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Lecture. 9
Second Stage

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HELICOBACTER PYLORI

Members of the genus ***Helicobacter*** **are usually spiral, curved, or fusiform rod-shaped Gram-negative bacteria**. *Helicobacter* species have been isolated from **the gastrointestinal and hepatobiliary tract of many different mammalian hosts,** including **humans, dogs, cats, pigs, cattle, and other domestic and wild animals.** The various helicobacters can be divides into two groups: *Helicobacter* species that primarily colonize the **stomach (gastric helicobacters),** and those that colonize the **intestines (enterohepatic helicobacters).** Humans are the primary host-reservoir for *H. pylori*, which is **Gram-negative, catalase- and oxidase-positive,**a **spiral-shaped, and urease positive rod**. *H. pylori* is associated with antral gastritis, duodenal (peptic) ulcer disease, gastric ulcers, gastric adenocarcinoma, and gastric mucosa-associated lymphoid tissue (MALT) lymphomas.

Morphology and Identification

A. Typical Organisms

Helicobacter species, including *H. pylori*, have many characteristics in common with campylobacters. ***Helicobacter*** **species are motile and have single and/or multiple monopolar flagella** that are typically sheathed and can vary greatly in their flagellum morphology.

B. Culture While *H. pylori* can be readily isolated from gastric biopsy specimens, culture sensitivity may be limited by several factors, including delayed specimen transport and processing, prior antimicrobial therapy, or contamination with other mucosal bacteria.

Special transport media (eg**, Stuart's transport medium**) should be used to main the organisms' viability when transport to the laboratory is anticipated to exceed 2 hours.

H. pylori usually grows within **3–6 days when incubated at 37°C** in a microaerophilic and humid atmosphere; however, incubation of up to 14 days may be necessary before resulting the culture as negative. To achieve a higher yield for recovery of the organism, the biopsy specimen may be homogenized prior to streaking onto the agar plate. The agar media for primary isolation include enriched agar media supplemented with blood and/or blood products (eg, **chocolate agar**) or antibiotic-containing media such as **Skirrow's medium**, in order to suppress overgrowth by other competing bacterial flora. The colonies have varying appearance on blood agar ranging from gray to translucent and are 1–2 mm in diameter.

C. Growth Characteristics

H. pylori is oxidase positive and catalase positive, and has a characteristic Gram-stain morphology; the organism is motile, and is a strong producer of urease.

Pathogenesis and Pathology

H. pylori is able to survive in the acidic environment of the stomach and ultimately establish lifelong colonization of the gastric mucosa in the absence of antimicrobial treatment. While *H. pylori* grows optimally at a **pH of 6.0–7.0**, it would be killed or not grow at the pH within the gastric lumen (**pH 1–3**). Several factors contribute to the organism's ability to overcome the acidic environment of the stomach, contributing to colonization, inflammation, changes in gastric acid production, and tissue destruction.

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Gastric mucus is relatively impermeable to acid and has a strong buffering capacity. On the lumen side of the mucus, the pH is low (1.0–3.0); on the epithelial side, the pH is about 5.0–7.0. After entering the stomach, *H. pylori* utilizes its urease activity to neutralize the gastric acid; intracellular urease activity as well as urease located on the bacterial cell surface allow for the **breakdown of urea into ammonia and CO 2**; NH3 is converted to ammonium (**NH4+**) and extruded from the bacterial cell leading to neutralization of the gastric acid.

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. Diagnostic testing methods are summarized in Table 1

B. Smears

The diagnosis of gastritis and *H. pylori* infection can be made histologically; this approach is generally more sensitive than culture. A gastroscopy procedure with biopsy is required. Routine stains (eg, hematoxylin & eosin stain) demonstrate acute/chronic gastritis, and Giemsa or special stains (eg, silver stains or immunohistochemical stains) can show the curved or spiral-shaped organisms.

C. Culture

Since *H. pylori* organisms adhere to the gastric mucosa, the bacteria cannot be recovered from stool specimens like other gastrointestinal pathogens. As described above, culture is usually performed when patients are not responding to treatment, and there is a need to perform antimicrobial susceptibility testing. Tissue for culture is obtained by endoscopy and biopsy of the gastric mucosa.

Table- 1: Diagnostic Testing Methods for *H. pylori*

Testing Modality	Advantages	Disadvantages
Invasive Testing		
Histology	Allows for detection of organism and assessment of the extent of tissue damage (eg, ulceration).	Requires mucosal biopsy and sample processing in Pathology. Requires several days for results.
Urease detection in tissue	Rapid test, with most positive results being obtained within 2 hours.	Requires mucosal biopsy. May give false-positive results with bacterial overgrowth. False-negative tests when patient receives PPI treatment.
Microbiologic culture	Allows for antimicrobial susceptibility testing.	Requires several days for results (slow growth of organisms); requires special and careful specimen processing (false-negative results due to prolonged specimen transport and processing in suboptimal conditions).
Noninvasive Testing		
Serology	Noninvasive; inexpensive; "rapid" turn-around-time for results. Useful for epidemiologic purposes and evaluation of symptomatic patients.	Provides no assessment of extent of tissue damage/pathology. Not suitable to assess completion of antimicrobial therapy. Usually cannot differentiate between acute and past infection.
Urea breath test	Relatively noninvasive and rapid. Valuable for assessment of therapy (eradication of infection).	Requires expensive instrumentation for testing; less convenient than serology. False-negative results when patient receives PPI therapy. Provides no assessment of extent of tissue damage/pathology.
Stool antigen test	Relatively noninvasive, convenient, rapid, and inexpensive. Most valuable for assessment of response to antimicrobial therapy.	Not useful to assess the extent of tissue damage/pathology.

D. Antibodies

Several assays have been developed to detect serum antibodies specific for *H. pylori*. While testing for IgG serum antibodies against *H. pylori* is useful to confirm the exposure to the organism, either for epidemiologic purposes or for the evaluation of a symptomatic patient, the antibody titers do not typically correlate with the severity of the disease. Furthermore, **IgM antibodies disappear rapidly during the initial course of an acute infection**, and are of little diagnostic value. The relevance of IgA testing remains controversial, **and both IgA and IgG serum antibodies persist even if the *H. pylori* infection is eradicated**. The role of antibody testing in differentiating active *H. pylori* infection from past infection and/or completion of therapy is therefore limited.