연수강좌 | 소강당

소화성 궤양 진단 및 치료

박 영 규
분당제생병원 가정의학과

목차

소화성 궤양의 정의

- 조

- 위 이하
까지

- 위

- 결 이란
(eros

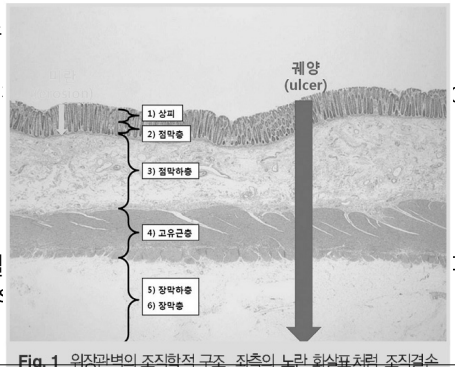
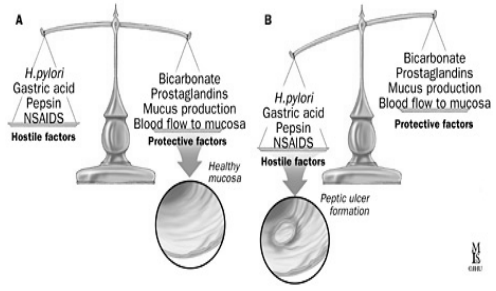


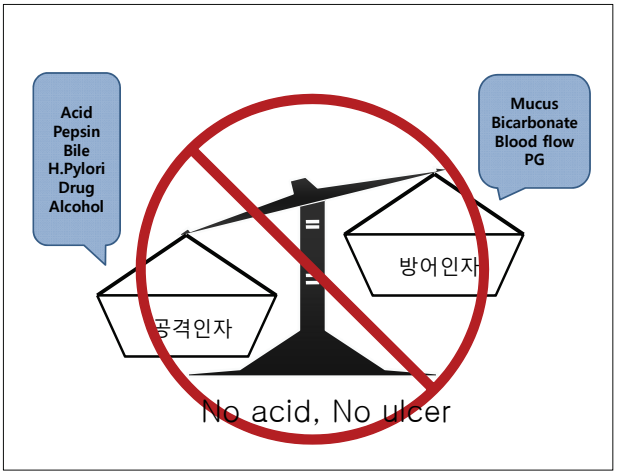
Fig. 1. 위장관벽의 조직학적 구조. 좌측의 노란 화살표처럼 조직결손

소화성 궤양의 유병율

1) 미국 – H. Pylori positive 환자 : 2% 내외
2) 국내
- 대한상부위장관-헬리코박터학회 : 대략 10%
(소화성궤양의 진단 가이드라인)
- 국내 다기관 연구 : 18.0~20.2%
3) 아시아권
- 대만 : 6,457명의 수검자대상으로 한 연구 10.9%

