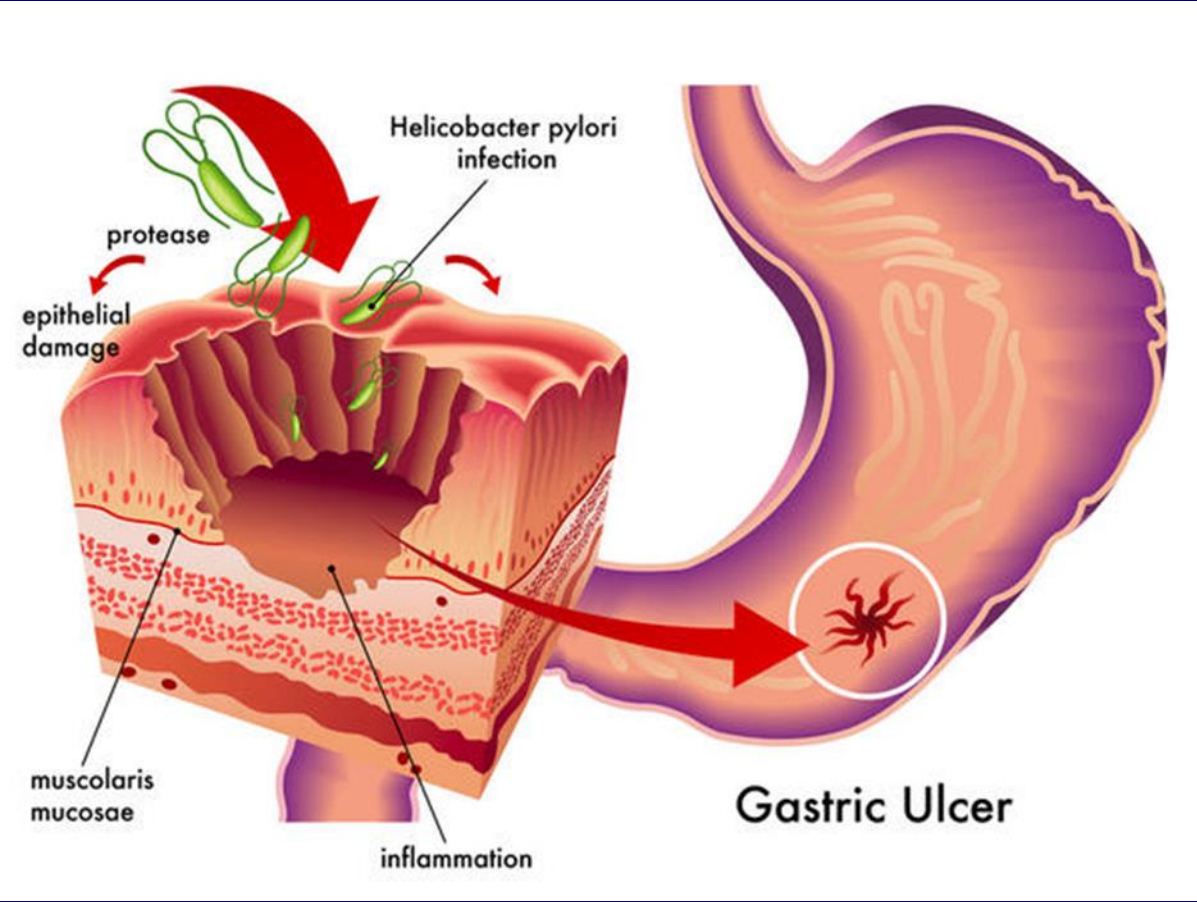


GIT

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# GIT infections

- *Helicobacter pylori (H.Pylori)*
- *Campylobacter*

# *Helicobacter pylori* (H. Pylori)

Organism classified first as *Campylobacter pylori*

Now *Helicobacter pylori*

Marshall and Warren cultured organism from human gastric mucosa and showed the association with gastric inflammation

## Important Human Pathogens:

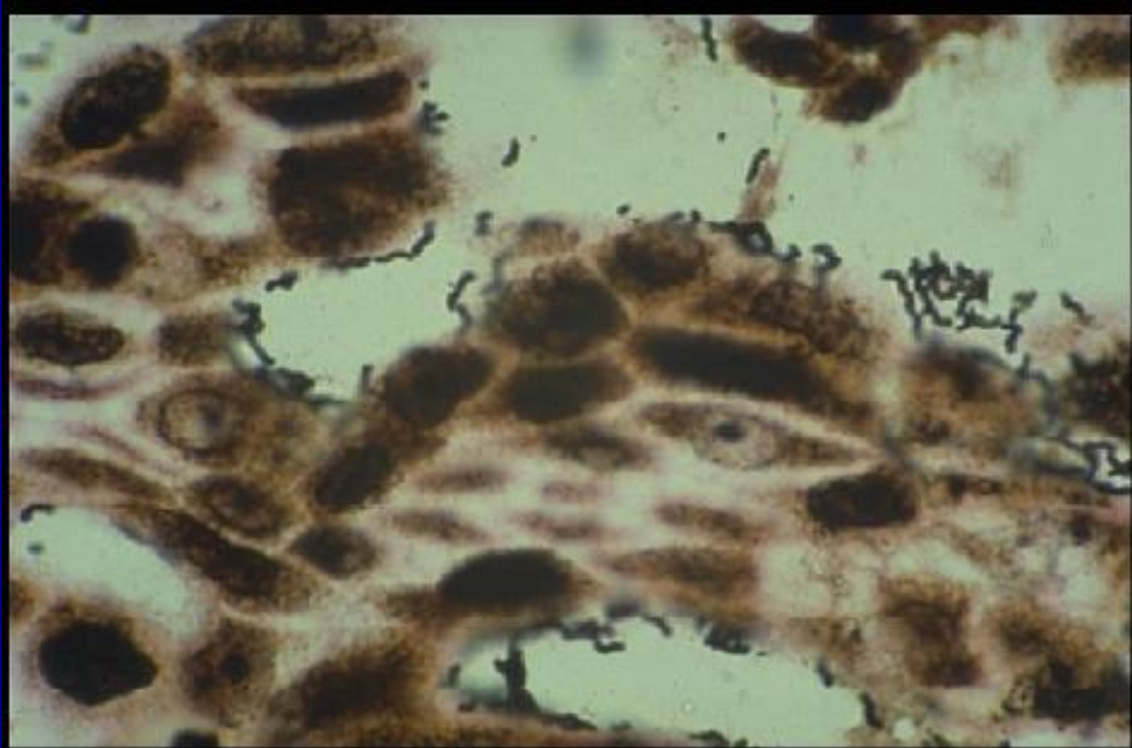
*Helicobacter pylori* (human; no animal reservoir)

*H. cinaedi* (male homosexuals; rodents)

