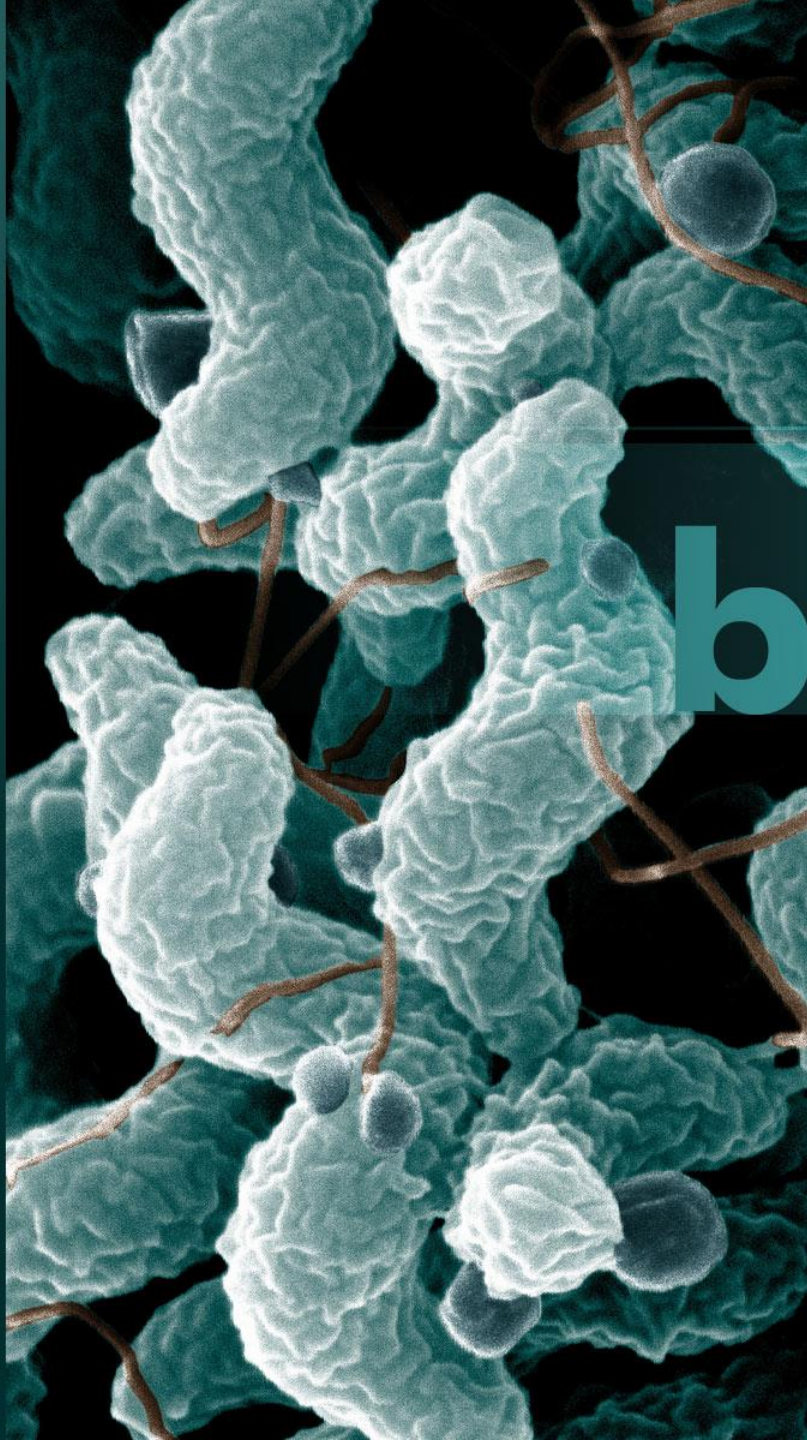


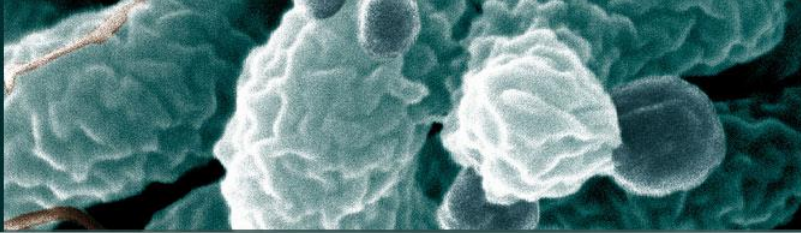
A scanning electron micrograph (SEM) showing a cluster of Helicobacter pylori bacteria. The bacteria are rod-shaped with a highly textured, wrinkled surface. They are surrounded by numerous thin, brown, hair-like flagella that extend outwards. The background is dark, making the light-colored bacteria stand out.

