EGYPHAR

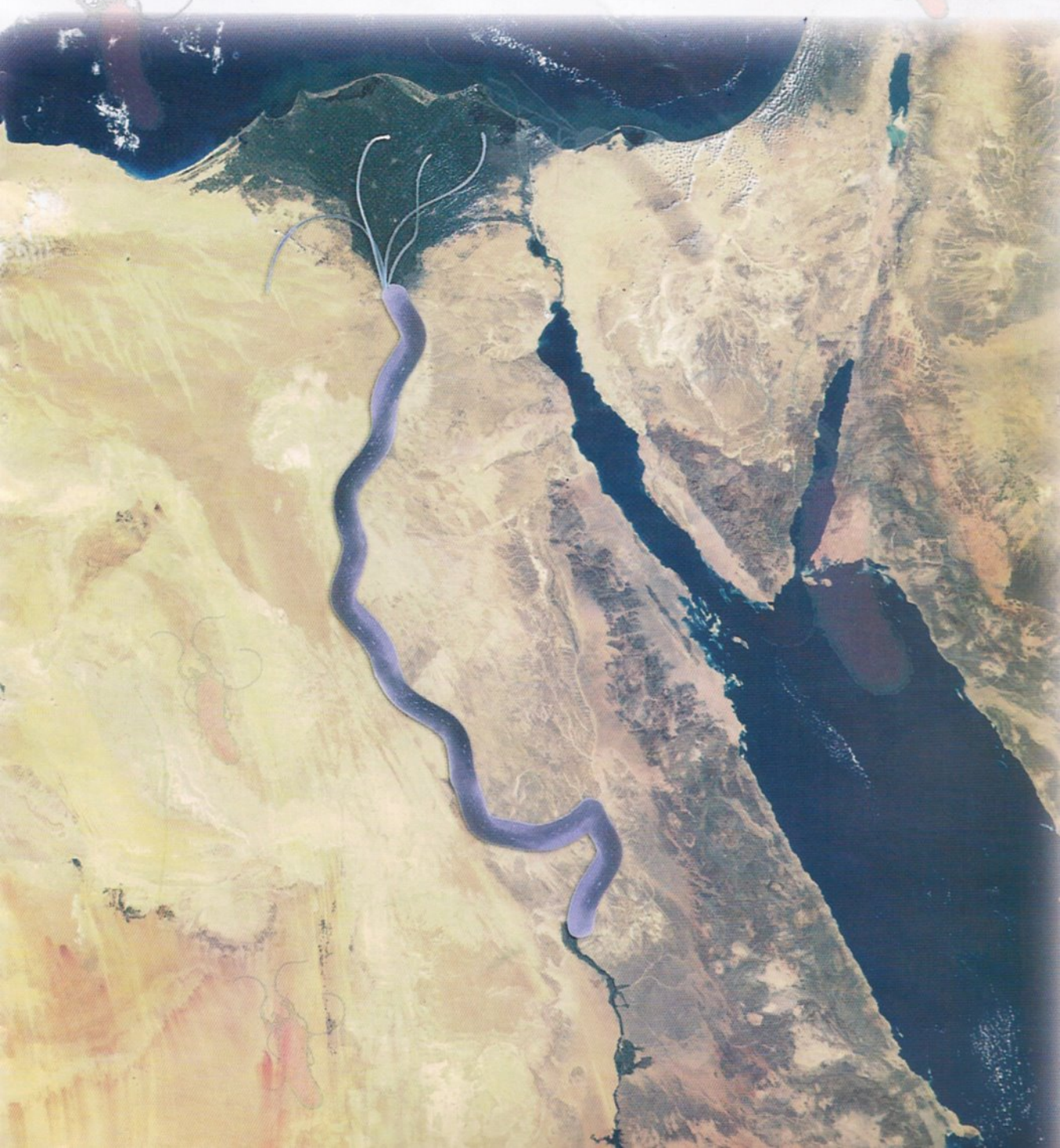# MEDICAL UPDATES

## A Word From EGYPHAR General Manager

It is our honor to launch the first issue of EGYPHAR MEDICAL UPDATES. Since EGYPHAR was established, 10 years ago, we continue extending the professional and scientific ties with the health care community, especially with the esteemed physician's community, and we have been committed to provide the market with versatile product range of high quality and affordable prices. In this issue of EGYPHAR MEDICAL UPDATED, you will notice that we are making our efforts to provide you with updated medical topics which we are certain that it will be of interest to you. We hope that you find it of value and we look forward to receiving your comments, if any, We thank you for your usual meaningful support and my best personal regards.