*H. fenneliae* (male homosexuals; rodents)

# *H. pylori*

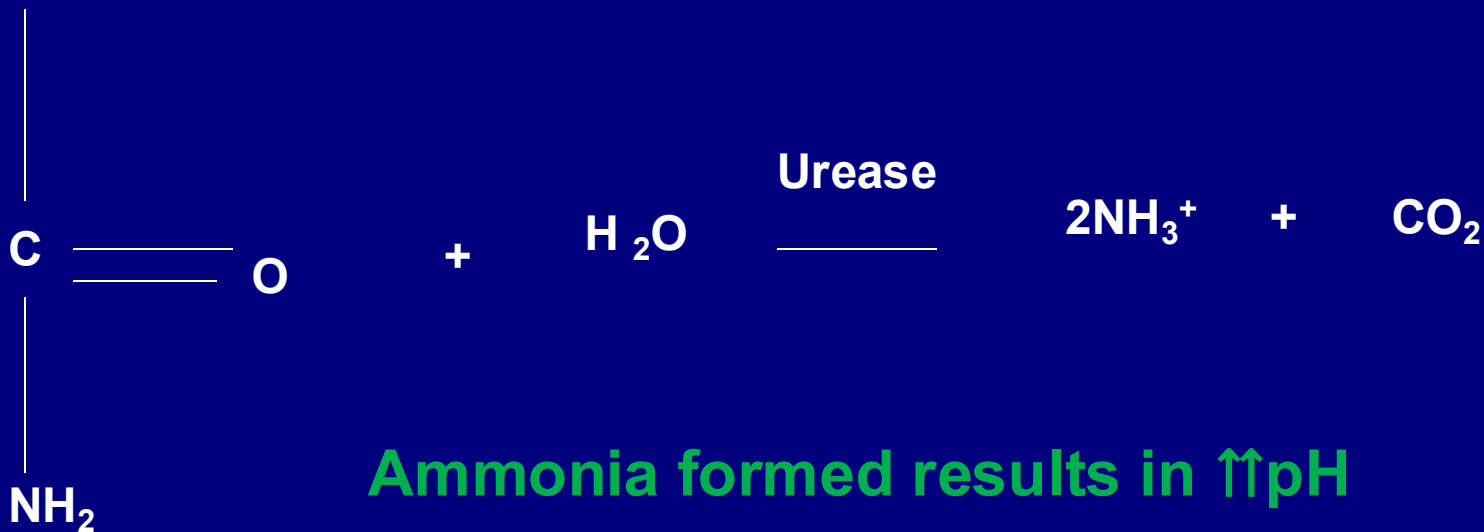
*H. pylori* on gastric mucus-secreting epithelial cells From Dr. Marshall's stomach biopsy taken 8 days after he drank a culture of *H. pylori* (1985) > stomach lining is infected



# H.pylori -Microbiology

- Gram negative rods, spiral, flagellated (motile) bacilli (0.5-0.9  $\mu\text{m}$  wide by 2-4  $\mu\text{m}$  long)
- This renders *H. pylori* motile in the mucus environment.
- urease that catalyzes urea hydrolysis to produce buffering ammonia which act as an acid-resistance mechanisms.

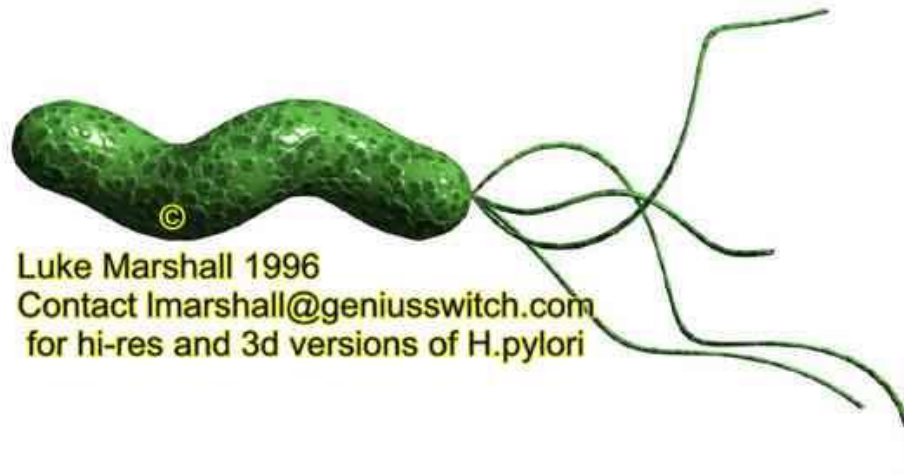
$\text{NH}_2$



Ammonia formed results in  $\uparrow\text{pH}$

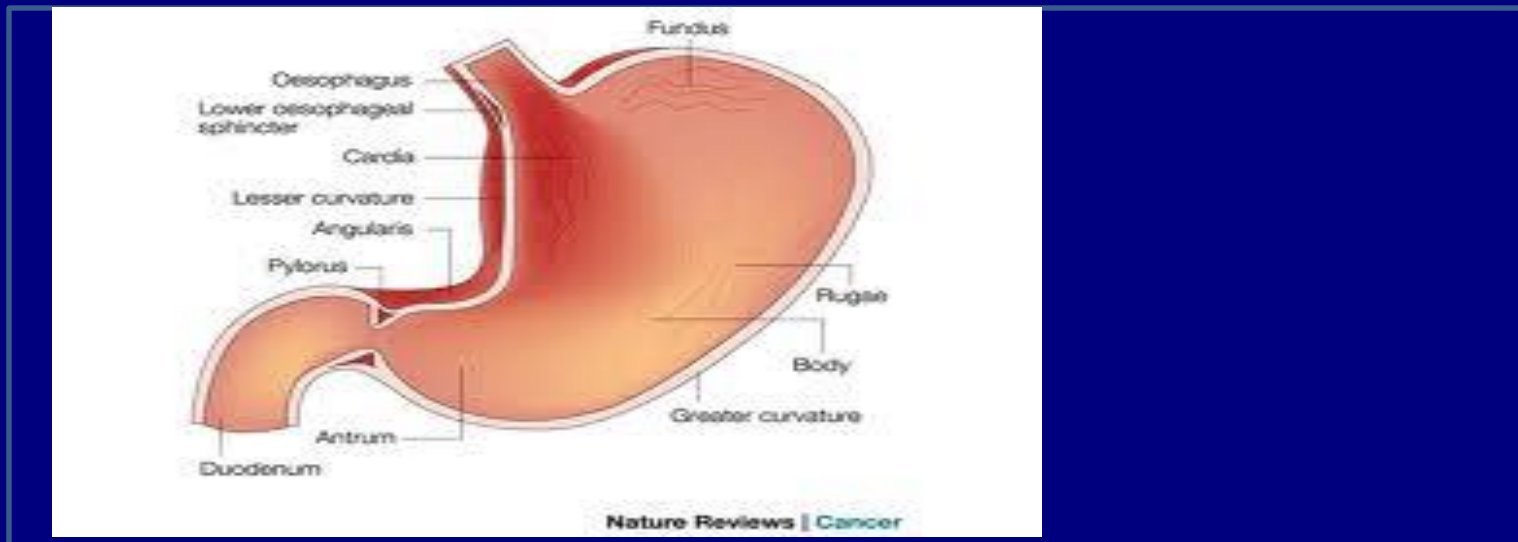
# *H. Pylori / Properties*

- Cells become rod-like and coccoid on prolonged culture
  - *H. pylori* have 4-6 sheathed flagella attached at one pole
  - Single polar flagellum on *H. fennellae* & *H. cinaedi*



