Helicobacter

Objectives of *Helicobacter*

Helicobacter pylori

Morphology and Identification

- Pathogenesis

Pathogenesis

- Pathology

- Clinical Findings

-Diagnostic Laboratory Tests

- Treatment

Helicobacter pylori

- *H pylori* is a spiral-shaped, gram-negative rod.
- *H pylori* is associated with gastritis, duodenal (peptic) ulcer disease, gastric ulcers, gastric adenocarcinoma, and gastric mucosa-associated lymphoid tissue (MALT) lymphomas.

Morphology and Identification

Typical Organisms

H pylori has many characteristics in common with campylobacters. It has multiple flagella at one pole and is actively motile.

Culture

- Culture sensitivity can be limited by prior therapy, contamination with other mucosal bacteria, and other factors.
- *H pylori* grows in 3–6 days when incubated at 37°C in a microaerophilic environment, as for *C jejuni*.
- The media for primary isolation include Skirrow's medium with vancomycin, polymyxin B, and trimethoprim, chocolate medium, and other

selective media with antibiotics (eg, vancomycin, nalidixic acid, amphotericin).

- The colonies are translucent and 1–2 mm in diameter.

Growth Characteristics

- *H pylori* is oxidase positive and
- catalase positive,
- is motile,
- and is a strong producer of urease.

Pathogenesis and Pathology

- *H pylori* grows optimally at a pH of 6.0–7.0 and would be killed or not grow at the pH within the gastric lumen.
- Gastric mucus is relatively impermeable to acid and has a strong buffering capacity.
- On the lumen side of the mucus, the pH is low (1.0–2.0); on the epithelial side, the pH is about 7.4. *H pylori* is found deep in the mucous layer near the epithelial surface where physiologic pH is present.
- *H pylori* also produces a protease that modifies the gastric mucus and further reduces the ability of acid to diffuse through the mucus.
- *H pylori* produces potent urease activity, which yields production of ammonia and further buffering of acid.
- *H pylori* is quite motile, even in mucus, and is able to find its way to the epithelial surface.
- *H pylori* overlies gastric-type but not intestinal-type epithelial cells. In human volunteers, ingestion of *H pylori* resulted in development of gastritis and hypochlorhydria. There is a strong association between the presence of *H pylori* infection and duodenal ulceration. Antimicrobial therapy results in clearing of *H pylori* and improvement of gastritis and duodenal ulcer disease.

- The mechanisms by which *H pylori* causes mucosal inflammation and damage are not well defined but probably involve both bacterial and host factors. The bacteria invade the epithelial cell surface to a limited degree. Toxins and lipopolysaccharide may damage the mucosal cells, and the ammonia produced by the urease activity may also directly damage the cells.
- Histologically, gastritis is characterized by acute and chronic inflammation. Polymorphonuclear and mononuclear cell infiltrates are seen within the epithelium and lamina propria. Vacuoles within cells are often pronounced. Destruction of the epithelium is common, and glandular atrophy may occur. *H pylori* thus is a major risk factor for gastric cancer.

Clinical Findings

Acute infection can yield an upper gastrointestinal illness with nausea and pain; vomiting and fever may also be present. The acute symptoms may last for less than 1 week or as long as 2 weeks. After colonization, the *H pylori* infection persists for years and perhaps decades or even a lifetime. About 90% of patients with duodenal ulcers and 50–80% of those with gastric ulcers have *H pylori* infection. Recent studies confirm that *H pylori* also is a risk factor for gastric carcinoma and lymphoma.

Diagnostic Laboratory Tests

A. Specimens

- Gastric biopsy specimens can be used for histologic examination or minced in saline and used for culture.
- Blood is collected for determination of serum antibodies.
- Stool samples may be collected for *H pylori* antigen detection.

B. Smears

The diagnosis of gastritis and *H pylori* infection can be made histologically. A gastroscopy procedure with biopsy is required. Routine stains demonstrate gastritis, and Giemsa or special silver stains can show the curved or spiral-shaped organisms.

C. Culture

As above, culture is performed when patients are not responding to treatment, and there is a need to assess susceptibility patterns.

D. Antibodies

Several assays have been developed to detect serum antibodies specific for *H pylori*. 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.

E. Special Tests

Rapid tests to detect urease activity are widely used for presumptive identification of *H pylori* in specimens. Gastric biopsy material can be placed onto a urea-containing medium with a color indicator. If *H pylori* is present, the urease rapidly splits the urea (1–2 hours), and the resulting shift in pH yields a color change in the medium. In vivo tests for urease activity can be done also. In urea breath tests, 13C- or 14C-labeled urea is ingested by the patient. If *H pylori* is present, the urease activity generates labeled CO2 that can be detected in the patient's exhaled breath. Detection of *H pylori* antigen in stool specimens is appropriate as a test of cure for patients with known *H pylori* infection who have been treated.

Immunity

- Patients infected with *H pylori* develop an IgM antibody response to the infection.
- Subsequently, IgG and IgA are produced, and these persist, both systemically and at the mucosa, in high titer in chronically infected persons.

Early antimicrobial treatment of *H pylori* infection blunts the antibody response; such patients are thought to be subject to repeat infection.

Treatment

- Triple therapy with metronidazole and either bismuth subsalicylate or bismuth subcitrate plus either amoxicillin or tetracycline for 14 days eradicates *H pylori* infection in 70–95% of patients. An acid-suppressing agent given for 4–6 weeks enhances ulcer healing.
- Proton pump inhibitors (PPIs) directly inhibit *H pylori* and appear to be potent urease inhibitors.
- The preferred initial therapy is 7–10 days of a PPI plus amoxicillin and clarithromycin or a quadruple regimen of a PPI metronidazole, tetracycline, and bismuth for 10 days.