Helicobacter Pylori and gastroduodenal disease

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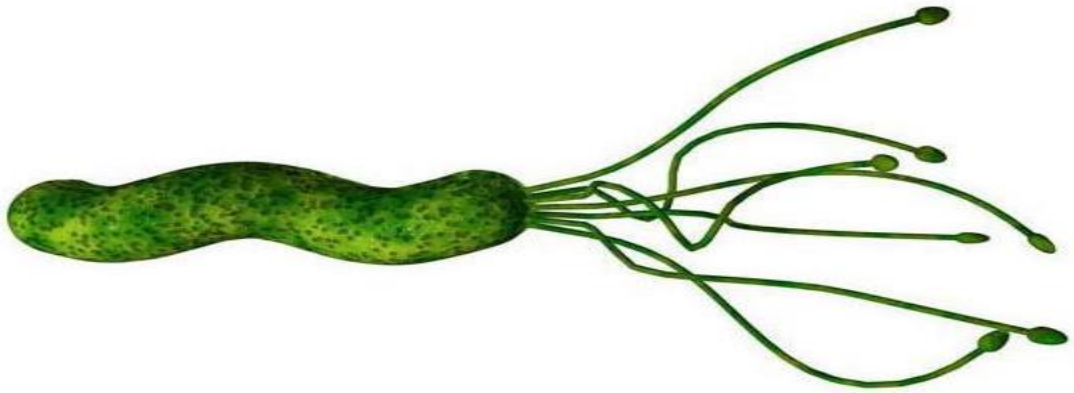
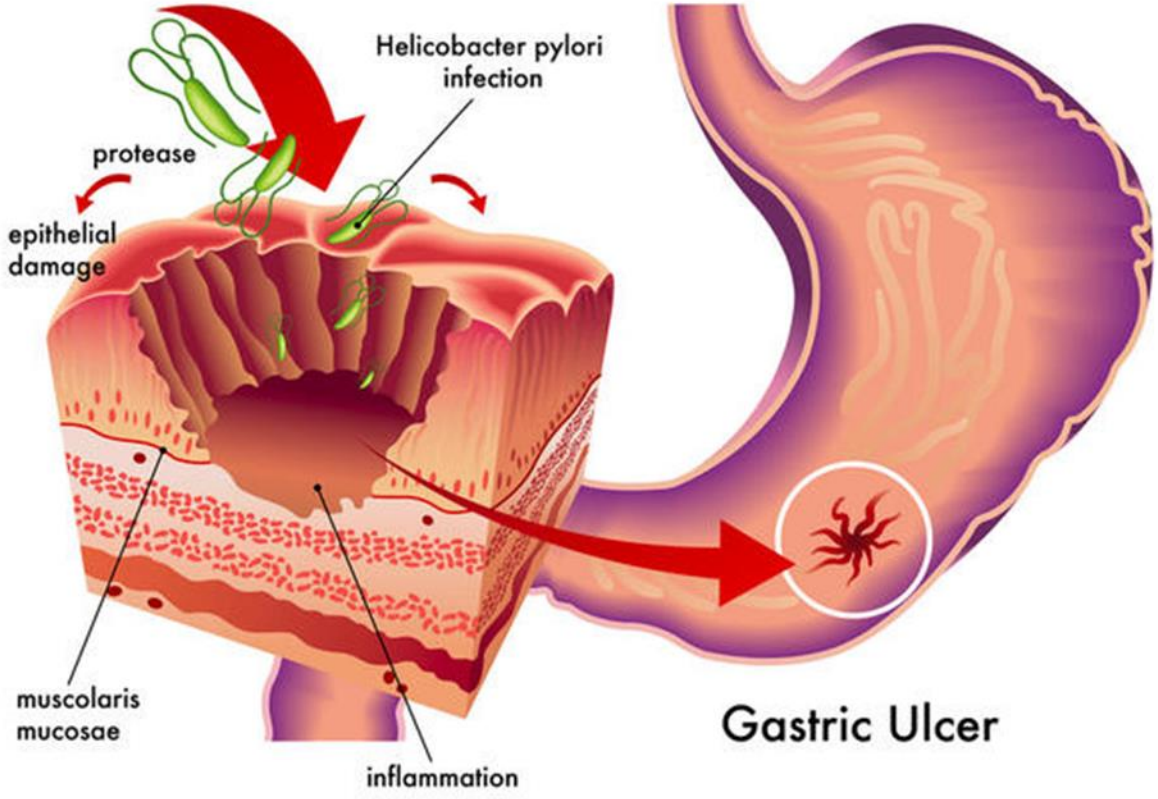
GIT Module




Helicobacter pylori
infection
protease
epithelial
damage
muscolaris
mucosae
inflammation
Gastric Ulcer

Contents/Aims of Lecture

- History
- Introduction
- Microbiology
- Epidemiology and Transmission
- Pathogenesis
- Clinical Outcomes of Infection
- Diagnosis
- Treatment Options
- Future

Objectives

To have a clear understanding of disease caused by *Helicobacter pylori* in terms of the above headings

History

The discovery of Helicobacter pylori is one of the greatest achievements in the modern history of gastroenterology.

In 1982, Australian physicians Robin Warren and Barry Marshall first cultured of a spiral-shaped bacterium from gastric biopsies of patients with gastritis.

