

PreCorso 2011

Firenze, 22 luglio 2011

Helicobacter pylori, un batterio causa di
molte malattie, dall'ulcera peptica al
cancro gastrico

Mario Milco D'ELIOS

Facoltà di Medicina e Chirurgia
Università degli Studi di Firenze
delios@unifi.it

Helicobacter pylori

- Quando è stato scoperto?
- Chi l'ha visto per primo?
- Da quanto tempo "conosce" l'uomo?
- Perché avvistato e non scoperto?
- Coincidenze delle grandi scoperte?
- Come vive nello stomaco?
- Quante persone sono infettate? illustri pazienti?
- Tutti gli infettati sono malati?
- E l'ospite (uomo) infettato che fa?
- Le **Relazioni Pericolose**





The Nobel Prize in Physiology or Medicine 2005

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

Barry J. Marshall
Australia

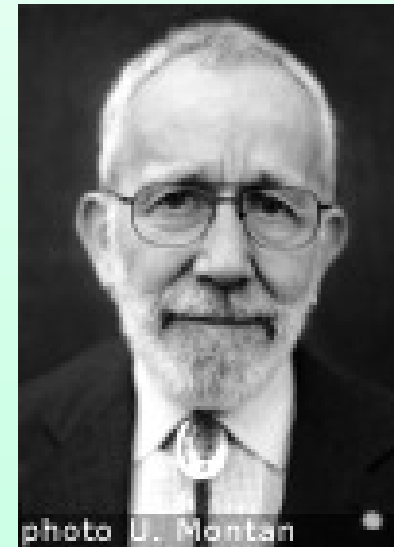
Helicobacter pylori
Research
Laboratory, QEII
Medical Centre;
University of
Western Australia
Australia

J. Robin Warren
Australia

Perth,
Australia



b. 1951



b. 1937

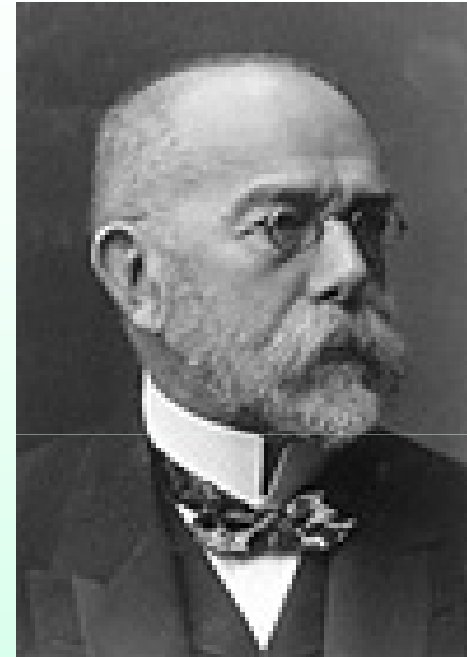
E 100 anni prima
Premio Nobel
a chi?

The Nobel Prize in Physiology or Medicine 1905



"for his investigations and
discoveries in relation to
tuberculosis"

Robert Koch



Germany
Institute for Infectious
Diseases
Berlin, Germany

b. 1843
d. 1910

Helicobacter pylori quando è stato scoperto?

Cultured for the first time on Easter Thursday 1982

- Patient 37, 70y.o. male
- DU, GU, artificial valve, anticoagulants
- **MRSA epidemic at Royal Perth**
 - Overworked microbiology technologists
 - No time to check the culture on Saturday
 - Not examined until Tuesday Not examined until Tuesday
 - Gram negative rods seen in pure culture
- **We had been using the right methods for**
 - Cultures were being discarded after 48 hours

From the 2005 Nobel Lecture by Barry Marshall

... e 100 anni prima?

Die Ätiologie der Tuberkulose.¹⁾

(Nach einem in der Physiologischen Gesellschaft zu Berlin am 24. März 1882 gehaltenen Vortrage.)

Von

Dr. R. Koch,

Regierungsrat im Kaiserl. Gesundheitsamt.

