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These lectures were prepared and performed for the students.

we published them in the MediTec websites to wider our educational aims.

With thanks to our team member Prof. Ismail Matalkeh for his efforts.

CHRONIC GASTRITIS & PEPTIC ULCER DISEASE
THE TALE OF A BACTERIUM AND NOBEL PRIZE

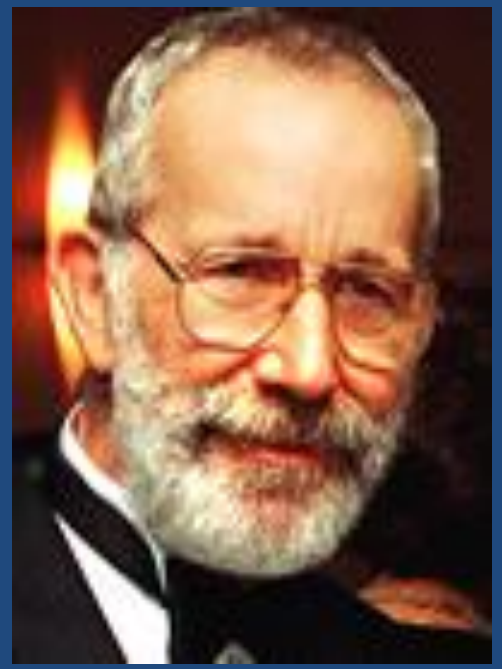
Ismail Matalka, FRCPath
Professor of Pathology
School of Medicine & King Abdullah University Hospital
Jordan University of Science & Technology

Marshall BJ, Warren JR. Unidentified curved bacilli in the human stomach. Lancet, 1983

Barry J Marshall & J Robin Warren

The Nobel Prize in Physiology/Medicine 2005

"for their discovery of the bacterium *Helicobacter pylori* and its role in gastritis and peptic ulcer disease"



The Marshall/Warren story

- Perth, Australia, late 70s: Robin Warren, Histopathologist, with 20 odd cases of a peculiar bacterial infection in the stomach
- Barry Marshall: young thrusting gastroenterologist in need of a project
- Dual publications in the Lancet in 1983

been transferred to the family Spirillaceae genus *Campylobacter*.[8] Campylobacters however, have "a single polar flagellum at one or both ends of the cell" and the campylobacter flagellum is unsheathed.[9] Warren's bacteria may be of the genus *Spirillum*.

The pathogenicity of these bacteria remains unproven but their association with polymorphonuclear infiltration in the human antrum is highly suspicious. If these bacteria are truly associated with antral gastritis, as described by Warren, they may have a part to play in other poorly understood, gastritis associated diseases (ie, peptic ulcer and gastric cancer).

I thank Miss Helen Royce for microbiological assistance, Dr J. A. Armstrong for electronmicroscopy, and Dr Warren for permission to use fig 1.

Department of Gastroenterology,
Royal Perth Hospital,
Perth, Western Australia 6001

BARRY MARSHALL

UNIDENTIFIED CURVED BACILLI ON GASTRIC EPITHELIUM IN ACTIVE CHRONIC GASTRITIS

SIR,—Gastric microbiology has been sadly neglected. Half the patients coming to gastroscopy and biopsy show bacterial colonisation of their stomachs, a colonisation remarkable for the constancy of both the bacteria involved and the associated histological changes. During the past three years I have observed small curved and S-shaped bacilli in 135 gastric biopsy specimens. The bacteria were closely associated with the surface epithelium, both within and between the gastric pits. Distribution was continuous, patchy, or focal. They were difficult to see with haematoxylin and eosin stain, but stained well by the Warthin-Starry silver method (figure).

I have classified gastric biopsy findings according to the type of inflammation, regardless of other features, as "no inflammation", "chronic gastritis" (CG), or "active chronic gastritis" (ACG). CG shows more small round cells than normal while ACG is characterised by an increase in polymorphonuclear neutrophil leucocytes, besides the features of CG. It was unusual to find no inflammation. CG usually showed superficial oedema of the mucosa. The leucocytes in ACG were usually focal and superficial, in and near the surface epithelium. In many cases they only infiltrated the necks of occasional gastric glands. The superficial epithelium was often irregular, with reduced mucinogenesis and a cobblestone surface.

When there was no inflammation bacteria were rare. Bacteria were often found in CG, but were rarely numerous. The curved bacilli were almost always present in ACG, often in large numbers and often growing between the cells of the surface epithelium (figure). The constant morphology of these bacteria and their intimate relationship with the mucosal architecture contrasted with the heterogeneous bacteria often seen in the surface debris. There was normally a layer of mucous secretion on the surface of the mucosa. When this layer was intact, the debris was spread over it, while the curved bacilli were on the epithelium beneath, closely spread over the surface (figure).

The curved bacilli and the associated histological changes may be present in any part of the stomach, but they were seen most consistently in the gastric antrum. Inflammation, with no bacteria, occurred in mucosa near focal lesions such as carcinoma or peptic ulcer. In such cases, the leucocytes were spread through the full thickness of the nearby mucosa, in contrast to the superficial infiltration associated with the bacteria. Both the bacteria and the typical histological changes were commonly found in mucosa unaffected by the focal lesion.

Curved bacilli on gastric epithelium.

Section is cut at acute angle to show bacteria on surface, forming network between epithelial cells. (Warthin-Starry silver stain; bar = 10 μm.)

Determinative Bacteriology. The stomach must not be viewed as a sterile organ with no permanent flora. Bacteria in numbers sufficient to see by light microscopy are closely associated with an active form of gastritis, a cause of considerable morbidity (dyspeptic disease). These organisms should be recognised and their significance investigated.

Department of Pathology,
Royal Perth Hospital,
Perth, Western Australia 6001

J. ROBIN WARREN

The Marshall/Warren story

The Lancet · Saturday 16 June 1984

UNIDENTIFIED CURVED BACILLI IN THE STOMACH OF PATIENTS WITH GASTRITIS AND PEPTIC ULCERATION*

BARRY J. MARSHALL J. ROBIN WARREN

Departments of Gastroenterology and Pathology, Royal Perth Hospital, Perth, Western Australia

Summary Biopsy specimens were taken from intact areas of antral mucosa in 100 consecutive consenting patients presenting for gastroscopy. Spiral or curved bacilli were demonstrated in specimens from 58 patients. Bacilli cultured from 11 of these biopsies were gram-negative, flagellate, and microaerophilic and appeared to be a new species related to the genus *Campylobacter*. The bacteria were present in almost all patients with active chronic gastritis, duodenal ulcer, or gastric ulcer and thus may be an important factor in the aetiology of these diseases.

Patients and Methods

Patients

All patients referred for gastroscopy on clinical groun eligible for the study which continued until there w participants who gave informed consent and in whom bio considered to be safe. The study was approved by our h human rights committee.

Questionnaire

Where possible patients completed a clinical questi designed to detect a source of infection or show any relat with "known" causes of gastritis or *Campylobacter* infectio than give a detailed account of each patient's history. The e was on animal contact, travel, diet, dental hygiene, and drug than symptoms.

Endoscopy

The gastroscopies were done by colleagues at the Roya Hospital. Participants fasted for at least 4 h before endosc

J Clin Pathol 1986;**39**:353–365

Review article

Campylobacter pyloridis, gastritis, and peptic ulceration

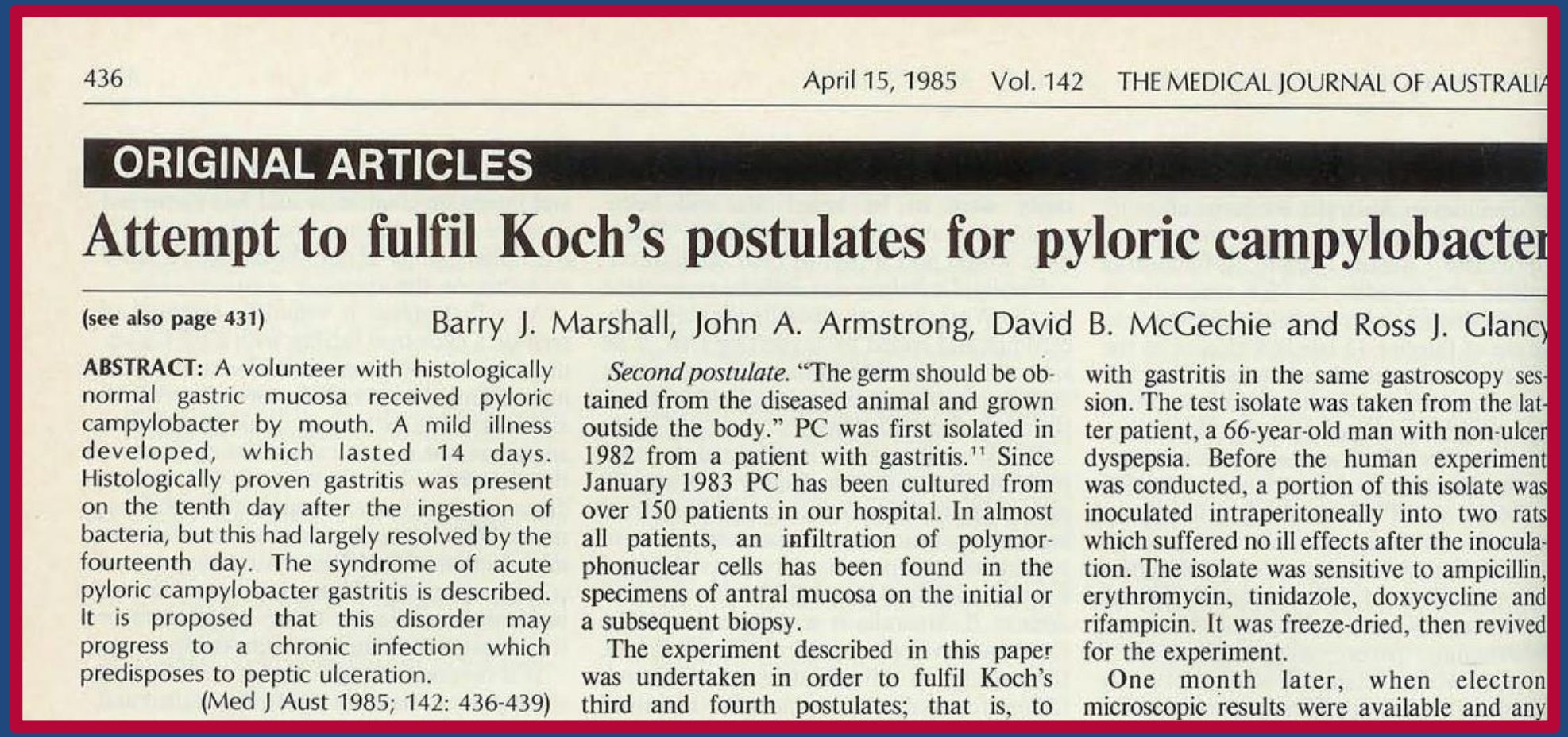
CS GOODWIN,* JA ARMSTRONG,† BJ MARSHALL‡

*From the Departments of *Microbiology, †Electronmicroscopy, and ‡Gastroenterology, Royal Perth Hospital, Western Australia*

SUMMARY *Campylobacter pyloridis* is a spiral bacterium which was seen by histopathologists several years before it was cultured in 1982 in Perth, Western Australia. It has unique cellular fatty acids, predominantly tetradecanoic acid and cis-11, 12 methylene octadecanoic acid. It also has a unique ultrastructure which is different from that of other campylobacters. *C pyloridis* possesses a powerful urease enzyme and produces large amounts of extracellular catalase. Both these features may be important virulence factors, allowing it to occupy a protected niche in the stomach below the mucus layer but above the gastric mucosa. Specific lesions are found in the gastric mucosa, and ultrastructural studies show the presence of adherence pedestals identical with those found with enteropathogenic *Escherichia coli* of the intestine. Histological examination of gastric biopsy tissue has shown that *C pyloridis* is strongly associated with active chronic gastritis, when polymorphonuclear leucocytes are present, and is not found on normal mucosa except when a biopsy specimen from elsewhere in the stomach shows active chronic gastritis. When patients with symptoms caused by gastritis are identified dual antibacterial treatment, combining the action of bismuth in the stomach with a systemic antibiotic, can eradicate *C pyloridis*, with remission of symptoms and restoration of normal epithelial morphology. Most peptic ulcers relapse after modern acid reducing treatment, and antibacterial treatment may be beneficial in preventing relapse.

The Marshall/Warren story

- A famous experiment Dr. Marshall conducted on himself was crucial in linking the bacterium to inflammation of the stomach, or gastritis, and showing that it resulted from an infection.



436 April 15, 1985 Vol. 142 THE MEDICAL JOURNAL OF AUSTRALIA

ORIGINAL ARTICLES

Attempt to fulfil Koch's postulates for pyloric campylobacter

(see also page 431)

Barry J. Marshall, John A. Armstrong, David B. McGechie and Ross J. Glancy

ABSTRACT: A volunteer with histologically normal gastric mucosa received pyloric campylobacter by mouth. A mild illness developed, which lasted 14 days. Histologically proven gastritis was present on the tenth day after the ingestion of bacteria, but this had largely resolved by the fourteenth day. The syndrome of acute pyloric campylobacter gastritis is described. It is proposed that this disorder may progress to a chronic infection which predisposes to peptic ulceration.

(Med J Aust 1985; 142: 436-439)

Second postulate. "The germ should be obtained from the diseased animal and grown outside the body." PC was first isolated in 1982 from a patient with gastritis.[11] Since January 1983 PC has been cultured from over 150 patients in our hospital. In almost all patients, an infiltration of polymorphonuclear cells has been found in the specimens of antral mucosa on the initial or a subsequent biopsy.

The experiment described in this paper was undertaken in order to fulfil Koch's third and fourth postulates; that is, to with gastritis in the same gastroscopy session. The test isolate was taken from the latter patient, a 66-year-old man with non-ulcer dyspepsia. Before the human experiment was conducted, a portion of this isolate was inoculated intraperitoneally into two rats which suffered no ill effects after the inoculation. The isolate was sensitive to ampicillin, erythromycin, tinidazole, doxycycline and rifampicin. It was freeze-dried, then revived for the experiment.

One month later, when electron microscopic results were available and any

The Marshall/Warren story

- Support & interest from Adrian Lee, Sydney, Australia & Drs Skirrow and McNulty, Worcester/Gloucester, UK
- Minimal, even negative, interest, including drug companies
- Only in late 80s, with support from Astra (omeprazole), was the importance of HP appreciated & money flowed into research…..
- Ultimate triumph of the 2005 Nobel Prize for Medicine

Two Win Nobel Prize for Discovering Bacterium Tied to Stomach Ailments

The New York Times

By LAWRENCE K. ALTMANOCT. 4, 2005

- The findings by the Australians in the early 1980's went so against medical thinking, which held that psychological stress caused stomach and duodenal ulcers, that it took many more years for an entrenched medical profession to accept it.

- In its citation, the Nobel committee from the Karolinska Institute in Stockholm said that Dr. Marshall and Dr. Warren "made an irrefutable case that the bacterium Helicobacter pylori" causes ulcers and other diseases.

- "It is now firmly established that H. pylori causes more than 90 percent of duodenal ulcers and up to 80 percent of gastric ulcers," the Nobel committee said.

- In the wake of the ulcer discovery, many scientists have been seeking unknown infectious agents as the cause of many chronic diseases. Examples include microbes that might produce atherosclerosis, the underlying basis of coronary artery disease; ulcerative colitis; regional enteritis (Crohn's disease); and rheumatoid arthritis.

Impacts

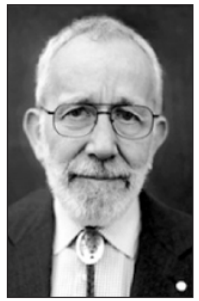
Helicobacter pylori and Ulcers

Richard G. Lynch, MD
Originally published in The ASIP Bulletin, Volume 8, Issue 1 - February 2005

MILESTONES

Warren JR, Marshall BJ:
Unidentified curved bacilli on gastric epithelium in active gastritis. *Lancet* 1983, i:1273-1275

Marshall BJ, Warren JR:
Unidentified curved bacilli in the stomach of patients with gastric and peptic ulceration. *Lancet 1984,* i:1311-1315



J Robin Warren

James B Marshall

These two landmark *Lancet* publications appeared almost 100 years after the first report of spiral bacteria in the human stomach and the initial speculation by several researchers that gastric ulceration was an infectious disease. Although more than 100 experimental studies suggesting a microbial cause of gastritis and peptic ulcers had been published in the first half of the 20th century, and several bacterial and viral species had been implicated as etiologic agents, the concept of an infectious pathogenesis for these common ailments was repeatedly rejected by influential authorities in both gastroenterology and unintentionally extending the incubation period from two to six days.

While the isolation of *Helicobacter pylori* was a breakthrough achievement, it did not establish that the microbe caused gastritis. It was already known from autopsy studies that curved rod-shaped bacilli were present in the stomachs of many individuals who had neither gastritis nor a history of stomach disease. The successful isolation of bacteria from gastric biopsies by Marshall and Warren satisfied the first two of Koch's four postulates, but all four had to be met to indisputably prove that the organism that had been isolated was the cause of the gastritis. In an amazingly daring feat that ultimately fulfilled Koch's postulates, Marshall and another volunteer ingested cultures of the bacteria. Both of them developed acute gastritis proven by endoscopic biopsies from which the suspected pathogen was re-isolated. These results confirmed the link between *H.*

H. Pylori has Revolutionized our Concept about PUD

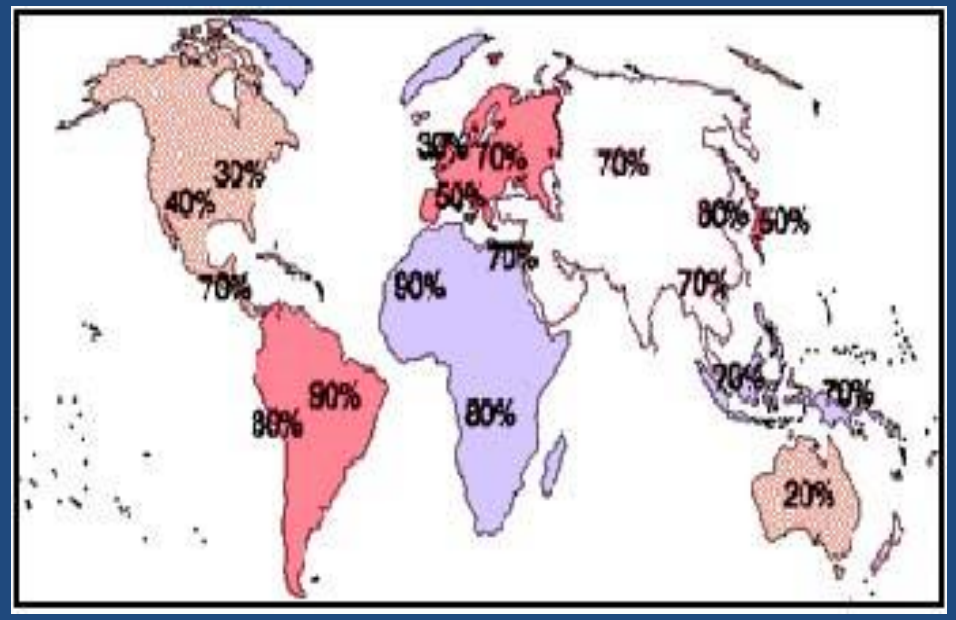
Before

- Peptic ulceration, a disease of world wide occurrence whose definitive treatment was surgical with high morbidity and mortality.
- A dogma that neoplasms are autonomous and neoplastic transformation is irreversible.

