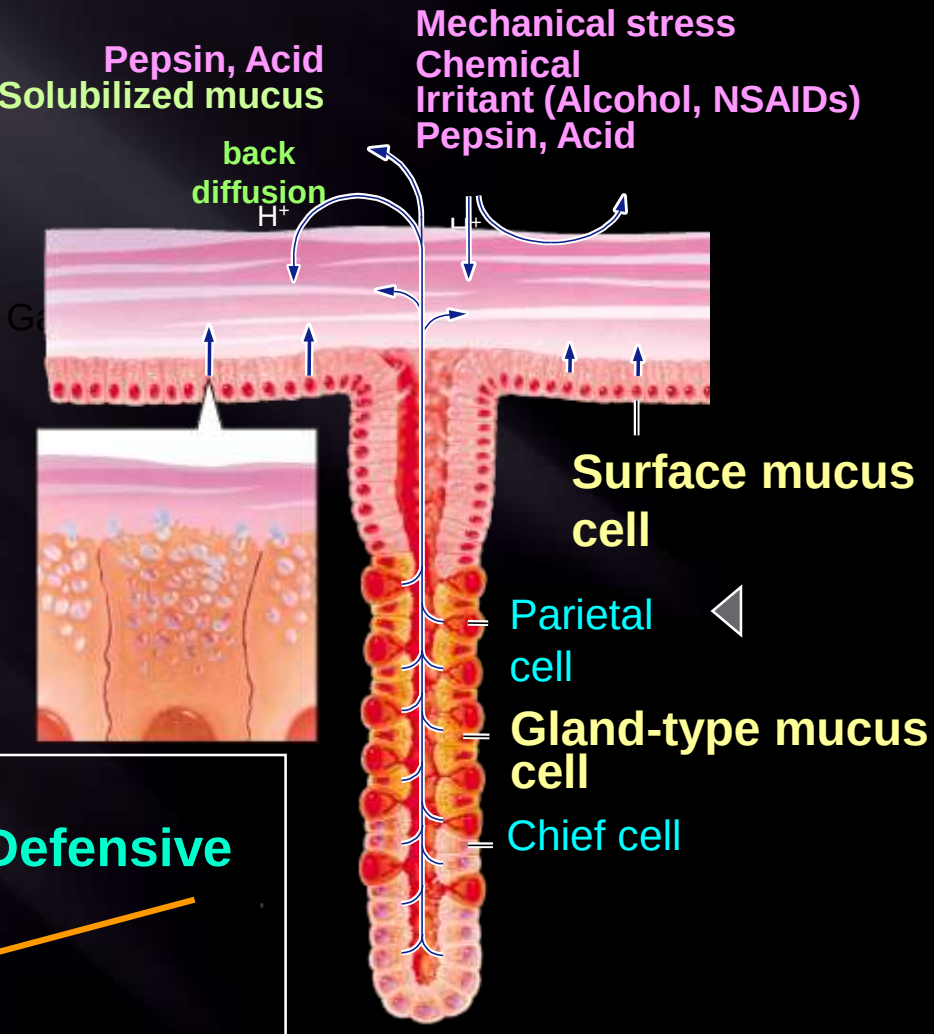


Pathophysiology of peptic ulcer diseases

Pathophysiology of peptic ulcer disease

Multiple causes of gastritis/ peptic ulcer disease

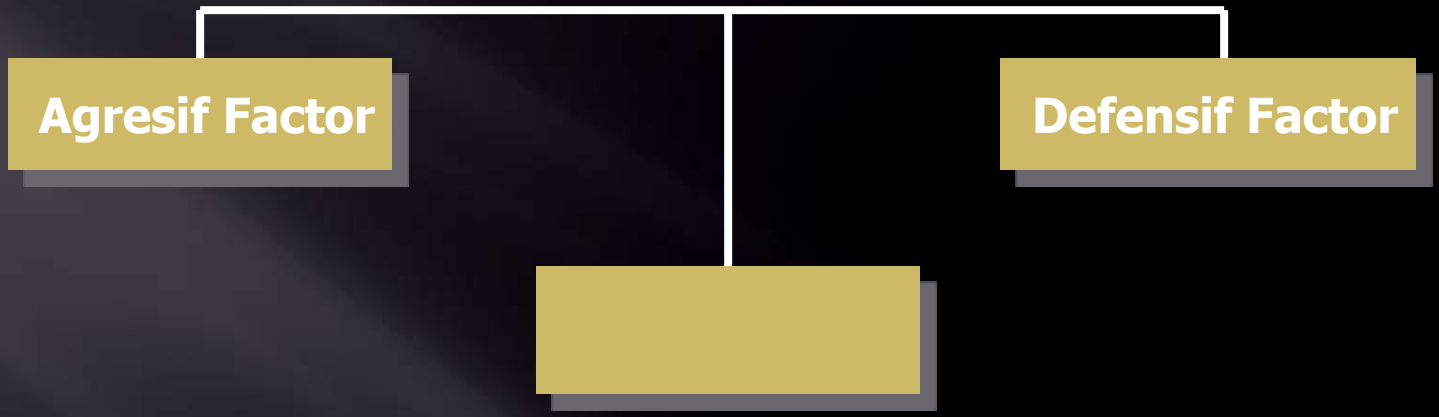




Shay & Sun's balance theory

Defensive

Aggressive



- Agresif Factor
  - Gastric Acid
  - Pepsin
  - Refluxs bile
  - Nicotin
  - Alcohol
  - Antiinflamation nonsteroid medicine
  - Cortikosteroid
  - *Helicobacter pylori*
  - *Free radical*

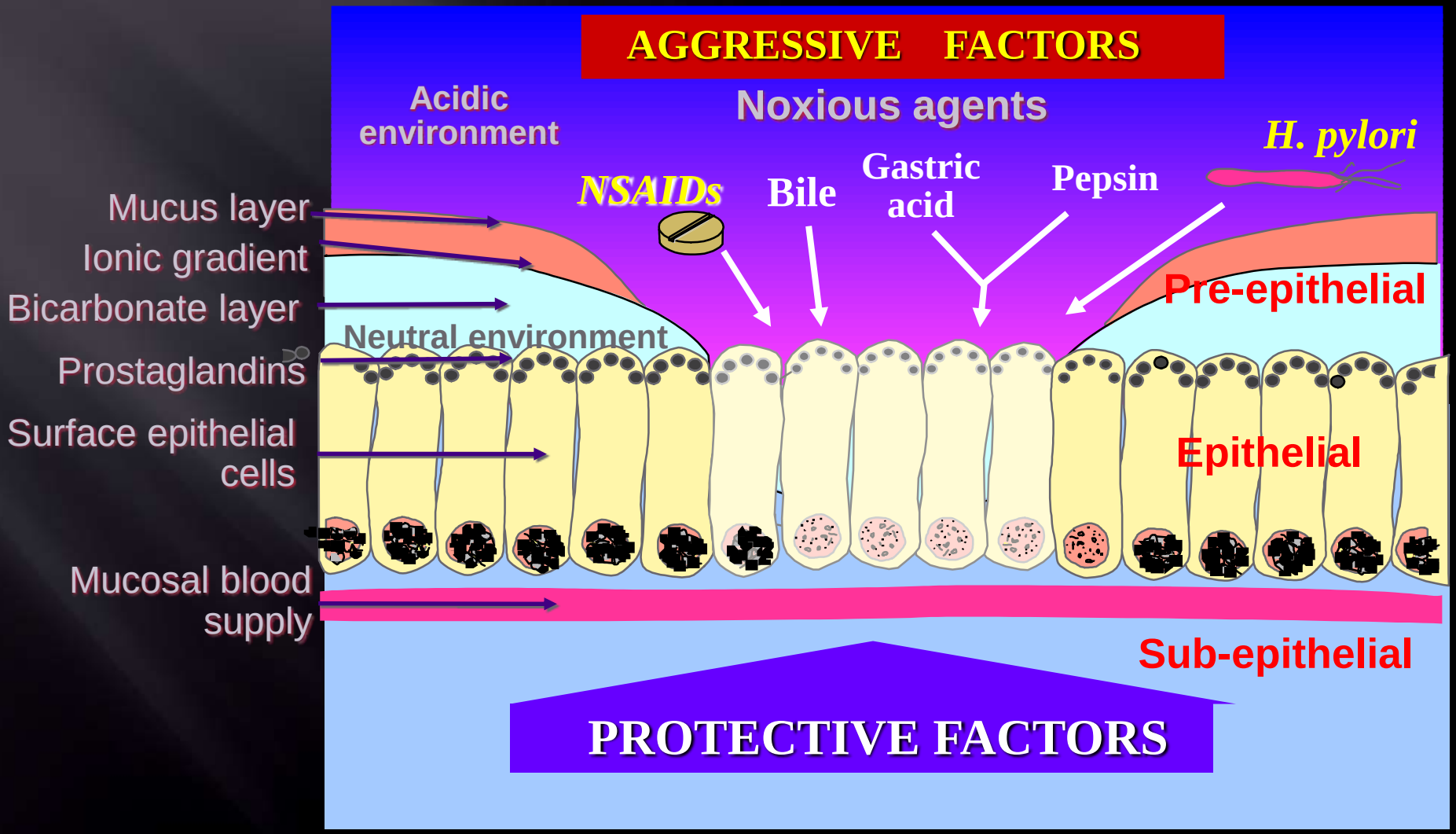
❑ Defensif Factor

Mucosa blood current (microsirculation)
Superficial epithel cell
Prostaglandin
Fosfolipid/*Surfactans*
Musin
Bikarbonat
Motilitas

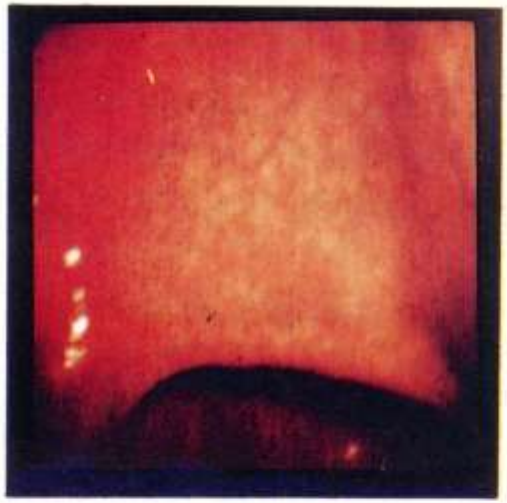
Diagram of the equlibrium theory of integration gastro-intestinal tractus mucosa especially gastric & duodenum

Pathophysiology of peptic ulcer disease

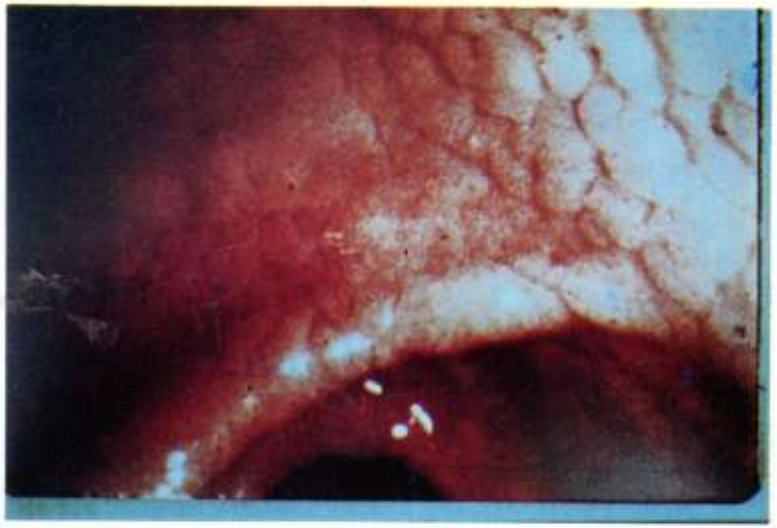
Imbalanced between aggressive factors and protective factors