# *H. Pylori* / Properties

- **Slow growing, requires complex media, microaerophilic (requires carbon dioxide, some Oxygen and Nitrogen)**
- **Oxidase, catalase and urease positive**
- **Proliferates in mucus overlying gastric antral mucosa > non invasive**



# *H. pylori*

- **Culture:**
- ***H. pylori* is easily cultured from vomitus and gastroesophageal refluxate and cultured from stool.**
- On special medium containing vancomycin, polymyxin and trimethoprim (Skirrow's)
- At 37 °C for 3-7 days in microaerophilic conditions.
  
- **Epidemiology:**
- **human** (Not zoonotic) appears to be the sole reservoir and source of *H. pylori*.
- How infection is **transmitted** is unknown, but it is presumed to be by the oral-oral or, possibly, faecal-oral route.

## *H. Pylori* / *epidemiology* cont'd

- Nosocomial infection from inadequately disinfected endoscopes has also occurred
- There is a steady rise in seropositivity with increasing age
- Remarkably, *H. pylori*, colonizes roughly half of the world's Population
  - ~ 20% below the age of 40 years are infected
  - 50% above the age of 60 years are infected
  - In developing countries, About 10% acquisition rate per year for children between 2 and 8 years of age (0.1% in developed)

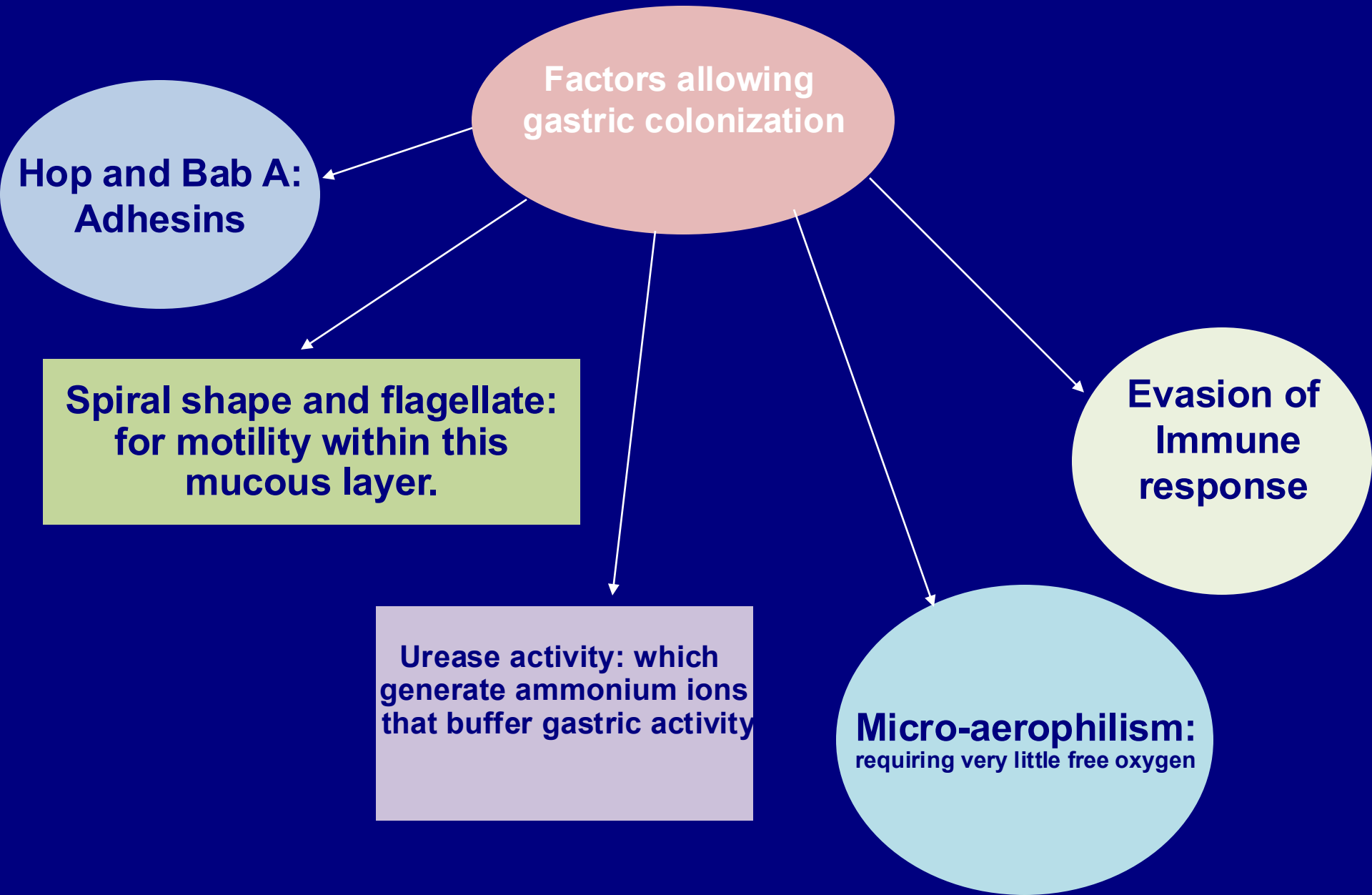
# *H. Pylori* / Pathogenesis

- sheathed flagella 'lophotrichous' > motile
  - enables penetration into viscous environment (mucus)
- Adhesins: Hemagglutinins; Sialic acid binding adhesin
- Mucinase: Degrades gastric mucus; Localized tissue damage
- Urease converts urea (abundant in saliva and gastric juices) into bicarbonate (to CO<sub>2</sub>) and ammonia
  - Neutralize the local acid environment
  - Localized tissue damage