Pathogenesis of peptic ulcer





NO ACID NO ULCER

→ *H. pylori infection*

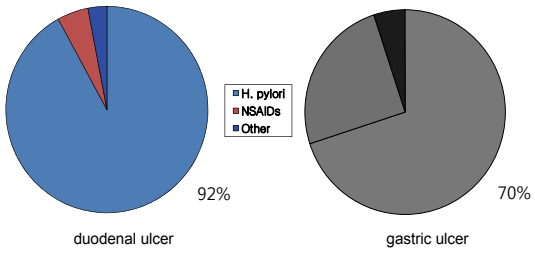
Pathogenesis of peptic ulcer

<Table 1> 대표적인 소화성 궤양의 원인 및 위험인자

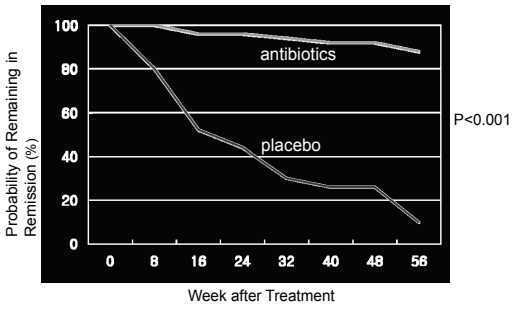
주요 원인 및 위험인자
1. 헬리코박터 (*H. pylori*) 감염
2. 비스테로이드성 소염제 사용
그 외 원인 및 위험인자
1. 위산분비 항진 증후군
1) 가스트리노마(Gastrinoma)
2) 비만세포 증식증
3) 호염기세포 증가증
4) 전정부 G세포 기능항진증
2. 선천적 기형
1) 십이지장 폐쇄증
2) 윤성췌장
3. 방사선치료
4. 항암화학요법
5. 생활습관
1) 흡연
2) 과량의 음주
3) 식이 – 커피, 과다한 염분섭취, 저섬유식
6. 정신적 스트레스

Hostile Factors

Peptic ulcer and *H. pylori*



H. pylori and duodenal ulcer recurrence

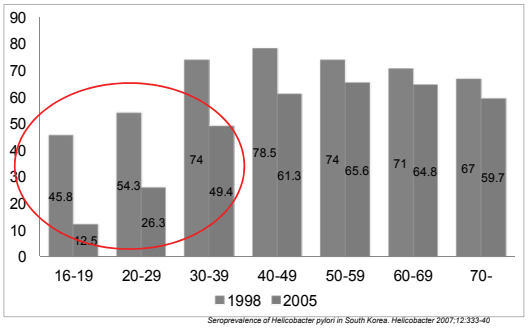


Hentschel E. NEJM. 1993

Seroprevalence of Helicobacter pylori in South Korea

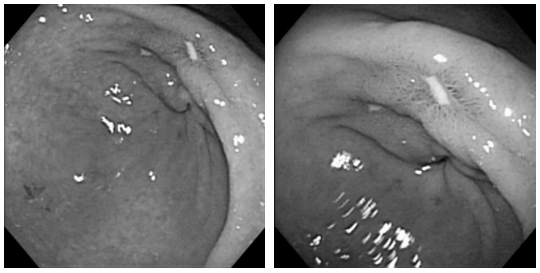
Seroprevalence of Helicobacter pylori in South Korea. Helicobacter 2007;12:333-40

Seroprevalence of Helicobacter pylori in South Korea

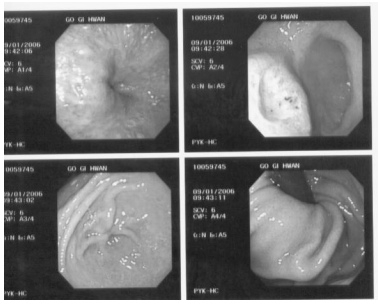


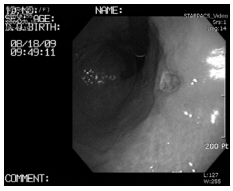
Seroprevalence of Helicobacter pylori in South Korea. Helicobacter 2007;12:333-40

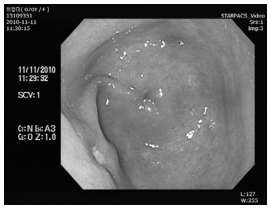
NSAID-induced gastric ulcer (aspirin)