Gastritis



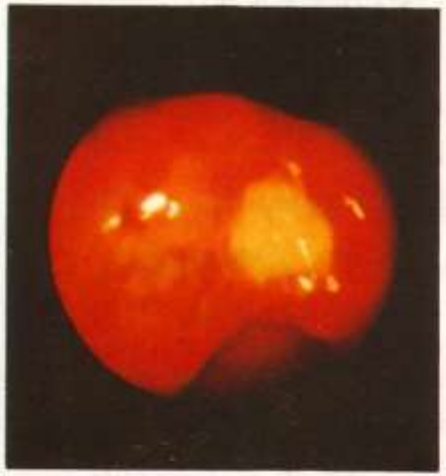
Gambar 8-3. Gastritis kronis atropik



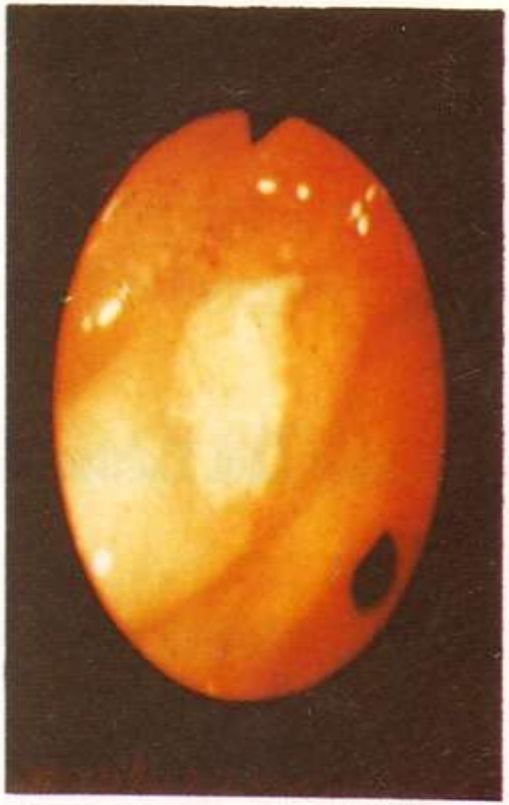
Gambar 8-4. Gastritis kronik hipertropik

Ulkus peptikum

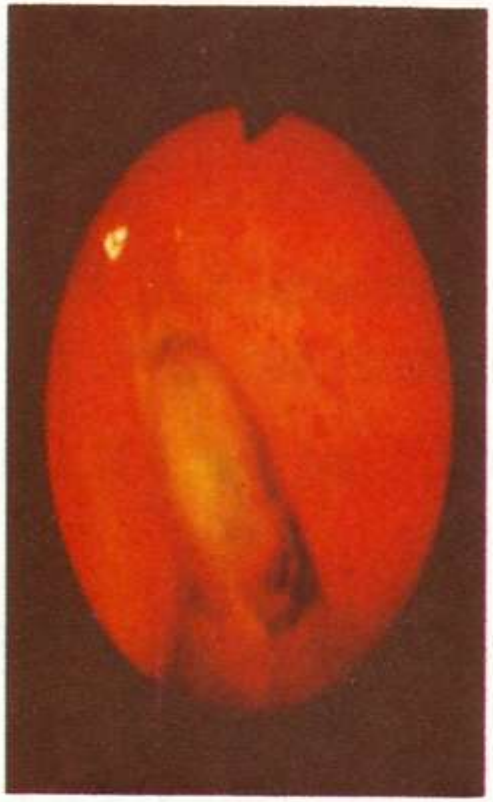
Gambar 9-1. Tukak peptik jinak sekitar angulus



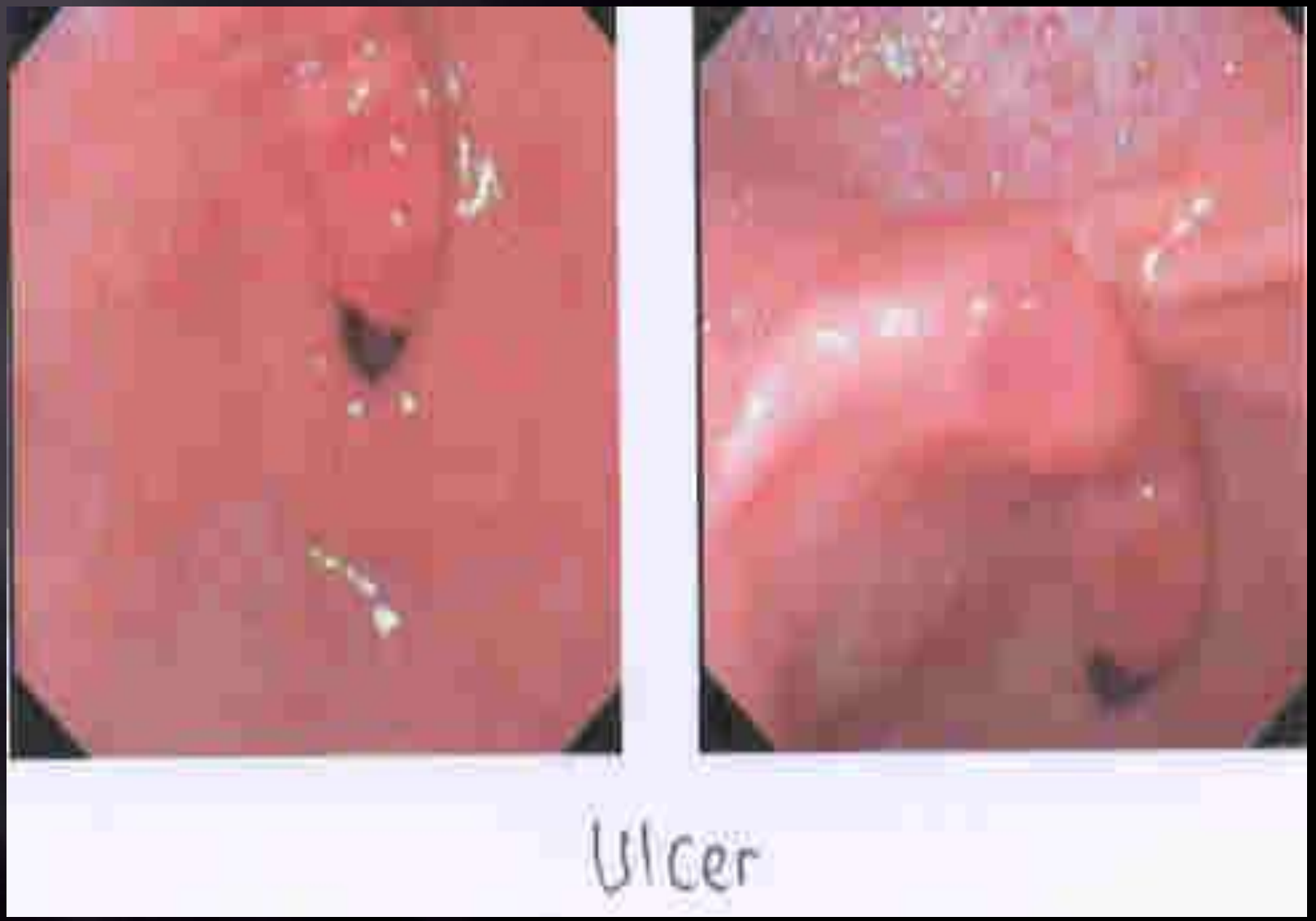
Gambar 9-2. Tukak lambung, bentuk bulat batas tajam, rata, dasar tertutup massa putih kekuningan, stadium aktif.