H. Pylori Infection

A Systemic Disease

bacteria

Bashar Almasri, MD
Assad University Hospital
Damascus



*Barry Marshall 1984
Nobel Prize in Physiology or Medicine in 2005*

Relation of *Helicobacter pylori* infection and coronary heart disease

Michael A Mendall, Patrick M Goggin, Nicola Molineaux, Joanna Levy, T Toosy, David Strachan, A John Camm, Timothy C Northfield

Abstract

Background—There is evidence suggesting that early life experience may influence adult risk of coronary heart disease (CHD). Chronic bacterial infections have been associated with CHD.

Objective—To determine whether *Helicobacter pylori*, a childhood acquired chronic bacterial infection, is associated with an increased risk of coronary heart disease in later life.

Design—Case-control study controlling for potential confounding variables with an opportunistically recruited control group.

Subjects—111 consecutive cases with documented CHD were recruited from a cardiology clinic and 74 controls from a general practice health screening clinic. All were white men aged 45–65.

Methods—Serum was analysed for the presence of *H pylori* specific IgG antibodies by ELISA (98% sensitive and 94% specific for presence of infection).

bacterial infection of the stomach that is usually acquired in childhood.⁴ It causes an active gastritis in all subjects infected with it and is strongly associated with gastric cancer and peptic ulcer disease, conditions that occur more commonly than by chance in association with CHD.^{5,6} Acquisition of *H pylori* is associated with poverty.⁴ This chronic bacterial infection may be a causative agent that explains part of the link between childhood poverty and adult CHD.

We used a case-control comparison to investigate whether *H pylori* infection was associated with adult CHD. We also studied possible associations of *H pylori* infection with cardiovascular risk factors in the control population.

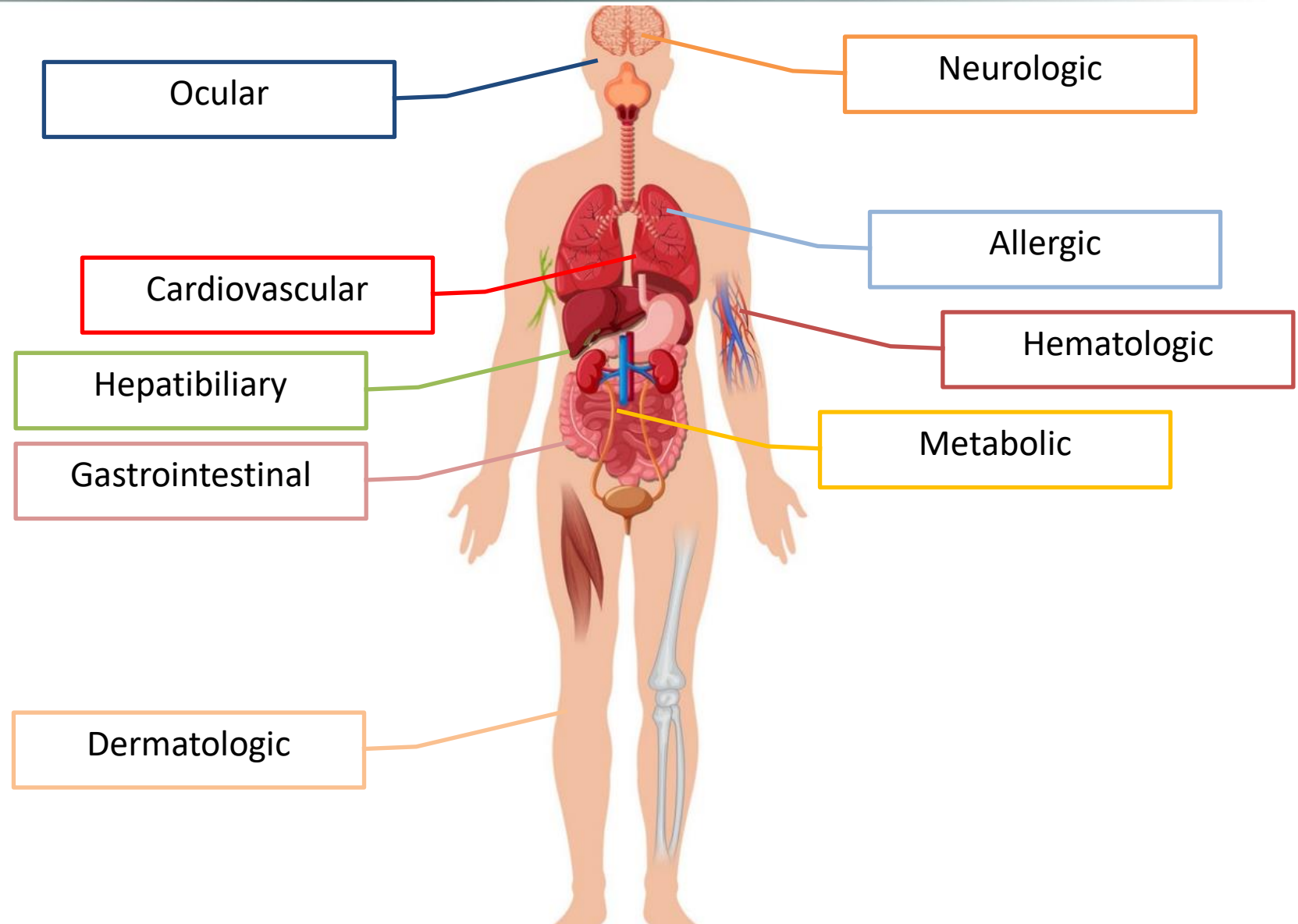
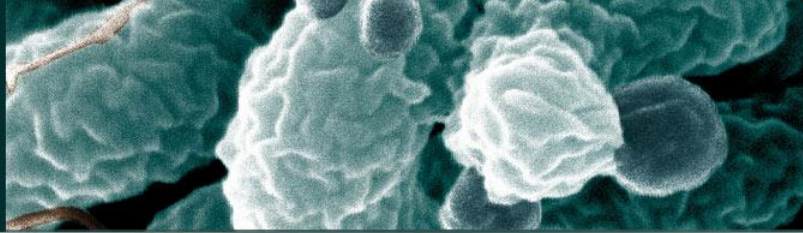
Patients and methods