Die von V i l l e m i n gemachte Entdeckung, daß die Tuberkulose auf Tiere übertragbar ist, hat bekanntlich vielfache Bestätigung, aber auch anscheinend wohlbegründeten Widerspruch gefunden, so daß es bis vor wenigen Jahren unentschieden bleiben mußte, ob die Tuberkulose eine Infektionskrankheit sei oder nicht. Seitdem haben aber die zuerst von C o h n h e i m und S a l o m o n s e n, später von B a u m g a r t e n ausgeführten Impfungen in die vordere Augenkammer, ferner die Inhalationsversuche von T a p p e i n e r und anderen die Übertragbarkeit der Tuberkulose gegen jeden Zweifel sichergestellt und es muß ihr in Zukunft ein Platz unter den Infektionskrankheiten angewiesen werden.

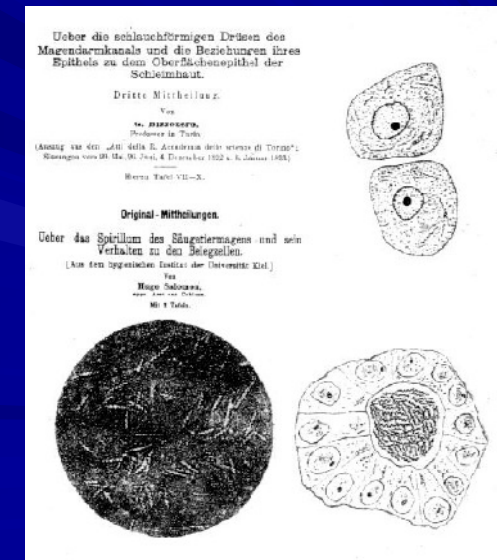
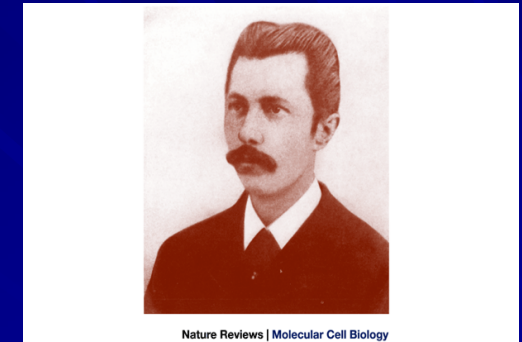
Wenn die Zahl der Opfer welche eine Krankheit fordert, als Maßstab für ihre Bedeutung zu gelten hat, dann müssen alle Krankheiten, namentlich aber die gefürchtetsten Infektionskrankheiten, Pest, Cholera usw. weit hinter der Tuberkulose zurückstehen.

The first report on the etiology of tuberculosis was presented on March 24, 1882 in Berlin.

Helicobacter

chi l'ha visto per primo? **quando?**

- Giulio Bizzozzero
- **1893**, *Arch f mikr Anat* 42: 82-152.
"Ueber die schlauchformigen drusen des magendarmkanals und die beziehungen ihres epithels zu dem oberflachenepithel der schleimhaut."
- **1892**, *Atti della Reale Accademia delle Scienze di Torino* 28: 233-251.
"Sulle ghiandole tubulari del tubo gastroenterico e sui rapporti del loro epitelio coll'epitelio di rivestimento della mucosa."



Helicobacter

altri avvistamenti

- La presenza di batteri spiraliformi nello stomaco fu descritta a più riprese nel secolo scorso, tra gli altri da **Freedberg** nel **1940** a **Steer** e **Colin-Jones** nel **1975**.
- **Ito** descrisse e fotografò batteri spiraliformi in biopsie derivate dal suo stomaco, nel suo famoso Textbook of Physiology del **1966**.
- Tra gli anni **20** e **50** del '900 altri scienziati, quali **Luck** e **Fitzgerald**, provarono la presenza di attività enzimatica di tipo **ureasica** nello stomaco di gatti e cani.
- Nel **1959** **Lieber** dimostrò che l'attività ureasica gastrica poteva essere soppressa con una terapia antibiotica a base di tetracicline. Nel **1968** **Delluva** osservò che animali mantenuti in condizioni asettiche non presentavano attività ureasica nello stomaco.
- Ma...la presenza di **batteri** nello stomaco e l'attività **ureasica** **non** furono **poste in relazione** all'insorgenza di **patologie** gastroduodenali

H. pylori

perché avvistato e non scoperto?