Dr. Mohammad Roushdy
General Manager

# Chronic gastritis, peptic ulcer, and gastric cancer

Involvement of ras and ap-1 in helicobacter pylori-induced expression of cox-2 and inos in gastric epithelial ags cells.

**Helicobacter pylori (h. Pylori) is an important risk factor For chronic gastritis, peptic ulcer, and gastric cancer.**

Cho so, lim jw, kim kh, kim h

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The genetic differences of h. Pylori isolates play a role in the clinical outcome of the infection. Inflammatory genes including cyclooxygenase-2 (cox-2) and inducible nitric oxide synthase (inos) are involved in h. Pylori gastritis. Transcription factor ap-1 is composed of c-fos and c-jun and mediates inflammation and carcinogenesis.

Ras acts as a regulator for ap-1 activation in various cells. We investigated whether h. Pylori in a korean isolate (hp99), a caga (+), vaca (+) strain, induces the expression of c-fos and c-jun for ap-1 activation to induce cox-2 and inos and whether hp99-induced expressions of cox-2 and inos are mediated by ras and ap-1, determined by the expressions of c-fos and c-jun, in gastric epithelial ags cells, using transfection with mutant genes for ras (ras n-17) and c-jun (tam-67).

As a result, hp99 induced the expression of c-fos and c-jun and the expressions of cox-2 and inos in ags cells. Transfection with mutant genes for ras or c-jun suppressed hp99-induced expressions of cox-2 and inos in ags cells. In conclusion, h. Pylori in a korean isolate induces the expression of cox-2 and inos via ap-1 activation, which may be mediated by ras and the expression of c-fos and c-jun in gastric epithelial cells.

# 90%

**Helicobacter pylori in the developing world is associated with many unique challenges not encountered in an industrialized setting.**

Enteric Disease Research Program, US Naval Medical Research Unit #3, Cairo, Egypt. FrenckR@namru3.med.navy.mil

Helicobacter pylori in the developing world is associated with many unique challenges not encountered in an industrialized setting. The 20% prevalence of infection with H. pylori among adolescents in the United States pales in comparison to infection rates exceeding 90% by 5 years of age in parts of the developing world. While H. pylori within the developed world is associated with gastritis, which may lead to peptic ulcer and gastric carcinoma, the infection in the developing world appears to also be linked with chronic diarrhea, malnutrition and growth faltering as well as predisposition to other enteric infections, including typhoid fever and cholera. Once identified, treatment of H. pylori within the developing world presents increased difficulties due to the frequency of antibiotic resistance as well as the frequency of recurrence after successful treatment. Control, and possibly eradication, of H. pylori could likely be achieved through increased standards of living and improved public health, as it has in the industrialized world. However, these measures are distant objectives for most developing countries, making long-term control of the organism dependent on the development and administration of an effective vacci

Frenck rw jr, clemens j.

**Infection rates exceeding 90% by 5 years of age in parts of the developing world**

From the department of tropical medicine and biochemistry department, minofyia university, minofyia, egypt.

# Common problems in egypt

**Helicobacter pylori infection, peptic ulcer and gastric cancer are common problems in egypt**

Helicobacter pylori infection, peptic ulcer and gastric cancer are common problems in Egypt. We investigated the prevalence of cagA-positive Helicobacter pylori infections among Egyptian adults in relation to presentation (e.g. dyspepsia vs asymptomatic controls) in Minofyia, Egypt. Patients included men or women seeking care for at least 3 months of upper gastrointestinal symptoms. Helicobacter pylori status was determined by rapid urease test and gastric histopathology in patients and by anti-Helicobacter pylori

Prevalence of caga in relation to clinical presentation of helicobacter pylori infection in egypt.