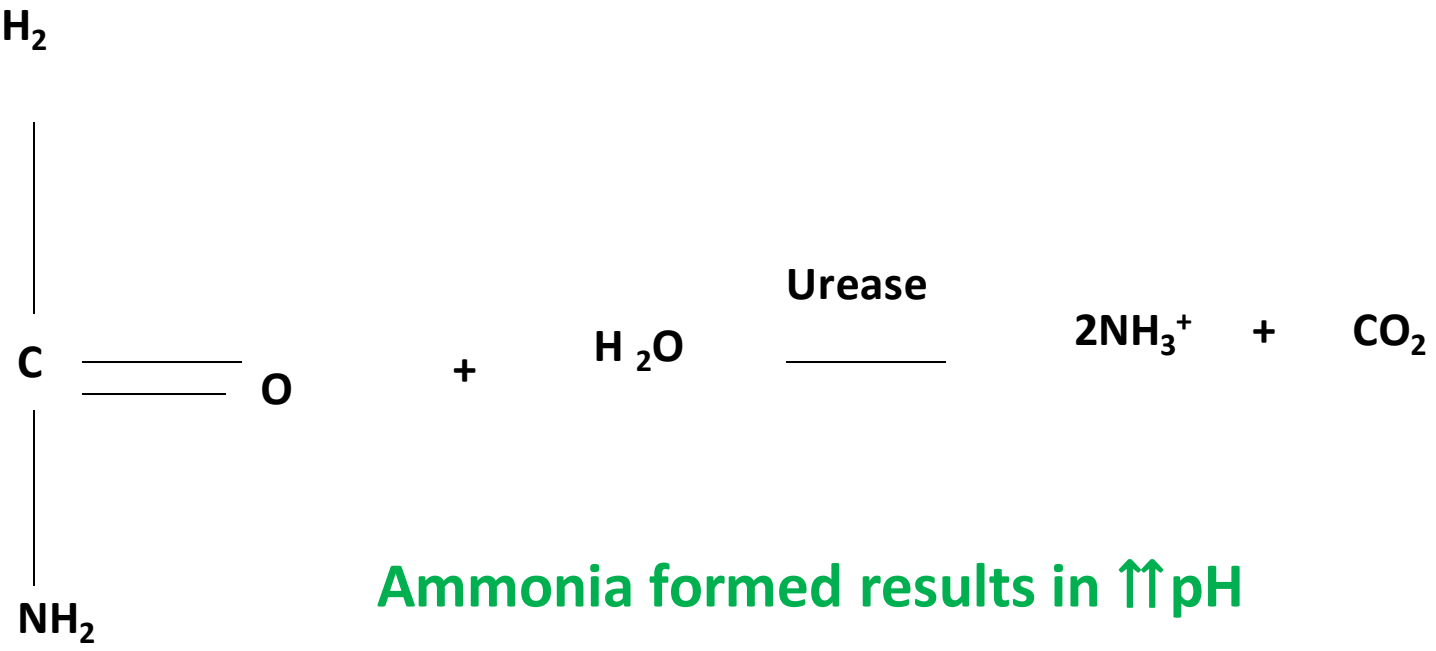
They concluded that the bacterium, not stress or diet, causes ulcers.

Barry Marshall

Robin Warren

H.pylori -Microbiology

- Small curved microaerophilic gram-negative rods 2-4ų 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.