- Acid environment kills organisms
- The normal stomach is sterile
- Bacteria seen are contaminant passing through, dead or secondary to gastric lesions such as peptic ulcer. Just a secondary infection, due to gastritis
- “If it is true, why were they not recognised before...”

(From the 2005 Nobel Lecture by Robin Warren)

... perché?

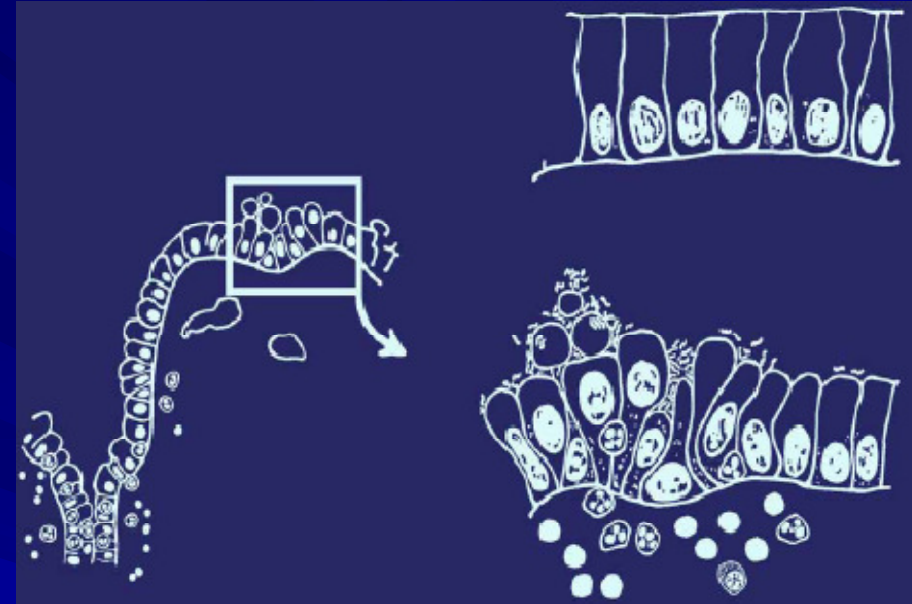
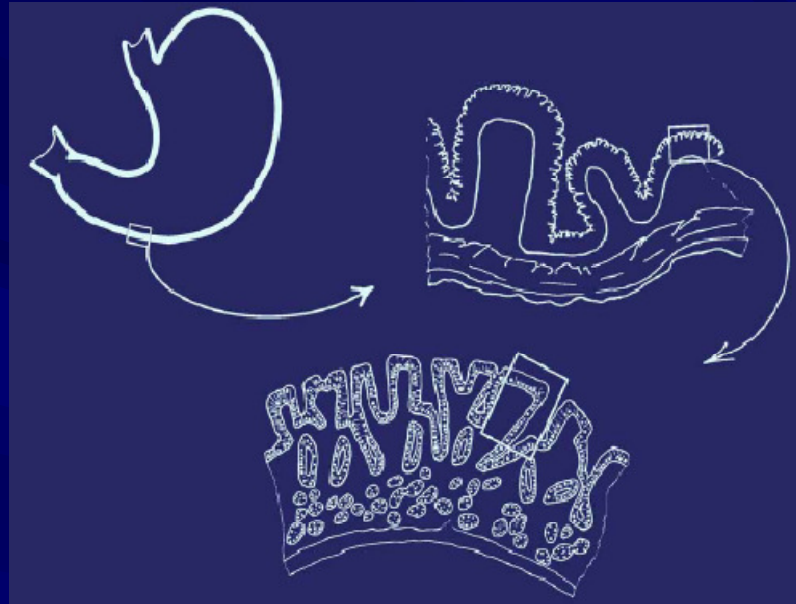
- “L’uomo, per sua natura, ha più paura della verità che della morte...”