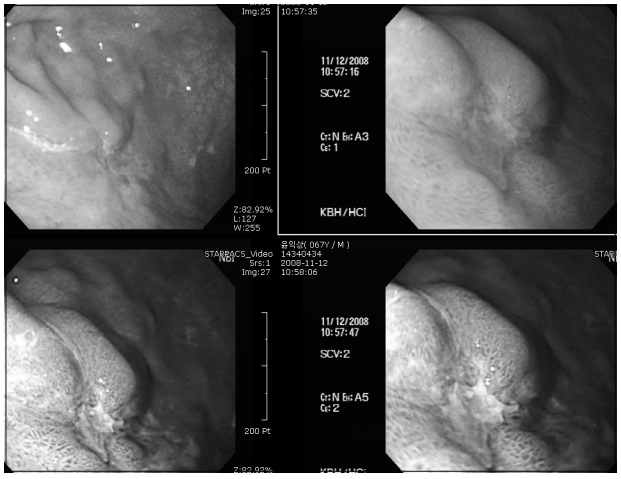


H.Pylori induced

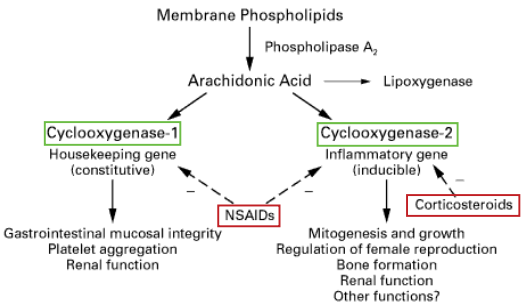


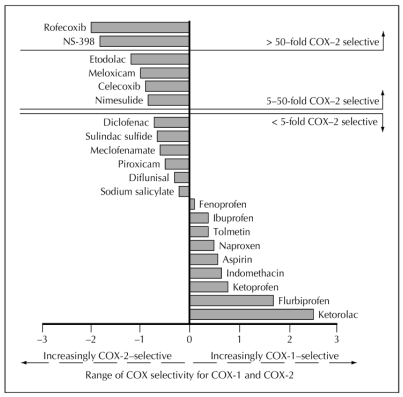






COX-1 & COX-2





Risk factors for NSAID-induced gastro-duodenal ulceration

Established	possible
Advanced age	Concomitant infection with *H. pylori*
History of ulcer	Cigarette smoking
Concomitant use of steroid	Alcohol consumption
High-dose NSAIDs	
Multiple NSAIDs	
Concomitant use of anticoagulant	
Serious or multisystem disease	

Miscellaneous pathogenic factors of peptic ulcer

- Cigarette smoking
- Genetic predisposition
- Psychological stress
- Diet
- Specific chronic disorders

→ Systemic mastocytosis, chronic pulmonary disease, CRF, LC, nephrolithiasis, antitrypsin deficiency....

Clinical Features of Peptic Ulcer

Symptoms

	Duodenal ulcer	Gastric ulcer
Epigastric pain	90 min to 3 h after a meal (hunger pain)	precipitated by food
	70% awakes the patient from sleep (between midnight and 3 A.M.)	Nausea and weight loss occur more common
	frequently relieved by antacids or food	

Symptoms

- The mechanism of abdominal pain in ulcer : **unknown**.

  - Acid-induced activation of chemical receptors in the duodenum
  - Enhanced duodenal sensitivity to bile acids and pepsin
  - Altered gastroduodenal motility

Suggestion of ulcer complication

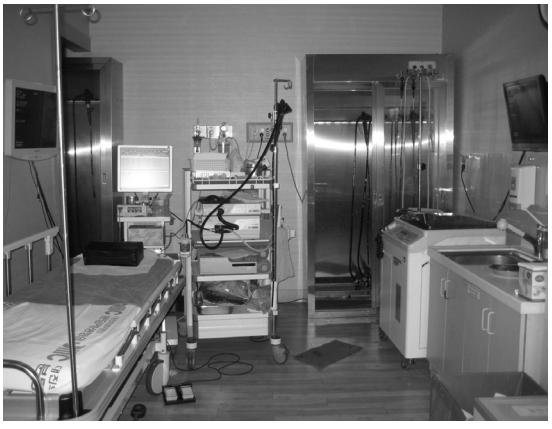
- Dyspepsia constant, not relieved by food or antacids, or radiates to the back
  → **penetrating ulcer** (pancreas)
- Sudden onset of severe, generalized abdominal pain
  → **perforation**
- Pain worsening with meals, nausea, and vomiting of undigested food
  → **gastric outlet obstruction**
- Tarry stools or coffee ground emesis
  → **bleeding**

감별진단

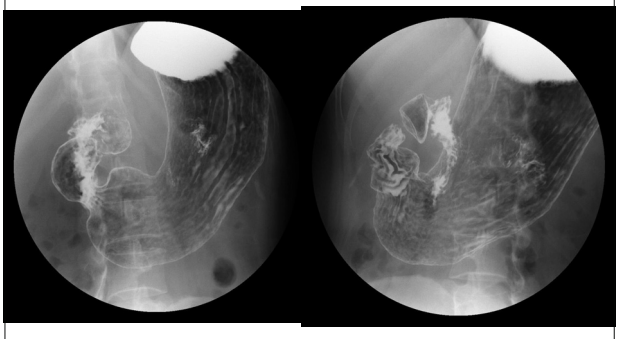
- 기능성 위장관질환(FGID) – Functional dyspepsia(FD), Non-ulcer dyspepsia(NUD)
- 위암같은 소화기계 질환
- 관상동맥질환 – 협심증, 심근경색
- 췌장질환 – 급성 췌장염, 만성 췌장염
- 담도계질환 – 급성 담낭염, 만성 담낭염
- 정신적질환 – 신경증, 신체화 장애