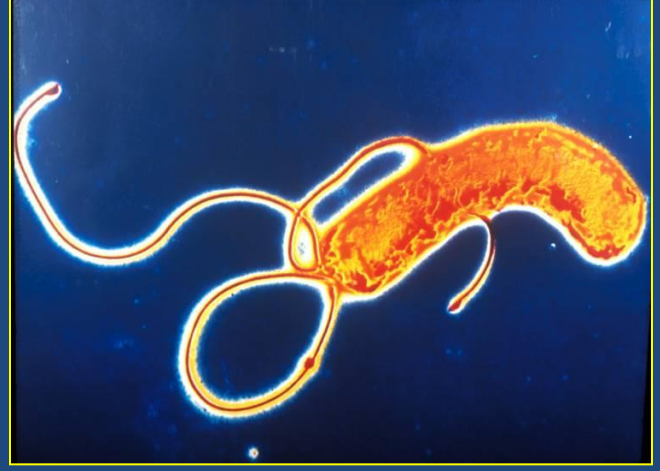
After

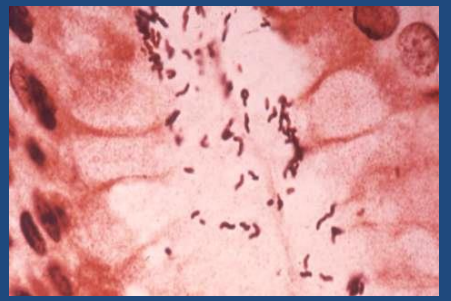
- PUD could be treated and cured with antibiotic
- Designation of H. pylori as a Class I carcinogen by the World Health Organization International Agency for Research in Cancer.
- MALT Lymphoma can be treated by Antibiotics
- Very significant decrease in Gastric Carcinoma and Lymphoma

Epidemiology



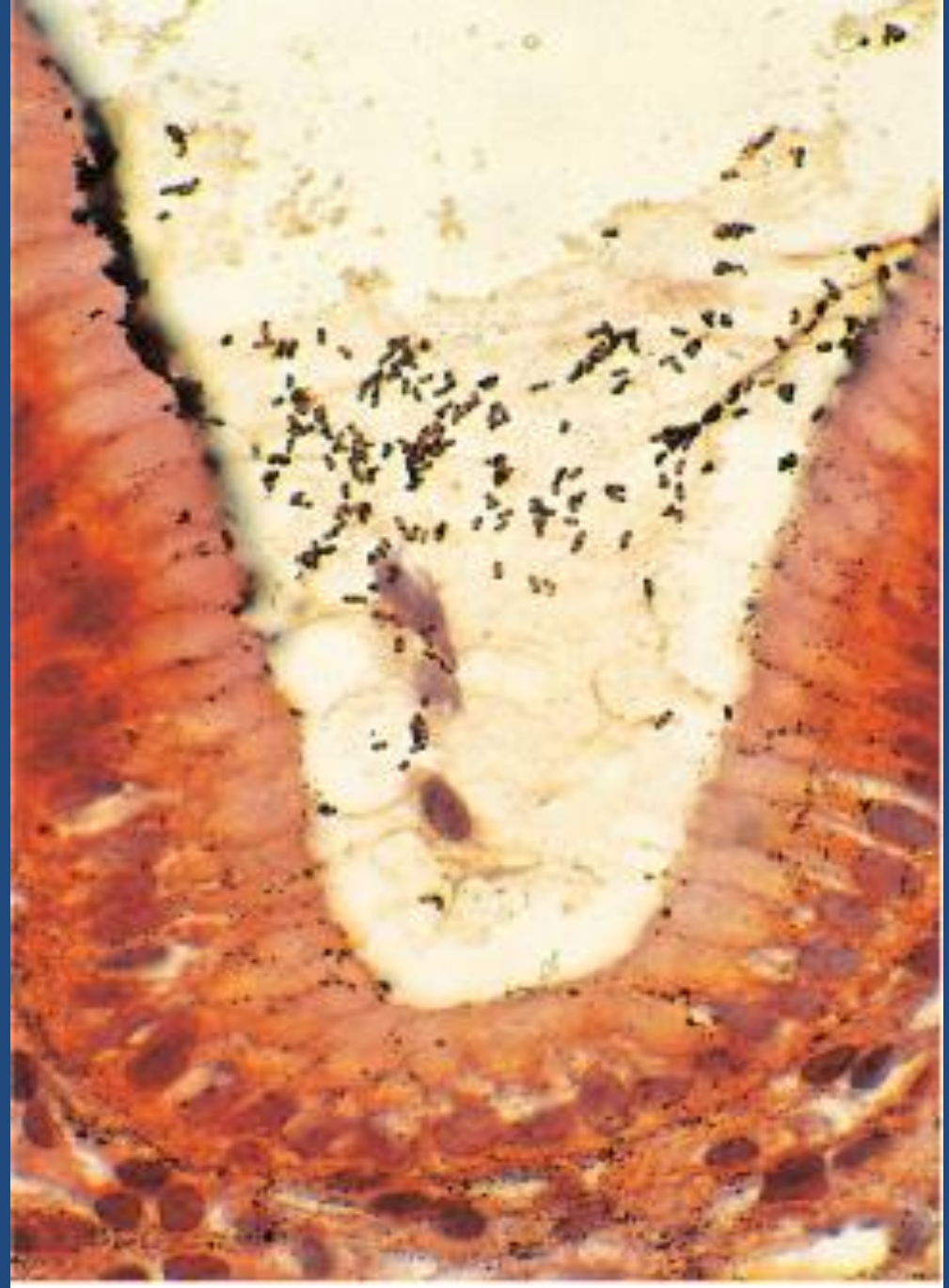
- infects over half the world's population
- infection probably acquired via faecal-oral route
- untreated, infection persists throughout life





- Gram negative motile bacillus 2.5μ long
- usually spiral shaped but can be coccoid under stress/in old cultures
- fastidious slow-growing organism

Although the new organism was only cultured in 1982, the Italian anatomist Giulio Bizzozero had reported its manifestations in the scientific literature 100 years earlier .



GASTRITIS

- Inflammation of the gastric mucosa
- Overused term and underdiagnosed condition
- Classification:

Acute gastritis

Chronic gastritis: most cases

prevalence exceeds 50% in adults >50 years

usually asymptomatic or cause few symptoms

(upper abdominal discomfort, nausea and vomiting)

- Helicobacter pylori associated gastritis: main cause
- Autoimmune (atrophic) gastritis
- Hypertrophic gastritis (gastropathy)
- Granulomatous gastritis; eosinophilic gastritis

The ABC classification of chronic gastritis

Wyatt & Dixon 1988

Type	Cause	Synonyms	Pathology
A for auto-immune (or atrophic)	auto-immune	Chronic atrophic gastritis	Chronic atrophic gastritis with IM
B for bacterial	bacterial	Chronic superficial gastritis	Chronic active gastritis
C for chemical	Chemical, bile reflux, drugs	Reflux gastritis, reactive gastritis	Foveolar hyperplasia, oedema, telangiectasia

HELICOBACTER PYLORI ASSOCIATED CHRONIC GASTRITIS

- Commonest form of gastritis
- *H. pylori* is a widespread noninvasive curved gram -ve rod, which is present in gastric mucosal surface of 50% of adults >50 yrs old
- Infection may be acquired in childhood
- Most infected individuals have gastritis but are asymptomatic
- Clinical features are variable

Adaptive features of *H pylori*

urease
- hydrolyses urea to CO_2 & ammonia
- necessary for colonisation but not for survival

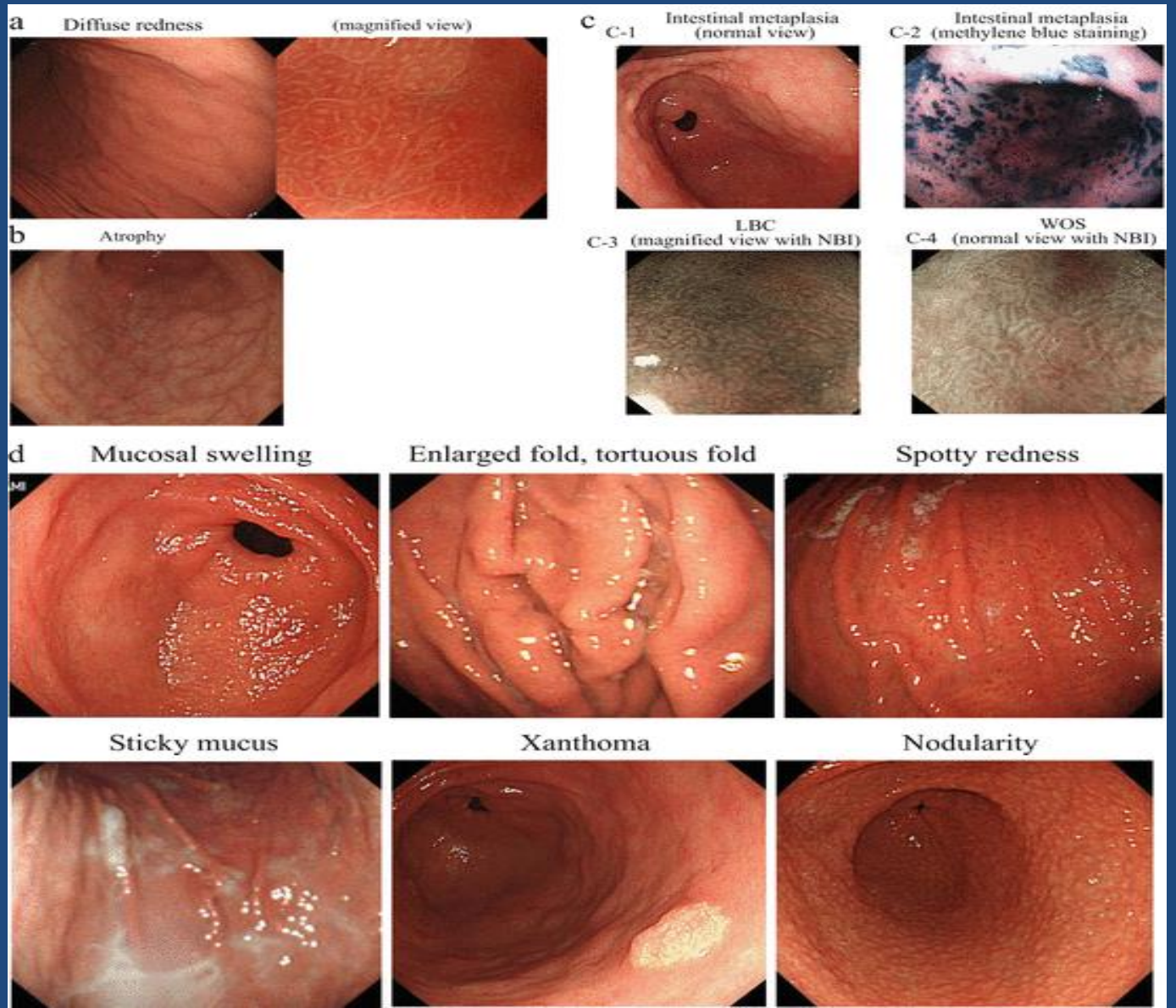
flagellae
- enable motility to areas of low acidity

adhesins
- allow adherence to epithelial surface

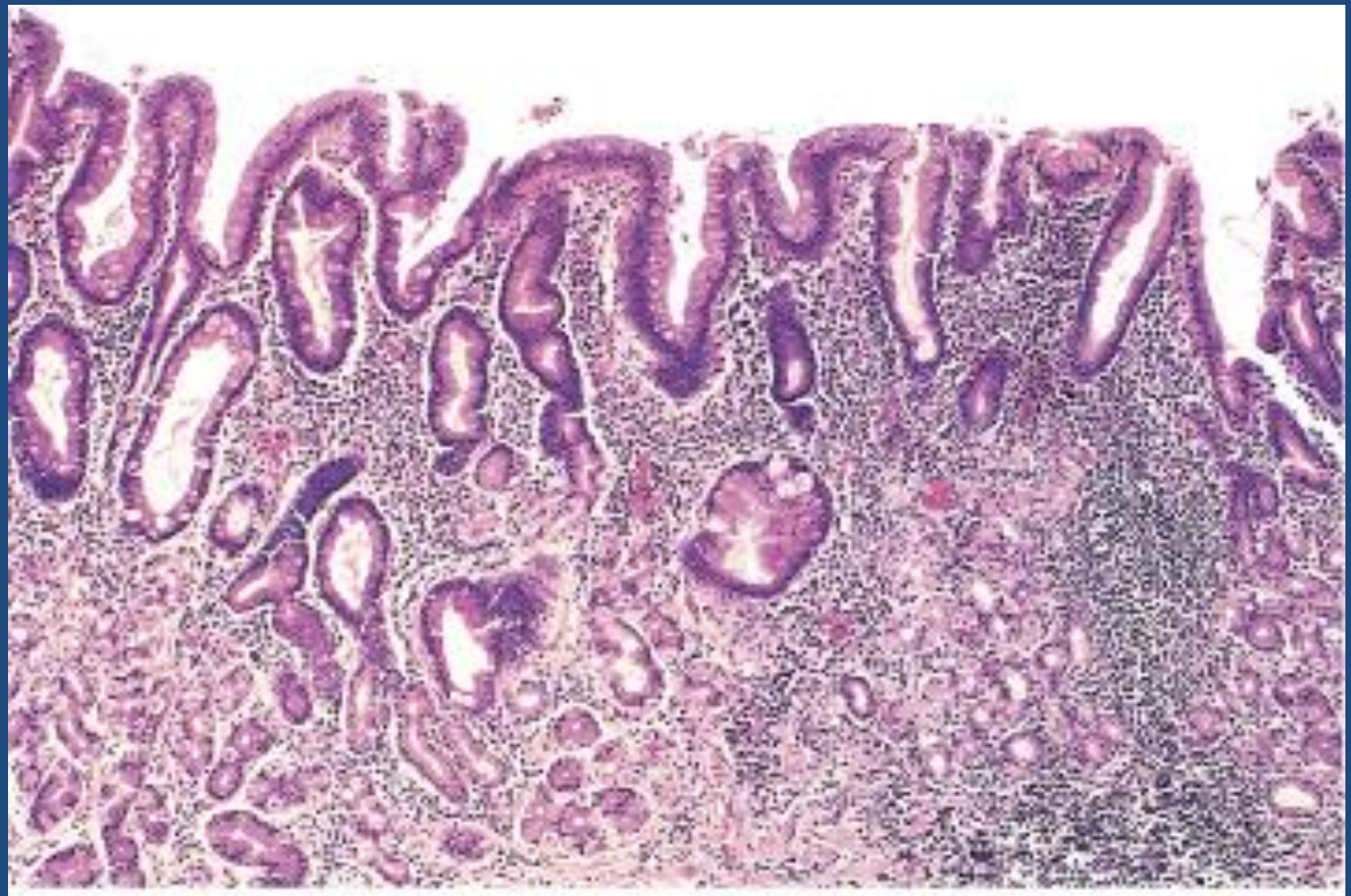
lipopolysaccharide (LPS) coat
- evades host defence mechanisms

Pathogenesis: Directly by bacterial enzymes & toxins, and indirectly by recruitment of PMNs which release noxious chemicals