Soren Kierkegaard

- “...Il più grande ostacolo alla conoscenza non è l’ignoranza bensì l’illusione della conoscenza”

Daniel Boorstein

Warren First Report



(From the 2005 Nobel Lecture by Robin Warren)

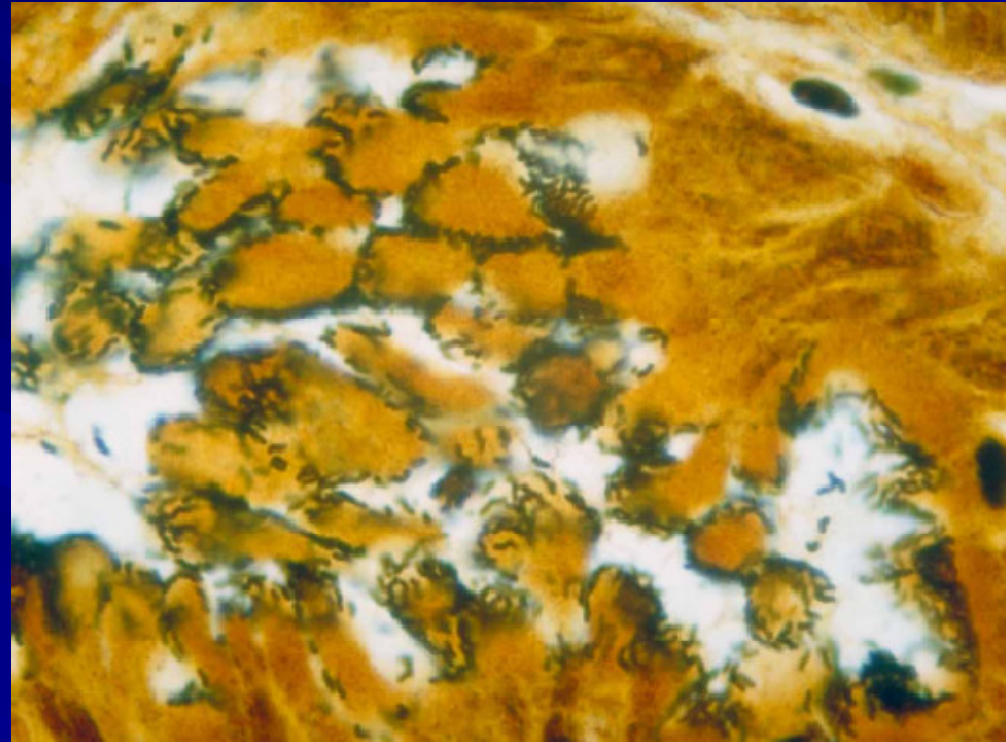
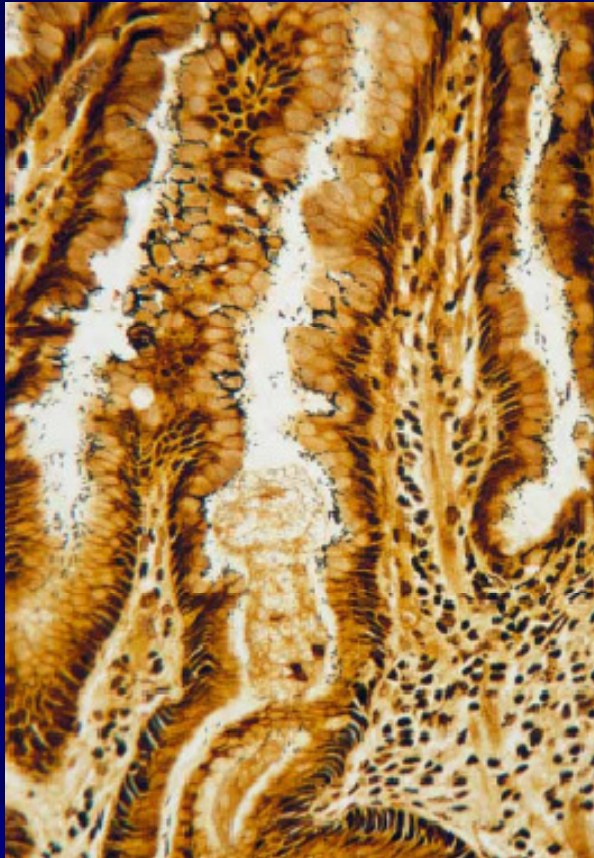
Conclusion:

There is chronic gastritis with a small erosion. The quality of the surface mucus appears slightly more dense than normal in many areas, and it contains numerous bacteria in close contact with the surface epithelium. These bacteria have the morphology of *Campylobacter*. They appear to be actively growing and not a contaminant. I am not sure of the significance of these unusual findings, but further investigation of the patient's eating habits, gastro-intestinal function and microbiology may be worthwhile.