PATIENTS

We studied men aged 45–65. The controls came from a single general practice screening clinic and the cases from a series of consecu-

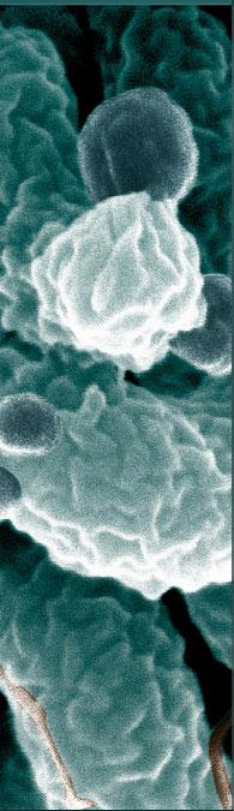


fppt.com



WHY ?????

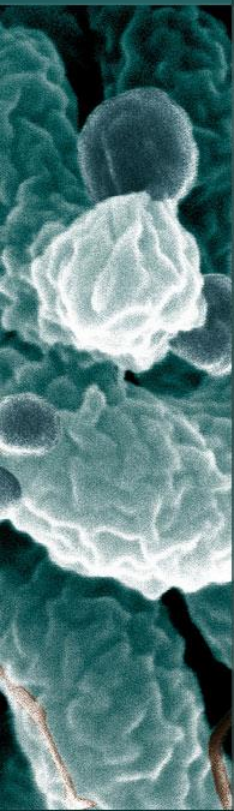
- LPS
- TNF α and low inflammatory state
- Modulation of immune cells
- Molecular mimicry
- Alteration of gastric acidity
- Translocation of microbiome to other sites
- Activation of platelets and factors involved in coagulation



GI diseases

- *Recurrent aphthous stomatitis* ... No obvious relationship BUT eradication of the infection may affect the clinical course of the oral lesions by undetermined mechanisms
- *GERD* ... discordant data
- *IBD* ... suggested protective role of chronic *H. pylori* infection due to immune tolerance and Treg stimulation

Gomes CC et al. Med Oral Patol Oral Cir Bucal. 2016
Yang YU et al. Cell Death & Disease. 2018



Neurologic diseases

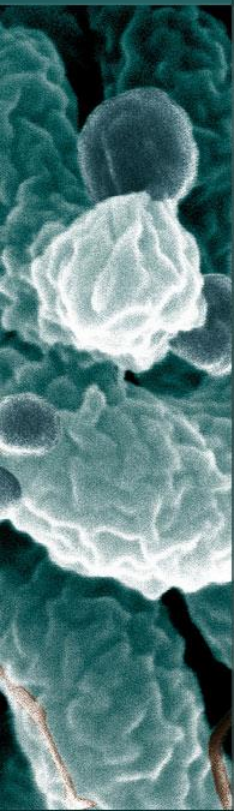
- CagA-positive strains were statistically significant risk factors for *Ischemic stroke*
- High anti-HP IgG in CSF and 1.6 Relative risk of *Alzheimer's disease*
- *Multiple sclerosis* (controversial)
- Increased risk of *PD* among individuals ≥ 60 years old
- High anti-HP IgG in CSF in *Guillain-Barré syndrome*



Wang ZW et al. J Neurol. 2012

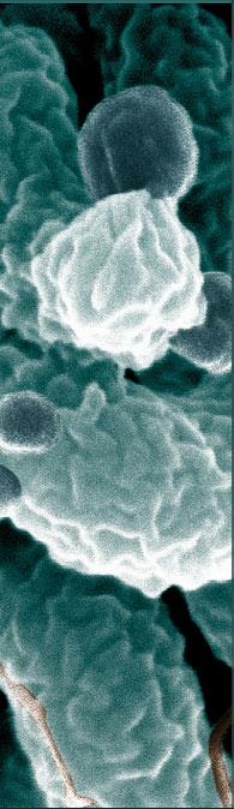
Huang Ws et al. J Clin Neurosci. 2014

Huang HK et al. Parkinsonism Relat Disord. 2018



Dermatologic diseases

- HP eradication successfully treats *Rosacea* in 97%
- Anti-*H. pylori* IgG was higher in patients with *Autoimmune bullous diseases (AIBD)* than in controls
- Association with *Psoriasis, alopecia aerata* and *Chronic urticaria* is still controversial
- *Schöenlein-Henoch purpura* (Few reports)