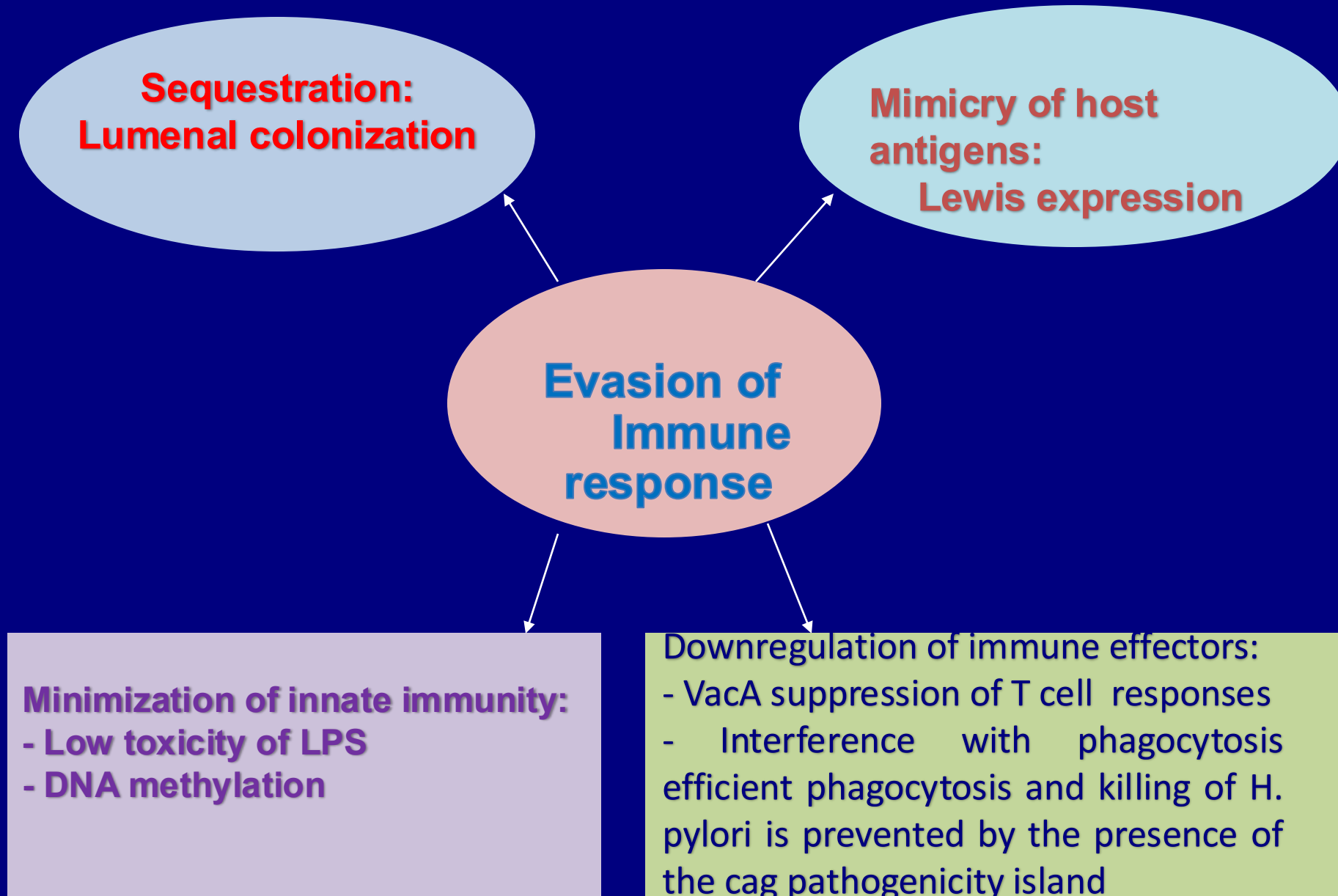
# *H. Pylori* / Pathogenesis

- vacuolating toxin (VacA) and cytotoxin (CagA) > Epithelial cell damage
- The vacuolating toxin has been associated with pore formation in host cell membranes, the loosening of the tight junctions between epithelial cells (thus affecting mucosal barrier permeability causing vacualation)
- Protection from phagocytosis & intracellular killing:
  - Superoxide dismutase
  - Catalase

# Pathology and Pathogenesis



# Pathology and Pathogenesis



## Mimicry of host antigens: Lewis expression

- H. pylori LPS mimics host Lewis antigens, often matching the specific Lewis phenotype of the host's gastric epithelium,
- Role in Adhesion/Colonization: Lewis antigens are essential for H. pylori to attach to human gastric cells, acts as a receptor for the H. pylori BabA adhesion protein. They are more prevalent in the antrum

# Pathology and Pathogenesis

**Most *H. pylori* colonized persons do not develop clinical sequelae due to differences in:**

1. Variability of virulent genes among different strains
2. Host susceptibility to disease
  - ✓ Polymorphisms in cytokines encoding genes
  - ✓ For example, colonized people with polymorphisms in the interleukin (IL) 1 gene that cause the production of large quantities of this cytokine in response to *H. pylori* infection are at increased risk of gastric adenocarcinoma.
3. Environmental factors.
  - Smoking increases the risks of ulcers and cancer in *H. pylori*-positive individuals.
  - Diets high in salt and preserved foods increase cancer Risk
  - Whereas diets high in antioxidants and vitamin C are protective.

# Pathology and Pathogenesis

## Variability of virulent genes among different strains

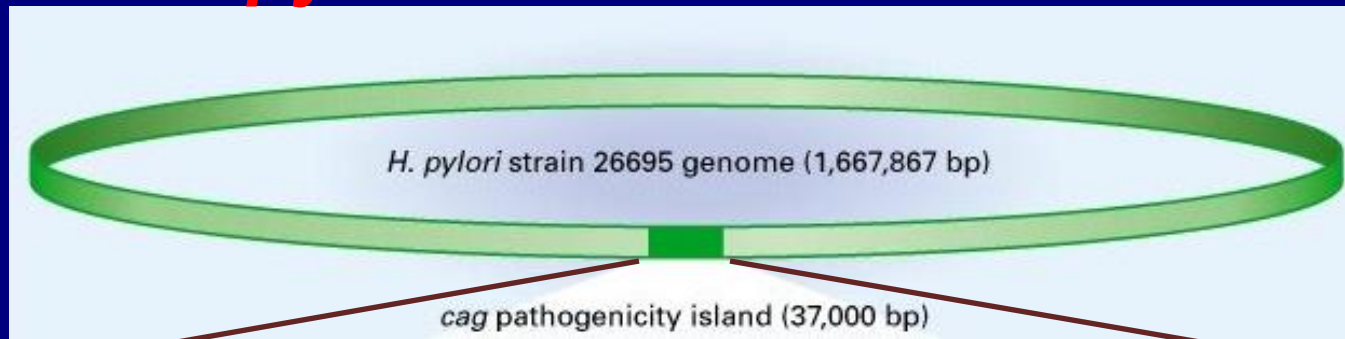
### 1. *cagA* and *cag* Pathogenicity Island (*cag* PAI):