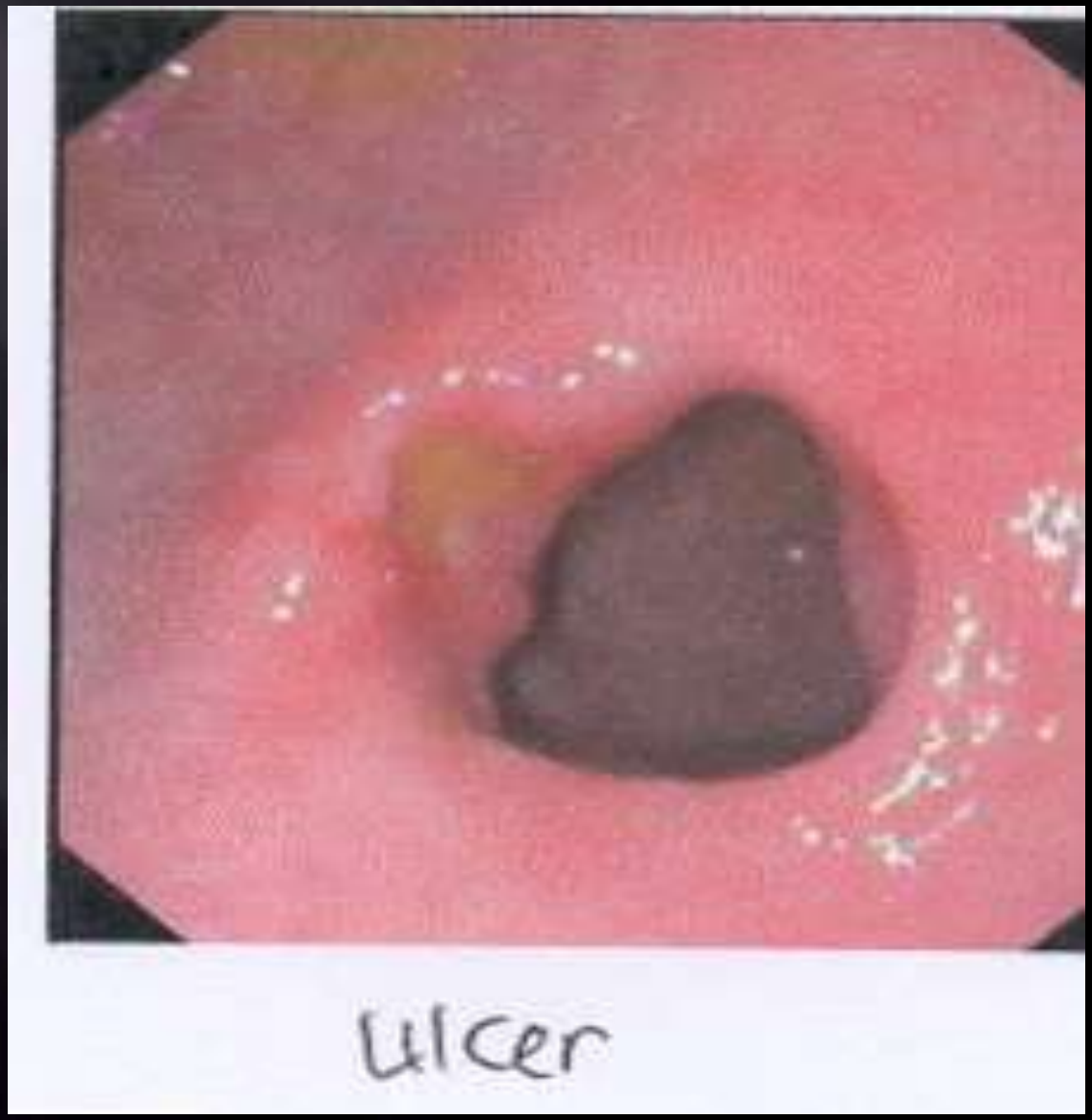


Gambar 9-3. Tukak jinak di antrum bentuk bulat



Gambar 9-4. Tukak lambung bentuk bulat lonjong *(ellipse)*


Ulcer

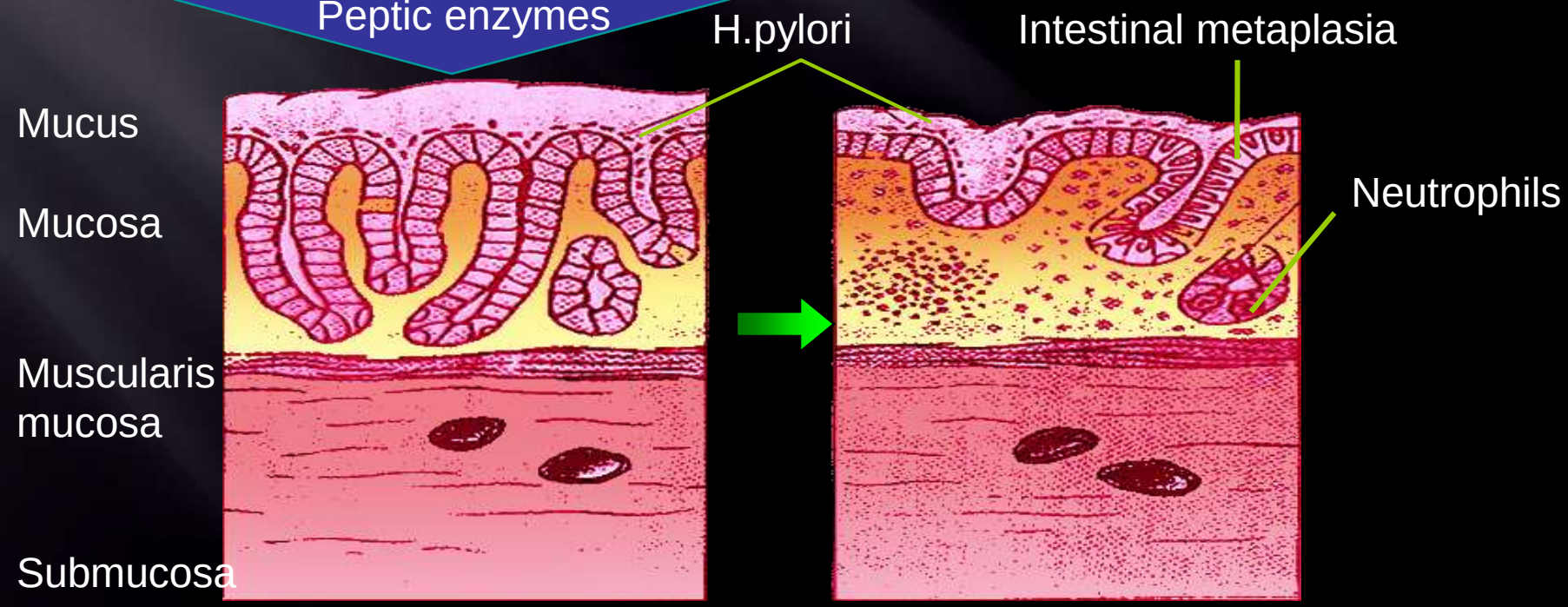

Ulcer

Gastric mucous layer in normal gaster and gastritis

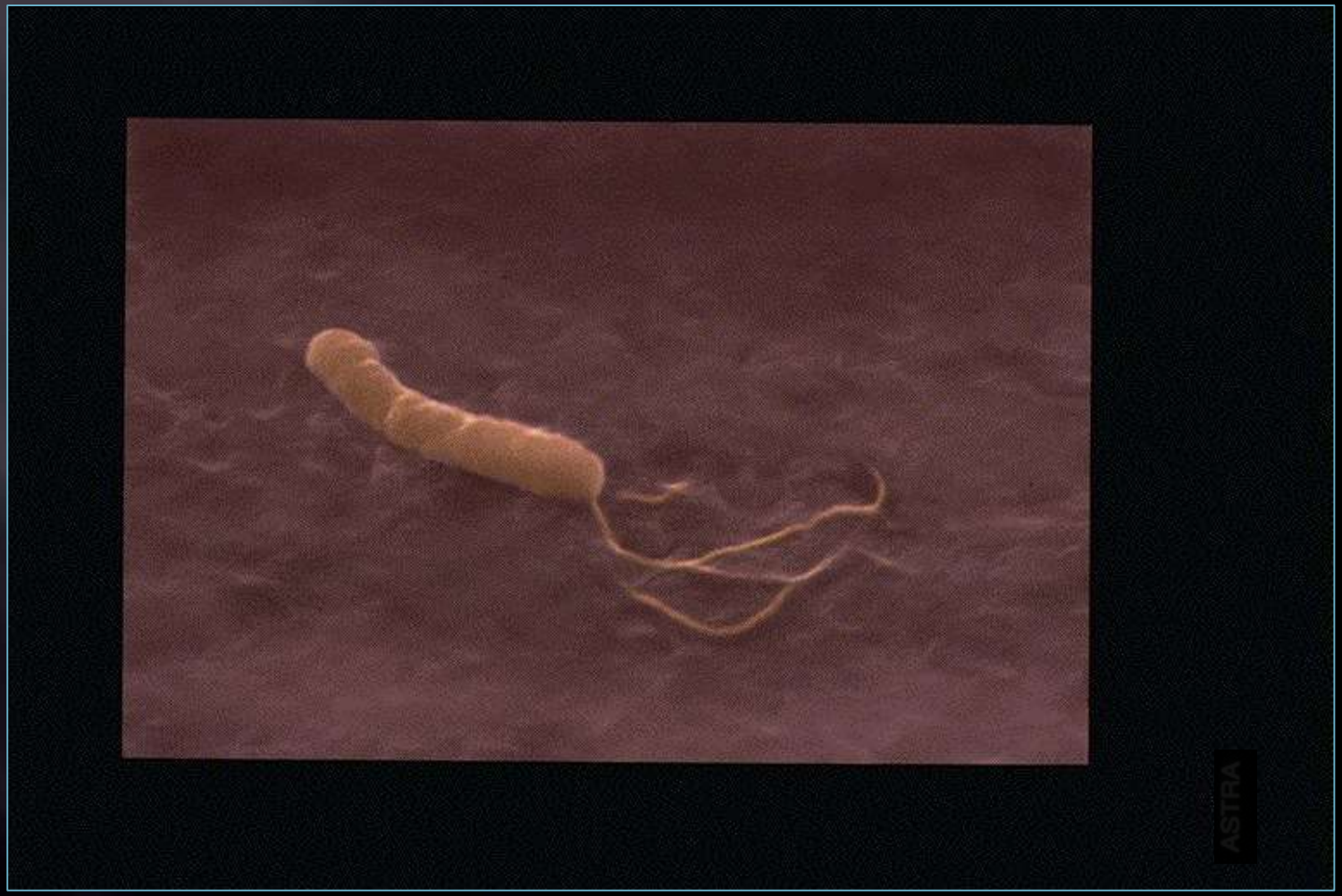
INFECTION

Damaging influences :
Helicobacter pylori
urease
toxins
Gastric acidity
Peptic enzymes

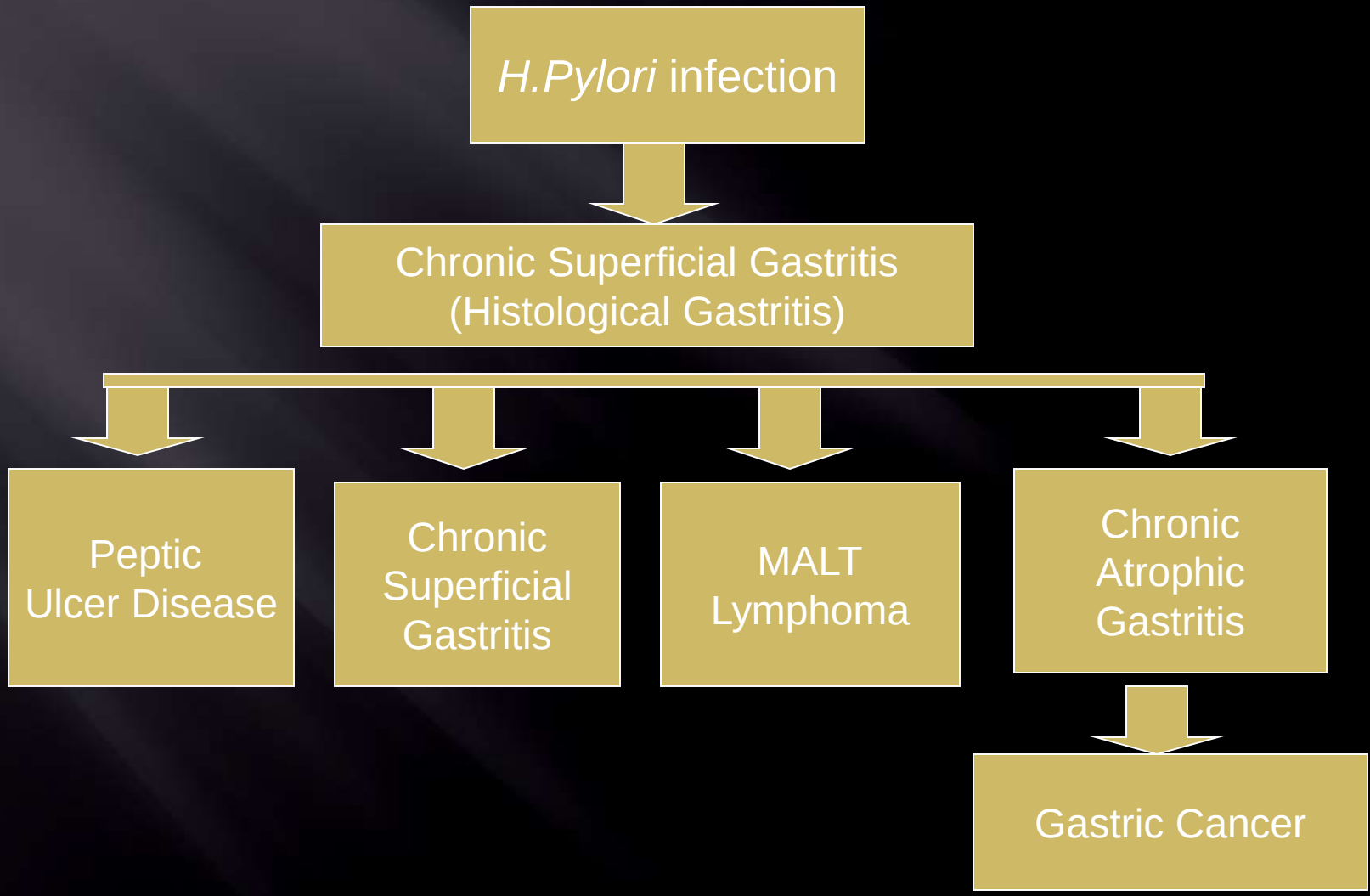
CHRONIC GASTRITIS
Atrophy
Intestinal metaplasia
Lymphoid aggregates
Neutrophil infiltrates