Gravina A et al. United European Gastroenterol J. 2015

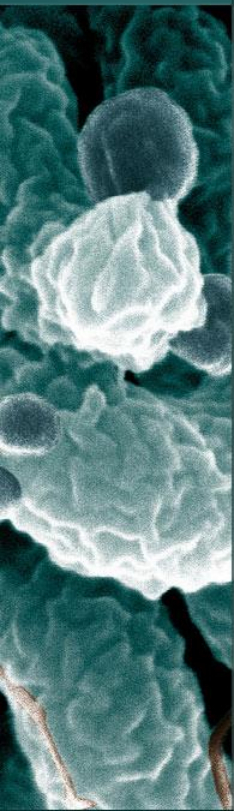
Yoshimasu T, Furukawa F. Allergol Int. 2014

Mortazavi H et al. Int J Dermatol. 2015

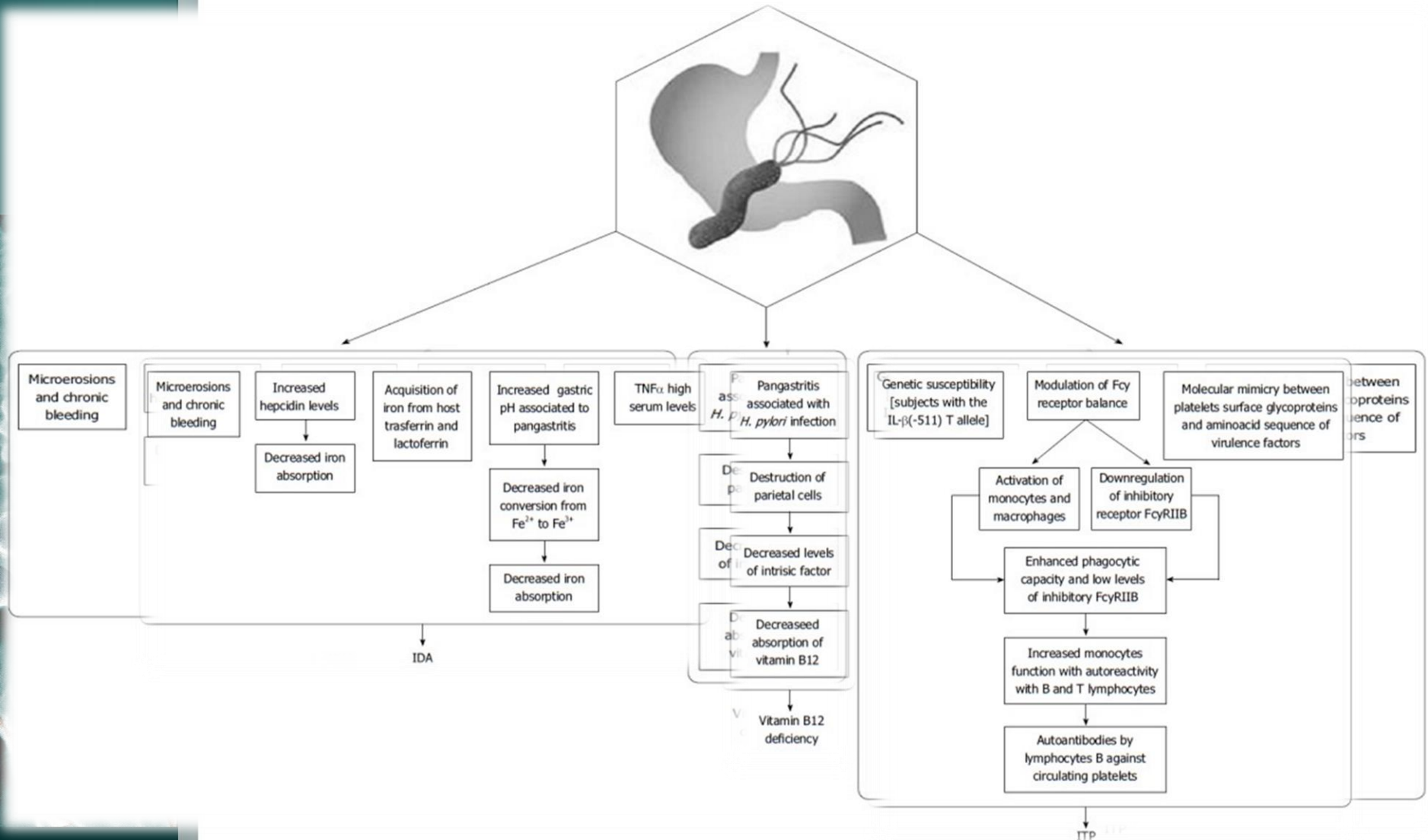
Hematologic diseases

- Close association with Iron deficiency anemia, B12 deficiency, and ITP
- *CagA+ strains are related to refractory IDA*
- Infection **should be eradicated** in cases of IDA and ITP according to guidelines
- Other disorders: *autoimmune neutropenia (AN)*, *anti-phospholipid syndrome (AS)*, and *plasma cell dyscrasias (PCD)*