IgG antibodies in controls. CagA status was determined using an anti-cag A ELISA. 99 Helicobacter pylori infected patients were entered including 90 dyspeptic patients (30 each with gastric cancer, peptic ulcer, and non-ulcer dyspepsia) and 9 non-dyspeptic healthy controls. Age ranged from 27 to 78 y (mean 49.5 y); 50% were men. Anti-cagA antibodies were present in 62.2% of dyspeptic patients compared with 11% of asymptomatic controls (p=0.004). Anti-cagA antibodies were more prevalent among dyspeptic patients with gastric cancer or peptic ulcer (73.3%) compared to those with non-ulcer dyspepsia (40%) (p=0.004). The prevalence of cagA in Egypt was related to the clinical presentation of Helicobacter pylori infection being lowest in asymptomatic controls (11.1%) and increasingly prevalent in non-ulcer dyspepsia (40%), peptic ulcer (66.7%), and gastric cancer (89%).

Essa as, nouh ma, ghaniam nm, graham dy, sabry hs.
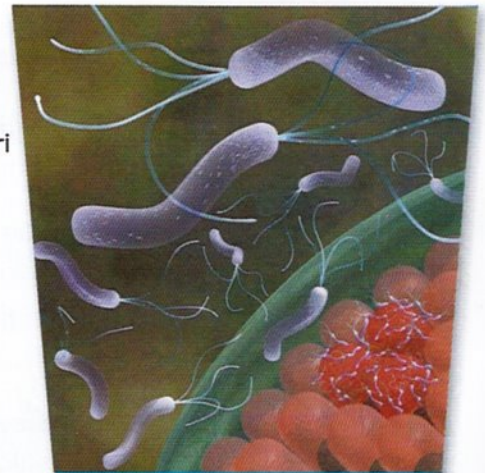
# Epidemiological

## The prevalence of h. Pylori antibodies in asymptomatic young egyptian persons

Department of internal medicine, faculty of medicine, high institute of public health, university of alexandria, egypt.

Developing countries show a higher incidence of h. Pylori infection than developed countries. Also, an earlier age of acquisition of such infection is reported. This study was conducted on sera from 89 persons who were either admitted for surgical conditions or seen on an outpatient basis and having no g.I. Symptoms or signs; all aged below 30 years. Sera were tested by eia technique for the presence of h. Pylori antibodies. The sera of 78 (87.6%) Were positive for h. Pylori antibodies while only 11(12.4%) Were negative. In those below 10 years, 10 (53%) were positive, while 29 (100%) in those between 11 - 20 years were positive and 39 (95%) of those between 21 - 30 years were positive. Ninety one percent of females but only 79% of males were positive. This study clearly illustrates that infection with h. Pylori occurs in egypt very early during childhood below the age of 10. It also shows that the detection of h. Pylori antibodies, in egypt, is of epidemiological and not clinical utility.

Salem oe, youssri ah, mohammad on.

The detection of h. Pylori antibodies, in egypt, is of epidemiological and not clinical utility.

# Empirical treatment of h. Pylori infection

What is the best strategy for diagnosis and treatment of helicobacter pylori in the prevention of recurrent peptic ulcer bleeding? A cost-effectiveness analysis.

**In patients with bleeding peptic ulcer, empirical treatment of h. Pylori infection immediately after feeding is restarted is the most cost-effective strategy for preventing recurrent hemorrhage.**

Gené e, sanchez-delgado j, calvet x, gisbert jp, azagra r.
Servei d'urgències, hospital de sabadell, corporació parc taulí, barcelona, spain.