Gambar *H. pylori*



Natural History of *H.Pylori* Infection



cover, T.L., et al. :ASM Nwes, 61(!),21,1995

Proposed natural history of *Helicobacter pylori* infection in humans

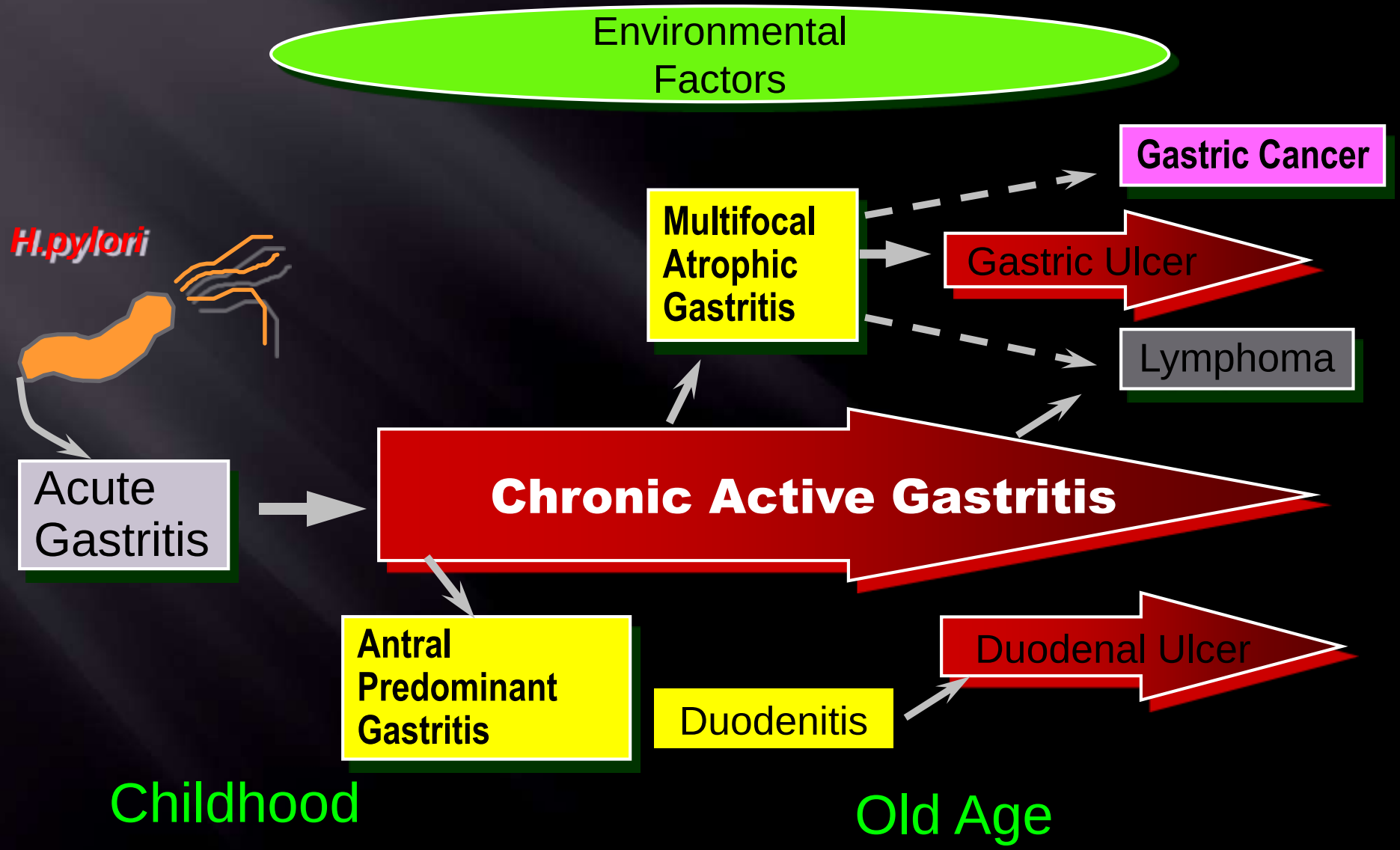


Table 1. Test for detection *of H.pylori*

Test	Sensitivity/specifity, %	Comments
INVASIVE (ENDOSCOPY/BIOPSY REQUIRED)		
Rapid urease	80 - 95/95 – 100	Simple, false negative with recent use of PPIs, antibiotics, or bismuth compounds
Histology	80 – 90/>95	Requires pathology processing and information
Culture	--/--	Time-consuming, expensive, dependent on experience; allows determination of antibiotic susceptibility
NON-INVASIVE		
Serology	>80/>90	Inexpensive, convenient; not useful for early follow-up
Urea breath test	>90/>90	Simple, rapid; useful for early follow-up; false negatives with recent therapy (see rapid urease test); exposure to low-dose radiation with ^{14}C test
Stool antigen	>90/>90	Inexpensive, convenient; not established for eradication but promising

Gastric cancer related to persistent presence of *H. pylori*-associated inflammation

Normal mucosa → Superficial gastritis → Atrophic gastritis → Intestinal metaplasia → Dysplasia → Gastric adenoCa.

Salt → Superficial gastritis

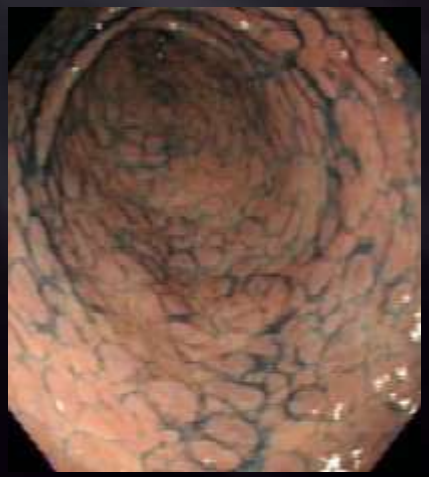
Higher pH → Atrophic gastritis

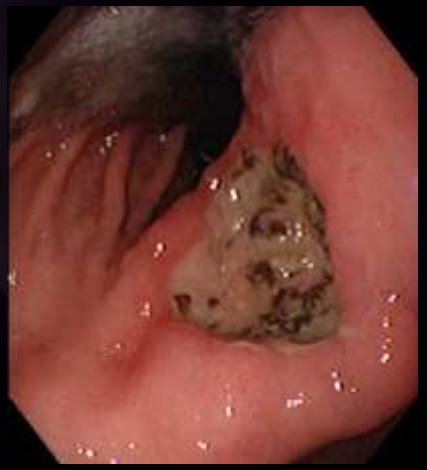
Salt
N-nitroso carcinogens
Inflammatory cell carcinogens → Dysplasia

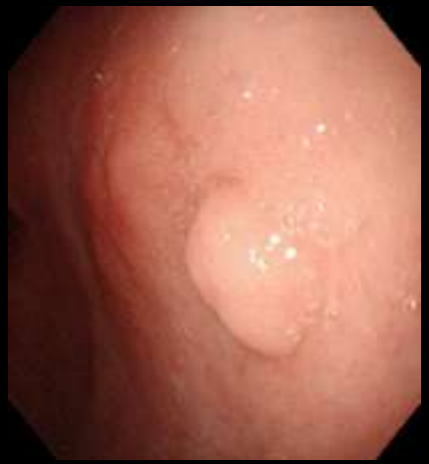
Ascorbic acid ⊣ Atrophic gastritis

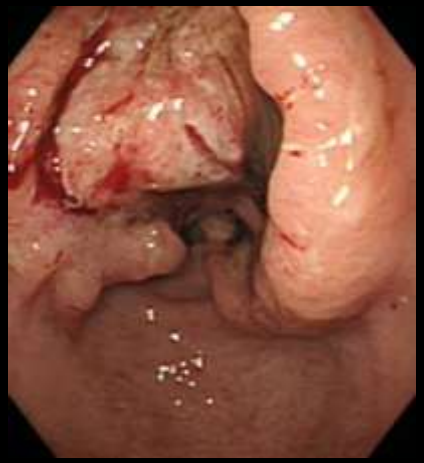
β-carotene ⊣ Intestinal metaplasia

H. pylori → Gastric adenoCa.



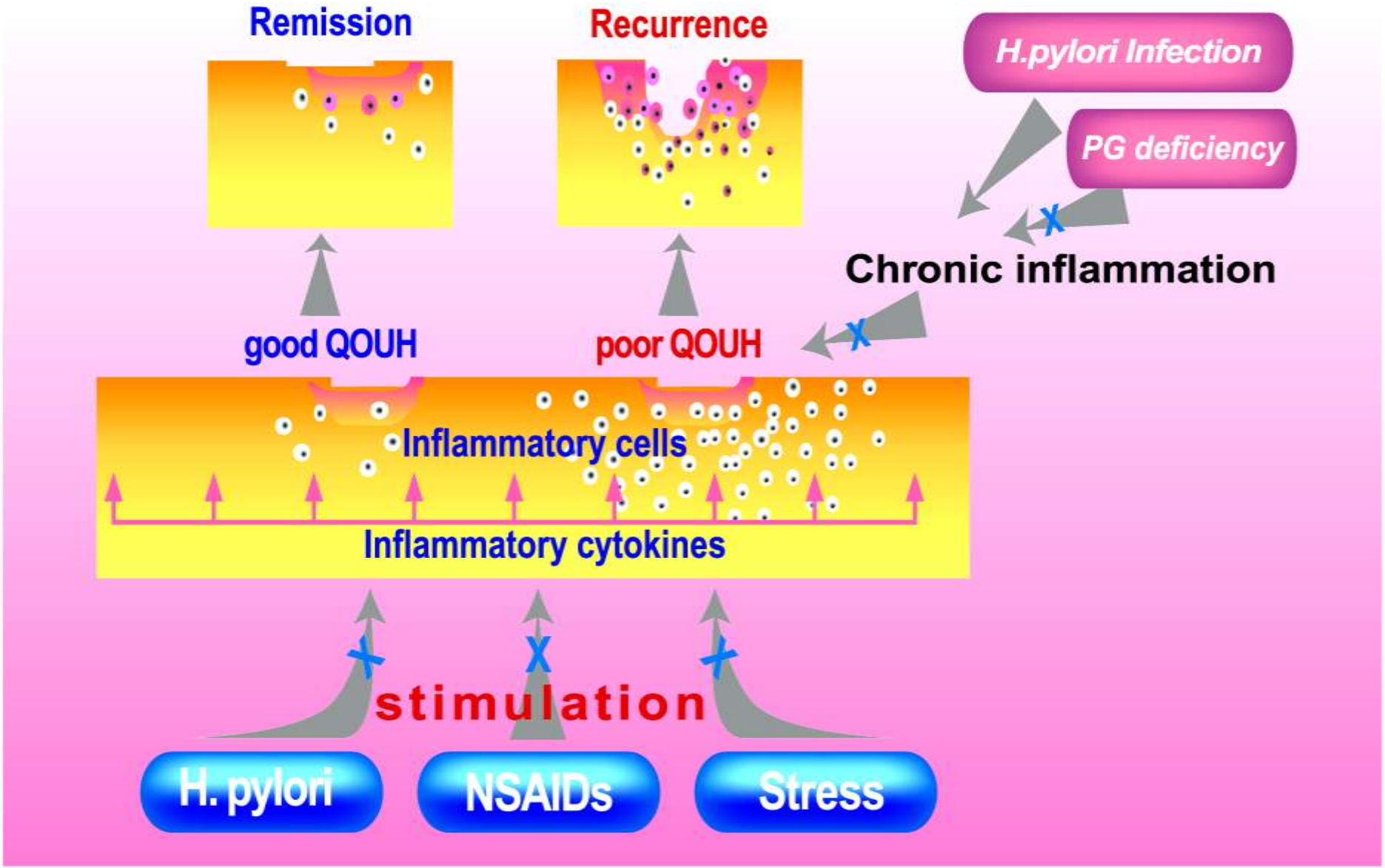






Chronic atrophic gastritis □ Gastric ulcer □ Gastric adenoma with dysplasia □ Gastric cancer