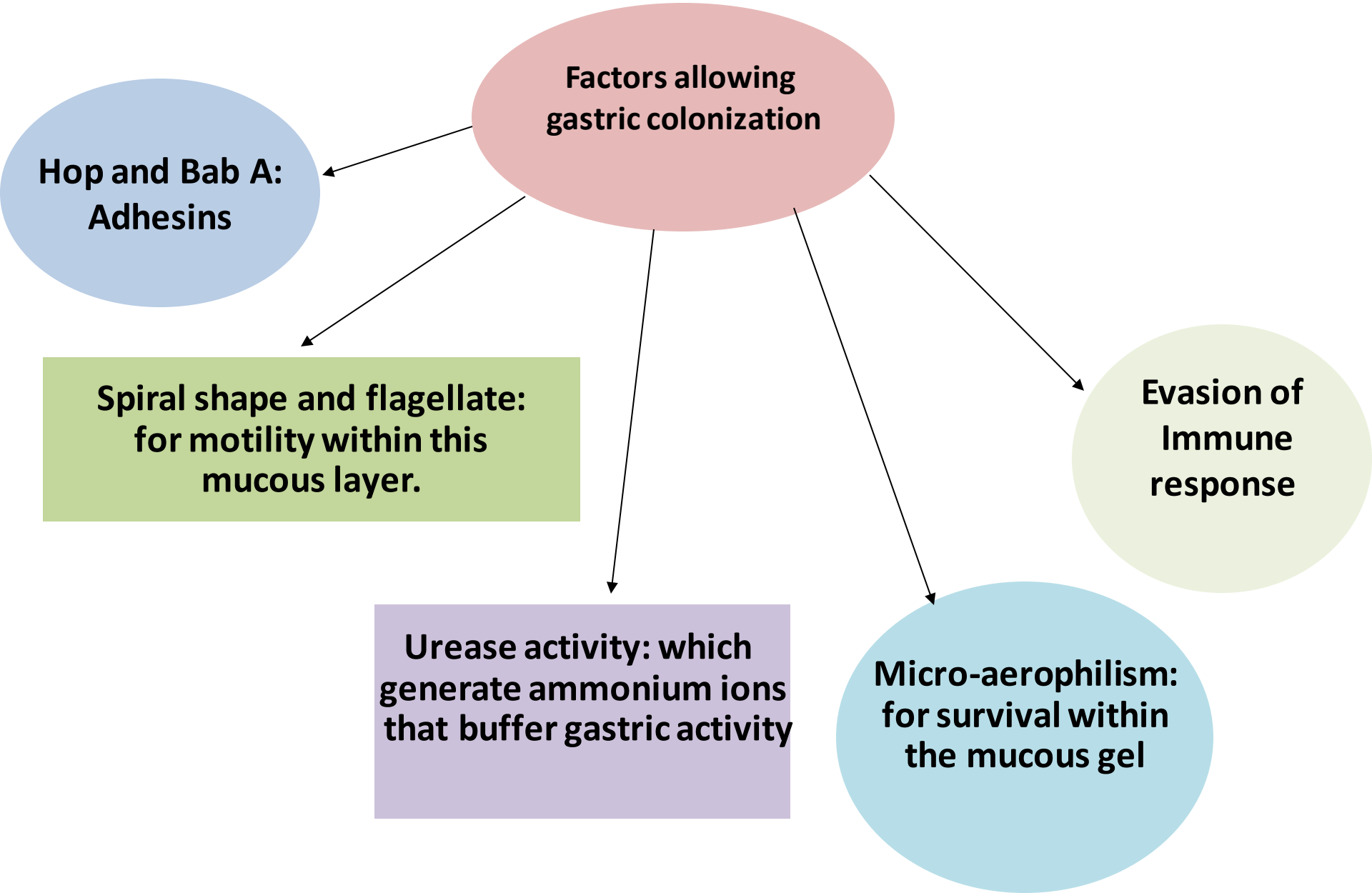


Ammonia formed results in ⇑⇑pH

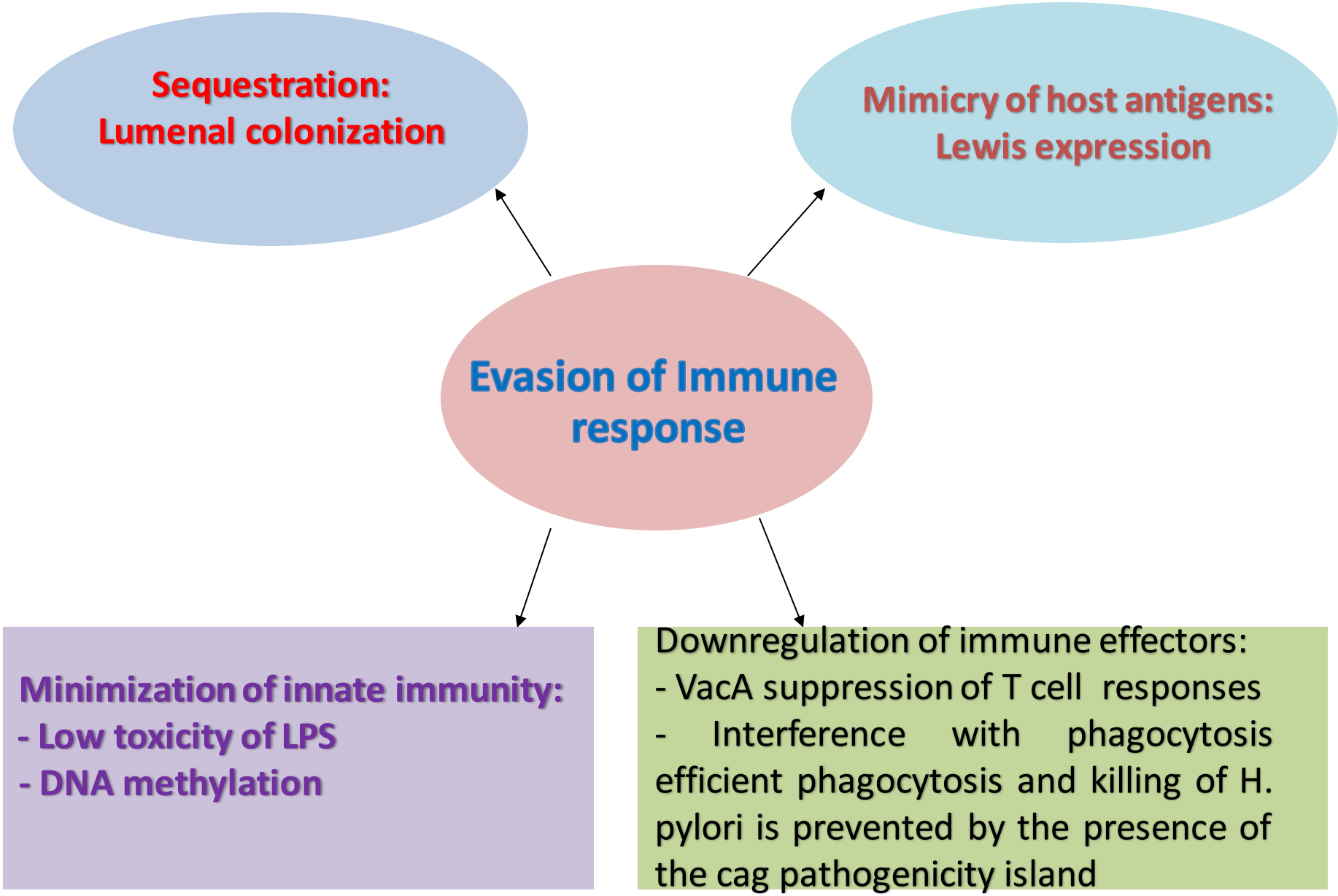
Epidemiology and Transmission

- Infection occurs worldwide
- Humans are the only important reservoir of H. pylori.
- Prevalence will depend on the country and population groups
- Children may acquire the organism from their parents (more often from the mother) or from other children.
- Tranmission by fecal-oral or oral-oral
- H. pylori is easily cultured from vomitus and gastroesophageal refluxate and is less easily cultured from stool.
- Overall *prevalence* strongly correlates with socio-economic conditions
- In Middle aged adults in developing countries prevalence is 80%, in industralised countries 20-50%.