J. R. Warren 1979

H. pylori

black bacilli line the pits, easily seen (silver stain)



(From the 2005 Nobel Lecture by Robin Warren)

Lancet Letters 1983

A new species

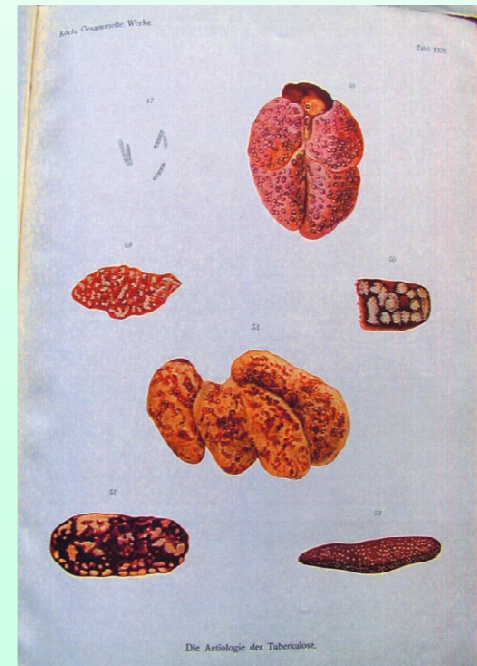
Bacteria linked to gastritis

- “since the new bacteria are associated with gastritis as described by Warren, then they may play a role in other poorly understood gastric diseases i.e. peptic ulcer and gastric cancer.”

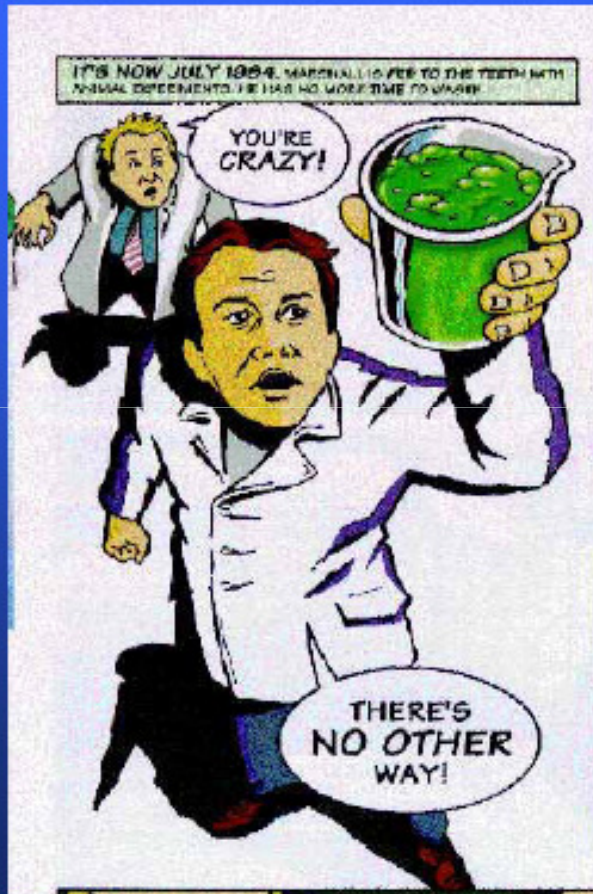
From the 2005 Nobel Lecture by Barry Marshall

Koch's Postulates ...

- 1. The same organism must be present in every case of the disease.**
- 2. The organism must be isolated from the diseased host and grown in pure culture.**
- 3. The isolate must cause the disease, when inoculated into healthy, susceptible animal.**



Koch's Postulates and *H. pylori*.....