Gravina AG et al. World J Gastroenterol. 2018
Malfertheiner P et al. Gut. 2017

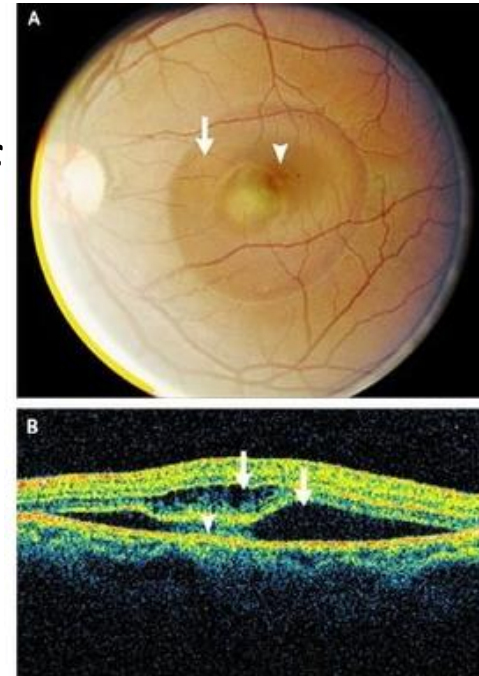


Hematologic diseases

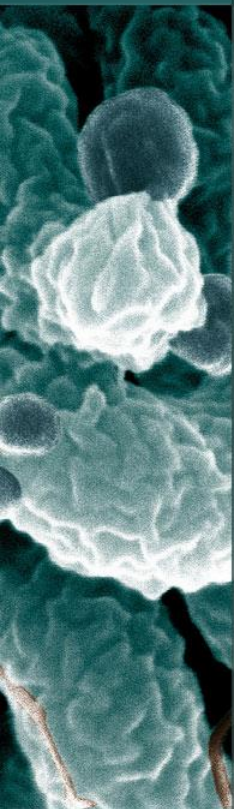


Ocular diseases

- Significant association between *H. pylori* infection and *Open Angle glaucoma*
- *H. pylori* infection is a possible risk factor for the occurrence of *central serous chorioretinitis*
- *Blepharitis* ... data are highly discordant



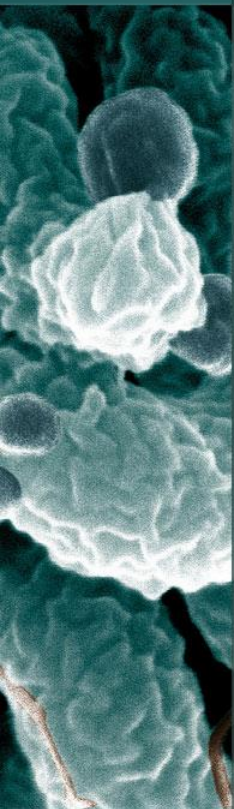
Testerman TL, Morris J. World J Gastroenterol. 2014
Liu B, Deng T, Zhang J. Retina. 2016