Pathology and Pathogenesis



Pathology and Pathogenesis



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

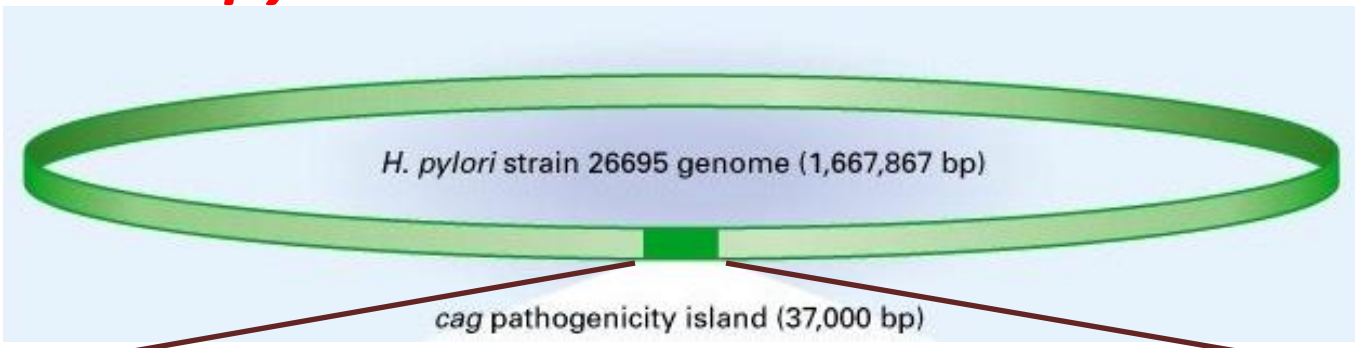
1. cagA and cag Pathogenicity Island (cag PAI):

- 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

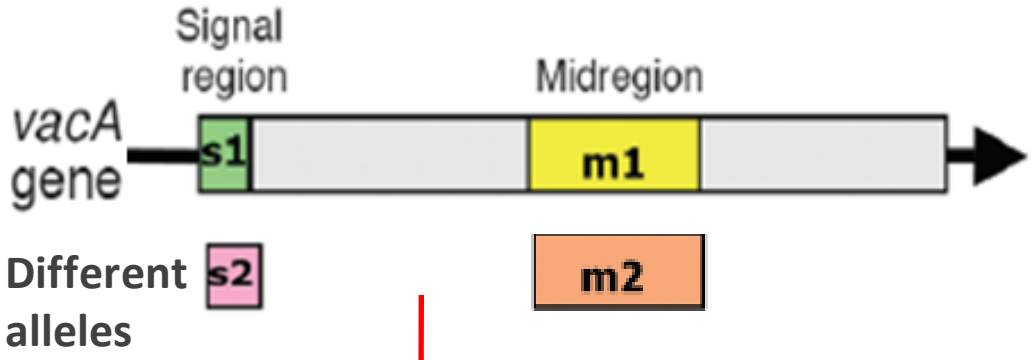
Growth factor–like response in host cell, cytoskeletal rearrangements

Pathology and Pathogenesis

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.

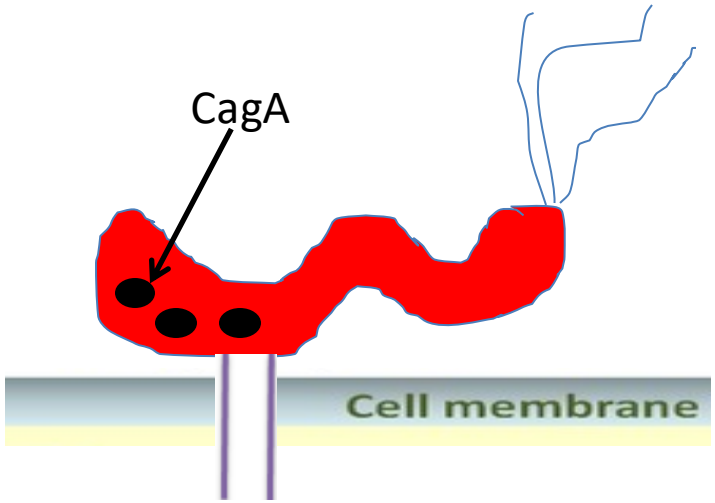


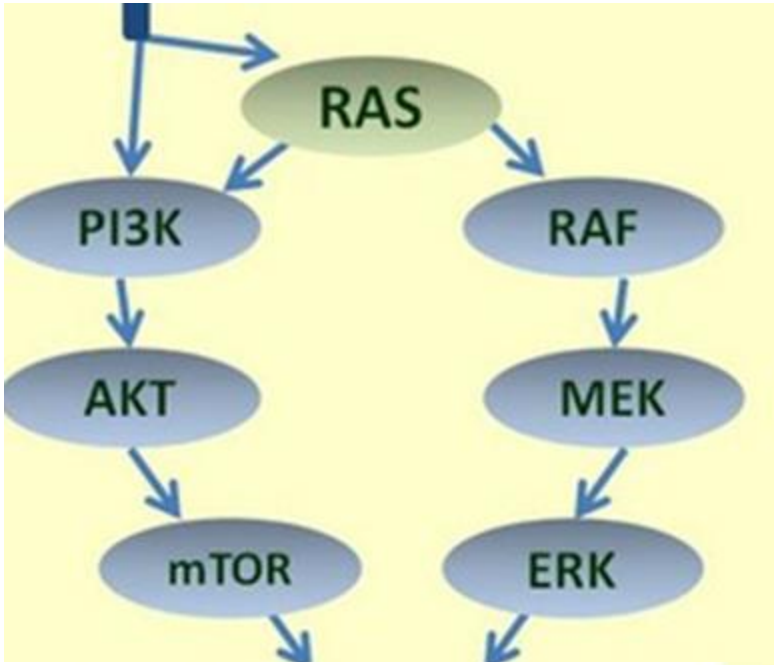
Possible genotypes:
- s1m1: exhibits the highest toxocity (vaculation)
- s1m2: moderate level of toxicity.
- s2m1: nontoxic
- s2m2: nontoxic