Abstract background: clinical trials provide evidence of the high effectiveness of helicobacter pylori eradication for preventing recurrent ulcer-related gastrointestinal hemorrhage. The best strategy for curing the infection in this setting is, however, still under debate. Objective: to evaluate four different strategies for prevention of rebleeding in patients with peptic ulcer hemorrhage: 1) test for h. Pylori and treatment, if positive; 2) proton pump inhibitor maintenance; 3) no preventive treatment; 4) empirical h. Pylori eradication immediately after bleeding. Methods: a decision analysis model was used, with a time horizon of 2 years and a third-party payer perspective. Costs were estimated for two different settings: a low-cost-for-care area (spain) and a high-cost area (usa). Main outcome measure was incremental cost-effectiveness ratio for each upper gastrointestinal hemorrhage avoided. Results: empirical h. Pylori eradication was the dominant strategy: its estimated rate of recurrent bleeding was lower (6.1%) Than those of strategies 1 (7.4%), 2 (11.1%), And 3 (18.4%) And it was the least expensive strategy. The results remained stable when variables were changed inside a wide range of plausible values. Sensitivity analysis also showed that the prevalence of h. Pylori in bleeding ulcer was the variable that most influenced the results: when it was below 45% in spain or below 51% in the united states, empirical eradication was not a dominant strategy although it remained cost-effective. Conclusion: in patients with bleeding peptic ulcer, empirical treatment of h. Pylori infection immediately after feeding is restarted is the most cost-effective strategy for preventing recurrent hemorrhage.

# The most frequent

**Gastric mucosa as a target of persistent proinflammatory aggression: pathogenic models of chronic gastritis.**

Servicio de aparato digestivo, fundación jiménez díaz, universidad autónoma, madrid, españa.

There are several causes of damage and regeneration of the gastric epithelium (erosive gastropathy) and/or histological inflammation of the gastric mucosa (acute or chronic gastritis). After outlining the usual morphology of chronic gastritis, the authors attempt to identify the biological profile of the main pathogenic models. The first, and by far the most frequent, is the model associated with Helicobacter pylori, which, without crossing the mucosal epithelium, provokes an immune reaction. Although incapable of eradicating this bacterium, this immune reaction contributes to the inflammatory lesion provoked by H. pylori in the mucosa. The second -and much less frequent- model is that causing progressive atrophic gastritis through a humoral and cellular autoimmune mechanism. In third place are a group of models defined by a peculiar cytohistologic pattern of inflammation (granulomatous, lymphocytic or eosinophilic gastritis), suggesting similar pathogenic mechanisms for each of these

**There are several causes of damage and regeneration of the gastric epithelium**

**The first, and by far the most frequent, is the model associated with helicobacter pylori,**

rare morphological forms of gastritis. Lastly, there is a model barely fitting within the scope of this review, which is that provoking chemical gastropathies (bile reflux, NSAIDs, etc.) with minimal cellular inflammation, i.e., minimal gastritis. To aid understanding of the article, the authors provide a brief outline of the functional histology of the gastric wall and the mechanisms defending its integrity in physiological conditions.

Sánchez-fayos calabuig p, martín relloso mj, porres cubero jc

# The association is much
## stronger than estimated

infection is an established risk factor for chronic atrophic gastritis. However, estimates of the strength of this association have varied widely, possibly due to clearance of the infection in severe stages of chronic atrophic gastritis, which may lead to underestimation of the association. We assessed the association of H. pylori infection with chronic atrophic gastritis according to severity of disease. METHODS:: We measured serum pepsinogen I and II (as surrogates for chronic atrophic gastritis) and antibodies againstH. pyloriby ELISA in 9444 men and women aged 50&cjs0023;74 years in a population-based study in Saarland, a state of Germany. The association between H. pylori and chronic atrophic gastritis (defined as pepsinogen I &cjs0060;70 ng/mL and pepsinogen I/II-ratio &cjs0060;3) was analyzed after stratification of chronic atrophic gastritis cases by quintiles of pepsinogen I as proxy marker for severity of chronic atrophic gastritis. RESULTS:: When all cases were included, the odds ratio for the association with Chronic atrophic gastritis forH. pyloriinfectionalone was 2.9 (95% confidence interval 2.3&cjs0023;3.6); it was 4.1 (3.2&cjs0023;5.2), for H. pylori infection that was positive for the presence of Ig G antibodies specific to the cytotoxin-associated gene A (CagA)protein&cjs0024;a well-established virulence factor of H. pylori.