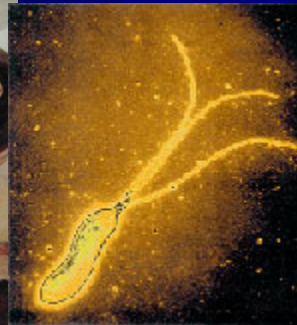


An attempt to Fulfill Koch's Postulates for *Campylobacter pyloridis*

Med J. Aust 1984

From the 2005 Nobel Lecture by Barry Marshall

H. pylori e pazienti nei secoli

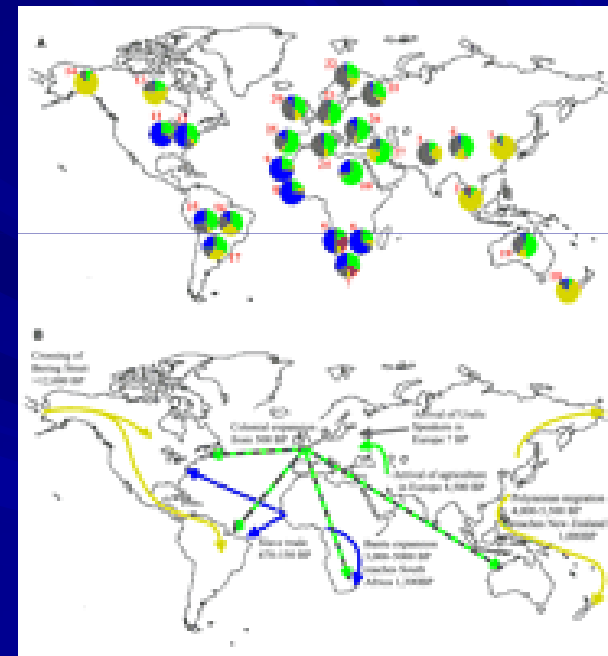
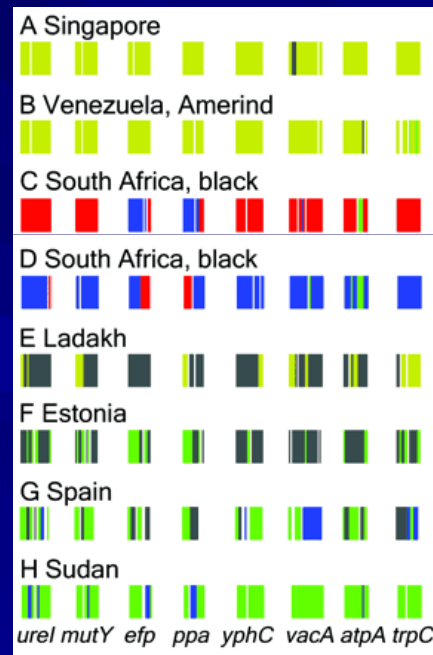
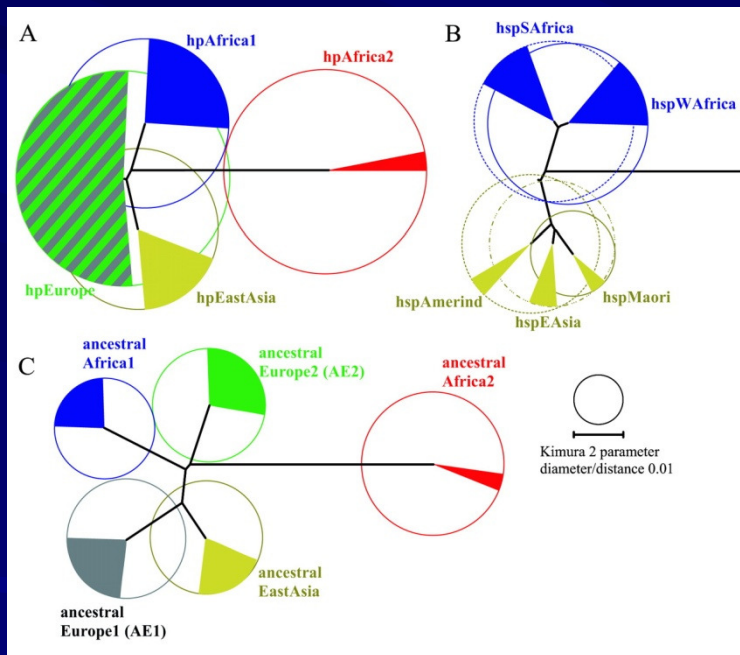


- **Napoleone**, a 52 anni, morì di “ulcera antrale maligna” (**cancro gastrico**). Così suo padre, suo nonno, almeno un fratello, una sorella.