- The *cag* island is a group of genes that encodes a bacterial secretion system through which a specific protein, CagA, is translocated into epithelial cells.
- CagA affects host cell signal transduction, inducing proliferative, cytoskeletal, and inflammatory changes

### 2. *vacA* gene mosaics

# Pathology and Pathogenesis

## Genome of *H. pylori*



The proteins encoded by these genes assemble to form a complex type IV secretion apparatus capable of delivering CagA from the bacterium into host cells

Translocation of CagA into gastric epithelial cells

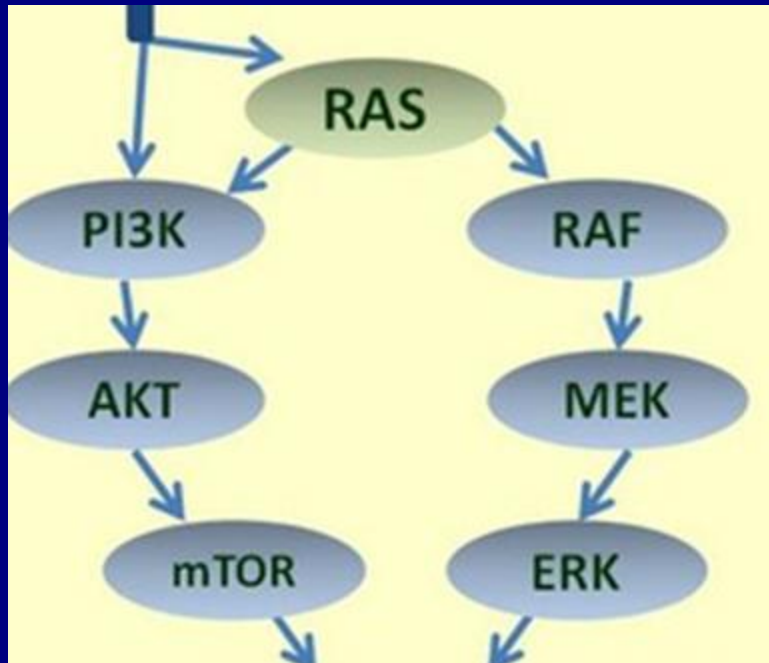
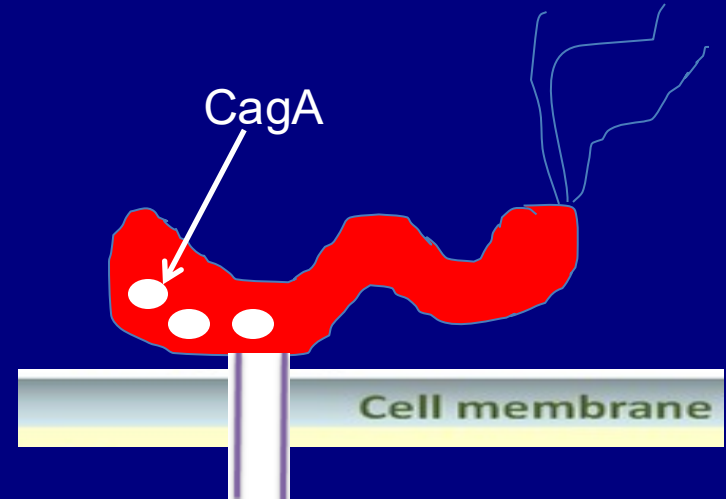
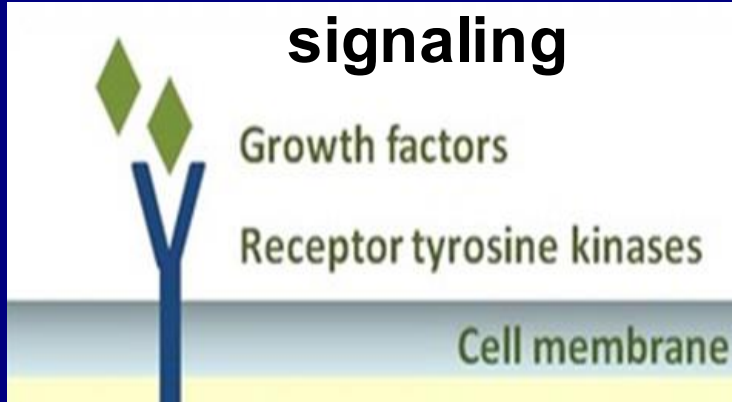
Phosphorylation of CagA by host-cell kinases c-Src and Lyn

Binding to and activation of cellular phosphatase SHP-2

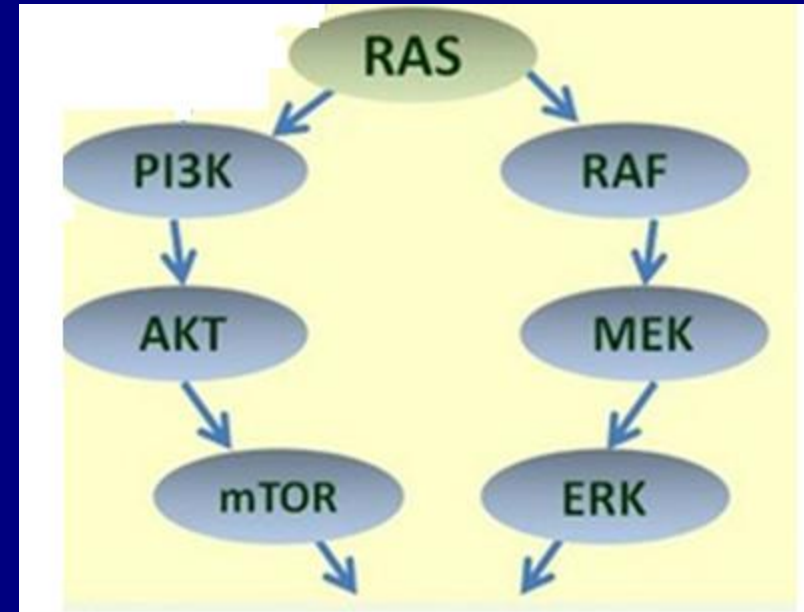
Growth factor-like response in host cell, cytoskeletal rearrangements