The illnesses caused by *H. pylori* inection are associted with the presence or absence of caga gene and the presence with different vaca alleles

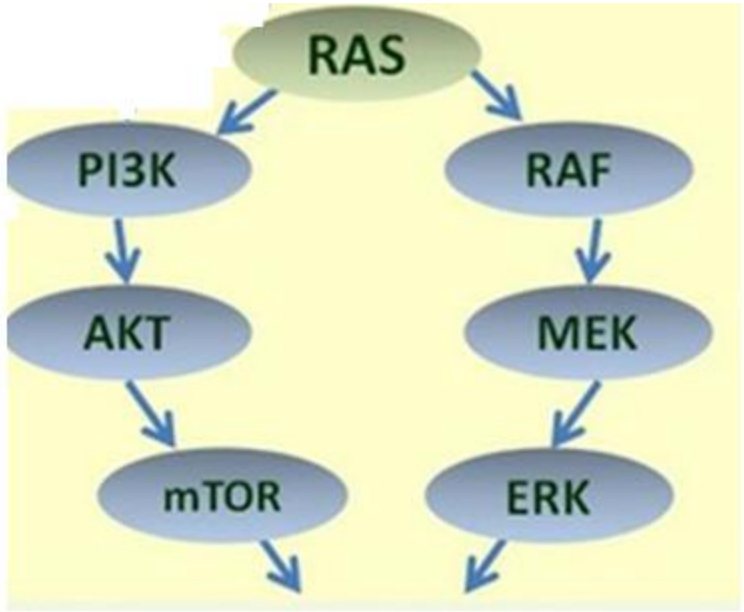
Pathology and Pathogenesis

Normal vs. CagA induced signaling



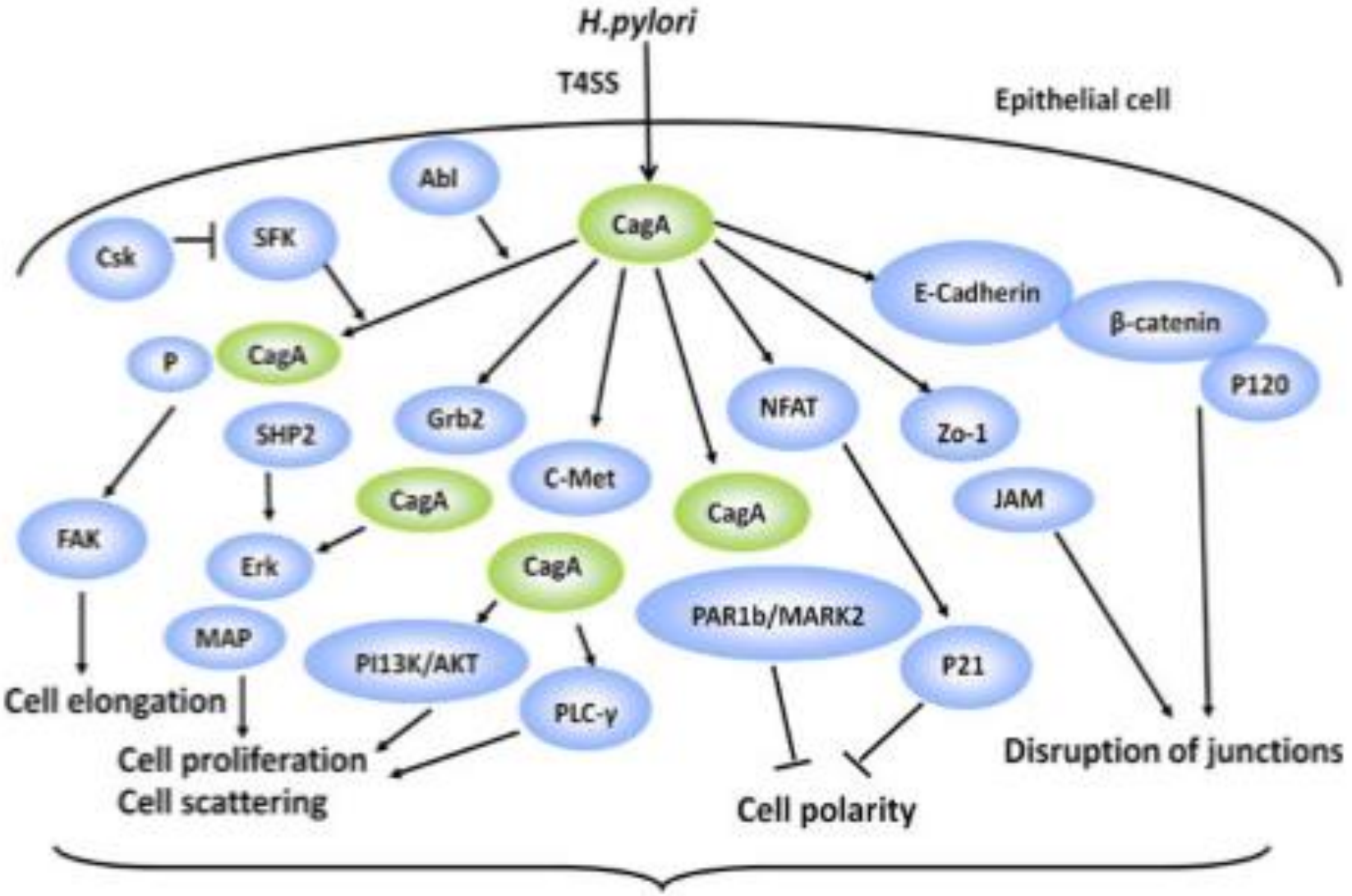


Cell growth and proliferation



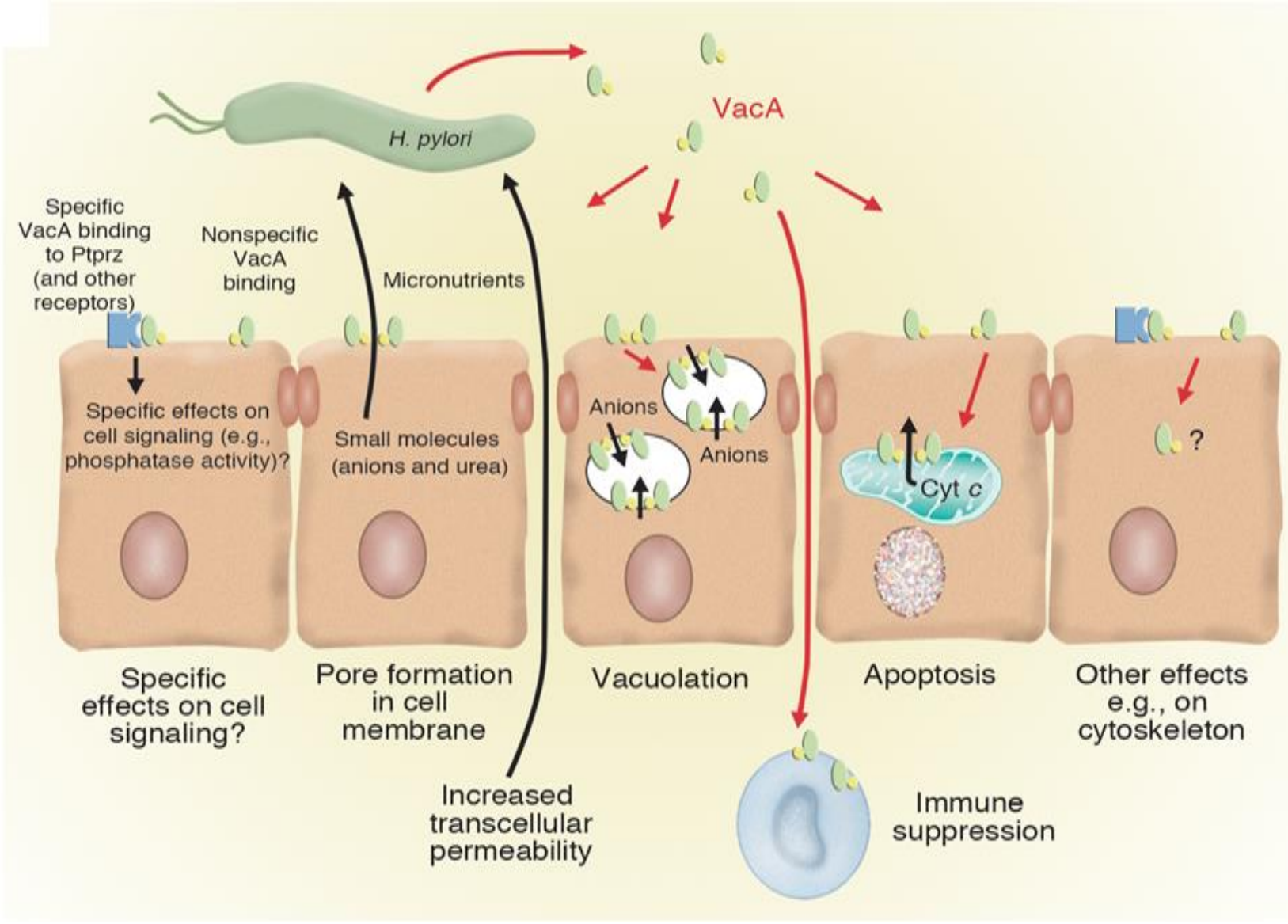
Cell growth and proliferation

Pathology and Pathogenesis

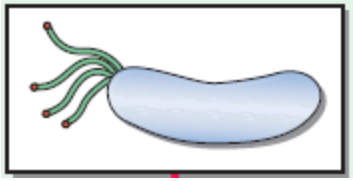


Pathology and Pathogenesis

The effects of VacA protein on the fate of cells



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

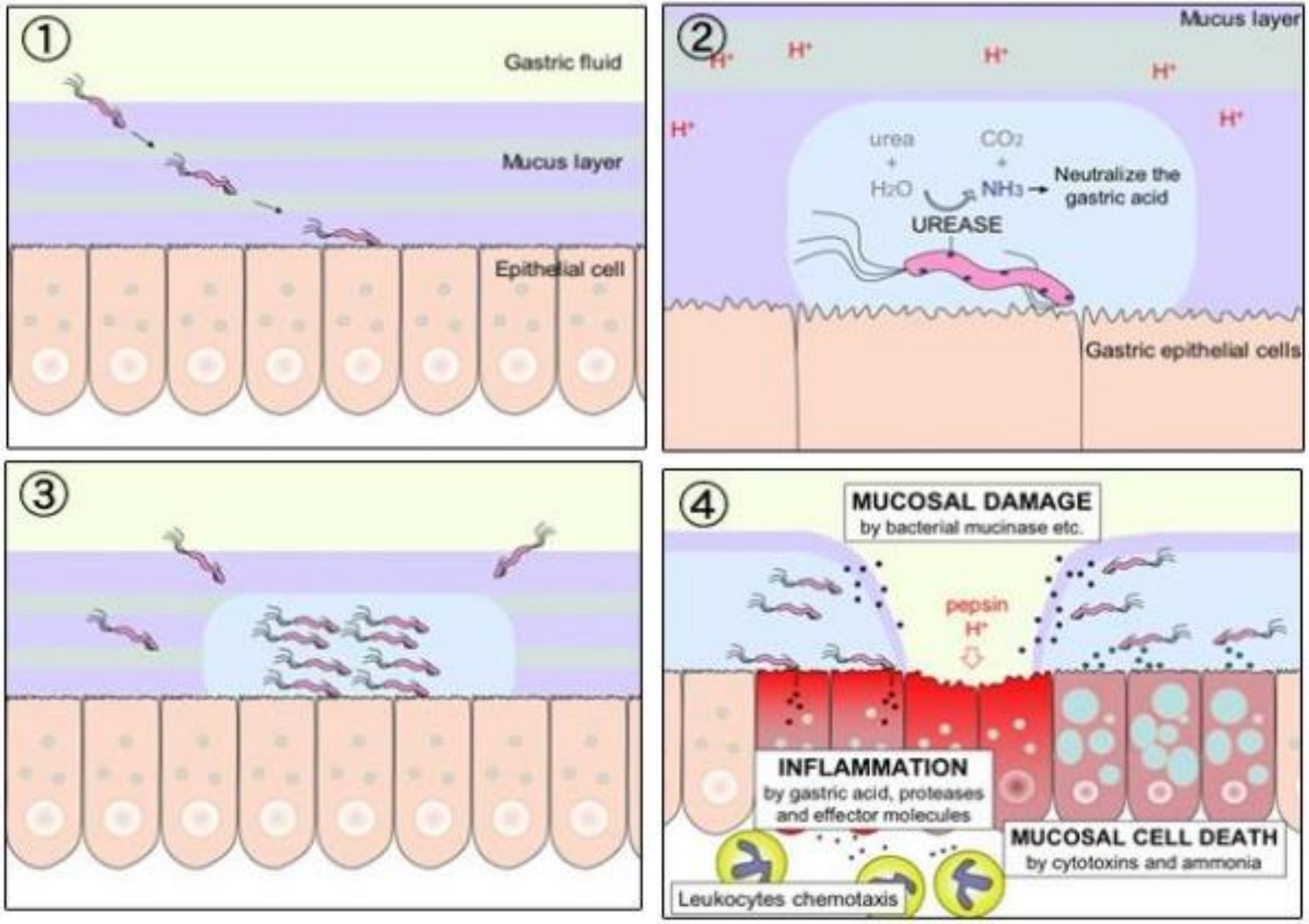
Pathology and Pathogenesis

Host responses to H. pylori and their role in disease:

Despite the mechanisms H. pylori has evolved to avoid and downregulate host immune responses, substantial immune activation occurs following H. pylori infection. This is manifested by continuous epithelial cell cytokine signaling and gastric mucosal infiltration by neutrophils, macrophages, and lymphocytes, all of which are more pronounced in colonization with a cag+ strain

IL-4 has not been detected in the gastric mucosa of most *H. pylori*-infected individualsTherefore, it has been concluded that *H. pylori* infection leads to a T helper cell (Th)1-polarized response