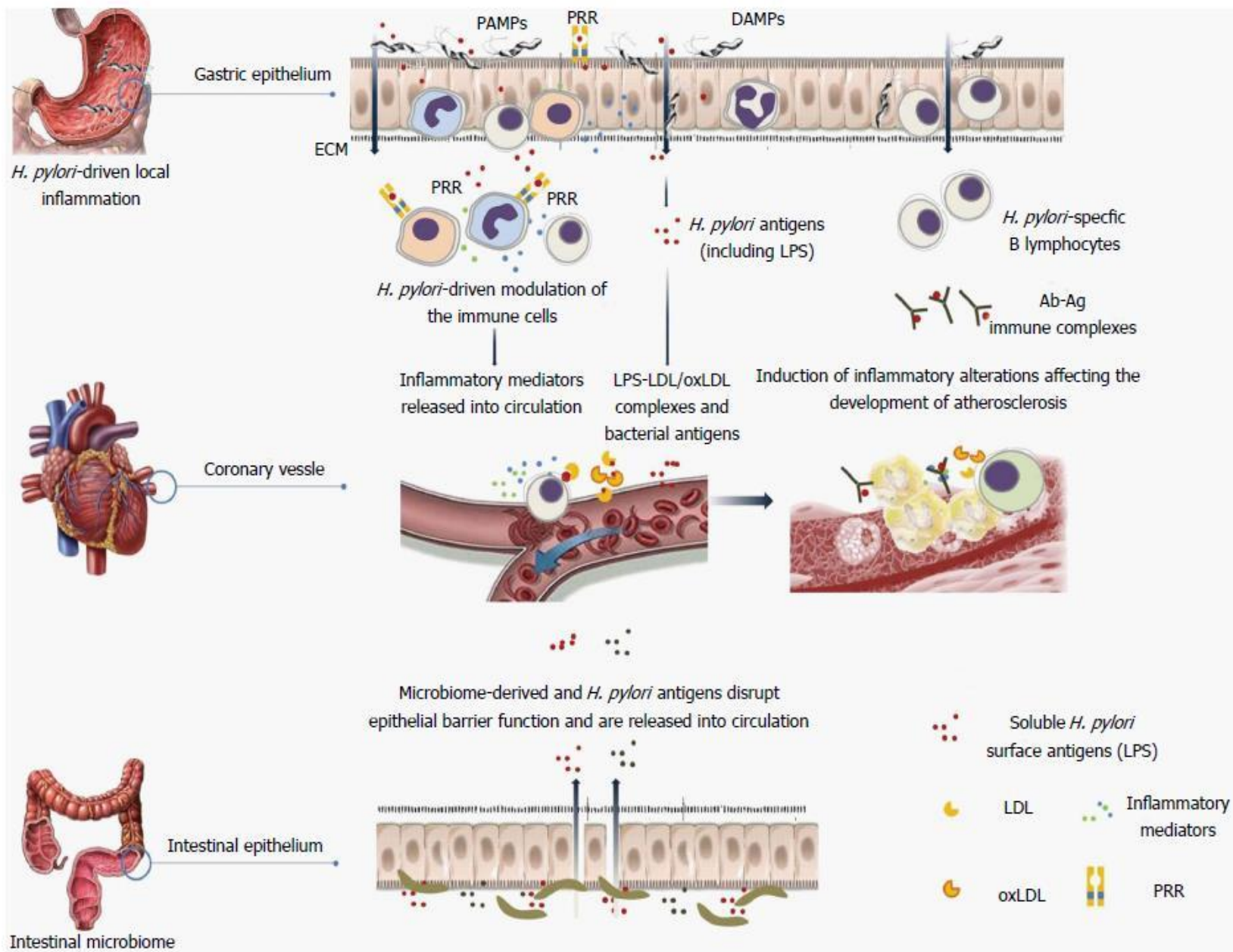


Cardiovascular diseases

- In 1994, first description of an association between *H. pylori* infection and *CAD*
- Atherosclerosis is an *inflammatory process*
- CagA-positive *H. pylori* strains were associated with an increased *risk of MI*
- Data in literature is still discordant

Gravina A et al. United European Gastroenterol J. 2015
Ikeda A et al. Atherosclerosis. 2013





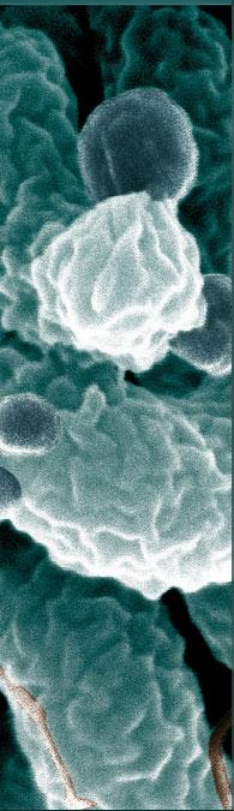
Chmiela M, Gajewski A, Rudnicka K. World J Cardiol 2015

Metabolic diseases

- Role of *H. pylori* infection in *diabetes mellitus*, *insulin resistance syndrome*, and *metabolic syndrome* is still controversial
- *H. pylori* (CagA+) → ↑ HbA1c, risk of microalbuminuria, neuropathy and heart disease in DM



Hsieh MC et al. Eur J Clin Invest. 2013
Chung GE et al. World J Gastroenterol. 2013

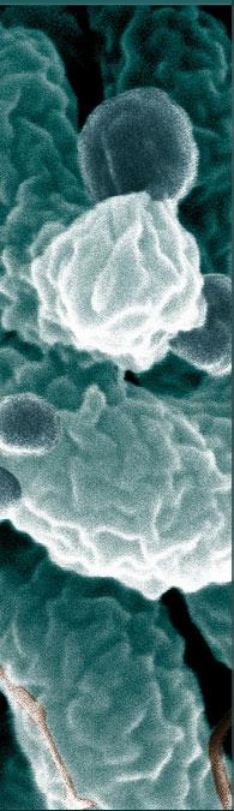


Metabolic diseases

- *HOMA-IR* is higher in patients with *H.pylori* infection than in control
- Serum *Chol* and *TG* levels were higher in infected male subjects