# Pathology and Pathogenesis

## Normal vs. CagA induced signaling



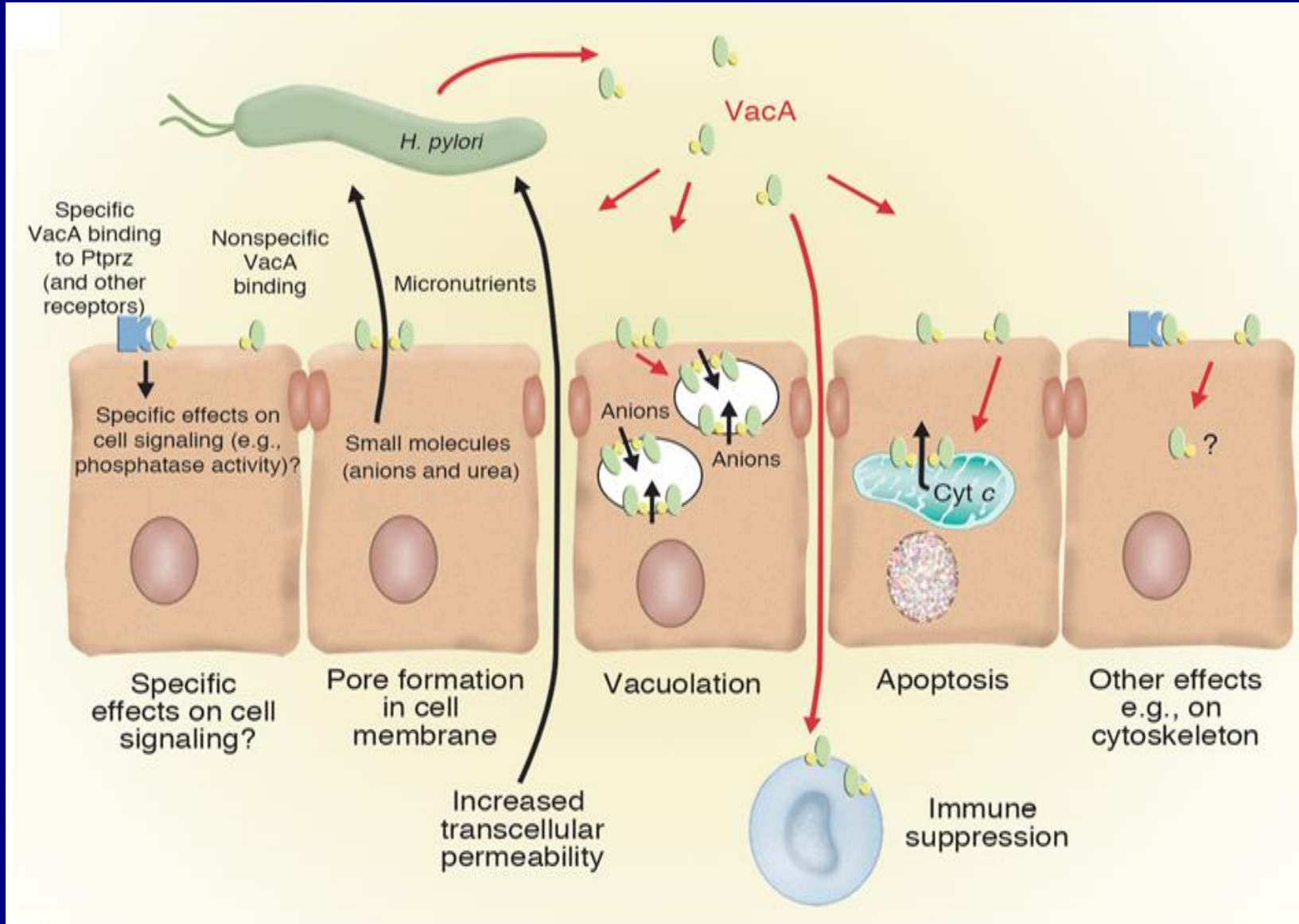
Cell growth and proliferation



Cell growth and proliferation

# Pathology and Pathogenesis

## The effects of VacA protein on the fate of cells

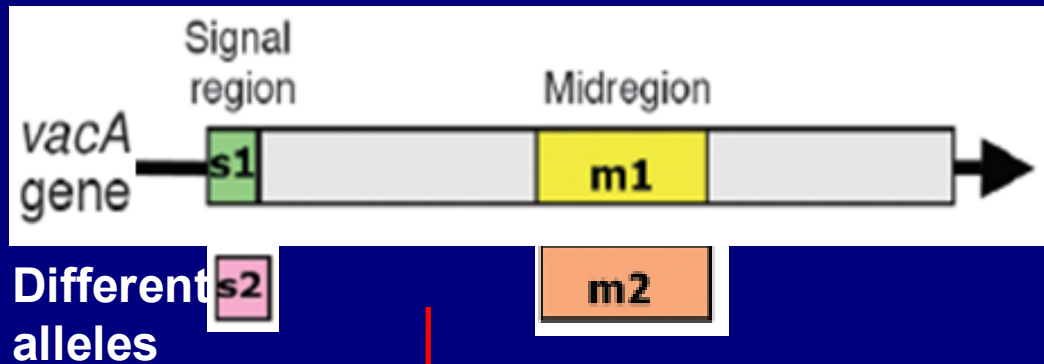


# Pathology and Pathogenesis

Fewer than 15% develop associated illnesses such as peptic ulceration, gastric adenocarcinoma, or gastric lymphoma

**(Why)**

1. Because not all *H. pylori* strains are positive for cagA gene.
2. Because of different alleles of vacA gene.



Possible genotypes:

- s1m1: exhibits the highest toxicity (vaculation)
- s1m2: moderate level of toxicity.
- s2m1: nontoxic
- s2m2: nontoxic

The illnesses caused by *H. pylori* infection are associated with the presence or absence of cagA gene and the presence with different vacA alleles

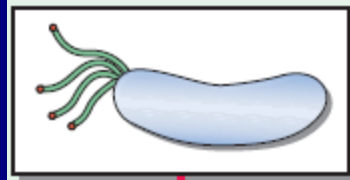
# *H. pylori*/ Clinically

- most infections are symptomless
- Acute infection: type A:
- Symptoms: Burning pain in the upper abdomen, nausea, vomiting, and frequent burping.
- Duration: Acute symptoms can last for less than one week, but may persist for up to 14 days.
- Diagnosis: Often diagnosed via urea breath tests, stool tests, or endoscopy.
- Treatment: A combination of at least two antibiotics (e.g., amoxicillin, clarithromycin, metronidazole) and acid-suppressing drugs (proton pump inhibitors or bismuth subsalicylate) is required for 14 days

# *H. pylori*/ Clinically

- chronic active gastritis; Type B.
- Peptic ulcer: Gastric (70%) and duodenal ulcers (more than 90%).
  - N.b: less than 20% of infected people will have peptic ulcers
  - GIT Haemorrhage, perforation, pyloric stenosis as complications
  - Other causes of ulcers: NSAIDS, Stress ulcers, chemotherapy...
- non-ulcer dyspepsia
- gastric malignancies.