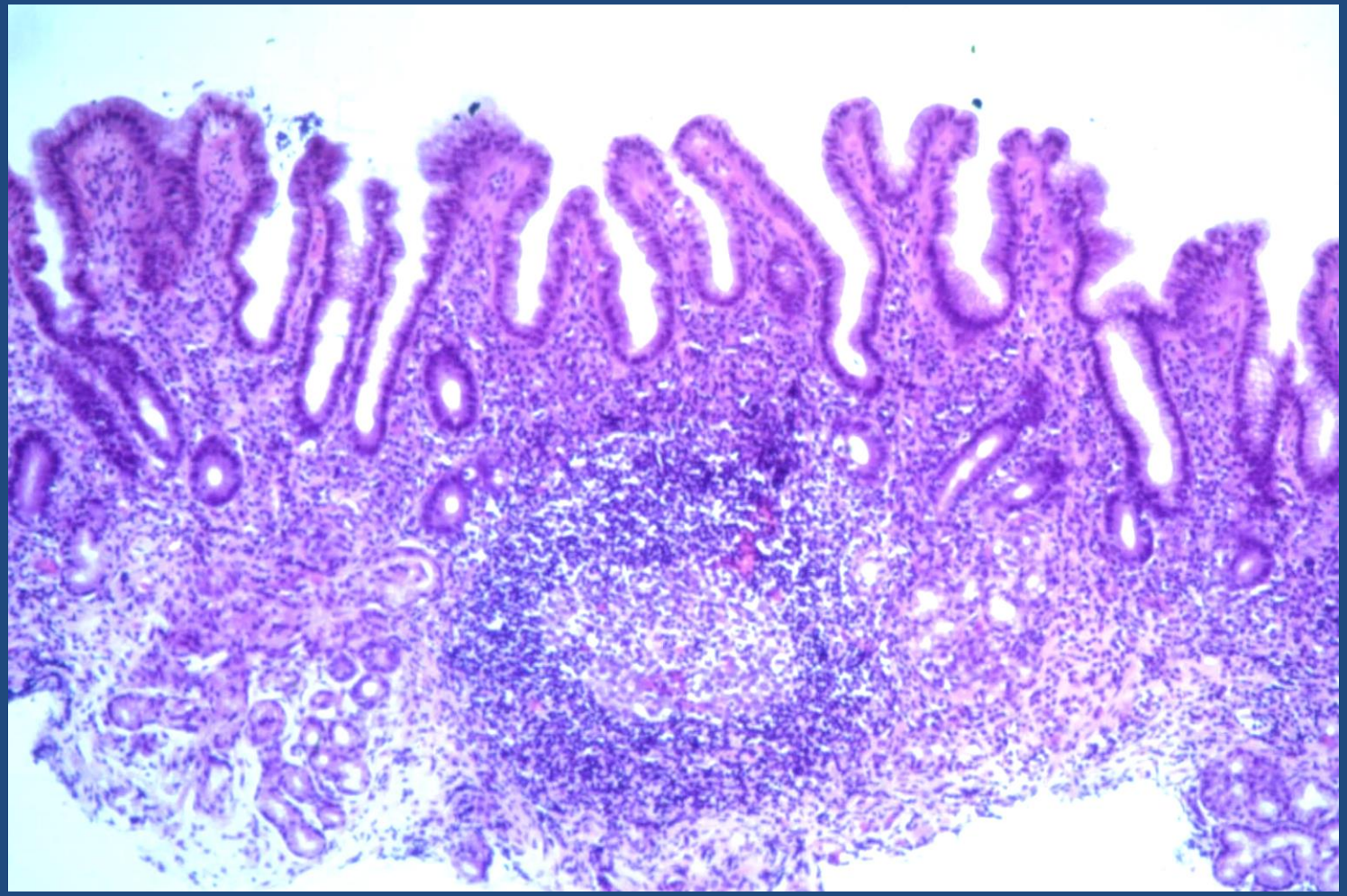
Endoscopic Appearance

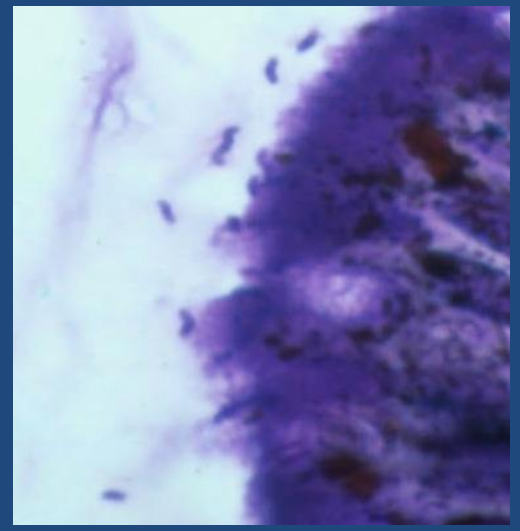


Histopathology

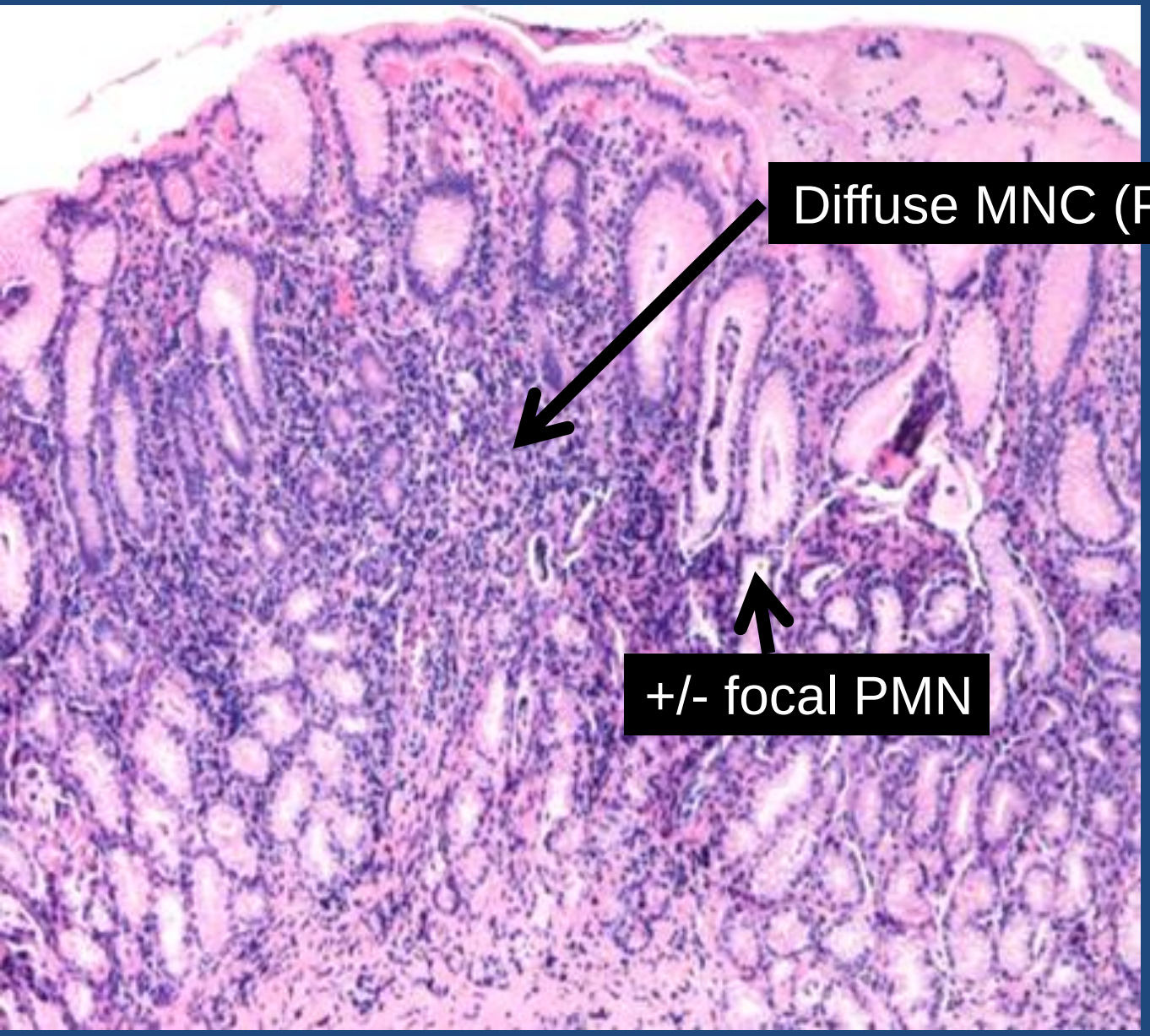


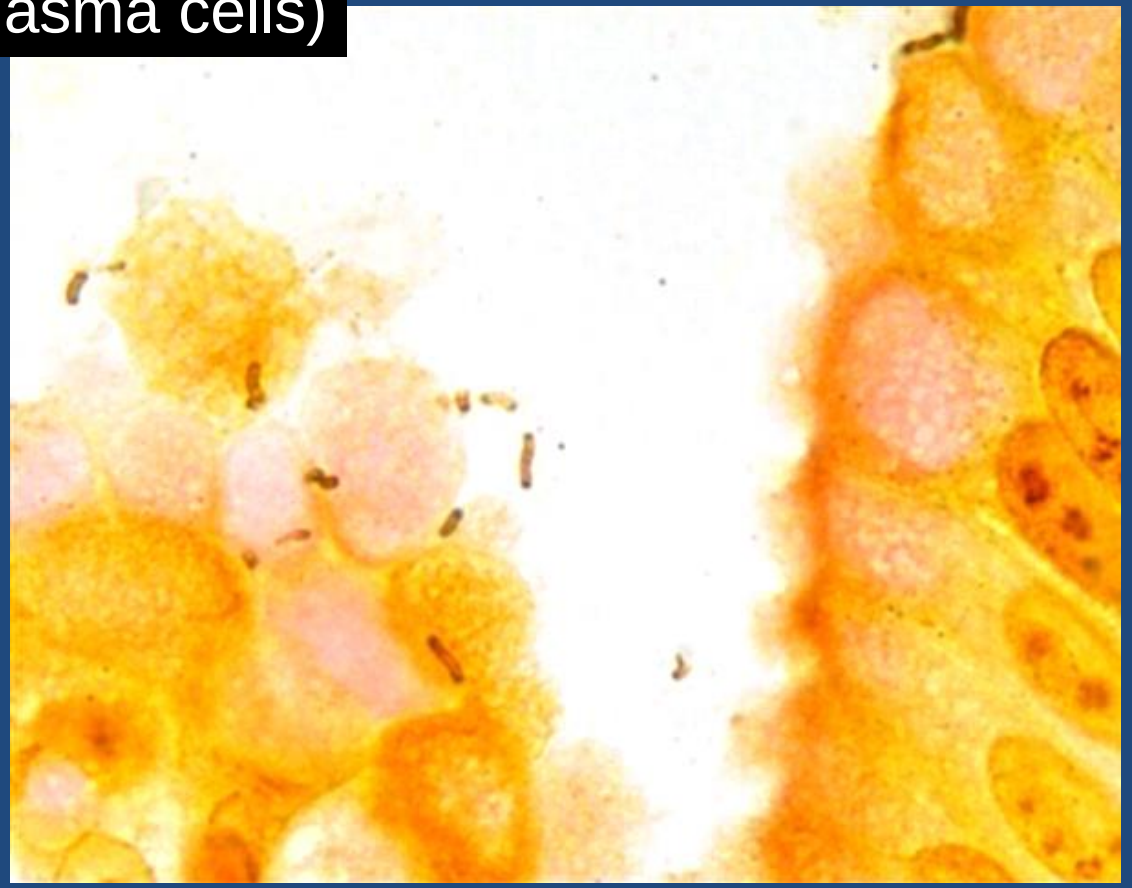
Helicobacter-associated chronic active gastritis