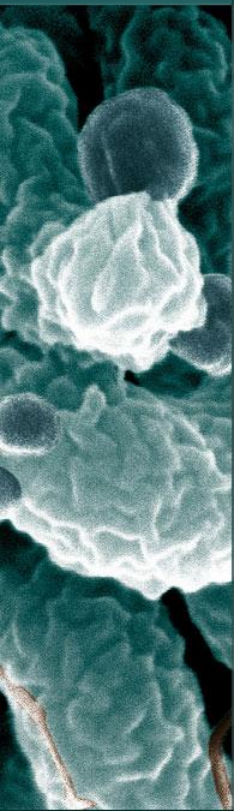
Eshraghian A et al. Dig Dis Sci. 2009
Niemelä S et al. Heart. 1996



Allergic diseases

- *Inverse association* is present between *H. pylori* infection and asthma
- *H. pylori* (CagA+) can protect against airway hyper-reactivity, broncho-alveolar eosinophilia, and lung inflammation
- IL-18 production by dendritic cells (DCs) following exposure to *H. pylori* stimulates Treg cells
- take into account the *hygiene hypothesis*

Zhou X, Wu J, Zhang G. Eur J Gastroenterol Hepatol. 2013
Oertli M et al. J Clin Invest. 2012



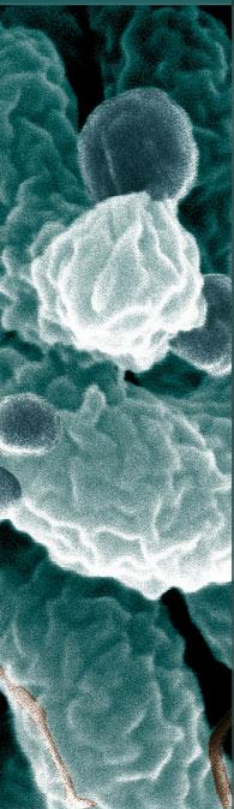
Hepatobiliary diseases

- Higher serum level of anti-*H. pylori* IgG in patients with **NAFLD** than in non-NAFLD



- Eradication of *H. pylori* → ↓ TNFα → Improvement of **NASH**

Chen CX et al. Appl Physiol Nutr Metab. 2017
Sumida Y et al. J Gastroenterol. 2015



Hepatobiliary diseases

H. pylori infection

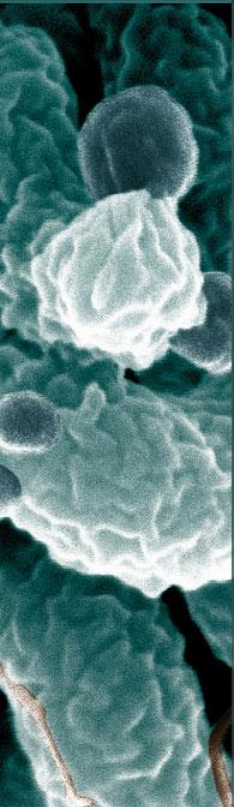


↑ *TGF-β1*-induced
pro-inflammatory

signaling pathways in hepatic stellate cells



accelerated *hepatic fibrosis*



Ki MR et al. Lab Invest. 2010

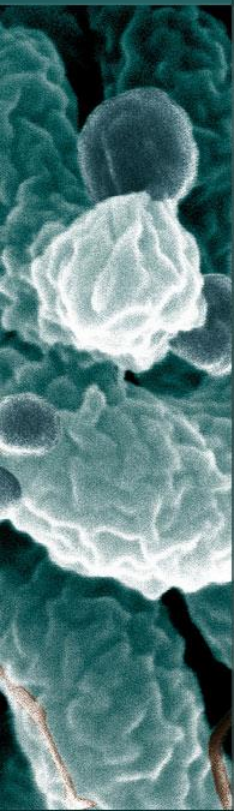
Hepatobiliary diseases

- Higher prevalence of anti-*H. pylori* IgG in patients with *PBC* compared to controls



- *H. pylori* was found in liver biopsies obtained from patients with *PBC* and *PSC*