# Pathology and Pathogenesis



Primary phenomenon:

Tissue response (inflammation)

Secondary phenomenon:

Hyperacidity

Antigenic stimulation

Atrophic gastritis

Clinical outcome:

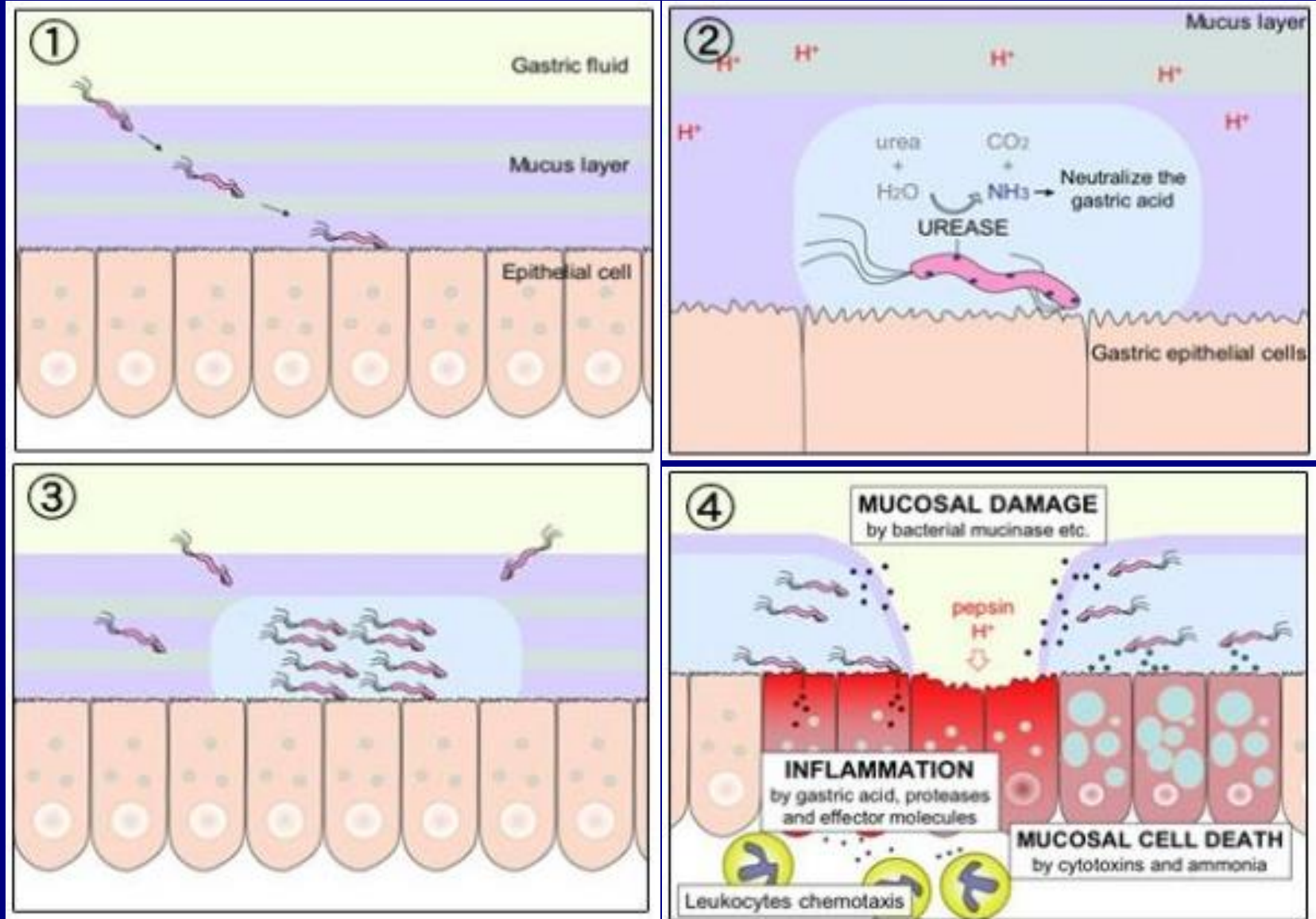
Duodenal ulceration

B-cell lymphoma

Noncardia gastric adenocarcinoma

Reflux esophagitis and sequelae

# Pathology and Pathogenesis



# Acidity during infection

- At the beginning; Antral-Predominant Infection: When inflammation is confined mostly to the antrum, it destroys somatostatin-producing D-cells. Since somatostatin usually inhibits acid, its loss leads to hypergastrinemia (excessive gastrin), which drives acid hypersecretion by parietal cells. This type of infection is strongly associated with duodenal ulcers.
- Later: Impact on Parietal Glands (Corpus/Body), If the inflammation extends from the antrum to the corpus (body) of the stomach, where the acid-producing parietal glands are concentrated, the effect on acid changes from high to low

# *H. Pylori* / Diagnosis

Definitive tests for *H. pylori* infection depend on finding the Organism in specimens of gastric mucosa obtained by biopsy. (In practice, non-invasive tests are used for initial screening).

## Non-invasive tests:

1. Urea breath test
2. Faecal antigen
3. PCR
4. Serology

# *H. Pylori* / Diagnosis

## 1. Urea breath test

- Detects bacterial urease activity in the stomach by measuring the output of carbon dioxide resulting from the splitting of urea into carbon dioxide and ammonia
- A capsule of urea labelled with carbon-14 or (13) is fed to the patient, and the emission of the isotope in carbon dioxide subsequently exhaled in the breath is measured
- Carbon-14 is radio-active so it is not used in children

# *H. Pylori* / Diagnosis

## Urease breath test cont'd:

The breath test is expensive but is becoming increasingly more available.

Other problems include false-negative results due to infection with coccoid forms of *H pylori* that do not produce as much urease or intake of antibiotics, bismuth, histamine 2 (H2) blockers, or proton pump inhibitors.

# *H. Pylori* / Diagnosis

## 2. Faecal antigen test :

Tests based on the use of monoclonal antibodies are more accurate than polyclonal antibody tests and have the potential to supplant serology for routine screening

## 3. Polymerase chain reaction (PCR):

- DNA probes for the direct detection of *H. pylori* in gastric juice, faeces, dental plaque and water supplies have been developed
- Some can also detect genes expressing antibiotic resistance and presence of the *cagA* pathogenicity island

## 4. Serology:

- mostly based on ELISA or latex agglutination
- detect IgG antibodies to *H. pylori*
- Indicates previous exposure
- Not good for follow up or as a test of cure

# *H. Pylori* / Diagnosis

## 2. Invasive tests (endoscopy guided biopsies):

- Ideally, patients for endoscopy should not have received antibiotics or proton pump inhibitors for 1 month before the test.
  - Mucosal biopsy specimens are taken from the gastric antrum within 5 cm of the pylorus, and preferably also from the body of the stomach
  - For maximum sensitivity, duplicate specimens are taken: one for histopathology , the other for culture
- > Specimens for culture must be processed as soon as possible, certainly on the same day, or placed in transport medium.

# *H. Pylori* / Diagnosis

## 1. Biopsy urease test :

This is a simple and cheap test that can be performed at the bedside.