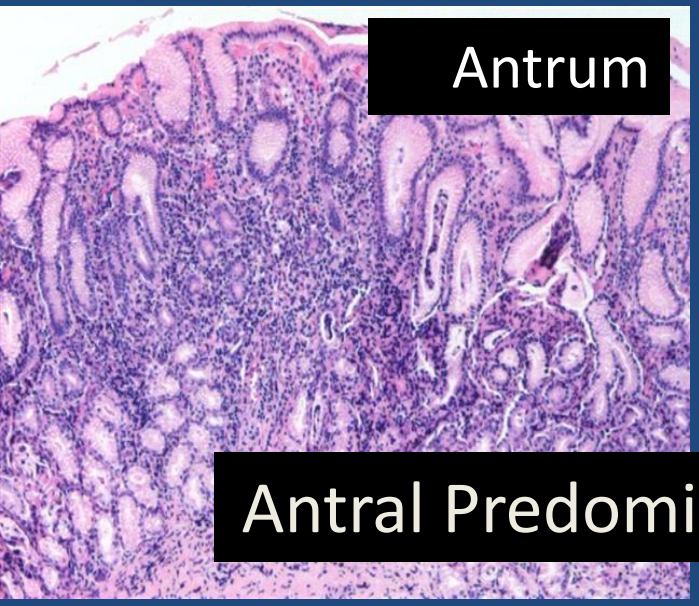


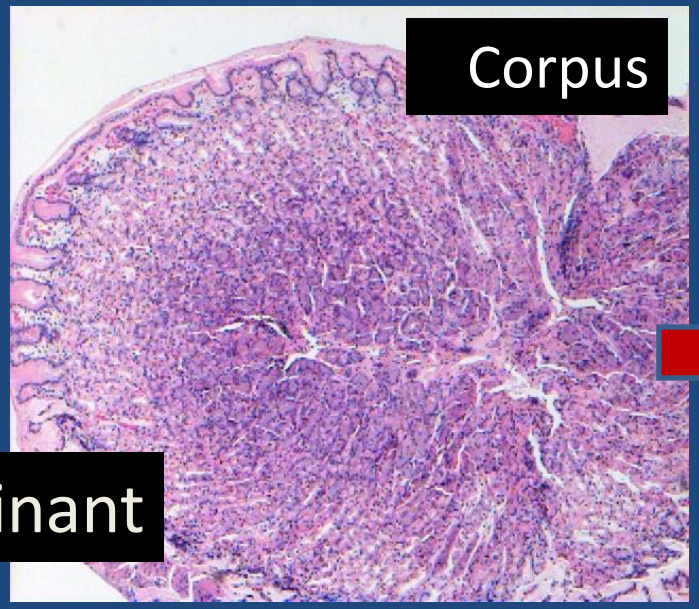


H. pylori

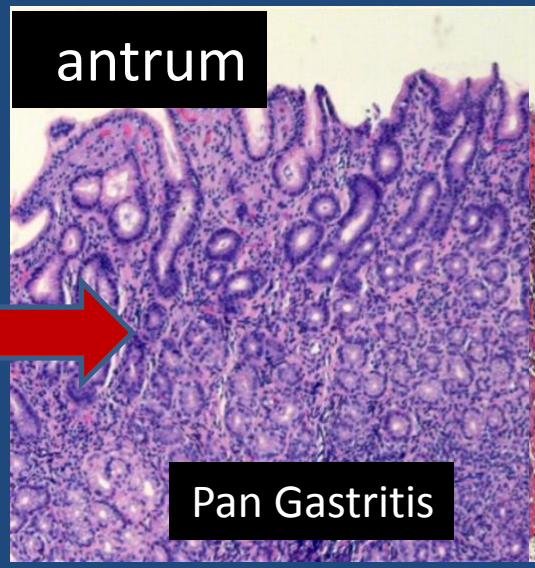




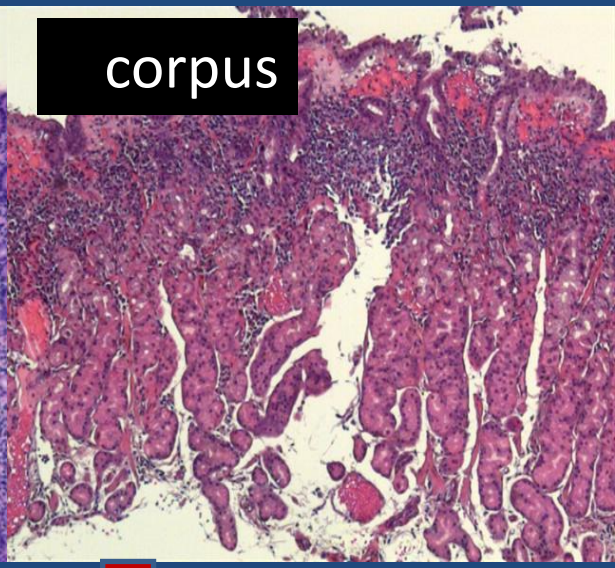


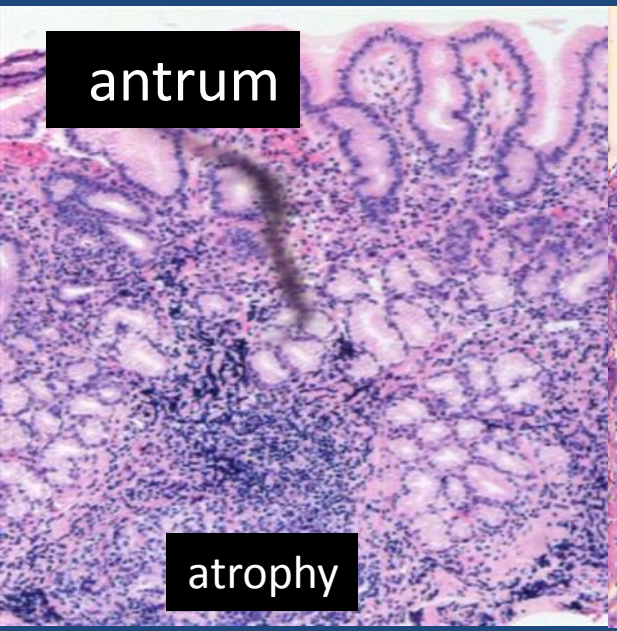


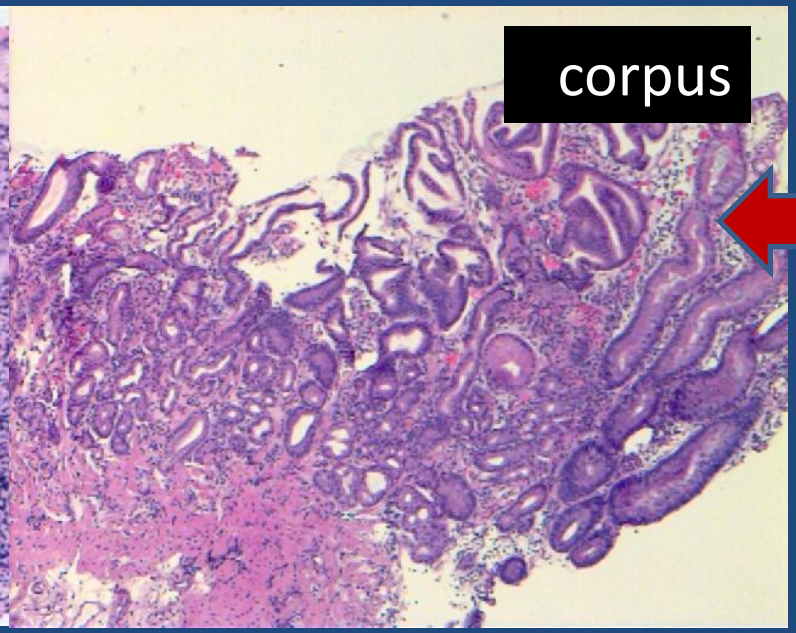
Antral Predominant

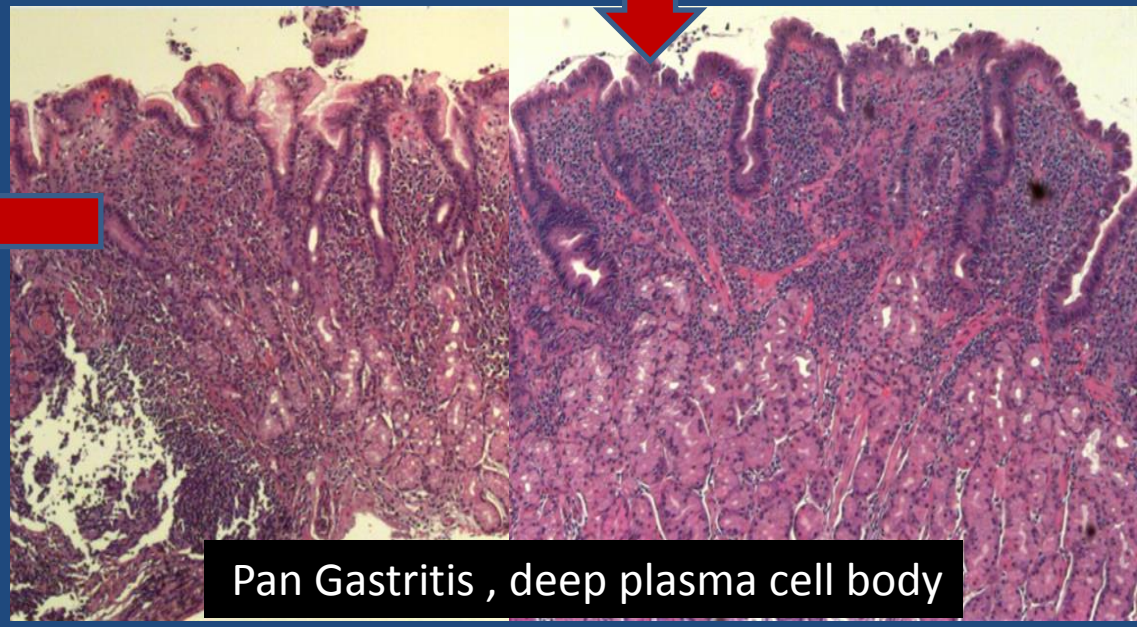


Pan Gastritis

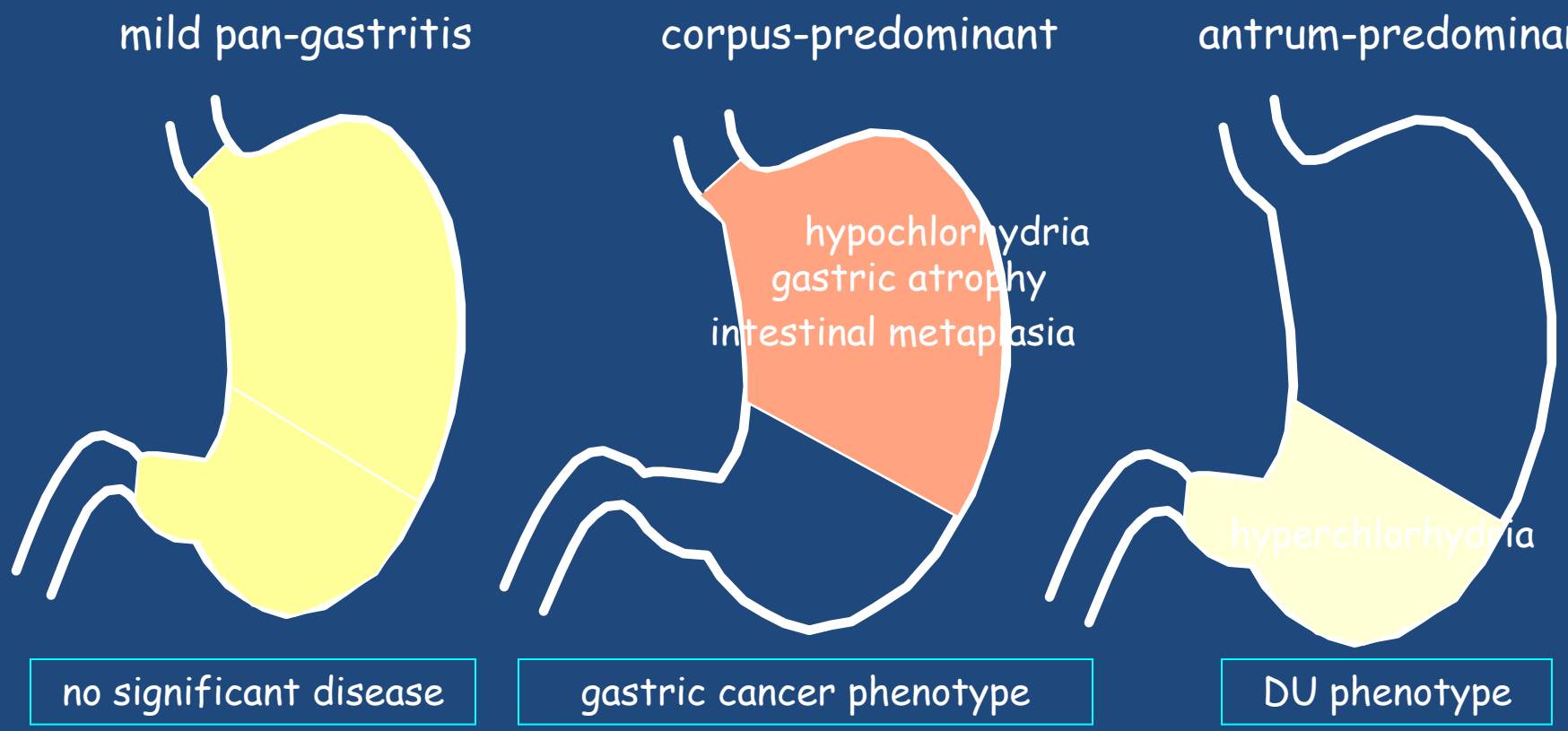








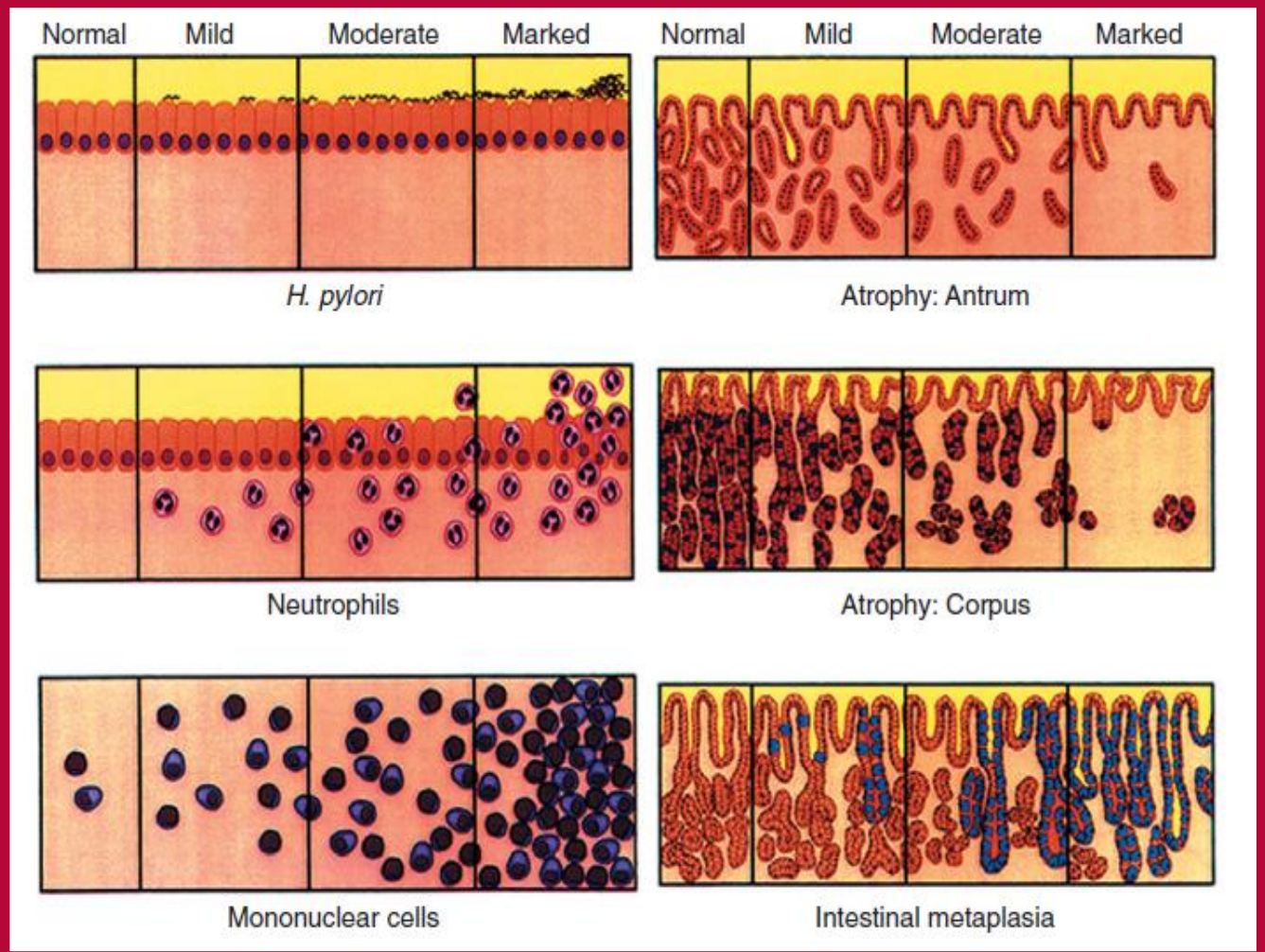
Phenotypes resulting from *H pylori* infection

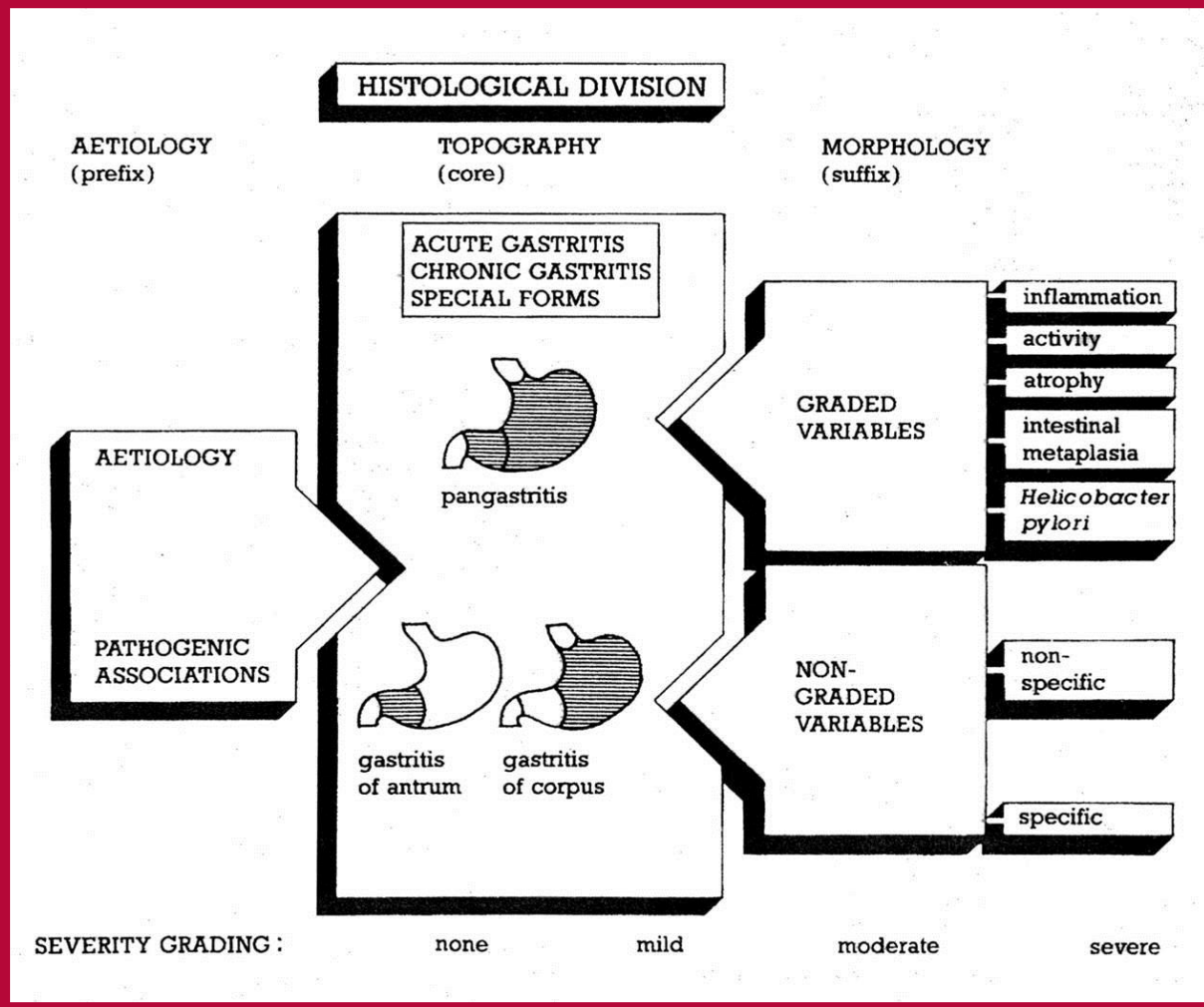


N. Shepherd Lecture

The Sydney classification

Price et al 1990





What determines the outcome of *H pylori* infection?

- genetically determined host responses (IL-1β and TNF-α)
- bacterial virulence factors
- environmental factors (Diet and Smoking)

Bacterial Virulence Factors

Proteins Mediating Establishment/Colonization, Persistence of Infection and Long-Term Damage to the Host

- The cytotoxin associated gene (cagA)

  Duodenal ulcer,gastric mucosal atrophy, and gastric cancer

- The vacuolating cytotoxin (VacA)

  Peptic ulcer patients and gastric cancer

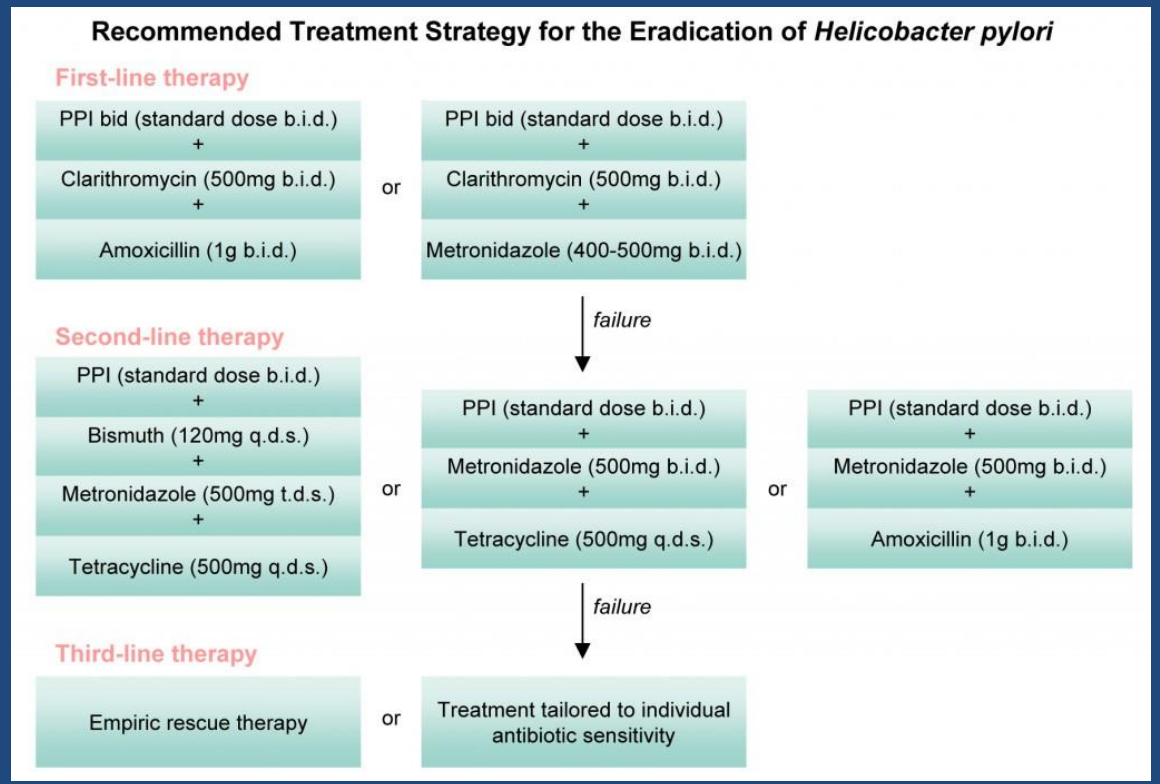
- The iceA gene (induced by contact with the epithelium)

  The IceA1 genotype was significantly associated with peptic ulceration and increased mucosal IL-8 concentrations

Nimri L , Bani-hani K E, Matalka I , Ibrahim M . Clinical Relevance of vacA, cagA, and iceA Genotypes of Helicobacter pylori. BMC Gastroenterol. 2006 Oct 4;6:27.