Shapira Y et al. Exp Mol Pathol. 2012
Nilsson HO et al. J Clin Microbiol. 2000

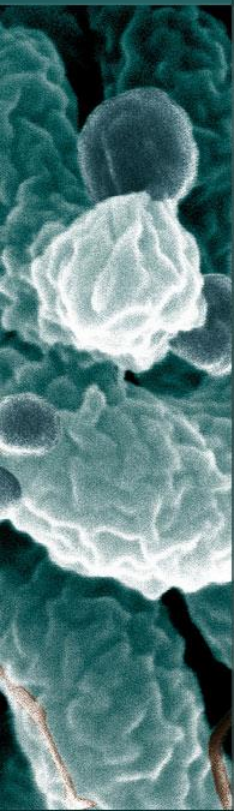


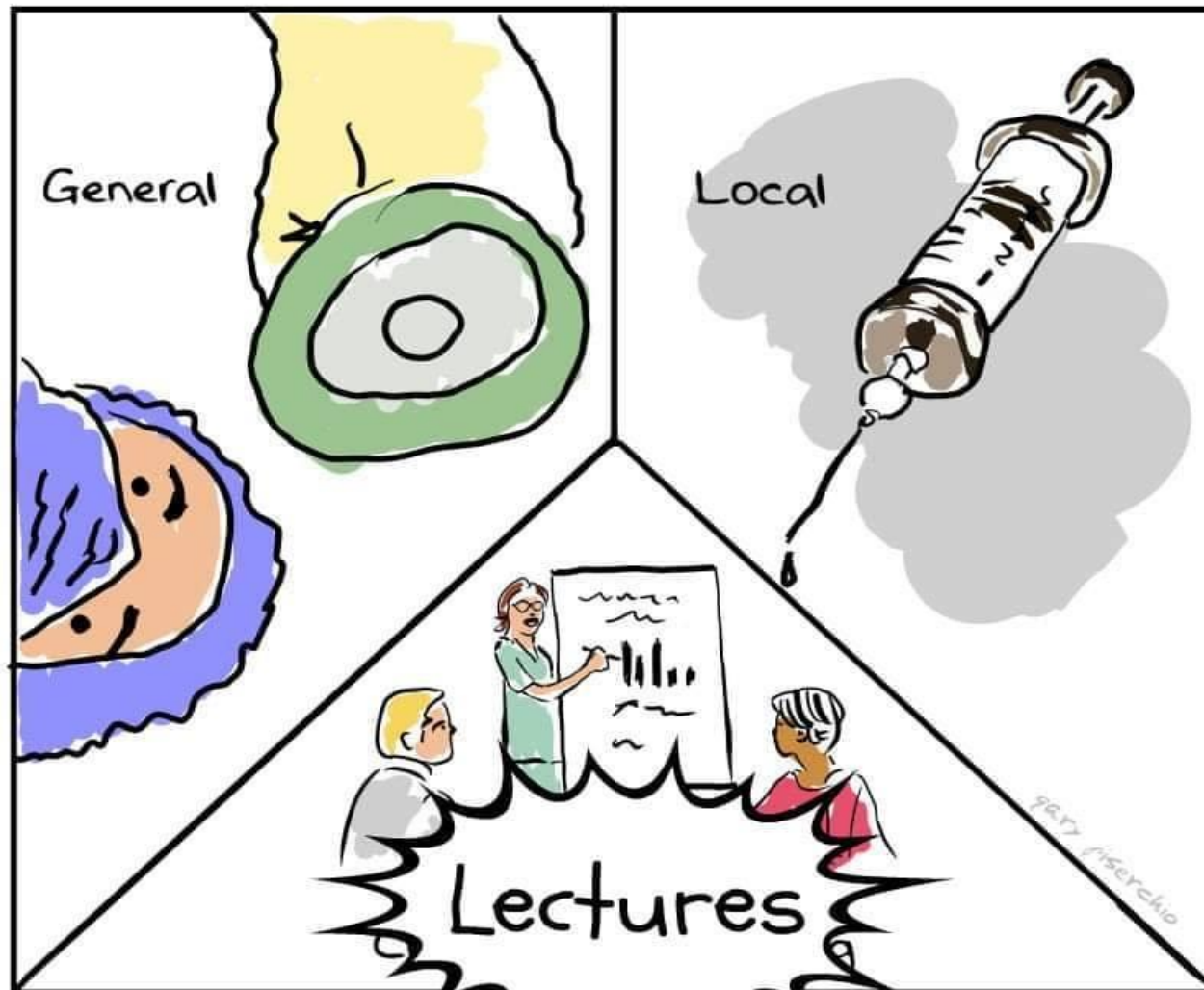
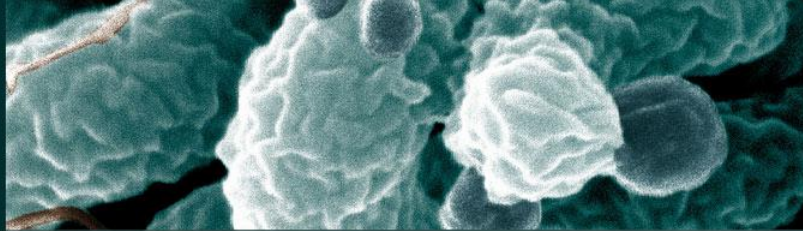
Hepatobiliary diseases

- Role of *H. pylori* in hepatic *carcinogenesis* is controversial
- Liver biopsies of *HCC* or *cholangiocarcinoma* were positive for *H. pylori*
- Positivity for *H. pylori* was higher in patients with HCC than in controls



Nilsson HO et al. Gastroenterology. 2001
Pellicano R et al. World J Gastroenterol. 2004





Three forms of anesthesia.

Conclusion

- Many extra-gastric manifestations have been reported to be linked to *H. pylori* infection
- Most evidences are derived from epidemiological studies
- It is *Hard to establish a cause-effect* correlation
- *H. pylori* infection should be sought and, if present, eradicated only in patients with hematologic disorders