Pathology and Pathogenesis



H. pylori/ Clinically

- chronic active gastritis;.

- Gastric (70%) and duodenal ulcers (more than 90%).
  - N.b: less than 20% of infected people will have peptic ulcers
  - UGIT Haemorrhage, perforation, pyloric stenosis as complications
  - Other causes of ulcers: NSAIDS, Stress ulcers, chemotherapy...

- non-ulcer dyspepsia

- gastric malignancies.

Clinical Manifestations

Symptoms

- Most people with H. pylori infection will never have any signs or symptoms.
- When signs or symptoms do occur with H. pylori infection, they may include:
  - An ache or burning pain in your abdomen –peptic ulcer

  Abdominal pain that's worse when your stomach is empty
  - Nausea
  - Loss of appetite
  - Frequent burping
  - Bloating
  - Unintentional weight loss
  - Blood in stools

Clinical Manifestations

Symptoms associated with gastric carcinoma

It's not common, but *H. pylori* infection can cause stomach cancer. The disease has few symptoms at first, such as heartburn. Over time, you may notice:

- Belly pain or swelling
- Nausea
- Not feeling hungry
- Feeling full after you eat just a small amount
- Vomiting
- Weight loss for no reason

Clinical Manifestations

When to see a doctor

Make an appointment with your doctor if you notice any persistent signs and symptoms that worry you. Seek immediate medical help if you experience:

- Severe or persistent abdominal pain
- Difficulty swallowing
- Bloody or black tarry stools
- Bloody or black vomit or vomit that looks like coffee grounds

Diagnosis

Divided into two groups:

1. **Invasive tests:**

   Require upper gastrointestinal endoscopy and are based on the analysis of gastric biopsy specimens

1. **Noninvasive tests**

   - Breath test
   - Stool test

Diagnosis

Invasive tests (endoscopy)

- Endoscopy often is not performed in the initial management of young dyspeptic patients without “alarm” symptoms but is commonly used to exclude malignancy in older patients. If endoscopy is performed, the most convenient biopsy-based test is the biopsy urease test, in which one large or two small antral biopsy specimens are placed into a gel containing urea and an indicator. The presence of H. pylori urease leads to a pH alteration and therefore to a color change, which often occurs within minutes but can require up to 24 h.
- Histologic examination of biopsy specimens for H. pylori also is accurate, provided that a special stain (e.g., a modified Giemsa or silver stain) permitting optimal visualization of the organism is used.

Diagnosis

Noninvasive tests

Urea breath test.