HELICOBACTER PYLORI ASSOCIATED CHRONIC GASTRITIS
Management and Prognosis

- Eradication Protocols : Anti-acid drugs and antibiotics



ANTIBIOTIC*	PROTON PUMP INHIBITOR
Amoxicillin 1g twice daily **and either:** Clarithromycin 500mg twice daily **or** Metronidazole 400mg twice daily**	Esomeprazole 20mg twice daily or Lansoprazole 30mg twice daily or Omeprazole 20–40mg twice daily or Pantoprazole 40mg twice daily or Rabeprazole 20mg twice daily
Penicillin allergy	
Metronidazole 400mg twice daily and Clarithromycin 250mg twice daily	

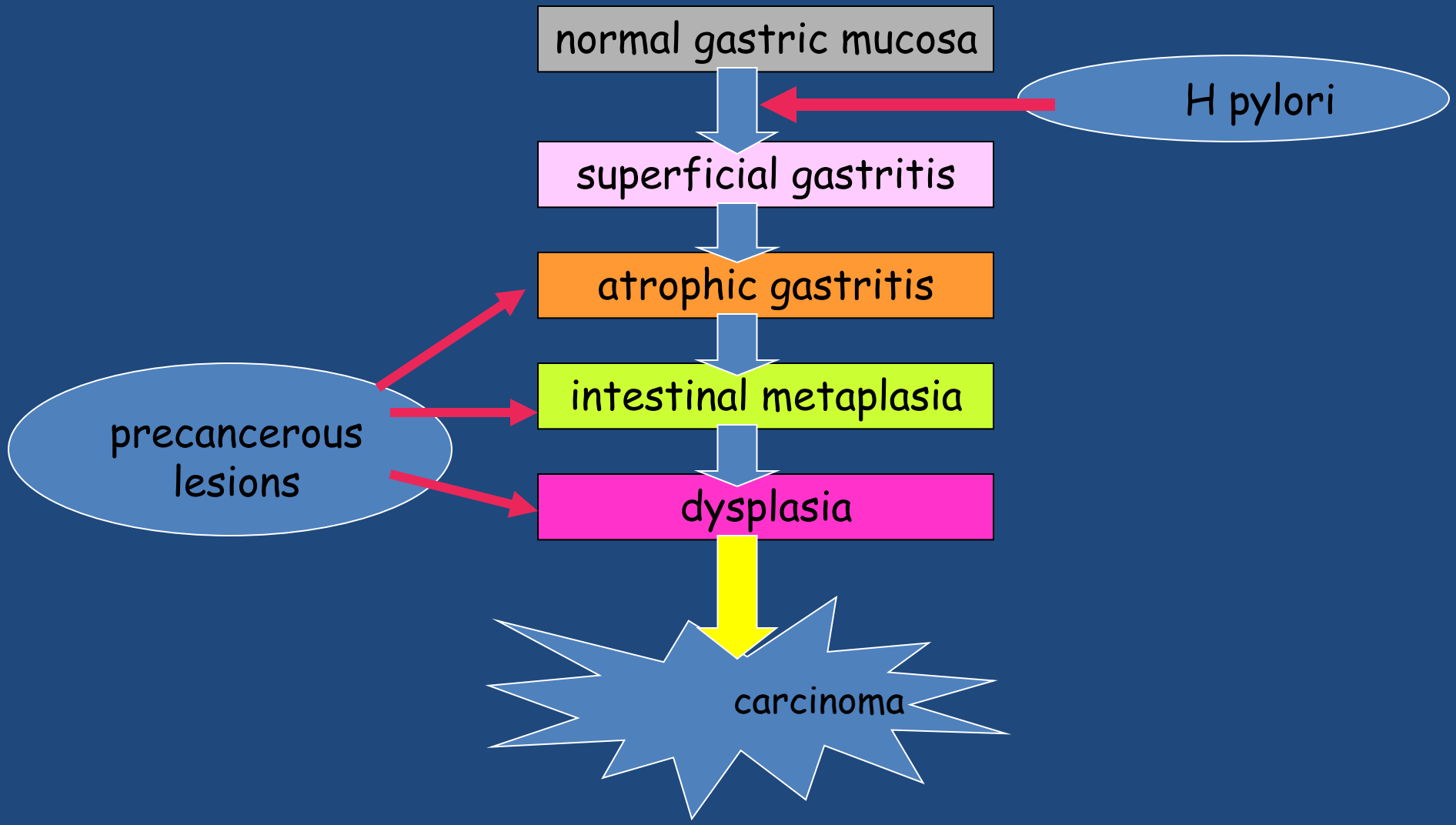
HELICOBACTER PYLORI ASSOCIATED CHRONIC GASTRITIS
Management and Prognosis

- Relapses are associated with reappearance of *H. pylori*; peptic ulcer disease; association with gastric lymphoma

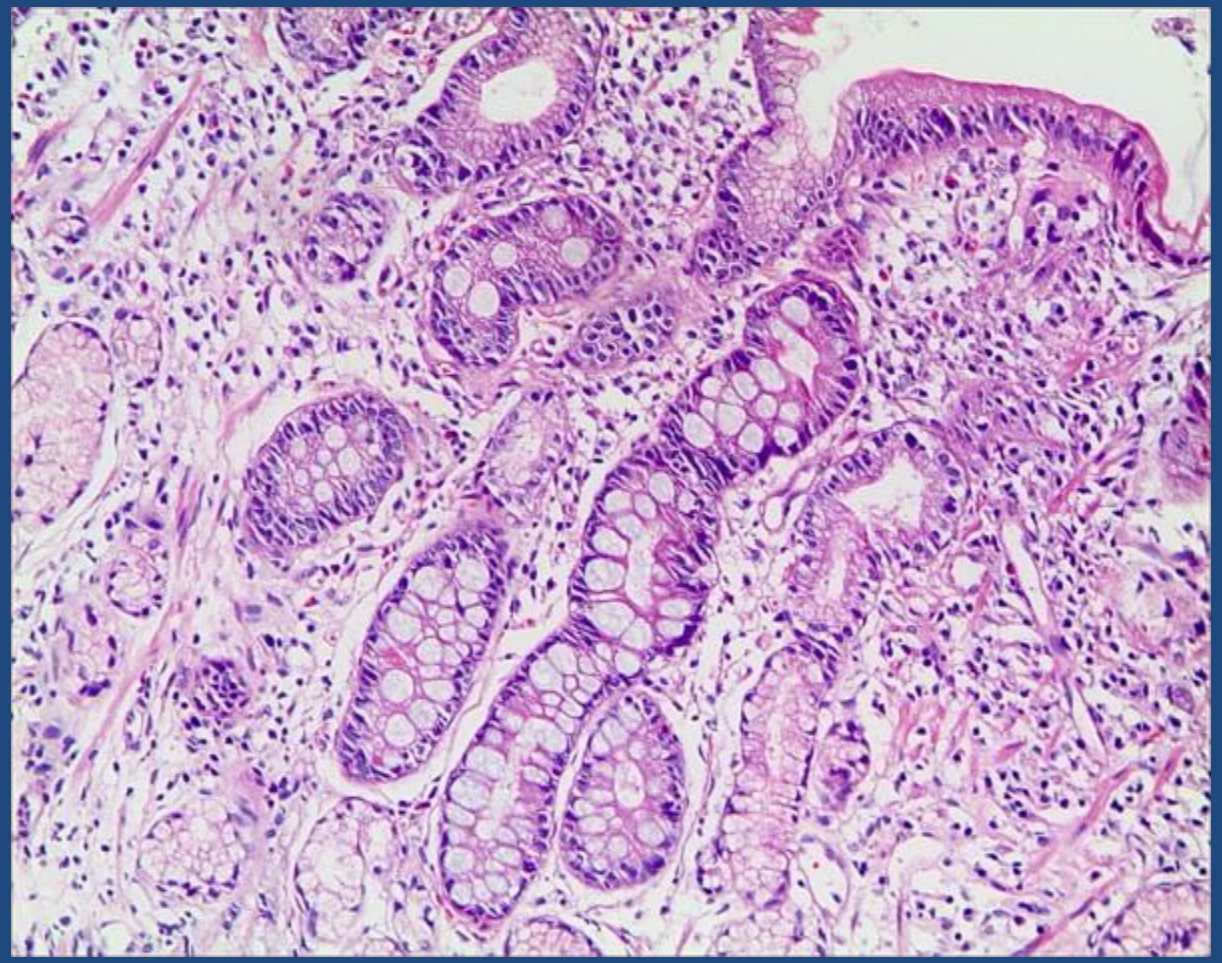
- Precancerous Lesions : Atrophy
  Intestinal Metaplasia
  Dysplasia

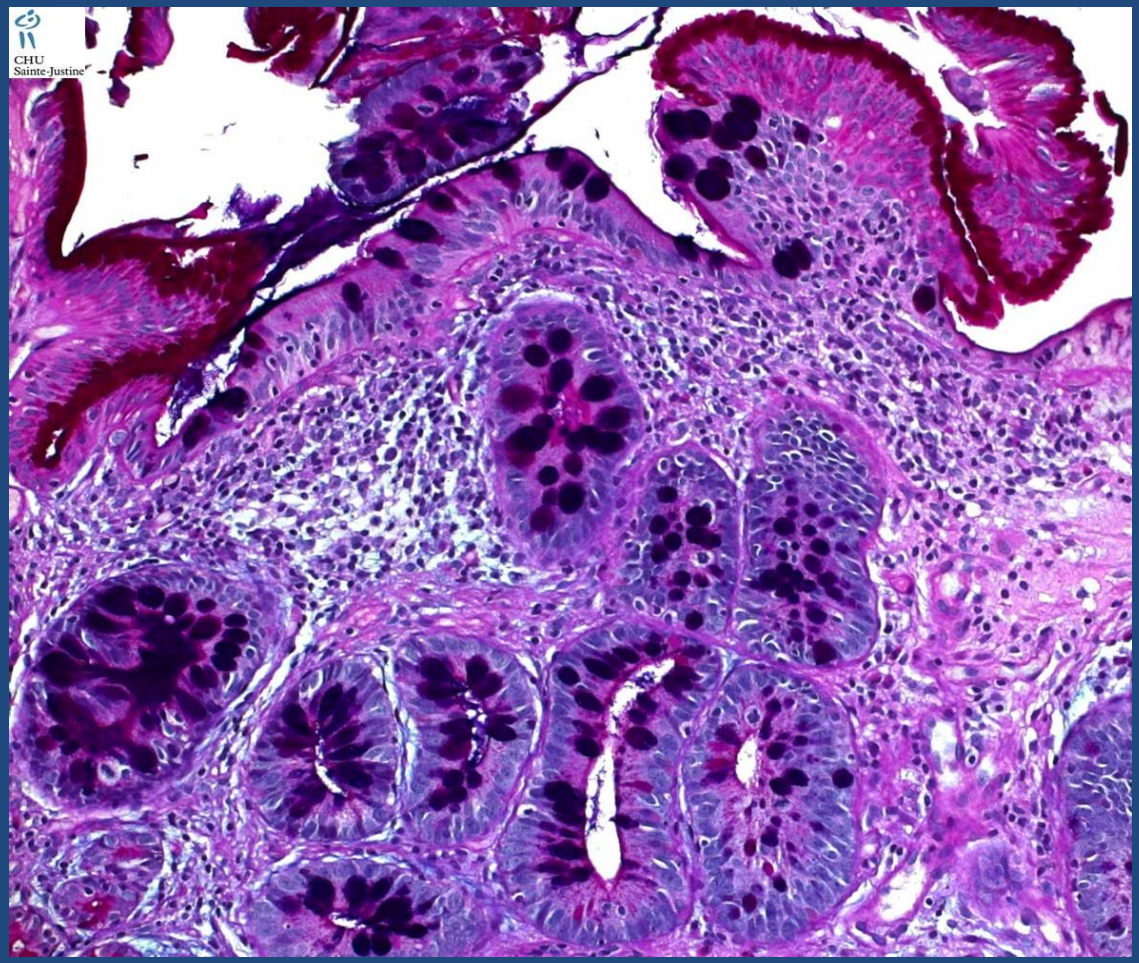
Stages in the development of gastric carcinoma

(after Correa)