소화성 궤양의 진단

- 소화성 궤양의 진단을 위해 시행할 수 있는 검사
  - Endoscopy
  - UGIS



UGIS



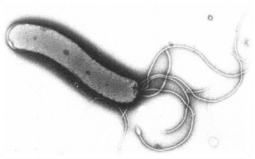
상부위장관 내시경(=위내시경) 검사

① 검사의 민감도와 정확도가 우수

② 촬영영상이 시각적이어서 환자에게 설명하기가 용이 (의사도 이해하기가 편함)

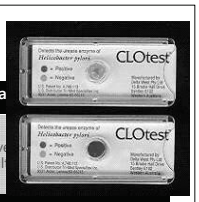
③ 악성종양을 감별하기 위한 조직검사

④ 헬리코박터균 검사가능 등의 장점



헬리코박터 파이로리 검사

Invasive Method



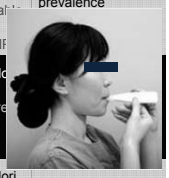
Invasive	Sensitivity(%)	Specificity(%)	Advanta	
Rapid urease test	80-95	95-100	Inexpensive rapid resul	
Histology	90-95	95-98	Excellent sensitivity and specificity	Expensive infrastructure and trained personnel
Culture	80-90	100	Excellent specificity antibiotic sensitivities	Expensive difficult to perform low sensitivity

American College of Gastroenterology guideline on the management of Helicobacter pylori infection. The American Journal of Gastroenterology 2007;102:1808-25.

Non-invasive Method

Non-invasive	Sensitivity(%)	Specificity(%)	Advantage	Disadvantage
Serol			ensive y availa good NP	PPV depend on prevalence
Urea breath test	90-95	86-95	active H. pylo infection Useful before and after therapy	
Stool antigen test	90-95	90-95	active H. pylori infection Useful before and after therapy	Polyclonal test less well validated Unpleasantness

양성자펌프 억제제 (PPI)는 최소 1~2주
항생제는 최소 2~4주 중지 후 검사 시행



American College of Gastroenterology guideline on the management of Helicobacter pylori infection. The American Journal of Gastroenterology 2007;102:1808-25.

complication

- Hemorrhage
- Perforation
- obstruction

Table 1. Factors associated with the occurrence and recurrence of peptic ulcer complications and with mortality after peptic ulcer complications

Risk factor	Occurrence	Recurrence	Mortality
Male sex	✓		
Increasing age	✓	✓	✓
Serious comorbidity	✓	✓	✓
PAI-1 4G/4G genotype		✓	
Tertiary education	✓		
High alcohol use	✓		
Smoking	✓		
NSAID use	✓	✓	
ASA use	✓	✓	
High-dose	✓		
Low-dose	✓		
Anticoagulant use		✓	
Immunosuppressant use		✓	
Corticosteroid use		✓	✓
Shock		✓	✓
Low hemoglobin levels at initial presentation		✓	✓
Low blood pressure		✓	✓
Treatment delay			✓
H. pylori infection	✓	✓	
History of peptic ulcer	✓		
No history of peptic ulcer			✓
Large ulcer size (>1 cm)	✓	✓	
Forrest class I–II		✓	✓
Recurrence of complication			✓

Treatment of Peptic Ulcers

Treatment: medical

- Acid Neutralizing / Inhibitory Drugs
  - Antacids
  - H_2 Receptor Antagonists
  - Proton Pump Inhibitors
- Cytoprotective agent
  - Bismuth
  - Sucralfate
  - Prostaglandin Analogues
- Therapy of *H. pylori*
- Therapy of NSAID-Related Gastric or Duodenal Injury.