The Relationship Between Quality Ulcer Healing and Recurrence



T. Arakawa. Dig dis Sci 1998

Treatment of peptic ulcer diseases

Tujuan Utama Pengobatan UP

1. Menghilangkan keluhan
2. Mempercepat penyembuhan luka
3. Mengobati komplikasi
4. Mencegah kekambuhan

Pengobatan Non-medikamentosa

1. Pendekatan pribadi

Penting mencari:

- faktor-2 yang berperan pada penyakit
- diagnosis dan pengobatan yang sesuai

2. Merubah cara hidup (life style)

Faktor yang perlu diperbaiki a.l.:

- rokok, alkohol, diet, cara makan, dll.
- stress psiko-sosial

Medikamentosa
Obat penyembuh luka UP

1. Antasida
2. Penghambat sekresi asam
    a. Anti-muskarinik
    b. Antagonis H2 -reseptor (H2RA)
    c. Penghambat pompa proton (PPI)
       Omeprazole, Rabeprazole, Pantoprazole, Lansoprazole

3. Sitoproteksi
    a. Sucralfate
    b. Cetraxate
    c. Colloidal Bismuth subcitrate
    d. Prostaglandin
    e. Teprenone
    f. Rebamipide

Obat Antasid & Anti-sekresi Asam

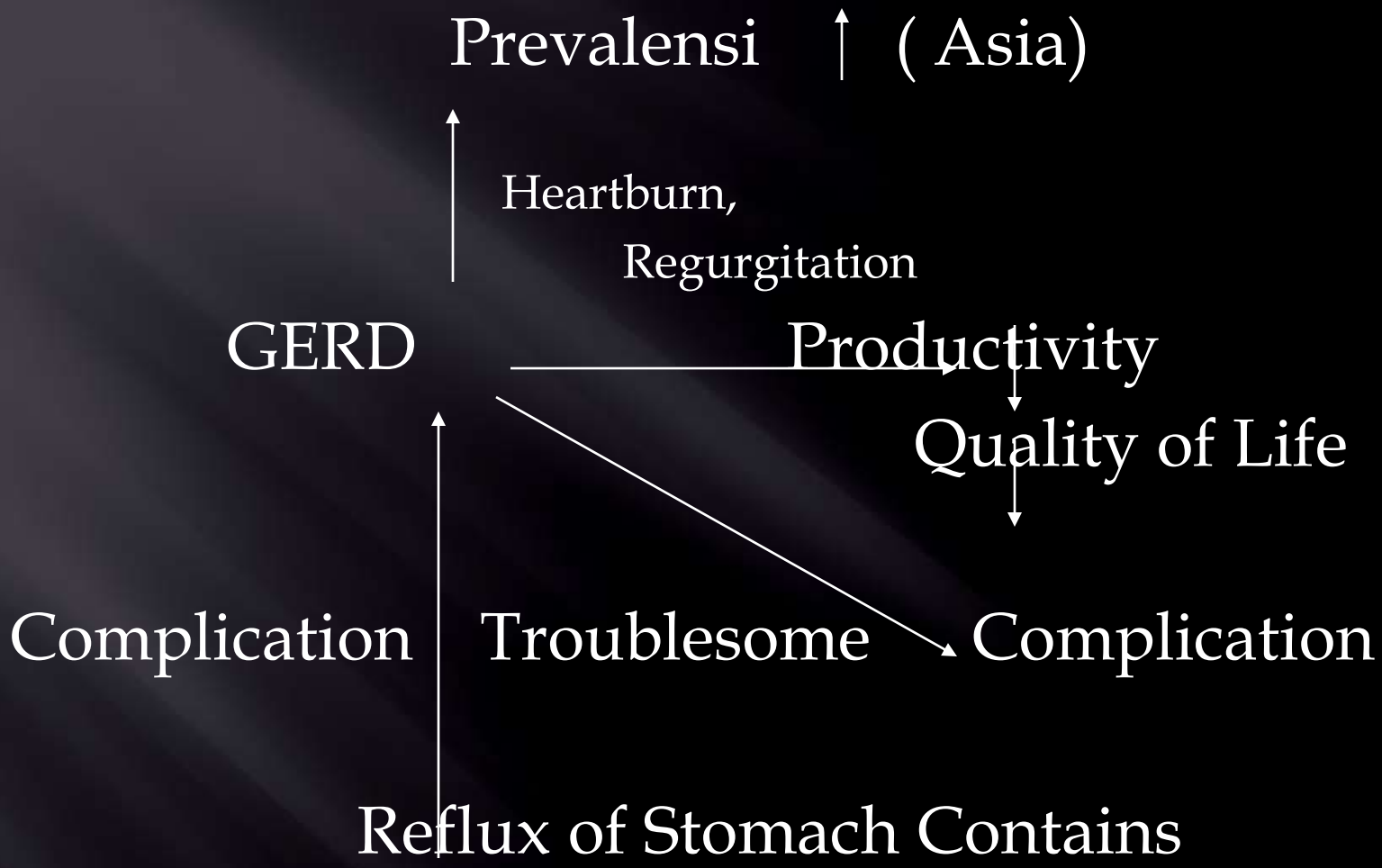
1. **Antasida**
   - *netralisir asam lambung, menghilangkan rasa sakit*
2. **Anti-kholinergik (muskarinik)**
   - *pirenzepin: selektif, ES ringan*
3. **Antagonis reseptor H2 (H2RA)**
   - *Cime-, Rani-, Famo-, Roxa-, Niza-tidin*
   - *efektif untuk pengobatan UP*
   - *(80% UD 8 mgg, UG 12 mgg)*
4. **Penghambat pompa proton (PPI)**
   - *Ome-, Lanso-, Panto-, Rabe-, Esome-prazol*
   - *paling efektif: UP, eradikasi Hp, GERD*
   - *> 90% UP sembuh, UD 4 mgg, UG 6 mgg*

Conclusions

- **Chronic inflammation is a major factor for the pathogenesis of serious gastroduodenal diseases and in the long term, is one of the most important factor in carcinogenesis.**
- Alarm features require immediate referral to a specialist for further investigation.
- **Helicobacter Pylori infection has a clinically important mechanism of chronic inflamation.**
- **Proton pump inhibitors improve ulcers healing and eradicate H. pylori more effectively.**

TERIMA KASIH
ATAS PERHATIANNYA

GUIDELINES AND GERD MANAGEMENT

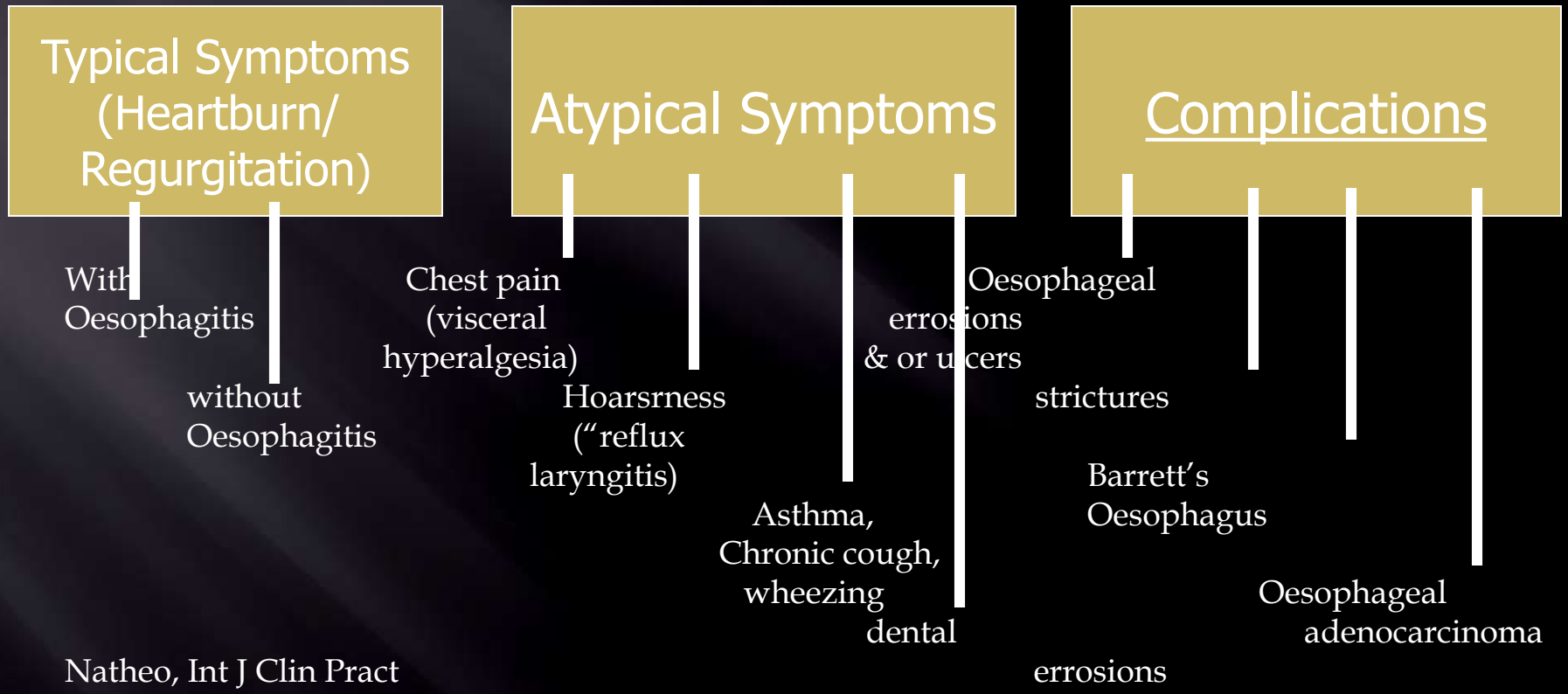

Prevalensi (Asia)
Heartburn,
Regurgitation
GERD
Productivity
Quality of Life
Complication
Troublesome
Complication
Reflux of Stomach Contains