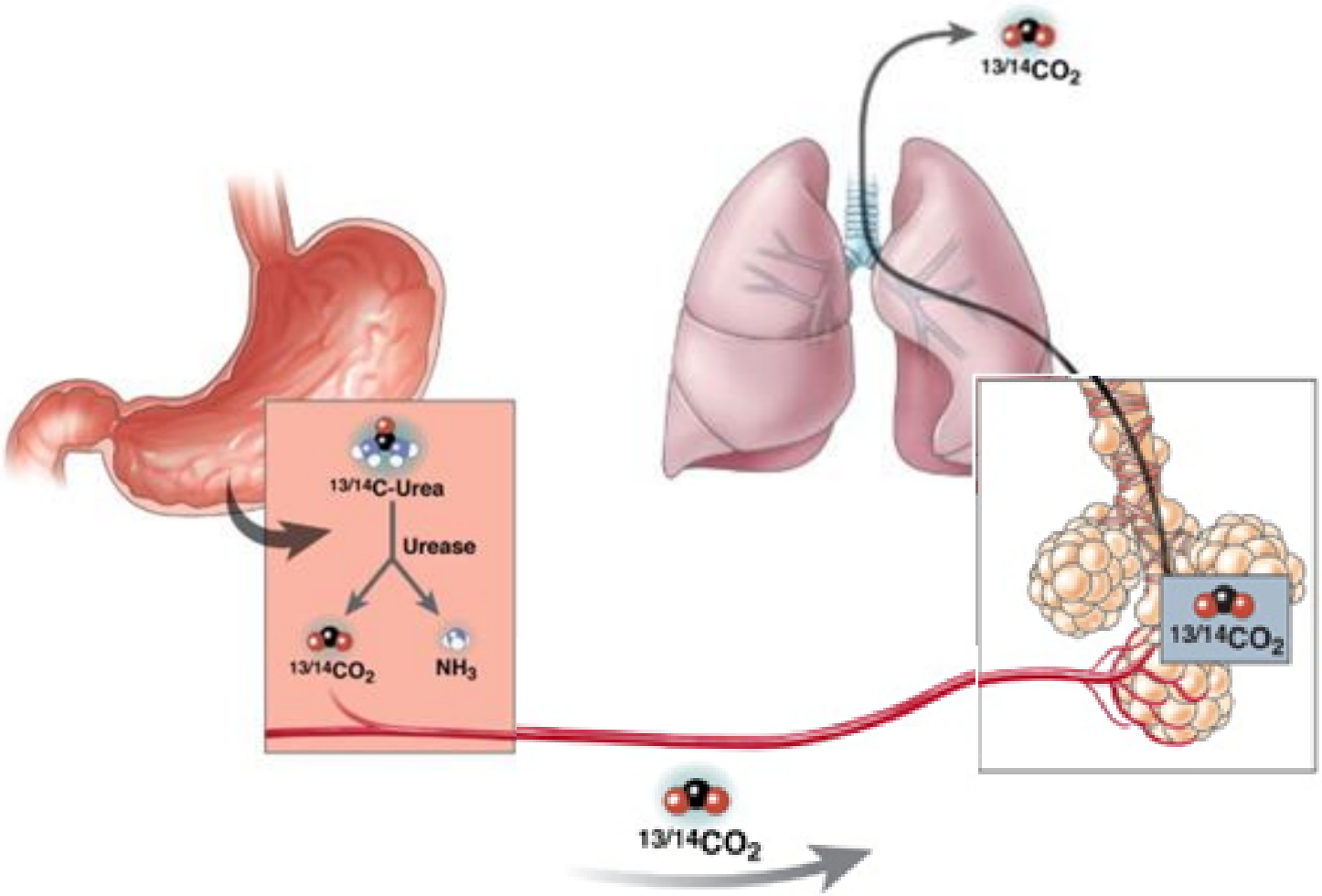
How is this breath test done?

- For the test, patients swallow a capsule containing urea made from an isotope of carbon. Isotopes of carbon can be measured with special testing machines.
- If *H. pylori* is present in the stomach, the urea is broken up and turned into carbon dioxide. The carbon dioxide is absorbed across the lining of the stomach and into the blood. It then travels in the blood to the lungs where it is excreted in the breath.
- Samples of exhaled breath are collected, and the isotopic carbon in the exhaled carbon dioxide is measured.

Diagnosis

Noninvasive tests

Urea breath test.



Diagnosis

How are the results of the urea breath test interpreted?

- If the isotope is detected in the breath, it means that *H. pylori* is present in the stomach. If the isotope is not found, *H. pylori* is not present. When the *H. pylori* is effectively treated (eradicated) by antibiotics, the test changes from positive (isotope present) to negative (isotope absent).

Are there any risks or complications of the urea breath test?

- There are no risks or complications of the urea breath test. There is no need to stop any medications (including proton pump inhibitors) prior to performing the urea breath test.

Diagnosis

Stool test.

A laboratory test called a stool antigen test looks for foreign proteins (antigens) associated with H. pylori infection in your stool.

Diagnosis

Diagnosis of suspected gastric carcinomea, 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)

H.pylori -Microbiology

- **Selective medium required for isolation-10% sheep blood agar + selective antibiotic supplement**
- **Incubated at 80-85% N_2, 5-10% CO_2, 5-10% H_2O at 37ºC**
- **Identified by urease, oxidase, catalase**

Antibody (IgG) detection

Antibodies to *H. pylori* can be detected in the patients serum by ELISA test.

The serum antibodies persist even if the *H pylori* infection is eradicated, and the role of antibody tests in diagnosing active infection or after therapy is therefore limited.

Polymerase chain reaction (PCR)

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 don't cause ulcers, they can keep them from healing quickly or make your pain worse. Talk to your doctor about ways to manage your stress, improve your diet, and, if you smoke, how you can get help to quit.

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.

Treatment

1st line triple drug therapy
Omeprazole + Clarithromycin + Metronidazole or Amoxicillin
given for 7 -14 dayes

↓

Urea breath test is done
If the 1st line regimen fails (Urea breath test +ve)

↓

2nd line quadruple drug therapy
Omeprazole + Bismuth subsalicylate + Metronidazole + Tetracycline
Given for 14 dayes

↓

If 2nd line quadruple drug therapy fails then –
Culture of endoscopic guided biopsy is done and treatment is
Given based on antimicrobial susceptibility test

Thank you