Treatment: antacids

- Rarely used as the primary therapeutic agent
- **For symptomatic relief** of dyspepsia
- Aluminum hydroxide: constipation
- Magnesium hydroxide: loose stools
- Commonly used antacids (e.g., Maalox, Mylanta)
  → combination of both aluminum and magnesium hydroxide in order to avoid these side effects
- Calcium carbonate and sodium bicarbonate

Treatment: H_2 receptor antagonist

- Cimetidine, ranitidine, famotidine, and nizatidine
- Different potency, all will significantly inhibit basal and stimulated acid secretion to comparable levels when used at therapeutic doses
- Renal excretion: reduce dose in renal impairment
- Adverse effects uncommon, but Cimetidine – serum aminotransferases, creatinine, and serum prolactin (gynaecomastia), confusion, psychosis

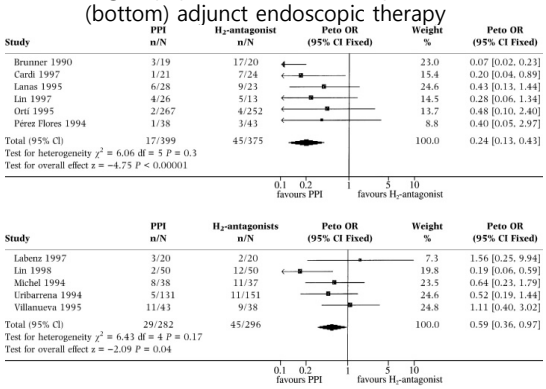
Be careful !!!

- Cimetidine inhibits Cytochrome P450 isoenzymes: inhibits metabolism of warfarin, phenytoin, carbamazepine, prednisolone, theophylline
  → careful monitoring
- Ranitidine, famotidine, nizatidine produce clinically insignificant inhibition

Treatment: PPI

- Covalently bind and irreversibly inhibit H+,K+-ATPase
- Potently inhibit all phases of gastric acid secretion
- Onset of action : 2 and 6 h after administration
- Duration of inhibition lasting up to 72 to 96 h

PPI vs H_2RA : Effect on persistent or recurrent bleeding of peptic ulcer without (top) and with (bottom) adjunct endoscopic therapy



Gisbert. Aliment Pharmacol Ther 2001;15(7):917-926

Treatment: sucralfate (Ulcermin®)

- Binding primarily to sites of active ulceration
  - providing a physicochemical barrier
- Trophic effect by binding growth factors
  - enhance prostaglandin synthesis
  - stimulate mucous and bicarbonate secretion
    Enhance mucosal defense and repair
- SE: Constipation (2 to 3%).

소화성 궤양의 치료에서 고려할 사항

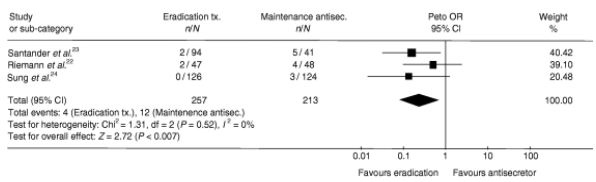
질문: 위궤양이 위암으로 발전하는가?

- 양성 위궤양이 위암으로 발전하지는 않는다.
- 양성 위궤양과 위암의 공통적인 위험인자가 있다.
- 위암이 처음에 양성 위궤양으로 잘 못 진단 되어지는 수가 있다.

헬리코박터 제균 치료

Long-term treatment for prevention of recurrent bleeding from peptic ulcer

- Hp eradication vs antisecretory treatment



Gisbert. Aliment Pharmacol Ther 2004;19(6):617-629

Indications

2007 American College of Gastroenterology Guideline
Established
Active peptic ulcer disease
Confirmed history of peptic ulcer disease
Gastric MALT lymphoma (low grade)
After endoscopic resection of early gastric cancer
Uninvestigated dyspepsia (depending upon H. pylori prevalence)
Controversial
Non-ulcer dyspepsia
Gastro-esophageal reflux disease
Persons using NSAIDs
Unexplained iron deficiency anemia
Populations at higher risk for gastric cancer