A biopsy specimen is placed into a small quantity of urea solution with an indicator that detects alkalinity resulting from the formation of ammonia.

Most infected patients (70%) give a positive result within 2 h; 90% after 24 h

# *H. Pylori* / Diagnosis

## 2. Histopathology and microscopy :

Histopathology provides a permanent record of the nature and grading of a patient's gastritis as well as detecting *H. pylori*.

Organisms can be seen in sections stained with haematoxylin and Eosin stain

The bacteria can also be seen in smears of biopsy material stained with Gram's stain

# *H. Pylori* / Diagnosis

## 3. Culture

- Is no more sensitive than skilled microscopy of histological sections,
- but has several advantages:
  - > isolates can be tested for antimicrobial resistance and typed for epidemiological studies;
  - > information about the presence of virulence factors can inform clinical outcome
- Plates are left undisturbed for 3 days and incubated for a week before being discarded as negative

# Treatment

Life style:Wash your hands

Ttriple therapies:

- Have reported cure rates from 85-90%.
- Administered for 10-14 days.
- The treatment regimens are (use one of them):
  1. Omeprazole, amoxicillin, and clarithromycin (OAC) for 10 days;
  2. Bismuth subsalicylate, metronidazole, and tetracycline (BMT) for 14 days;
  3. Lansoprazole, amoxicillin, and clarithromycin (LAC), which has been approved for either 10 days or 14 days of treatment.

# Diagnosis

Diagnosis of suspected gastric carcinoma, this includes:

- Physical exam
- Blood tests to check for anemia, when your body doesn't have enough red blood cells. It could happen if you have a tumor that bleeds.
- Fecal occult blood test, which checks your stool for blood that's not visible to the naked eye
- Endoscopy
- Biopsy, when a doctor takes a small piece of tissue from your stomach to look for signs of cancer. Your doctor may do this during an endoscopy.
- Tests that make detailed pictures of the insides of your body, such as a CT scan or magnetic resonance imaging (MRI)

# Prevention

- Wash your hands after you use the bathroom and before you prepare or eat food. Teach your children to do the same.
- Avoid food or water that's not clean.
- Don't eat anything that isn't cooked thoroughly.
- Avoid food served by people who haven't washed their hands.
- Avoid food served by people who haven't washed their hands.

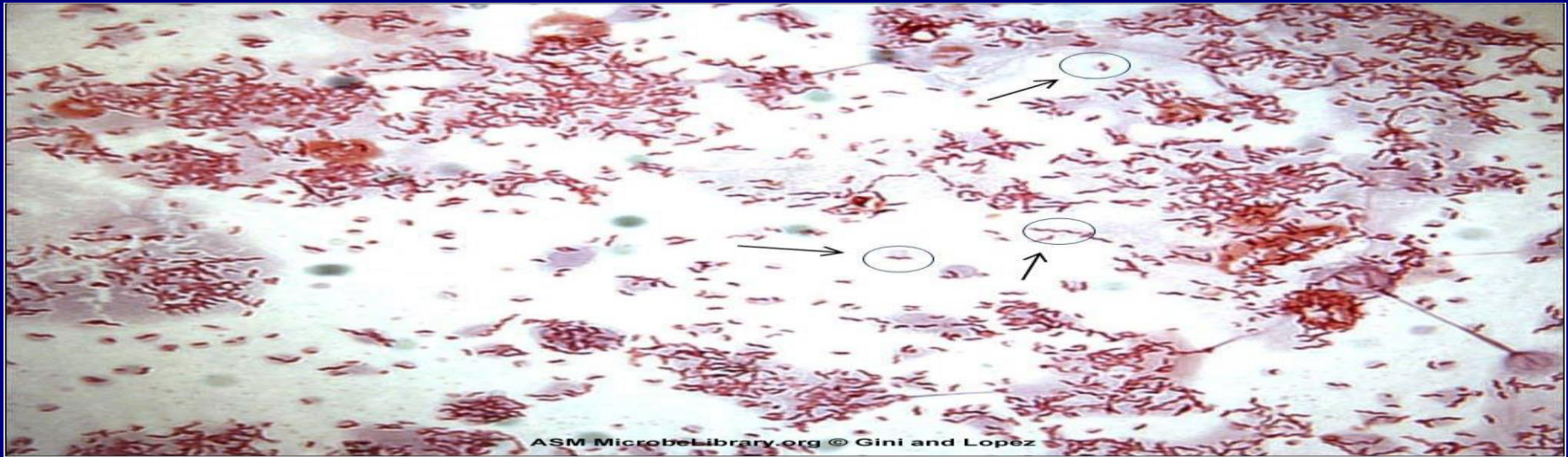
# Prevention

- Though stress, spicy foods, alcohol, and smoking make your pain worse.
- **What can I expect after *H. pylori* infection?**
- Most ulcers caused by *H. pylori* will heal after a few weeks of treatment. If you've had one, you should avoid taking NSAIDs for pain, since these drugs can damage your stomach lining. If you need pain medicine, ask your doctor to recommend some.

# Campylobacter

- The main human pathogenic is *campylobacter jejuni* (*C. jejuni*)
- Other species occasionally found in human gastrointestinal disease include *C. coli* and *C. fetus*
- **Habitat:**
  - Guts of various animal species such as chickens, domestic animals and **seagulls**
- **Pathogenesis:**
  - Enterocolitis, may penetrate beyond the mucosa

## Laboratory:



- Small gram negative, curved or spiral rods (Figure/seagull appearance)
- Highly motile (darting,), with a flagellum at one or both ends
- Microaerophilic (5% O<sub>2</sub>, 10-15% CO<sub>2</sub>, 80% Nitrogen)
- Growth at 42°C for 2 days (25°C no growth, 37°C some growth, 42°C enhanced growth).
- Needs a special media (Skirrow's)

# Campylobacter

- **Clinically:**

- Incubation period: 1-10 days

- Route of transmission:

Eating contaminated poultry, other meat or drinking milk

Faecal –oral between humans can occur

- Symptoms vary from asymptomatic to severe

- With or without prodromal phase (flu-like)

# Campylobacter / clinically

- Bloody diarrhoea with mucus (up to 20 stools a day > faecal incontinence)
- Abdominal pain is a prominent feature (mimicking appendicitis)
- Septicaemia with fever and rigors in severe cases
- Symptoms may last several days and relapses are common (usually self limiting)
- Guillain-Barre syndrome as a complication.

# Campylobacter

- Diagnosis
- Hx & Ex
- Stool sample for culture on Skirrow's medium
  
- Treatment:
- Erythromycin in severe cases.
- Ciprofloxacin as an alternative but resistance is increasing
  
- Control:
- Properly cooked food and personal hygiene
- Animals control: as usually harboured asymptotically

The End