> **Helicobacter pylori infection is an established risk factor for chronic atrophic gastritis**
>
> **The association between h.Pylori and chronic gastritis is much stronger than estimated by most epidemiologic studies to date**

These ORs ranged from 11 (5.2-22) and 16 (7.7-34) for the quintile of cases with highest pepsinogen I (least severe cases) to 1.0 (0.7-1.6) and 0.9 (0.5-1.5) for the quintile of cases with lowest pepsinogen I (most severe cases). Five of 7 cases with CagA-seropositivity but negative H. pylori serostatus (a pattern indicative of past infection) were in the group of most severe cases. CONCLUSIONS:: Our results support the hypothesis of major underestimation of the association ofH. pyloriand chronic atrophic gastritis, due to clearance of the infection in advanced stages of the disease. These results suggest that the association is much stronger than estimated by most epidemiologic studies to date.

Weck mn, gao I, brenner h
Background:: helicobacter pylori

# Gastric carcinoma

### Helicobacter pylori infection induces genetic instability of nuclear and mitochondrial dna in gastric cells.
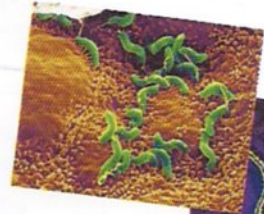
**Machado am, figueiredo c, touati e, máximo v, sousa s, michel v, carneiro f, nielsen fc, seruca r, rasmussen lj**

Department of science, systems and models, roskilde university, roskilde, denmark.

> **Helicobacter pylori is a major cause of gastric carcinoma.**

PURPOSE: Helicobacter pylori is a major cause of gastric carcinoma. To investigate a possible link between bacterial infection and genetic instability of the host genome, we examined the effect of H. pylori infection on known cellular repair pathways in vitro and in vivo. Moreover, various types of genetic instabilities in the nuclear and mitochondrial DNA (mtDNA) were examined. EXPERIMENTAL DESIGN: We observed the effects of H. pylori infection on a gastric cell line (AGS), on C57BL/6 mice, and on individuals with chronic gastritis. In AGS cells, the effect of H. pylori infection on base excision repair and mismatch repair (MMR) was analyzed by reverse transcription-PCR, Western blot, and activity assays. In mice, MMR expression was analyzed by reverse transcription-PCR and the CA repeat instabilities were examined by Mutation Detection Enhancement gel electrophoresis. Mutation spectra in AGS cells and chronic gastritis tissue were determined by PCR, single-stranded conformation polymorphism, and sequencing. H. pylori vacA and cagA genotyping was determined by multiplex PCR and reverse hybridization. RESULTS: Following H. pylori infection, the activity and expression of base excision repair and MMR are down-regulated both in vitro and in vivo. Moreover, H. pylori induces genomic instability in nuclear CA repeats in mice and in mtDNA of AGS cells and chronic gastritis tissue, and this effect in mtDNA is associated with bacterial virulence. CONCLUSIONS: Our results suggest that H. pylori impairs central DNA repair mechanisms, inducing a transient mutator phenotype, rendering gastric epithelial cells vulnerable to the accumulation of genetic instability and thus contributing to gastric carcinogenesis in infected individuals.

# Helicobacter pylori
— the bacterium causing peptic ulcer disease

### Infection
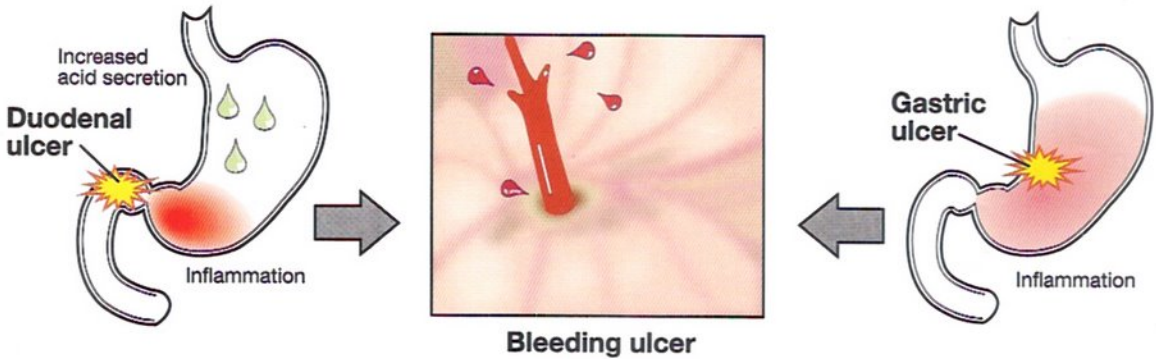*Helicobacter pylori* infects the lower part of the stomach, antrum.