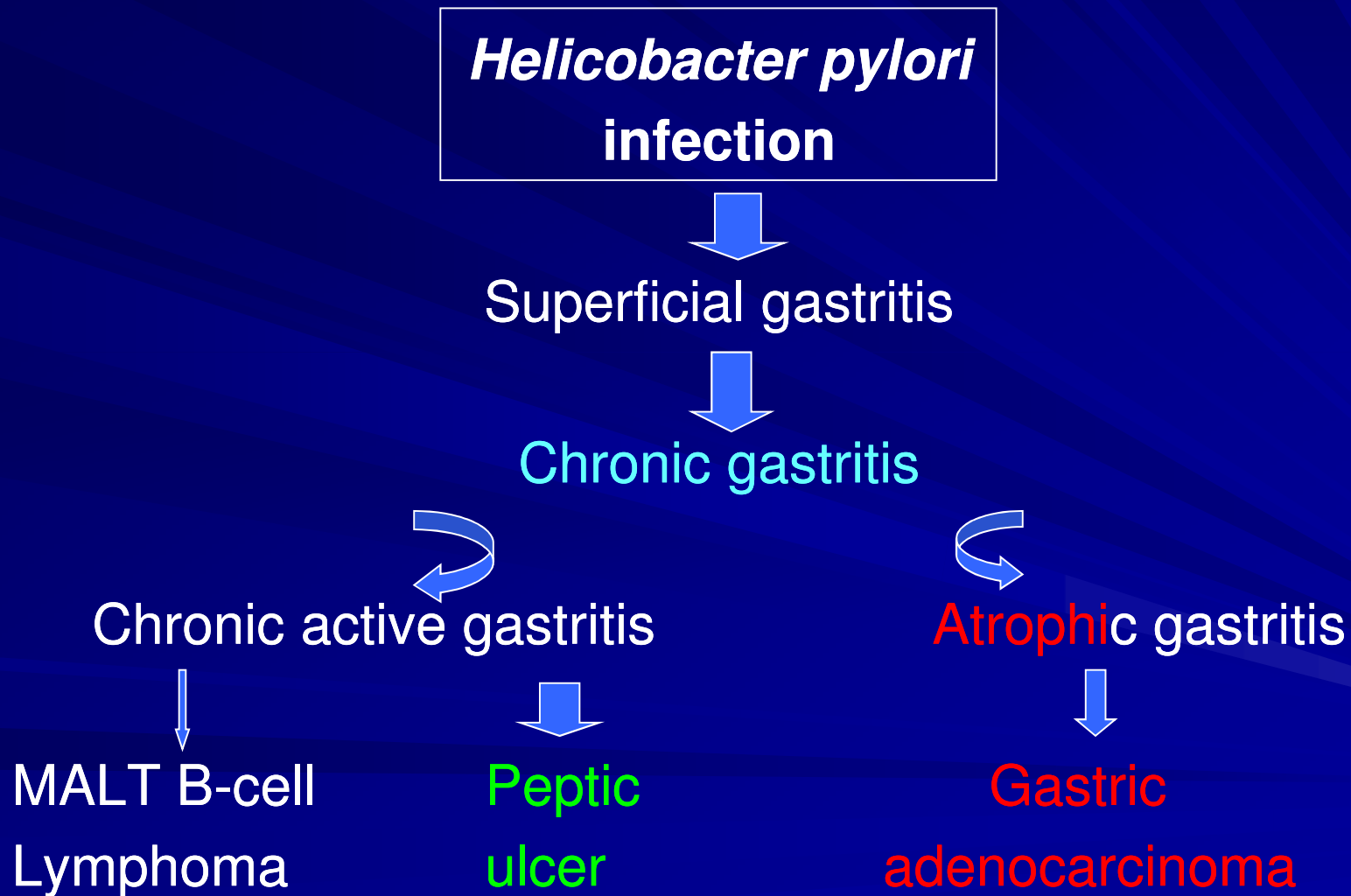
- Alfred **Nobel** soffriva di ulcera peptica!
- James **Joyce** morto di ulcera duodenale perforata.