Incompetence GEJ

Trans relax of LES
Hipotension of LES
Anatomic Disturbance

Hiatus hernia
Short LES
drugs
Hormonal

Range of Presentation GERD



Natheo, Int J Clin Pract 2001 ; 55 :465-9

The Montreal New Definition of GERD 2006

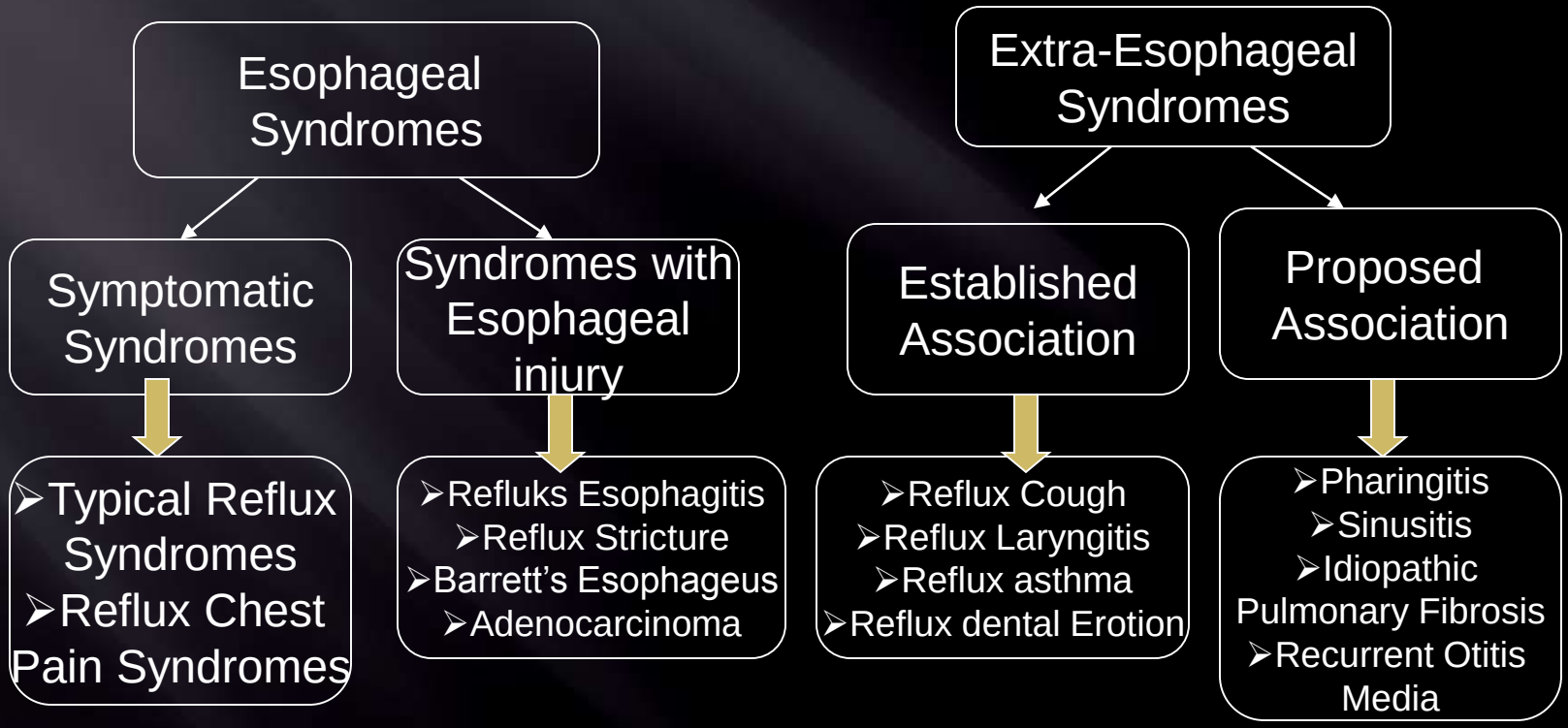
The Global Definition of GERD :

- GERD is a condition which develops when the reflux of stomach contents causes troublesome symptoms and/ or complications
- Symptoms related to gastro-esophageal reflux become troublesome when they adversly affect an individual's well-being
- Reflux symptoms that are not troublesome should not be diagnosed as GERD
- In Clinical Practice, the patients should determine if their reflux symptoms are troublesome

Schoeider HR. GERD. The Montreal definition and classification. SA Fam Pract 2007;49(1):19-26

The Montreal Definition of GERD 2006

GERD is a condition which develops when the reflux of stomach content causes trouble some symptoms and/or complications



Vakil N et al. Am J Gastroenterol 2006;101:1900-1920

What is GERD?

GERD is a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complication

Vakil N et al. Am J Gastroenterol 2006;101:1900-1920

Symptomatics Syndromes: the Troublesomeness of Reflux Symptoms is the Key to Diagnosis

"Symptoms related to Gastroesophageal Reflux become troublesome when they adversely affect an individual well-being"

"….mild symptoms occuring 2 or more days a week, or moderate/severe symptoms occuring more than 1 day aweek, are often considered troublesome by patient"

Vakil N et al. Am J Gastroenterol 2006;101:1900-1920

When do reflux symptoms become troublesome?

"In clinical practice, the patient should determine if their reflux symptoms are troublesome"

Vakil N et al. Am J Gastroenterol 2006;101:1900-1920

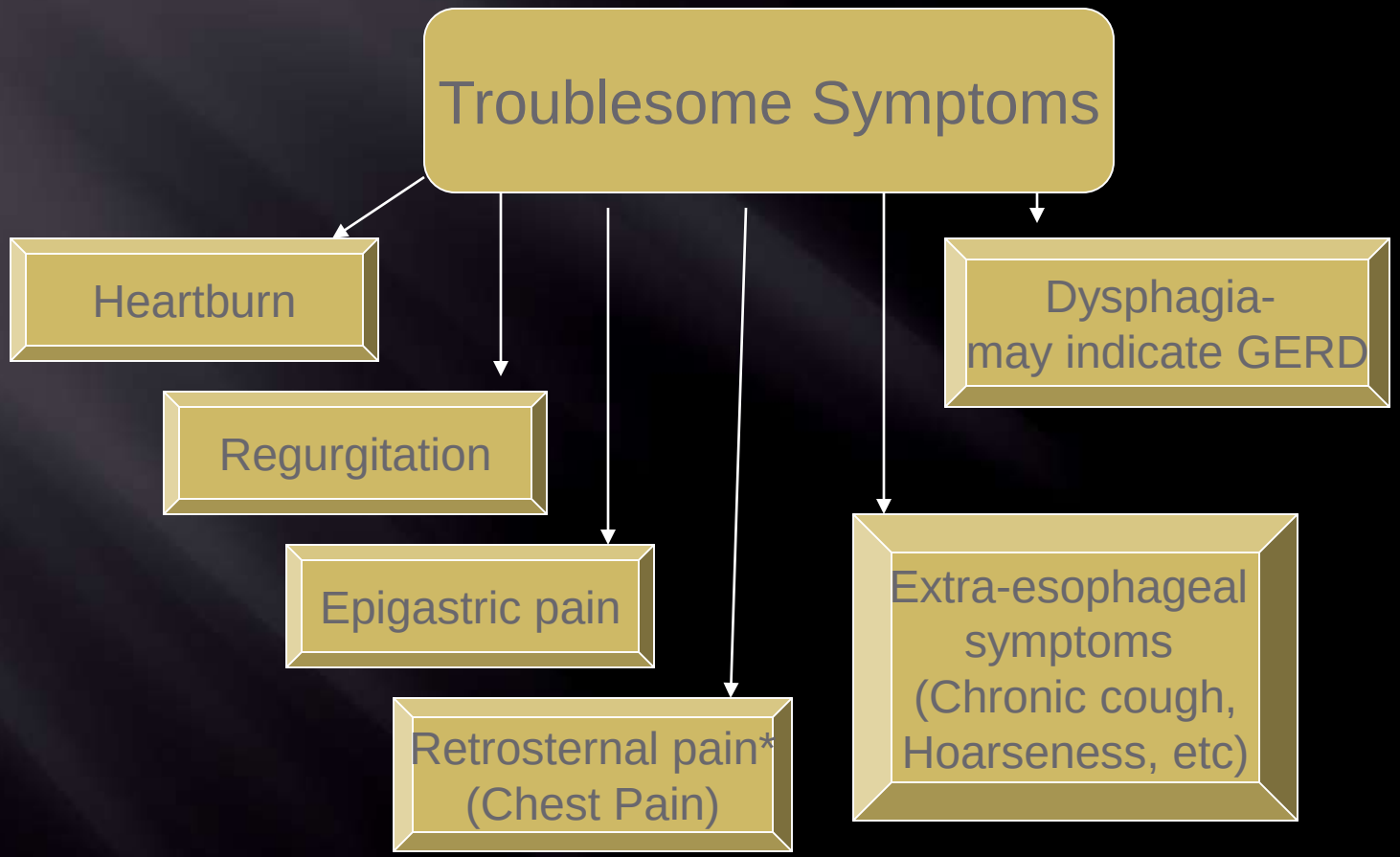
How Can Typical Reflux Syndrome/GERD be diagnosed?

"The Typical Reflux Syndrome can be diagnosed on the basis of characteristis symptoms, without diagnostic testing"

"Heartburn and regurgitation are the characteristic symptoms of the Typical Reflux Syndrome"

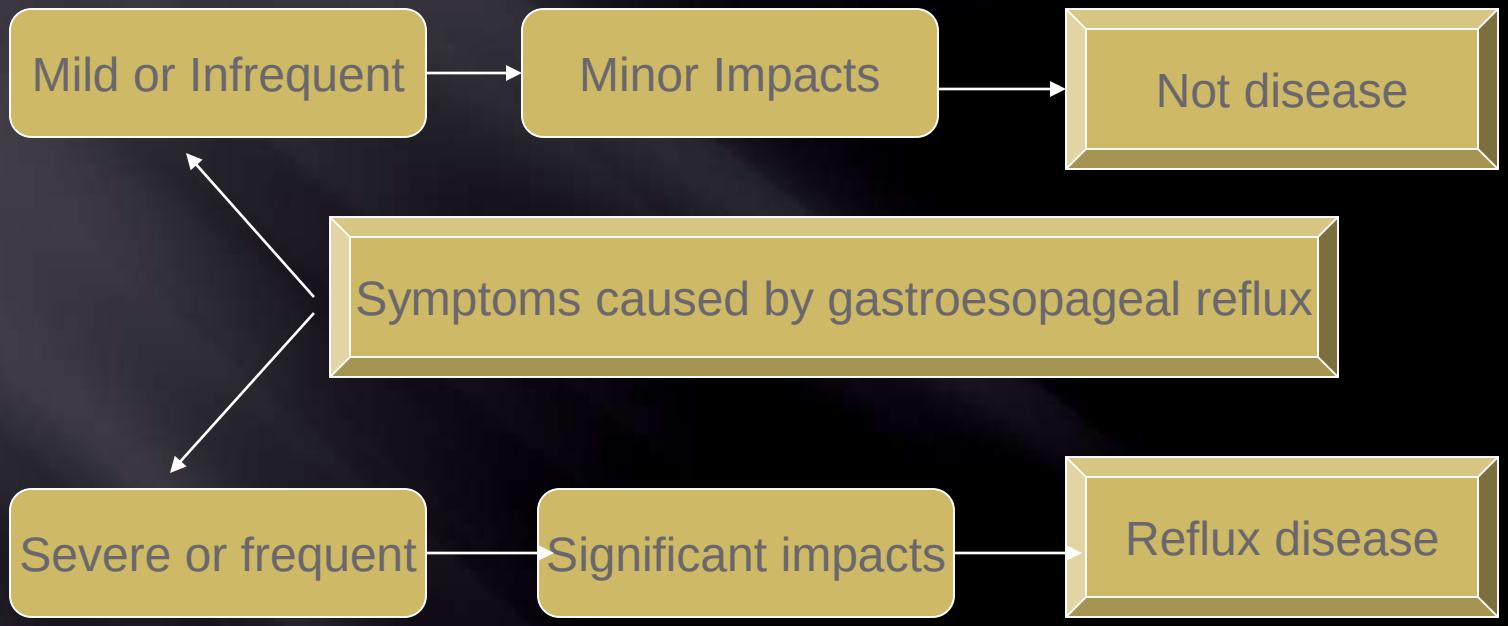
Vakil N et al. Am J Gastroenterol 2006;101:1900-1920