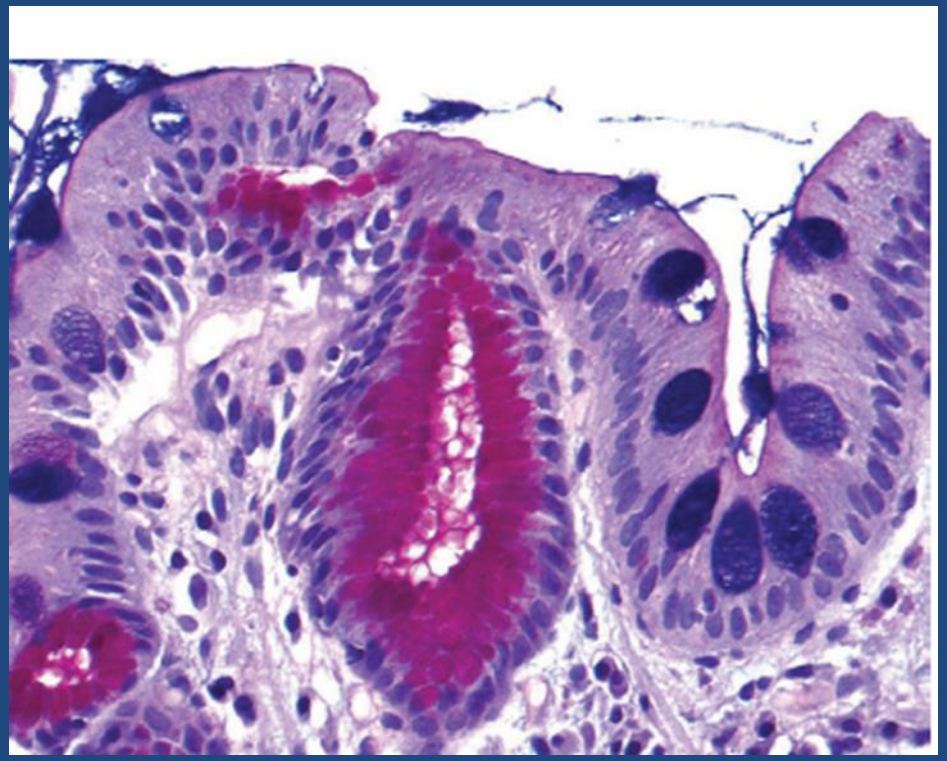


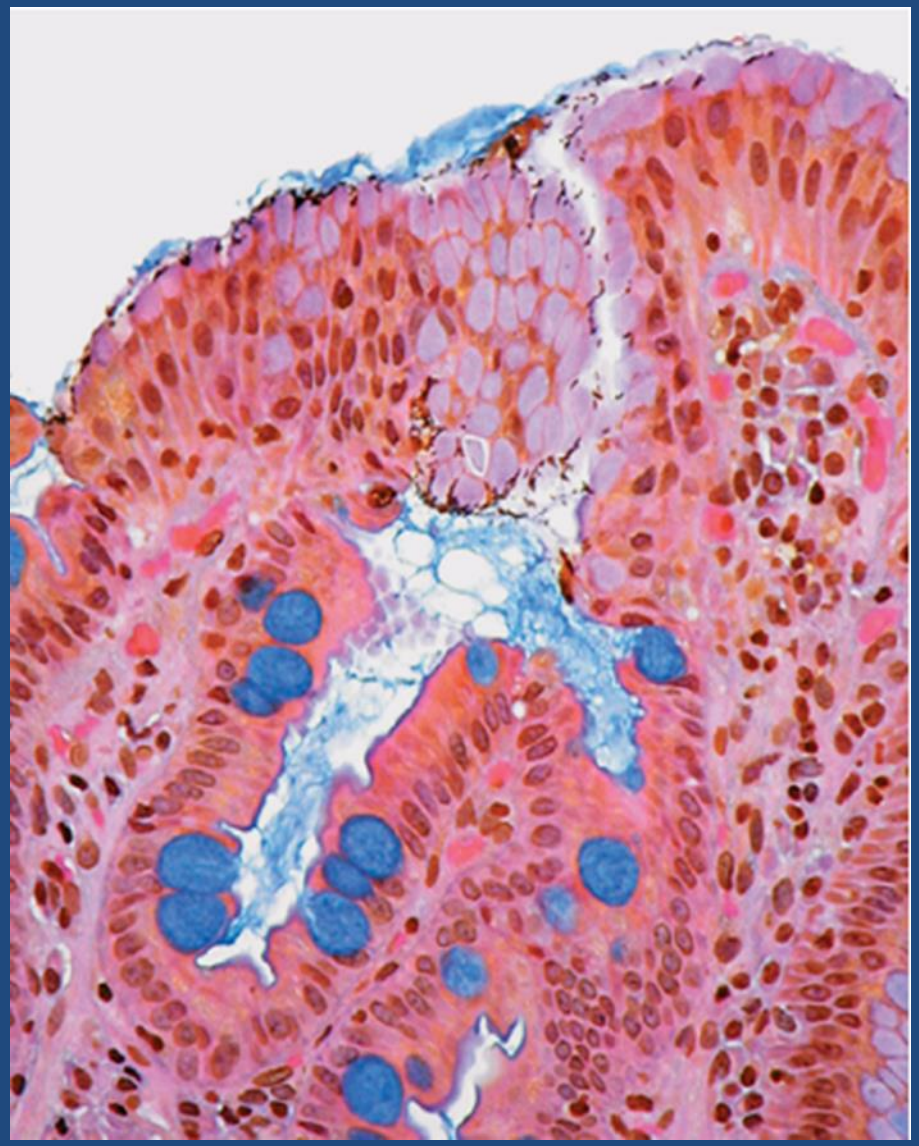
Intestinal Metaplasia



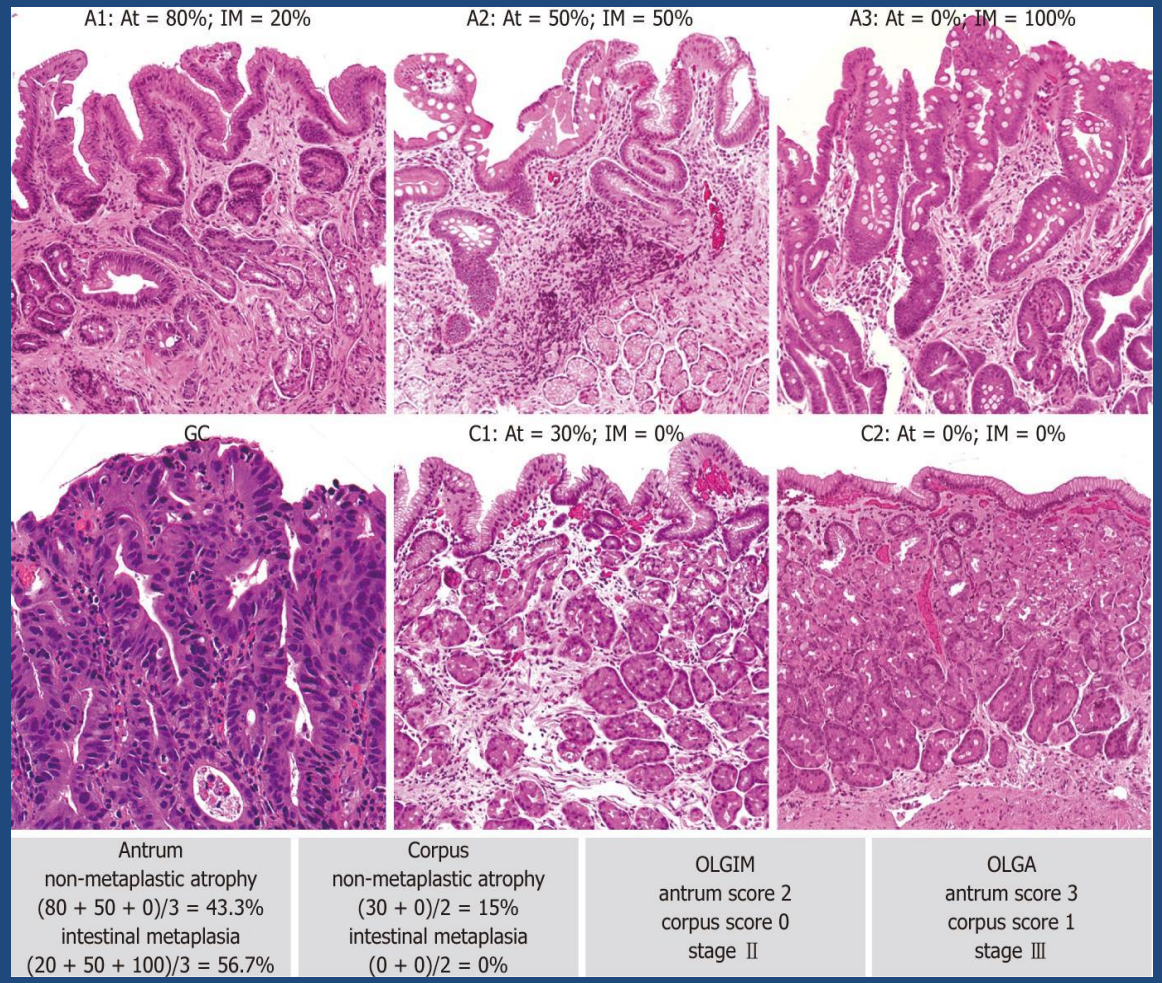


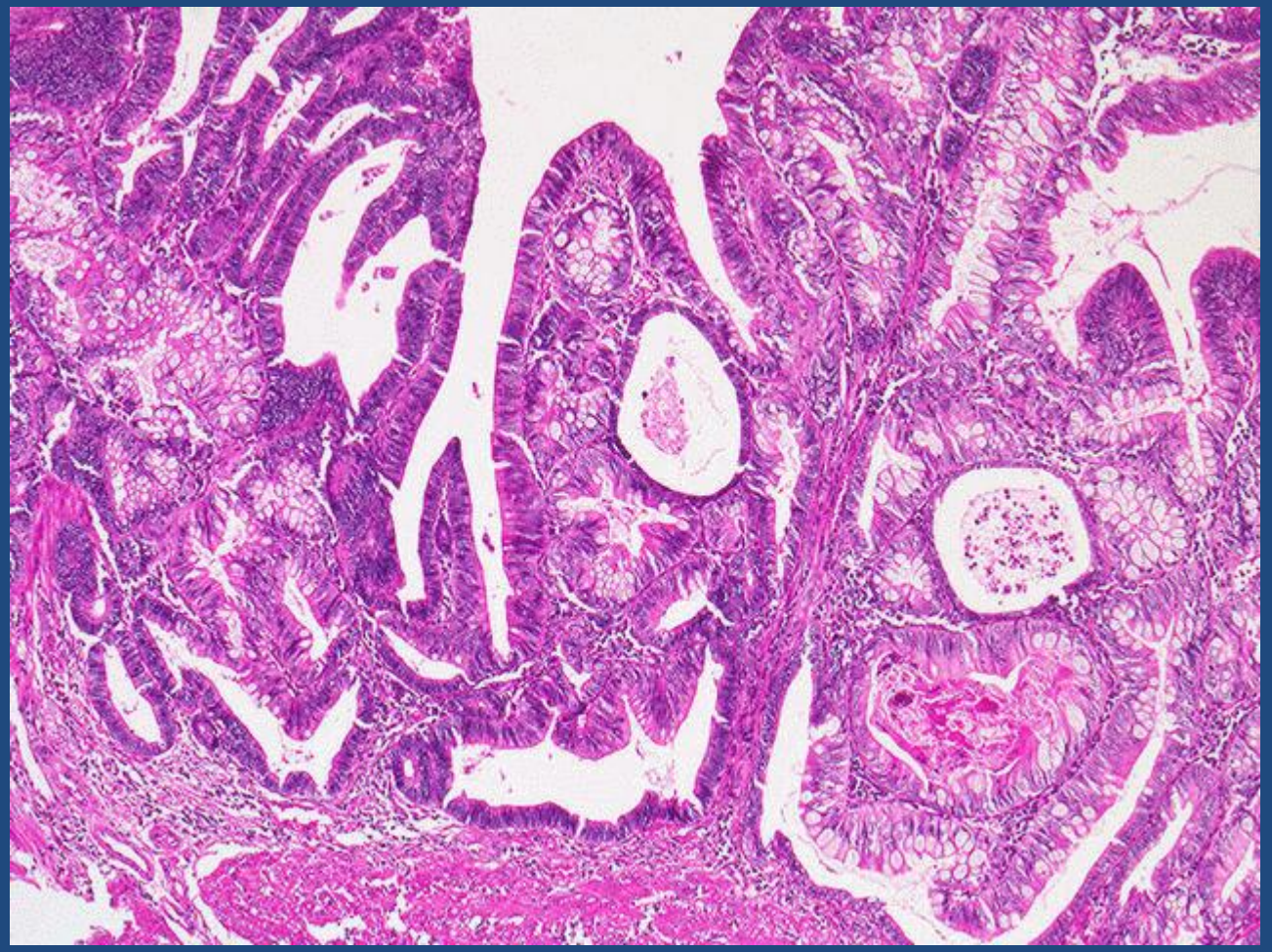
Intestinal Metaplasia



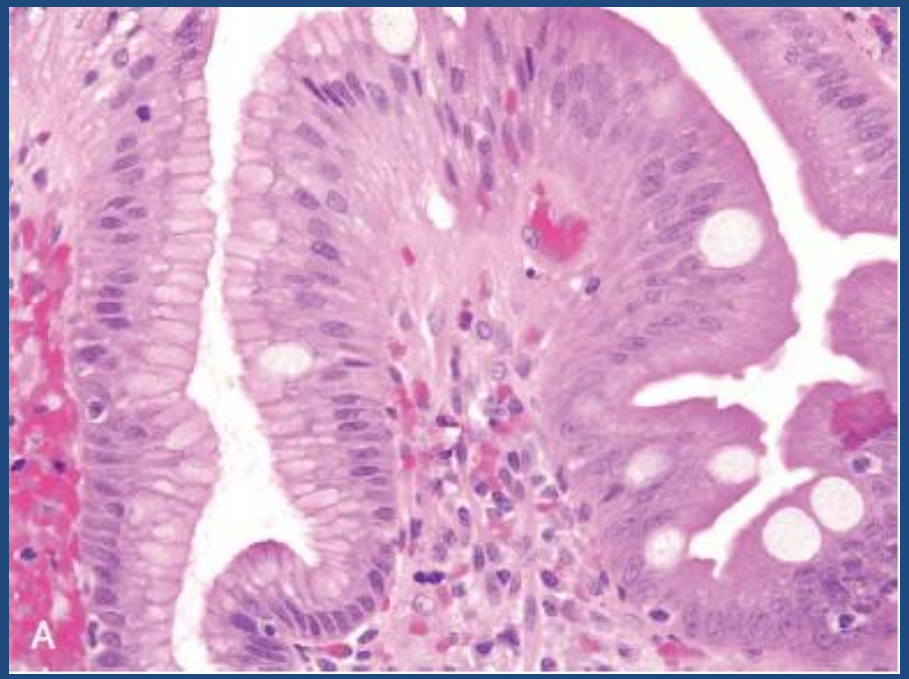


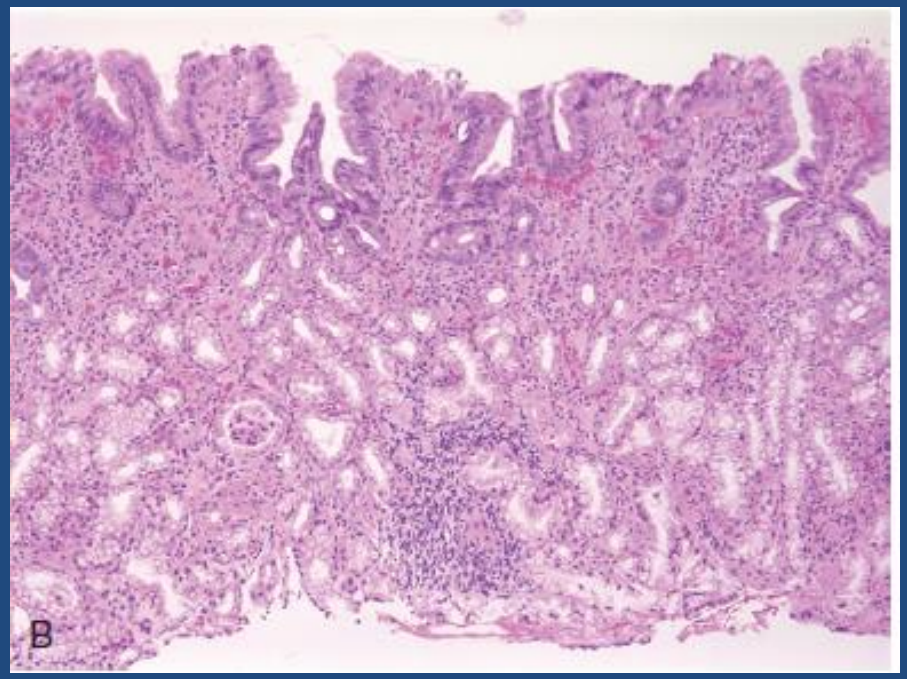
Gastric Mucosa Atrophy and Dysplasia





Peptic Duodenitis



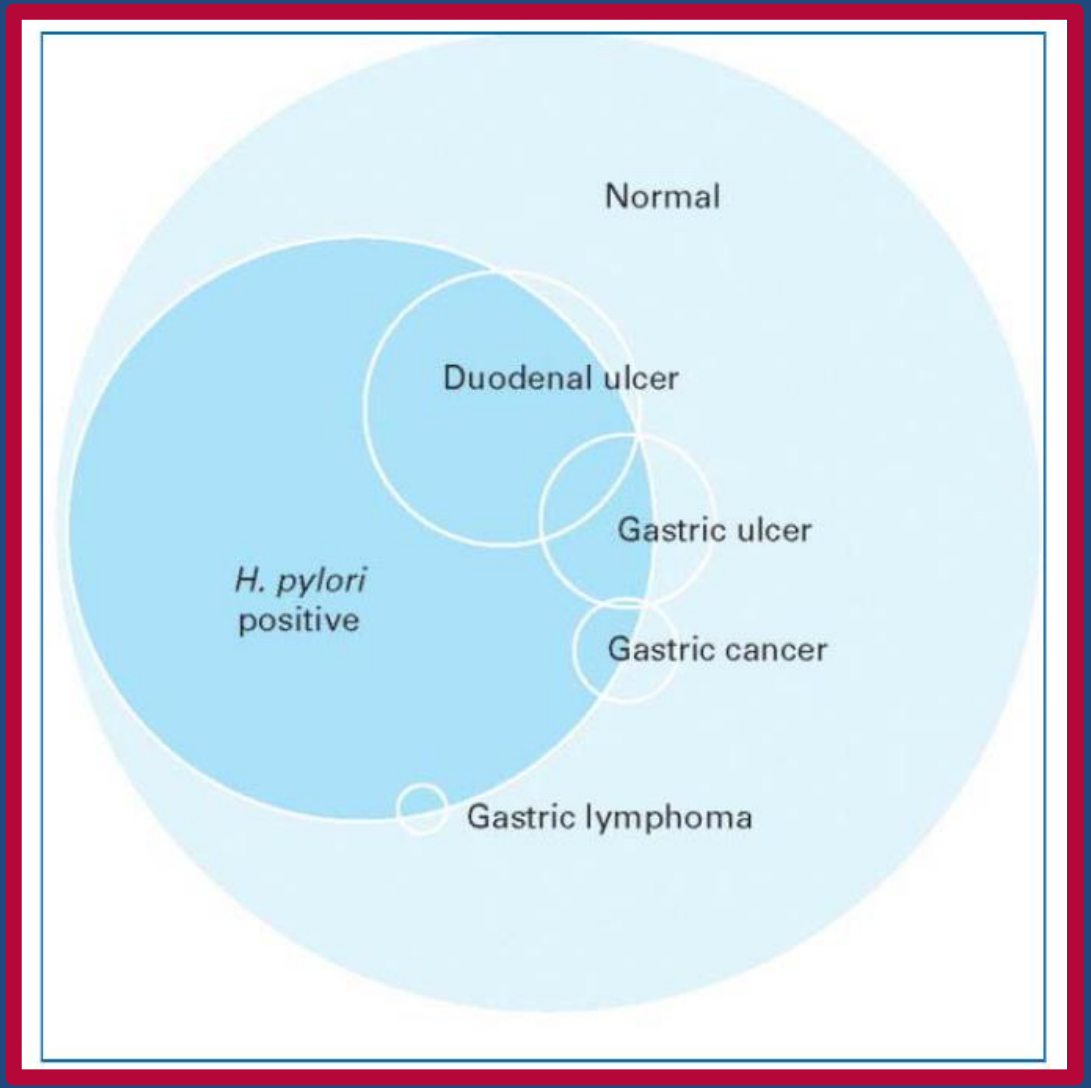


- Gastric Metaplasia of the first part of the duodenum

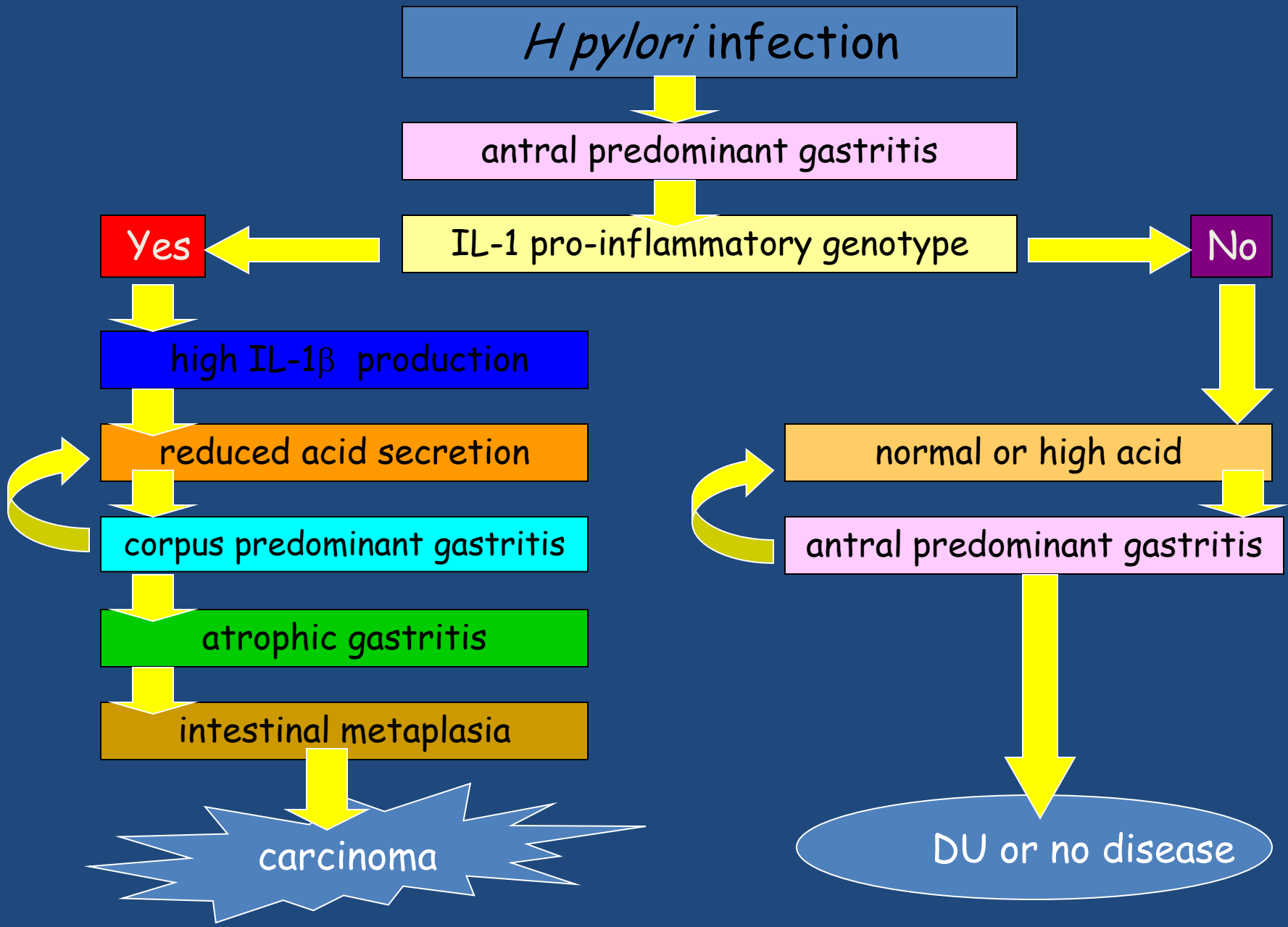
Diseases Associated with *Helicobacter pylori* Infection

Disease	Association
Chronic gastritis	Strong causal association
Peptic ulcer disease	Strong causal association
Gastric carcinoma	Strong causal association
Gastric MALT lymphoma*	Definitive etiologic role

Epidemiology and disease associations of Helicobacter pylori



Barry Marshall. Clinical Medicine, Volume 2(2).March/April 2002.147-152



N. Shepherd Lecture

H. Pylori and Gastric Cancer

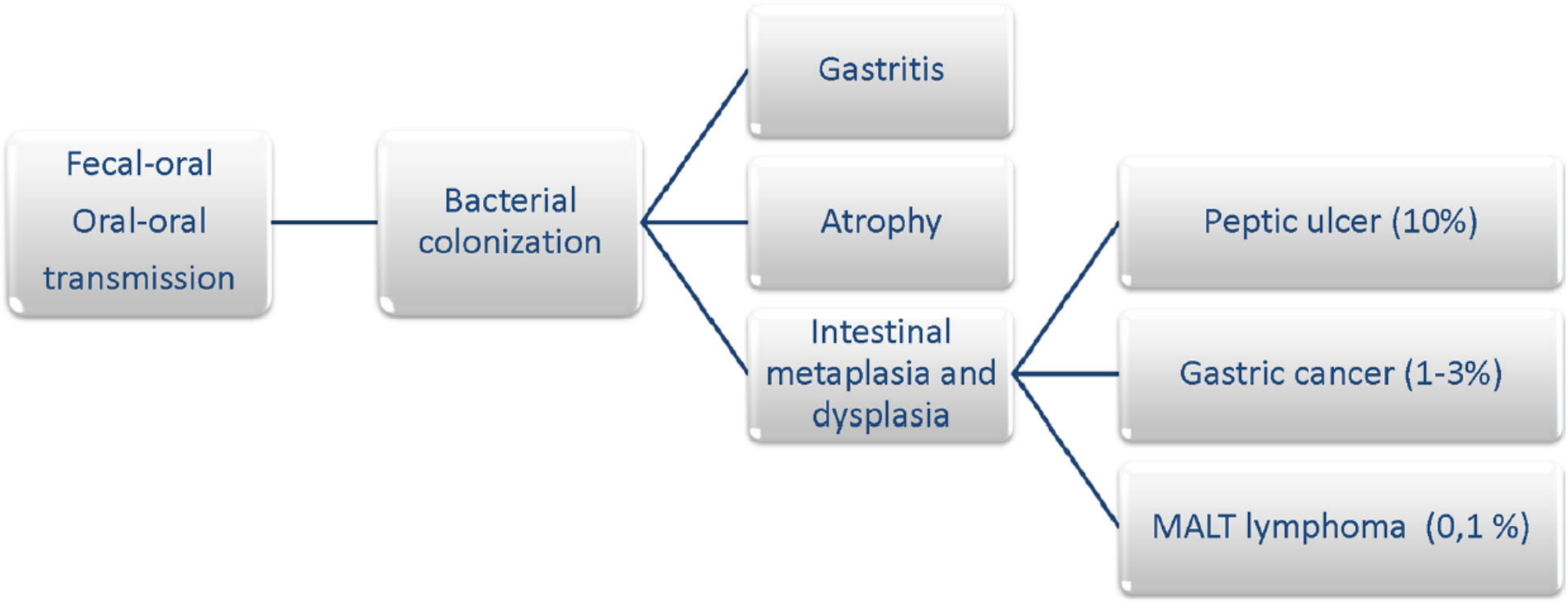


Fig. 1. Sequence of subsequent events from bacterial transmission to the host until precancerous and gastric lesions induced by *H. pylori*.