Indications

2009 대한 Helicobacter 및 상부위장관 연구학회		
Definite indication	**증거수준**	**권고등급**
H. pylori 에 감염된 소화성 궤양 환자 위의 저 악성도 B-세포 MALT 림프종 조기 위암	높음	높음
Highly recommended indication		
위암의 가족력이 있는 경우	중등도	중등도
Possible indication		
조직학적 검사 위축성 위염이 있거나 Serum pepsinogen I/II ratio가 3 이하인 경우	매우 낮음	매우 낮음
H. pylori 양성인 dyspepsia 환자		X
장기간 NSAID를 복용해야 하는 환자		X
H. pylori 에 감염된 환자의 배우자나 자녀		X
역류성 식도 질환으로 장기간 PPI 유지 요법을 해야 하는 환자		X
H. pylori 치료를 원하는 사람		?

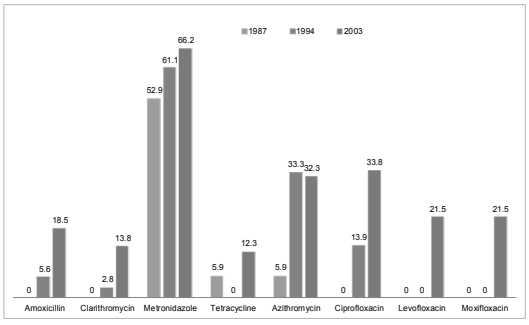
Treatment regimen (First-Line)

Regimen	Duration	Eradication rate	Comment
2005 Maastricht III Consensus Report			
PPI + AMX + CLA or MET	7-14		14 day treatment is more effective than 7 days In populations with less than 15-20% clarithromycin resistance
PPI + CLA + MET			In populations with less than 40% metronidazole resistance
Bismuth containing quadruple therapy	10-14		Alternative

Treatment regimen (First-Line)

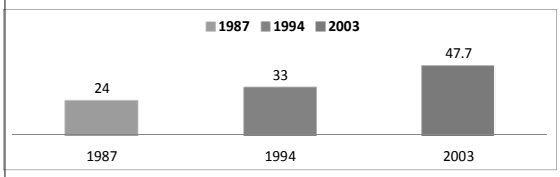
Regimen	Duration	Eradication rate	Comment
2007 American college of gastroenterology			
PPI + AMX + CLA	10–14	70-85%	Consider in nonpenicillin allergic patients who have not previously received a macrolide
PPI + CLA + MET	10–14	70-85%	Consider in penicillin allergic patients who have not previously received a macrolide or are unable to tolerate bismuth quadruple Therapy
Bismuth containing quadruple therapy	10–14	70-85%	Consider in penicillin allergic patients
PPI + AMX 1000 mg (BID) followed by: PPI + CLA 500mg (BID) + Tinidazole 500 mg (BID)	5 5	> 90%	Requires validation in North America

Antibiotic resistance among H. pylori isolates in Korea



Antibiotic resistance of Helicobacter pylori isolated from Korean patients. Korean J Gastroenterol 2006; 47: 337-49.

2개이상 항생제에 대한 내성 비율



The Effects of Resistance of Amoxicillin and Clarithromycin on the Eradication Rate

Amoxicillin	Clarithromycin	No. of patients	Success(%)	Failure(%)
Susceptible	Susceptible	31	97	3
Resistant	Susceptible	5	40	60
Susceptible	Resistant	5	0	100
Resistant	Resistant	2	0	100

Treatment regimen (Second-Line)

regimen	duration	Eradication Rate	comment
2009 대한 Helicobacter 및 상부위장관 연구학회			
PPI (BID) + Denol 120mg (QID) + MET 0.5g (TID) + TET 0.5g (QID)	7 - 14		
2005 Maastricht III Consensus Report			
PPI + Bismuth + MET + TET	7 -		Minimum for 7 days Remain the best second choice
PPI + AMX or TET + MET			If Bismuth is not available
2007 American college of gastroenterology			
PPI + Bismuth + MET + TET	7	68%	Accessible, cheap but high pill count and frequent mild side effects
Levofloxacin triple therapy PPI + AMX 1 g (BID) + LVF 500 mg (QD)	10	87%	Requires validation in North America