GERD can be diagnosed based on Symptoms alone



*when cardiac causes have been excluded

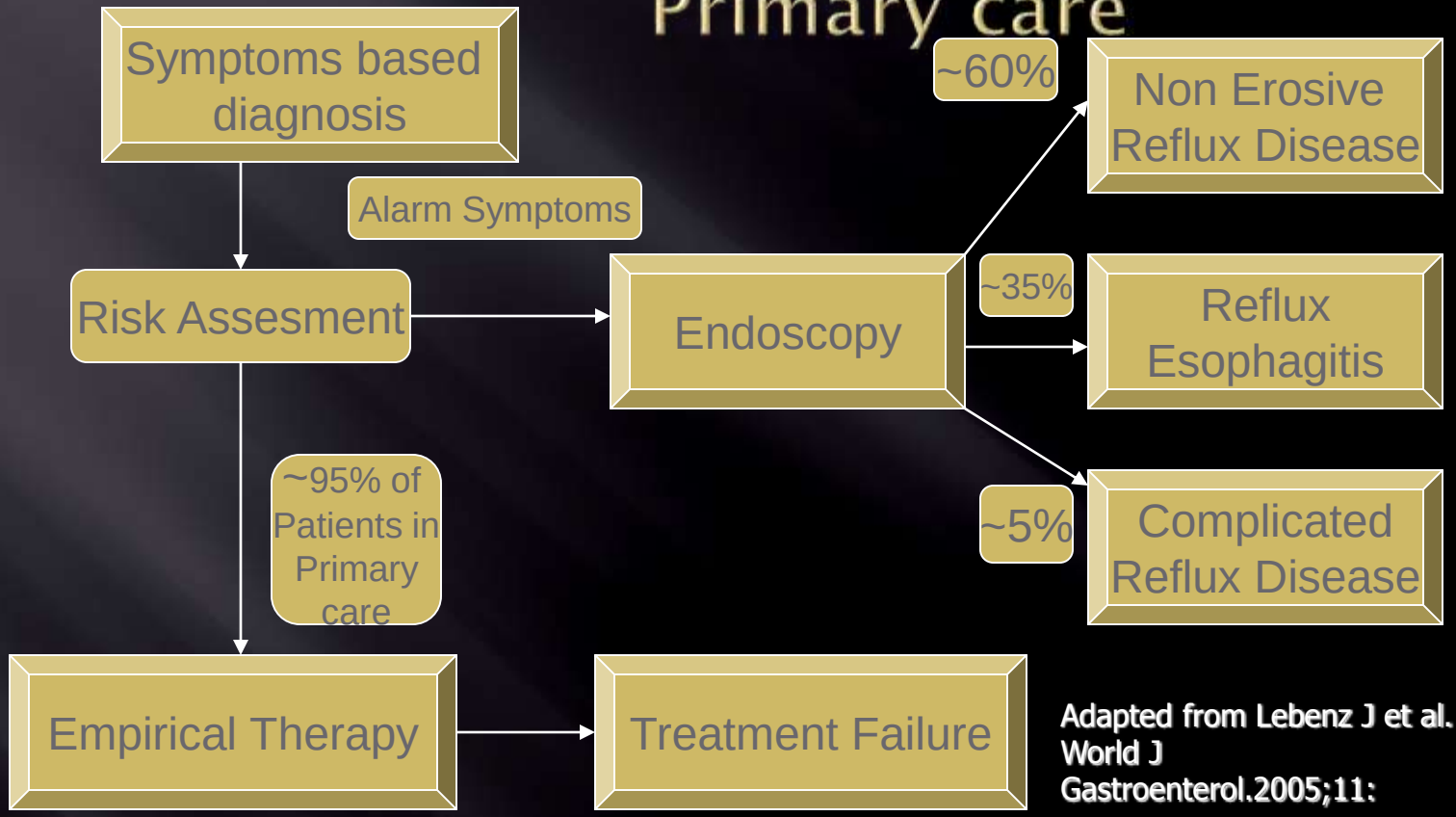
The Key Factor in Diagnosis are the frequency and severity of symptoms and their impact on patient lives



Mild or infrequent symptoms may, however, indicate reflux disease if they have a significant impact on a patient's daily life

Dent J et al. Gut 2005 :54 :710-7

Following a symptom-based diagnosis, almost all Patient can be managed in Primary care



Adapted from Lebenz J et al. World J Gastroenterol.2005;11: 4291-99

DeVault KR,Catell DO. Am J Gastroenterol 2005;100:190-200

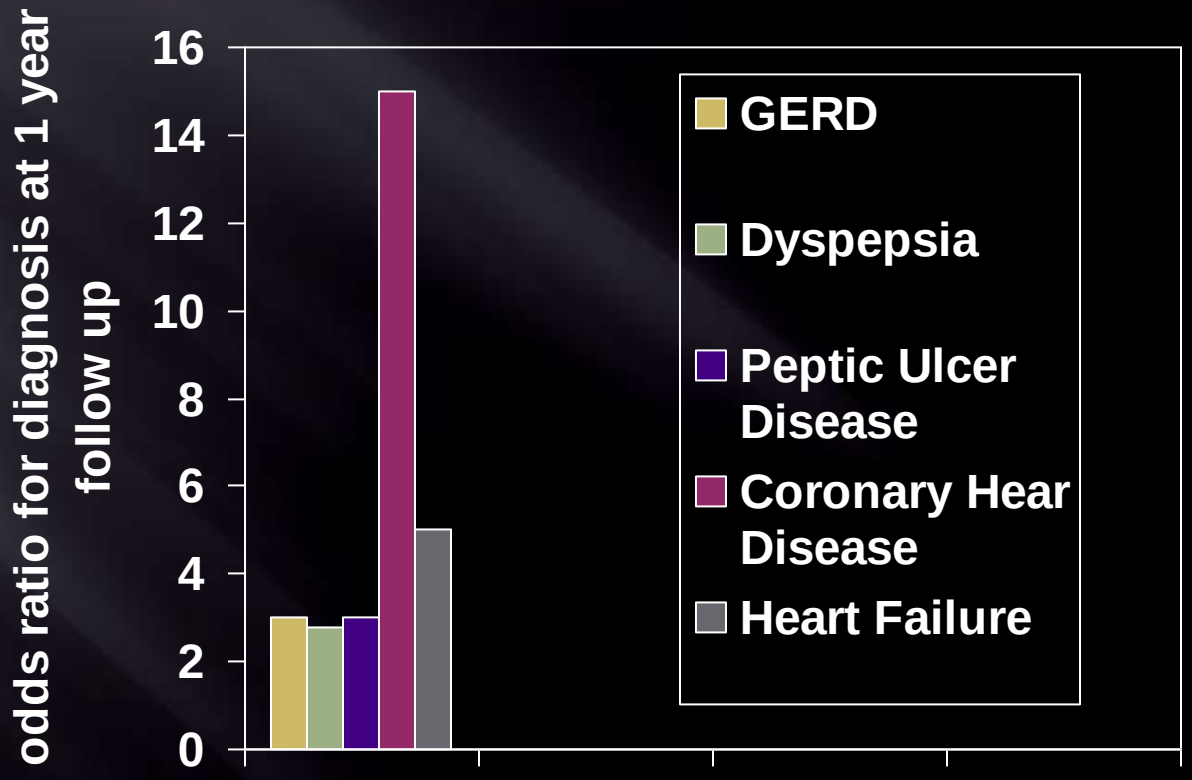
Rao G.J Fam Pract 2005;54(12 suppl):3-8

Gastroesophageal reflux may cause Reflux Chest Pain Syndrome

"Chest pain indistinguishable from ischemic cardiac pain can be caused by GERD"

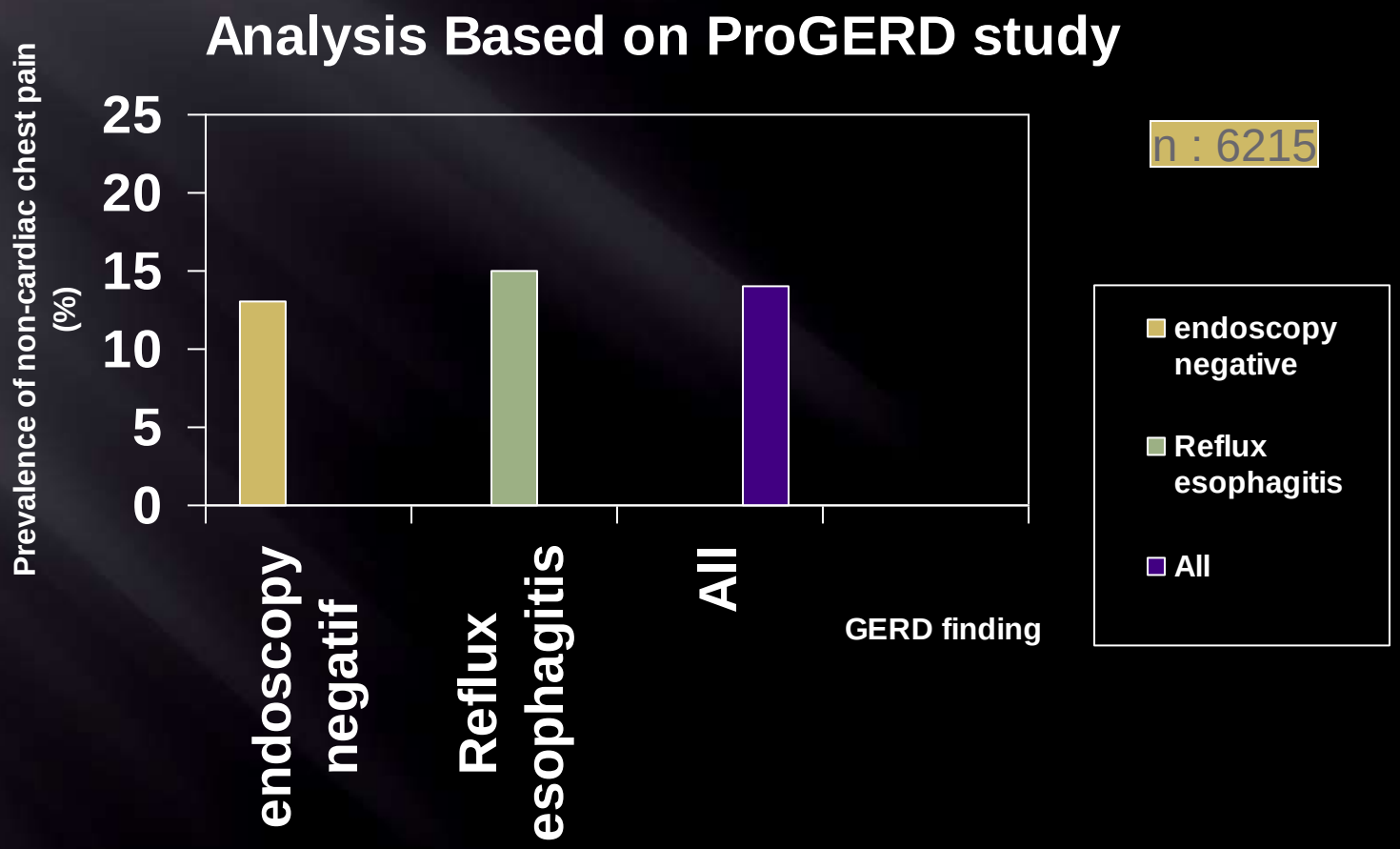
Vakil N et al. Am J Gastroenterol 2006.in press