Corpus

Duodenum

Pylorus  Antrum

*Helicobacter pylori*
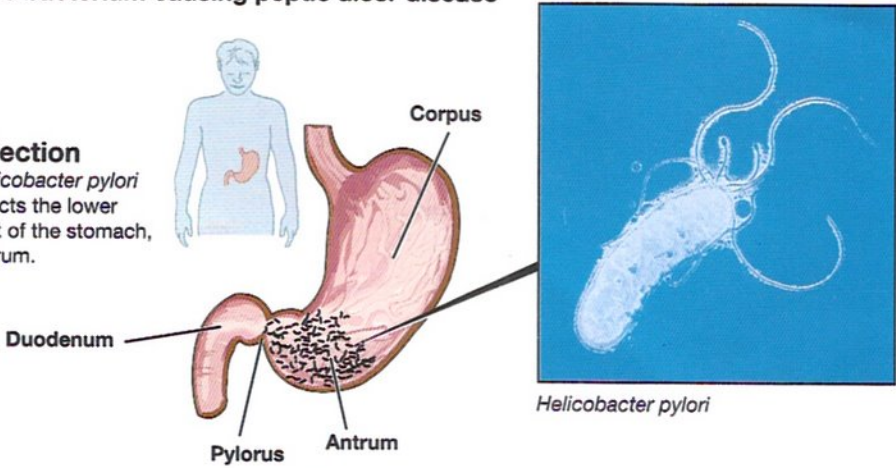
### Inflammation
*Helicobacter pylori* causes inflammation of the gastric mucosa (gastritis). This is often asymptomatic.

Gastric mucosa

*Helicobacter pylori*

Protective mucus

Inflammatory cells
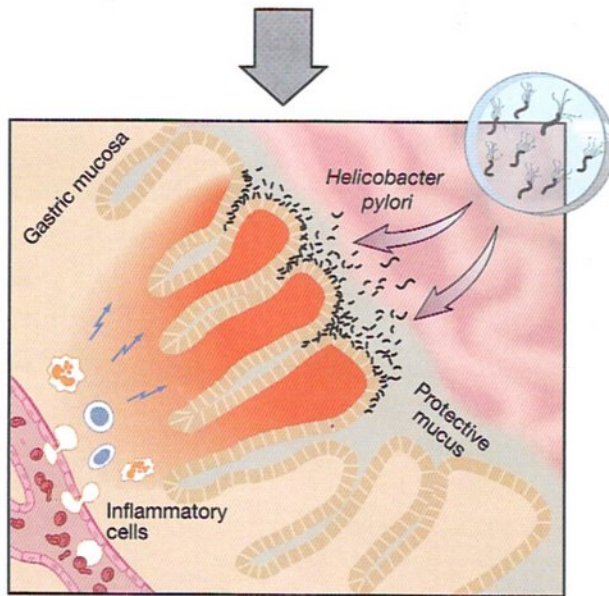
### Ulcer
Gastric inflammation may lead to duodenal or gastric ulcer. Severe complications include bleeding ulcer and perforated ulcer.

Increased acid secretion

**Duodenal ulcer**

Inflammation

**Gastric ulcer**

Inflammation

**Bleeding ulcer**

In patients with bleeding peptic ulcer, empirical treatment of h. Pylori infection immediately after feeding is restarted is the most cost-effective strategy for preventing recurrent hemorrhage.

Infection rates exceeding 90% by 5 years of age in parts of the developing world

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