Traces of human migrations in *H. pylori* populations

da quanto tempo "conosce" l'uomo?



H. pylori and related clinical outcomes



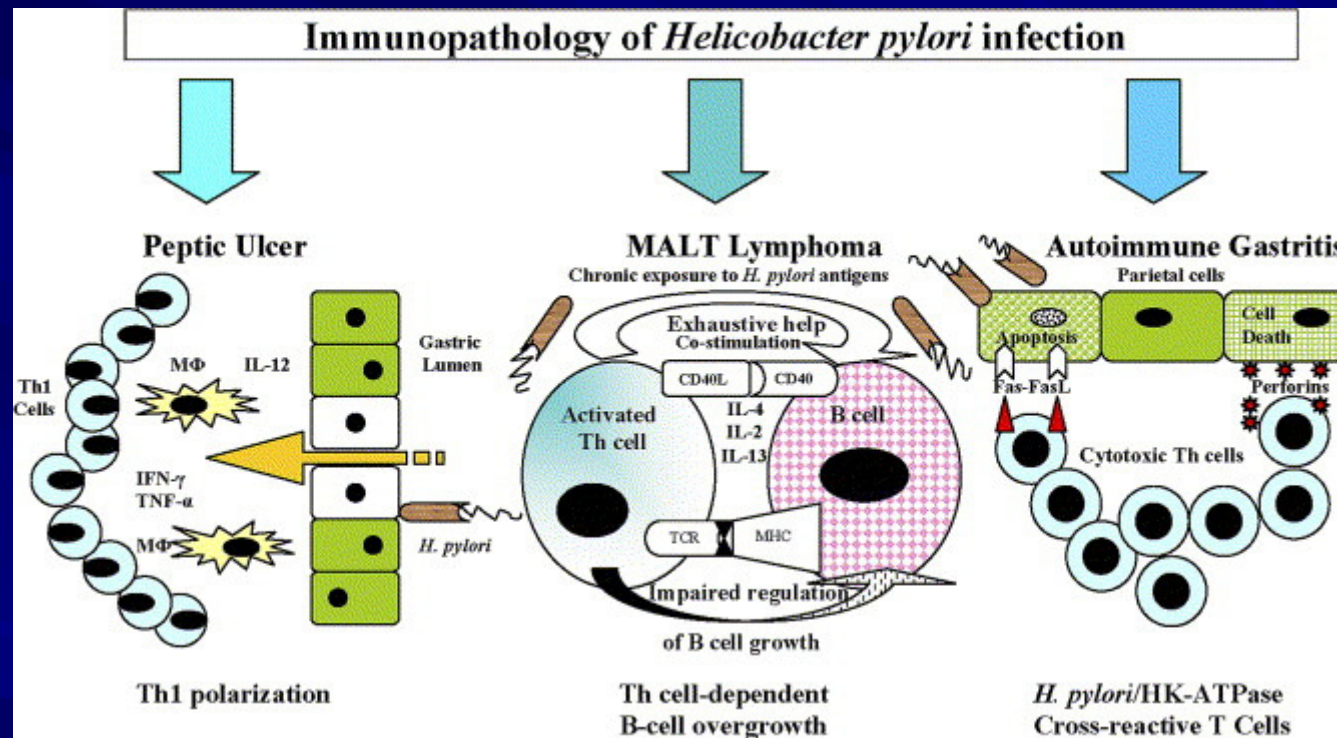
H. pylori, host response, and related clinical outcomes

- Bacterial factors (different strains, pathogenicity island)
- Host factors (genetics, cytokine / chemokine network, gastrin, somatostatin, pepsinogen, regulation of acid secretion)
- Inflammation (site, type, etc)

“..Qui pourrait ne pas frémir en songeant aux malheureux
qui ont causé une seule liaison dangereuse ...”

P. Choderlos De Laclos

Les liaisons dangereuses



D'Elíos et al., *J Immunol* 1997; *Gastroenterology* 99, 2001; *PNAS* 2003; *J Exp Med* 2003
Trends Mol Med 2004; *J Clin Invest* 2006; *Helicobacter* 2009;
Cancer Immunol Immunother 2009, *Expert Rev Anti Infect Ther* 2010