Chest Pain can be caused by GERD and other upper GI disease



Ruigomas A et al. Fam Pract 2006; 23:167-74

Prevalence of non-cardiac chest pain among patient with GERD



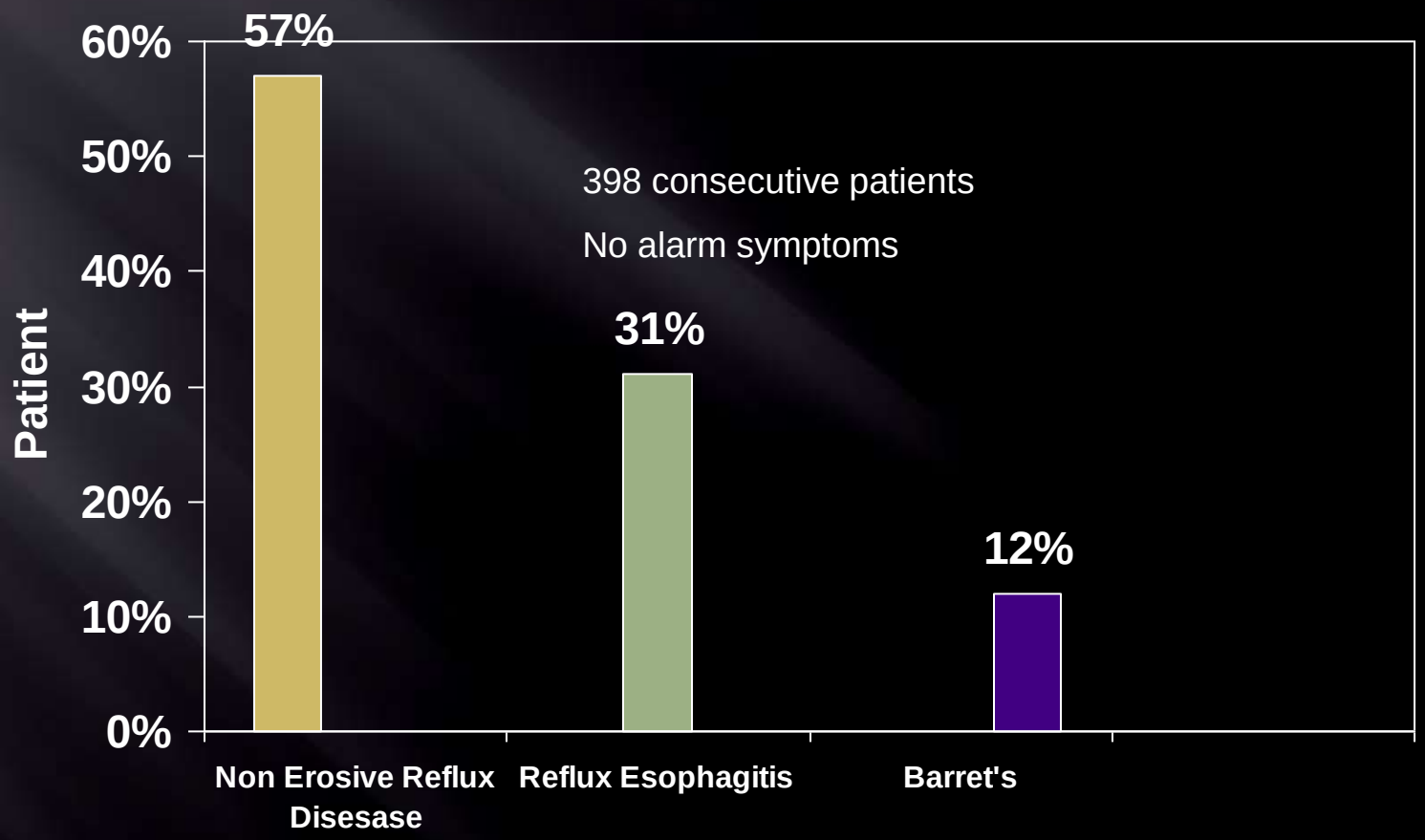
Jaspersen D A et al. Aliment Pharmacol Ther 2003; 17:1515-20

Syndromes with Esophageal Injury

"Esophageal complications of Gastroesophageal reflux disease are reflux esophagitis, hemorrhage, sticture, Barret's esophagus and adenocarcinoma"

Vakil N et al. Am J Gastroenterol 2006.in press

The most common findings during endoscopy for GERD



Sharma Pet al. Gatroenterology 1224 suppl 1 : A-584 (2002)

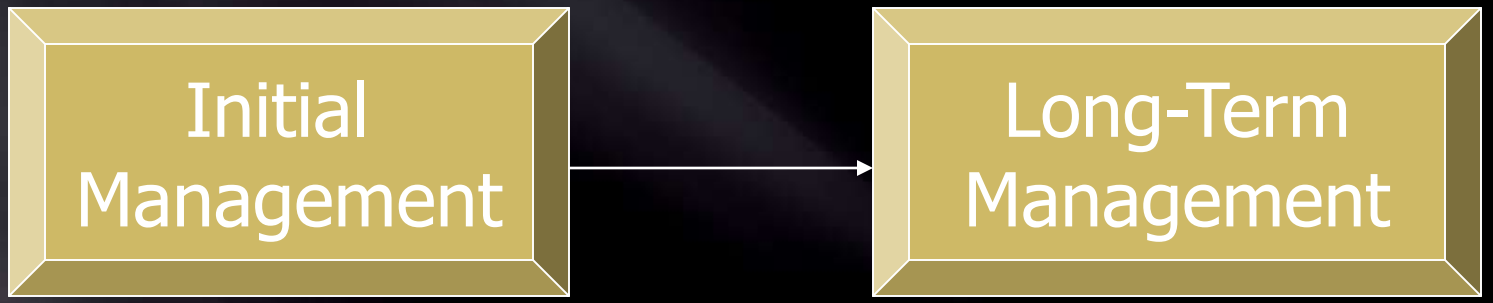
Management of GERD

- Life style Modification
- Medicamentosa
- Operatif Therapy/ Endoscopy

Life Style Modification

- ↑ the head side of the bed
- ↓ fat consumption
- Stop smoking
- Prevent : alcohol, chocolate, coffea, soda
- Prevent : lie down after eating
- Low weight
- Prevent : drugs which make LES tonus ↓

GERD : Clinical Management



Mainstream Options for Therapy of GERD

Highest Efficacy

Recommended

Current guidelines

Should be abandoned

Lowest Efficacy

- 2x daily PPI + H_2RA
- 2x daily PPI
- 1x daily PPI
- 1x daily ½ PPI
- Prokinetic + H2RA
- Prokinetic Or H2RA
- Antacide + lifestyle
- Antacide
- Lifestyle

*no clear dose-response established

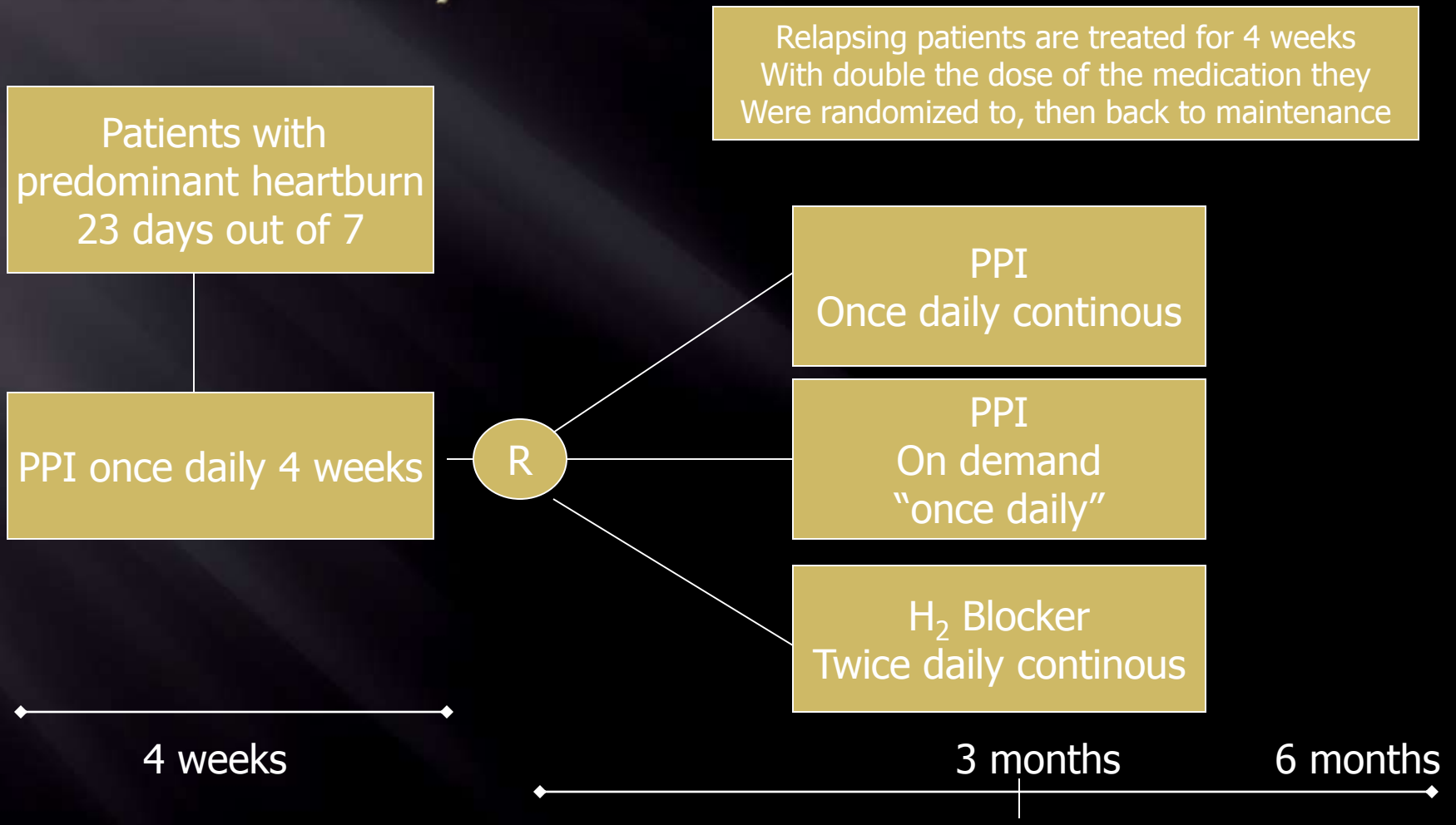
After Dent et al. Gut 1999 (Suppl 2)

GERD : Long Term Management

Dent & Talley, Aliment Pharmacol Ther 2003 (Suppl 1)

Dent et al. Gut 2004 (Suppl 4)

On Demand vs Contimous Therapy in Primary Care GERD Patients



Norman Hansen et al. Int J Clin Pract 2005

A trial Course of PPI therapy may aid diagnosis of GERD in patients with non-cardiac chest pain

Meta-analysis of data from six studies showed that for the diagnosis of GERD in patient with non-cardiac chest pain :

- The sensitivity of PPI test was 80% compared with 19% for placebo
- The summary diagnostic odds ratio of the PPI test was 19.35 compared with only 0.61 in the placebo group

A reduction in non-cardiac chest pain during PPI therapy is therefore indicative of GERD

Wang WH et al.Arch intern Med 2005;165;1222-8

What the Montreal Definition of GERD provides

- A patient-centered approach to diagnosis and management
- An evidence-based consensus definition and classification of GERD
- A globally applicable definition of GERD
- Clarified diagnostic criteria for Barrett's esophagus
- A rational classification for proposed esophageal disorders

Other Key point from the Montreal definition of GERD

- GERD can be diagnosed in primary care, based on troublesome symptoms-reducing the number of unnecessary referral for further investigations
- Acid plays a central role in the development of :

- **Symptomatic Esophageal Syndromes** (Typical reflux Syndrome, Reflux Chest Pain Syndromes)
- **Esophageal Syndromes with Esophageal Injury** (such as Reflux Esophagitis, Reflux Stricture, Barrett's Esophagus)
- **Extra-Esophageal Syndromes** (such as Reflux Cough, Reflux Laryngitis, Reflux Asthma)

THANK YOU