Molecular Mechanisms of Helicobacter pylori Pathogenesis. De Falco M et al, J Cell Physiol. 2015 Aug;230(8):1702-7.

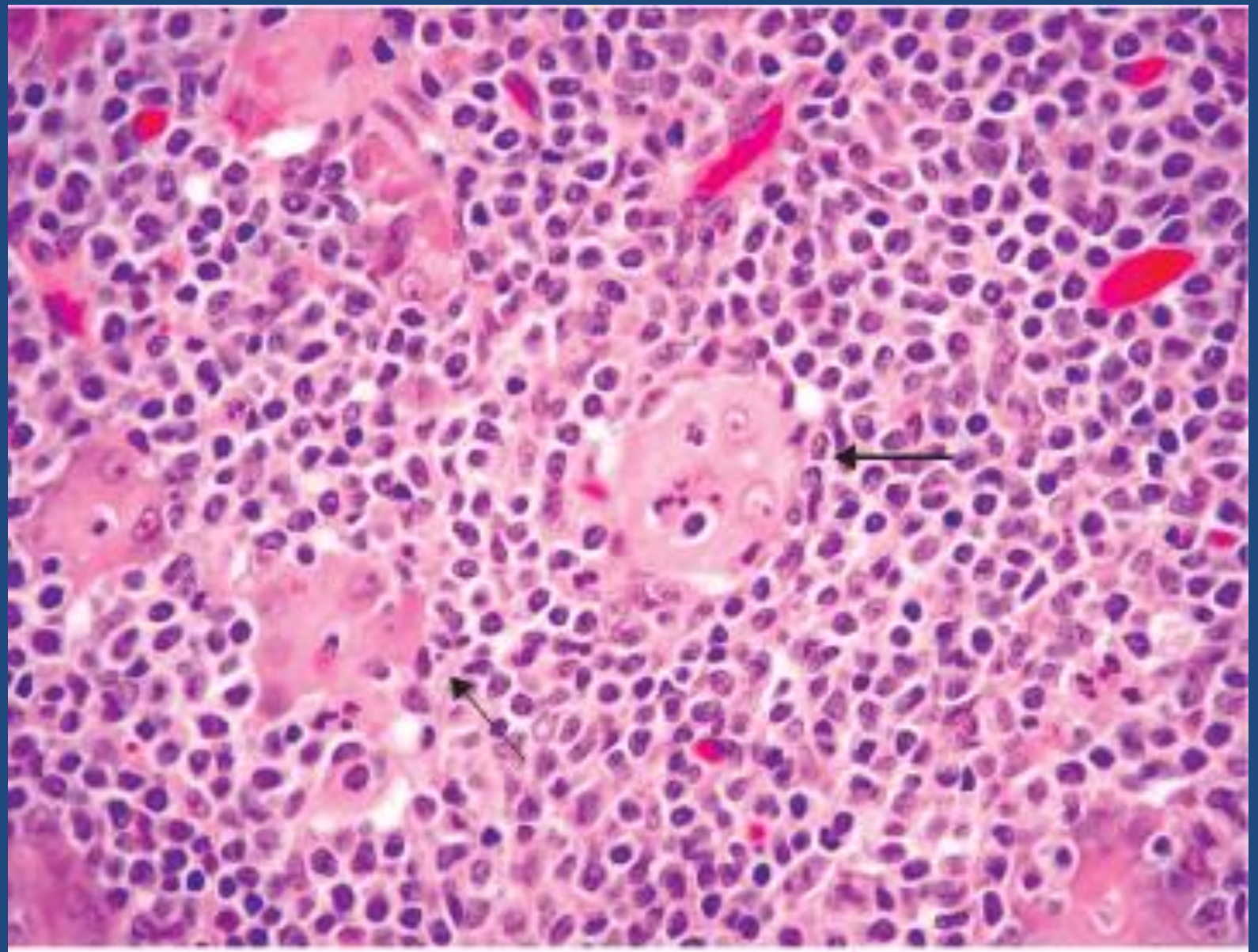
WADI MUJIB

GASTRIC LYMPHOMA

- Gastric Lymphoma represent 5% of all gastric malignancies
- Classification similar to nodal lymphoma; mostly B-cell type
- Stomach is the most common site of extra nodal lymphomas (20%)
  - MALT (Mucosa-Associated Lymphoid Tissue) Lymphomas are most common:
  - Related to *H. pylori* gastritis, with chronic antigenic stimulation giving rise to one or more clones of lymphoid cells
  - low grade, limited to mucosa or submucosa
  - lympho- epithelial lesions are characteristic
  - Prognosis: relatively good
  - Treatment: antibiotics, surgery, chemotherapy

Pathogenesis of MALT Lymphoma

- Extranodal marginal zone lymphomas commonly follow immune system dysregulation from sustained stimulation with chronic infections or autoimmune disorders.
- Susceptibility is thus influenced by both genetic and environmental factors.
- Marginal zone lymphoma of MALT (MALT lymphoma) is the most common indolent subtype and represents 7% of all non-Hodgkin lymphomas.
- The stomach is the most common extranodal site followed by eye/adnexa, lung, skin, and salivary glands .
- Nearly all patients with gastric MALT lymphoma are infected with Helicobacter pylori.
- Histological and endoscopic improvement commonly follows H pylori eradication.



Epidemiology of HP in Jordan

- high rates of HP infection in children and adults: 55.5%

  factors were rural areas, poor sanitation, overcrowding, low maternal educational level and low socioeconomic status

Bani-Hani KE et al. Prevalence and risk factors of Helicobacter pylori infection in healthy schoolchildren. Chin J Dig Dis 2006; 7: 55-60.

- studies of HP genetic diversity in Jordan

  vacA, cagA and iceA studies - illustrate the geographic nature of the genetic diversity of H. pylori, similar to those reported in neighbouring countries.

Nimri LF, Matalka I, Bani Hani K, Ibrahim M. Helicobacter pylori genotypes identified in gastric biopsy specimens from Jordanian patients. BMC Gastroenterol 2006; 6: 27.

Clinical outcome of *H pylori* infection

>80%	asymptomatic
5-15%	peptic ulcer disease
0-10%	non-ulcer dyspepsia
1-3 %	gastric adenocarcinoma
0.5%	gastric lymphoma

Bani-Hani KE, Yaghan RJ, Matalka I. Primary gastric lymphoma in Jordan with special emphasis on descriptive epidemiology. Leuk Lymphoma 2005; 46: 1337-43.

Epidemiology of HP in UAE

- The overall colonisation rate of H pylori was 90%, and there was no significant difference between groups of different ethnic origins.
  Helicobacter associated gastritis was the most common form of chronic gastritis (87%)
  Atrophy was mainly of low grade and increased the older the patient.

Zaitoun AM. Histological study of chronic gastritis from the United Arab Emirates using the Sydney system of classification. J Clin Pathol. 1994 Sep;47(9):810-5.

- H. pylori serology by IgG was positive in 167 industrial workers (78.4%) and 137 in referent workers (64.3%) respectively, ($p < 0.002$). The sensitivity and specificity of the IgG serology assay were 94.5%, and 97.2% respectively.

Bener A et al. **Prevalence of Helicobacter pylori infection among low socio-economic workers.** J Commun Dis. 2002 Sep;34(3):179-84.

Epidemiology of HP in UAE

- Point mutations A(2442/43)G and A(2142)C and the combination of both were common among our patients. Perhaps the highest reported yet. Mutation at A(2142/43)G is far more common than mutation at A(2142)C.

Alfaresi MS, Eltom AA, Alshaikh SS, Buchel EH, Saeed LS, Aljenaibi MM. Molecular prevalence of point mutations conferring resistance to clarithromycin in Helicobacter pylori in the United Arab Emirates. Saudi Med J. 2005 May;26(5):763-6.

- Clarithromycin resistance was common in this small collection of H. pylori isolates from the UAE. The A2142G and A2143G mutations were associated with clarithromycin resistance.

Alfaresi MS, Elkoush AA.Characterization of clarithromycin resistance in isolates of Helicobacter pylori from the UAE. Indian J Gastroenterol. 2010 Jun;29(3):116-20. doi: 10.1007/s12664-010-0034-z. Epub 2010 Jul 25.

Clinical significance of Helicobacter associated chronic gastritis

- Most common cause of chronic gastritis and peptic ulcer disease.
- Long term risk for gastric carcinoma (5 fold risk). gastric atrophy, intestinal metaplasia, and dysplasia role.
- Long term risk for gastric MALT-lymphoma.
- ?Future possible prophylactic vaccines

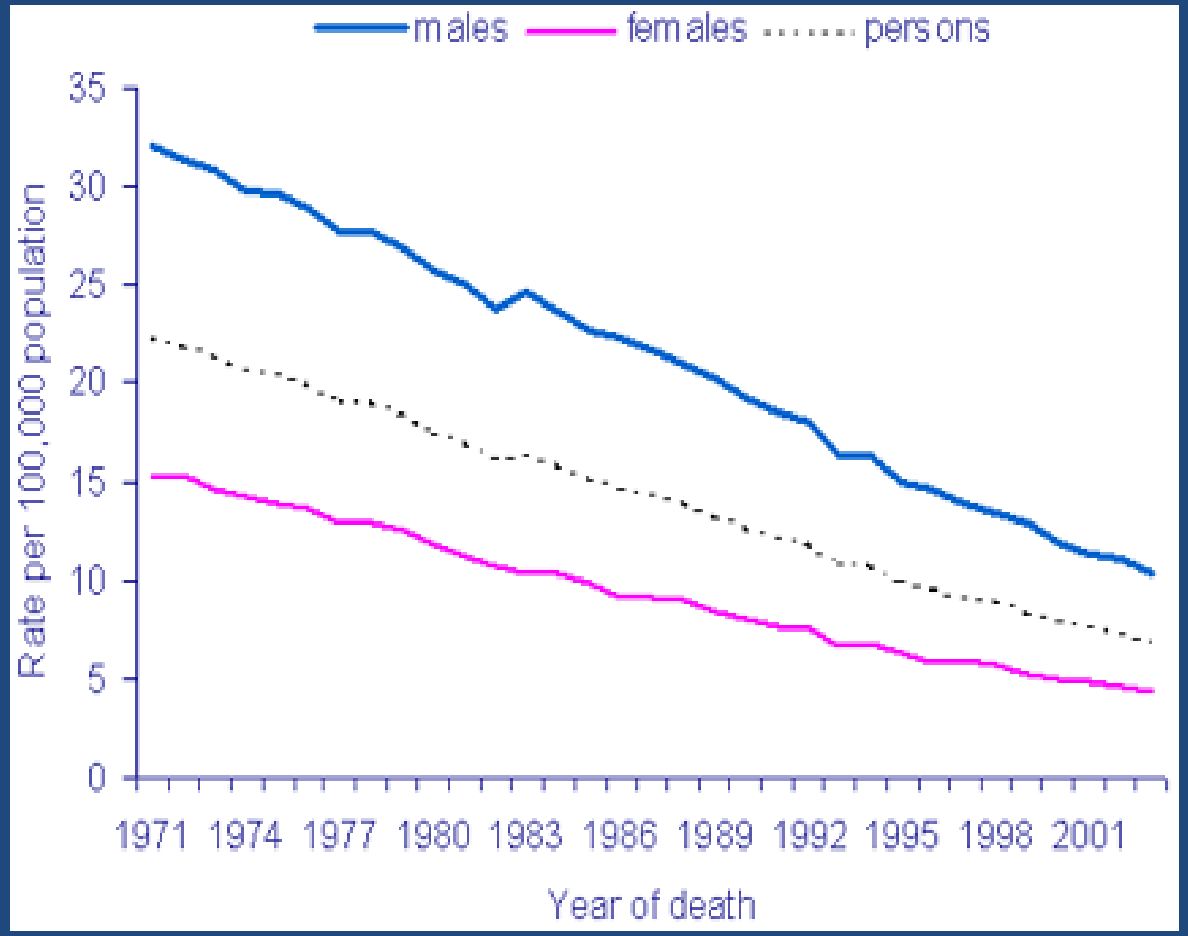
Epidemiological data linking *H pylori* and gastric carcinoma

- prospective studies

  Forman et al 1991, Parsonnet et al 1991, EUROGAST study 1993, Siman et al 1997, Uemura et al 2001

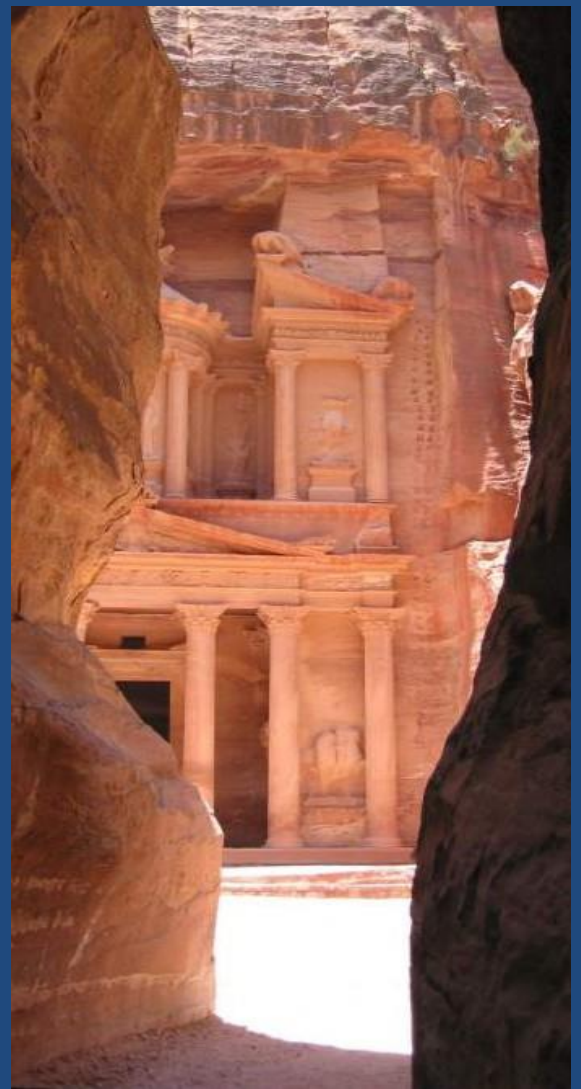
- HP now regarded as a Class 1 carcinogen

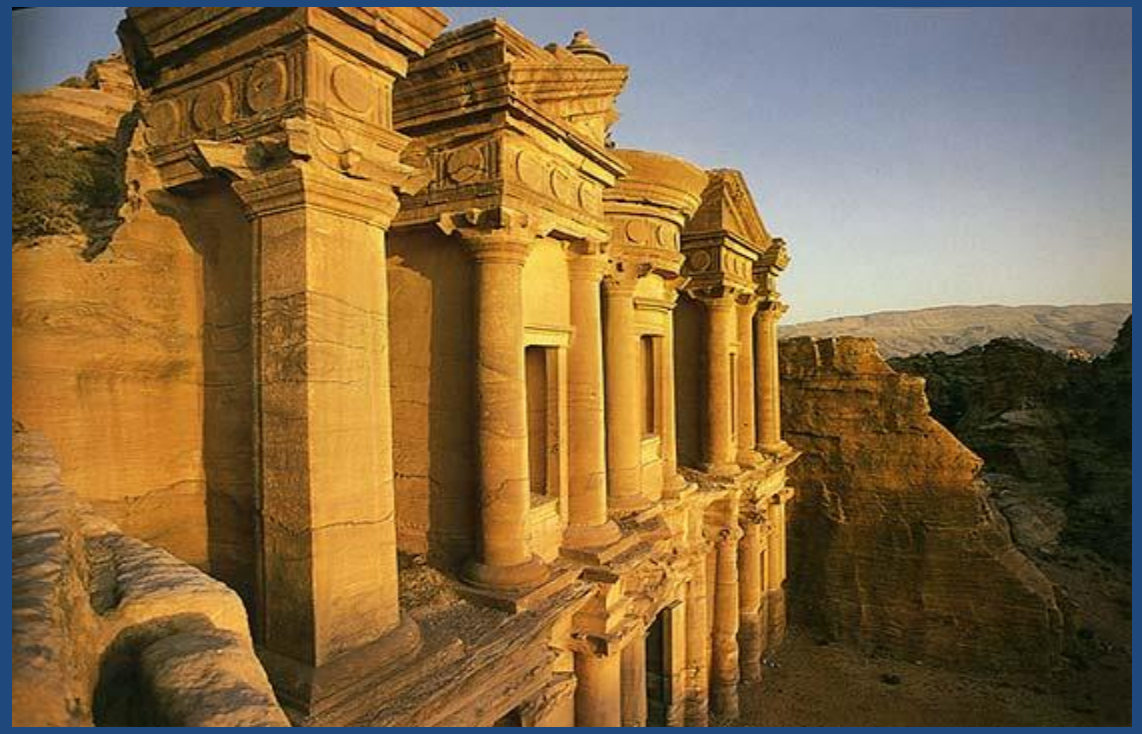
Gastric cancer mortality, UK, 1971-2003

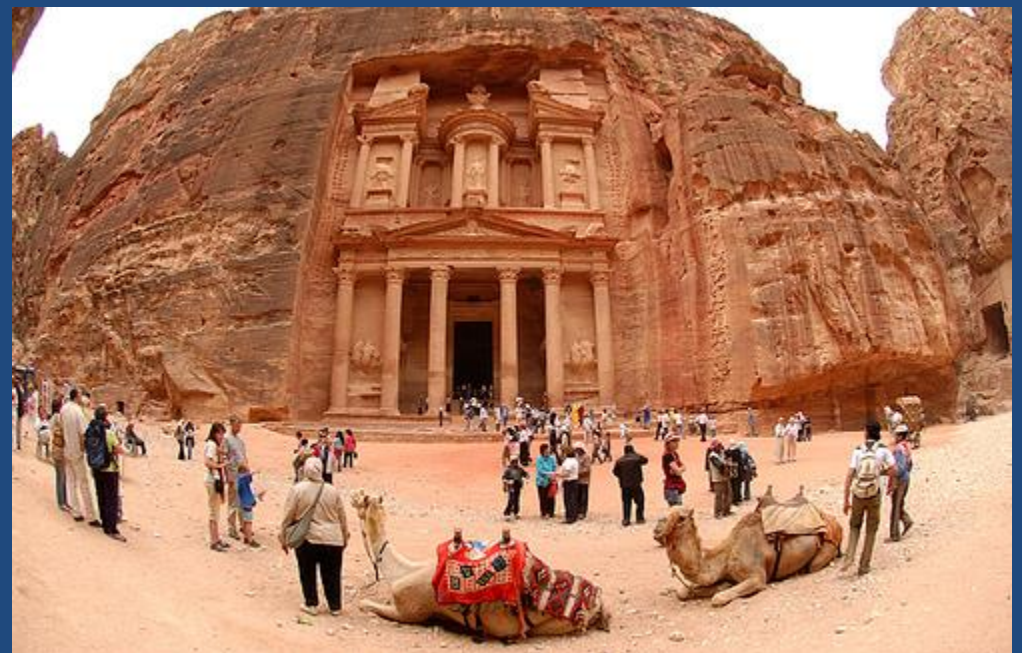


CRUK, 2006

Petra(Rose City)



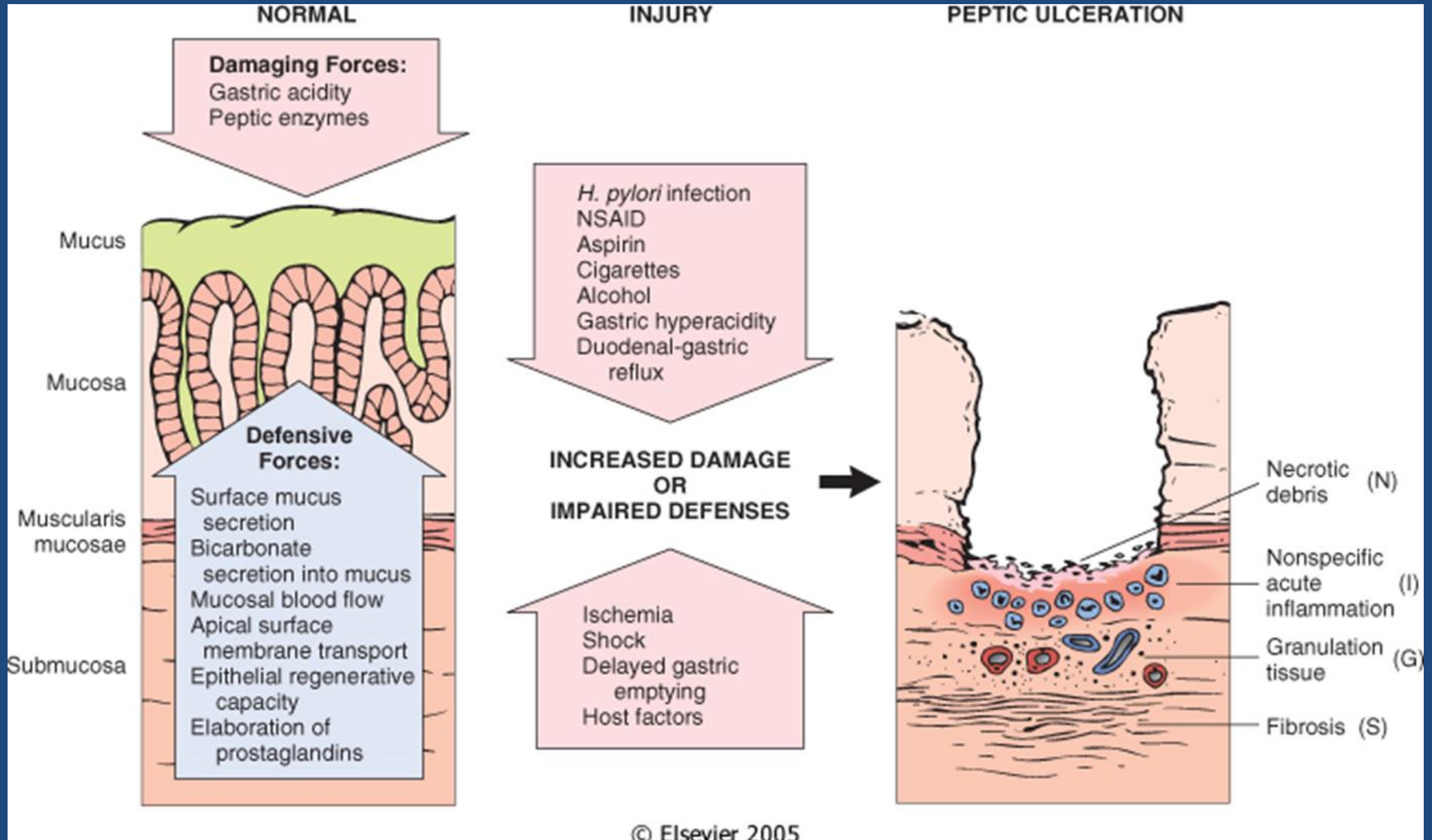




PEPTIC ULCER DISEASE

- Chronic, most often solitary, lesions that occur in any part of GIT exposed to aggressive action of acid-peptic juices
- Sites: 98% occur in either the duodenum or stomach
- Remitting-relapsing lesions, mostly in middle-aged to older adults
- Epigastric pain, worse at nights, 1-3 hrs after meals, may be relieved by alkalis or food; nausea, vomiting, bloating, belching, weight loss
- Pathogenesis: Two key facts are known:
  - Mucosal exposure to gastric acid & pepsin is a requisite (*"no acid, no ulcer"*)
  - Strong causal relationship with *H. pylori* infection

PATHOGENESIS OF
PEPTIC ULCER DISEASE



PATHOGENESIS OF
PEPTIC ULCER IN H.PYLORI INFECTION

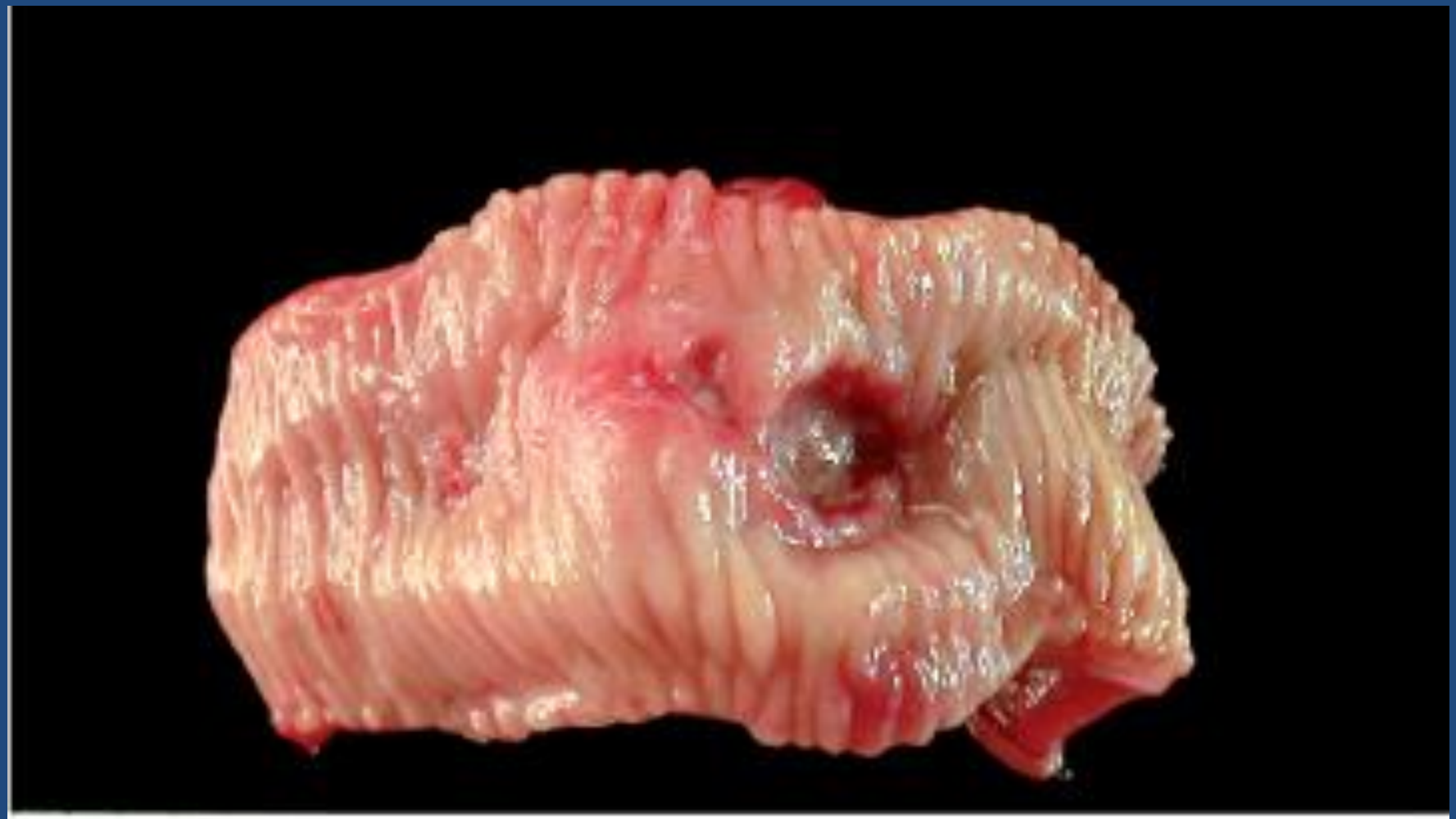
Helicobacter pylori infection

- Secretion of urease, protease & phospholipases
- Attracted PMNs release myeloperoxidase, which produces hypochlorous acid, & monochloramine (in the presence of ammonia)
- Colonization & direct damage of mucosal epithelial cells & lamina propria endothelial cells by release of bacterial enzymes & other factors e.g. LPS
- Leakage of tissue nutrients into surface sustaining bacillus
- Thrombotic occlusion of surface blood vessels by bacterial PAF
- Only 10-20% of infected individuals develop PUD

PATHOGENESIS OF PEPTIC ULCER DISEASE

Other factors have been associated with PUD

- Zollinger-Ellison syndrome: excess gastrin secretion by tumor leading to excess acid production
- Chronic use of NSAIDs & Aspirin suppresses mucosal PG synthesis
- Cigarette smoking: impairs mucosal blood flow & healing
- Alcohol: alcoholic cirrhosis
- Repeated use of high doses of corticosteroids
- Personality & psychological stress



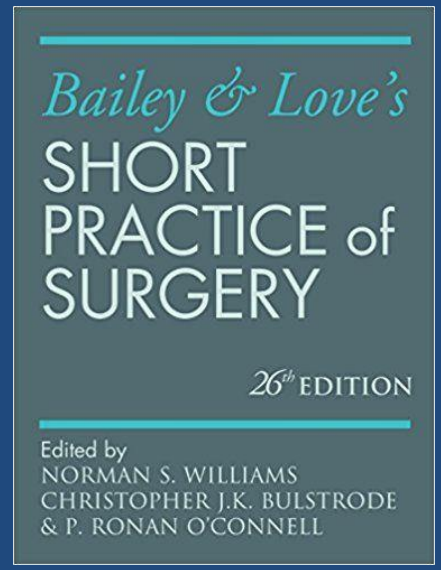
COMPLICATIONS OF PEPTIC ULCER DISEASE

- Hemorrhage: minimal to massive
- Perforation: uncommon but serious; peritonitis
- Pyloric channel obstruction: rare
- Malignant “transformation”: gastric ulcers

UM QAIS

Yet Another Story
When I was a medical student……

- Fourth year medical students during the surgery Rota
- A case of peptic ulcer disease for a surgery (Selective Vagotomy)
- Bed –side teaching by one of our best teachers
- The questions was about the causes of peptic ulcer disease
- Our reference was “ Baily & Love “ textbook



TWO ASSIGNMENTS

- What is the pathogenesis of Duodenal Ulceration in the context of Helicobacter Pylori Associated Chronic Gastritis ?

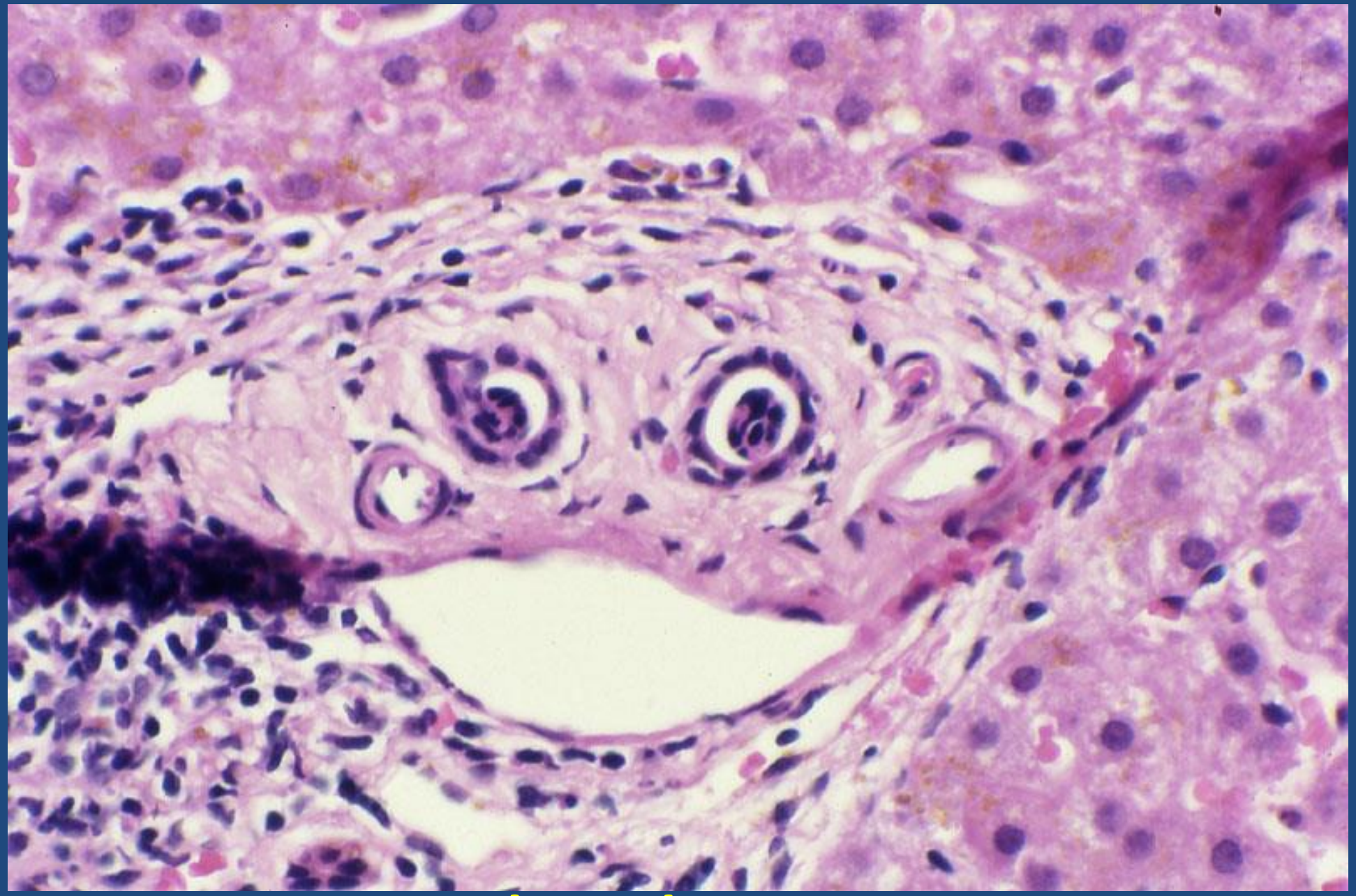
- What is the pathogenesis of NSAIDs induced Ulceration of the stomach ?

Conclusions on HP and neoplasia

- Worldwide *H pylori* is the commonest bacterial infection
- Gastric cancer is the 2nd leading cause of cancer-related deaths worldwide
- Pathogenesis of gastric cancer is complex & multifactorial but key pathophysiological events triggered by HP infection
- Host genetic factors, bacterial virulence factors and the environment all play an important role

There are several principles contained in the H. pylori story

- A recurrent element in the history of biomedical progress, is the vital role of the independent investigator
- Discoveries that change paradigms often come from young independent investigators working in situations that are permissive of the high risk research that challenges established dogma.
- Diseases are sophisticated experiments of nature whose elucidation yields extraordinary societal benefits.



Thank You

DANA

Wadi Rum (The Valley of The Moon)