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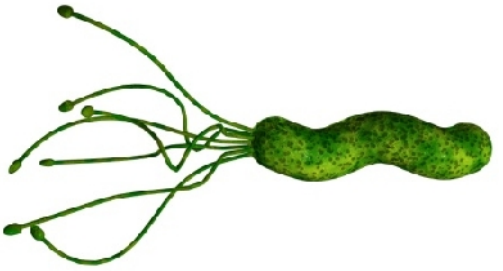
كليـــة الصيدلـــة

Helicobacter *pylori* infection



In 1983, Warren (a biologist) and Marshall (a clinician) described *Helicobacter pylori (HP)*. At first, they named the bacterium *Campylobacter pyloridis*. Later, it was named *Campylobacter pylori*. [2] Since then, a large number of reports have been produced on *H pylori* and its pathogenetic potential. H. pylori is a common gastric pathogen that causes gastritis, peptic ulcer disease.[1] In fact, although peptic ulcer disease is the most studied disease related to *H pylori* infection, this bacterium is seemingly involved in the pathogenesis of several extragastric diseases, such as mucosa-associated lymphoid tissue lymphomas (MALTomas), coronaritis, gastroesophageal reflux disease (GERD), iron deficiency anemia, skin disease, and rheumatologic conditions. However, at present, many of these associations remain largely uncertain, and the debate to confirm or refute causality related to these associations is still open. [2]

H. pylori is a spiral-shaped, gram-negative organism that has adapted to thrive in acid. In developing countries, it commonly causes chronic infections and is usually acquired during childhood. In the US, infection is less common among children but increases with age: by age 60, about 50% of people are infected. Infection is most common among blacks, Hispanics, and Asians.

The organism has been cultured from stool, saliva, and dental plaque, which suggests oral-oral or fecal-oral transmission (direct contact with saliva, vomit or fecal matter, or spread through contaminated food or water). Infections tend to cluster in families and in residents of custodial institutions. Nurses and gastroenterologists seem to be at high risk because bacteria can be transmitted by improperly disinfected endoscopes. [1,2]

Pathophysiology

Effects of H. pylori infection vary depending on the location within the stomach. Antral-predominant infection results in increased gastrin production, probably via local impairment of somatostatin release. Resultant hypersecretion of acid

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predisposes to prepyloric and duodenal ulcer. Body-predominant infection leads to gastric atrophy and decreased acid production. Patients with body-predominant infection are predisposed to gastric ulcer and adenocarcinoma. Some patients have mixed infection of both antrum and body with varying clinical effects. Many patients with H. pylori infection have no noticeable clinical effects.
Ammonia produced by H. pylori enables the organism to survive in the acidic environment of the stomach and may erode the mucus barrier. Cytotoxins and mucolytic enzymes (eg, bacterial protease, lipase) produced by H. pylori may play a role in mucosal damage and subsequent ulcerogenesis.
Infected people are 3 to 6 times more likely to develop stomach cancer. H. pylori infection is associated with intestinal-type adenocarcinoma of the gastric body and antrum but not cancer of the gastric cardia. Other associated cancers include gastric lymphoma and mucosa-associated lymphoid tissue (MALT) lymphoma, a monoclonally restricted B-cell tumor.

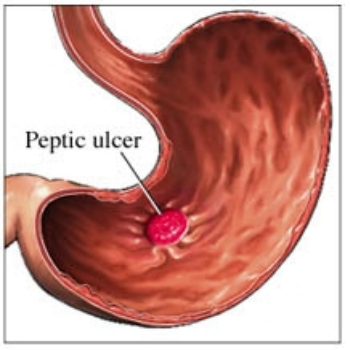
Symptoms

Infection may be asymptomatic (30-35% of patients) or result in varying degrees of dyspepsia. [1,2] Adults and children differ in immune response to *H pylori* infection. This is probably due to a physiologic lower density of neutrophils and T lymphocytes during childhood, especially in children younger than 8 years.

Although *H pylori* infection is not significantly related to recurrent abdominal pain, weekly pain is reported more often in children who are infected with *H pylori* compared with children who are not infected.

Abdominal discomfort is the most common symptom. This discomfort usually:

- is a dull, gnawing ache.
- comes and goes for several days or weeks.
- occurs 2 to 3 hours after a meal.
- occurs in the middle of the night (when the stomach is empty).
- is relieved by eating.
- is relieved by antacid medications.



Other symptoms include weight loss, poor appetite, bloating, burping, nausea and vomiting.[1,4]

Emergency Symptoms

Sharp, sudden, persistent stomach pain,bloody or black stools,bloody vomit or vomit that looks like coffee grounds. These could be signs of a serious problem, such as:
Perforation – when the ulcer burrows through the stomach or duodenal wall.
Bleeding – when acid or the ulcer breaks a blood vessel.
Obstruction – when the ulcer blocks the path of food trying to leave the stomach.[2]

Tests and diagnosis

Screening of asymptomatic patients is not warranted. Tests are done during evaluation for peptic ulcer and gastritis. Posttreatment testing is typically done to confirm eradication of the organism. Different tests are preferred for initial diagnosis and posttreatment.

Noninvasive tests:

Laboratory and **office-based serologic assays** for antibodies to H. pylori have sensitivity and specificity of > 85% and are considered the noninvasive tests of choice for initial documentation of H. pylori infection. However, because qualitative assays remain positive for up to 3 yr after successful treatment and because quantitative antibody levels do not decline significantly for 6 to 12 mo after treatment, serologic assays are not usually used to assess cure.

Urea breath

- The carbon 13 urea breath test (UBT) is based on the detection of the products created when urea is split by the organism.
- Patients are asked to drink urea (usually with a beverage) labeled with a carbon isotope (carbon 13 or carbon 14). The organism metabolizes the urea and liberates labeled CO2, which is exhaled and can be quantified in breath samples taken after 20 to 30 min. The concentration is high only when urease is present in the stomach. Because the human stomach does not produce urease, such a reaction is possible only with H pylori infection.
- The breath test is expensive but is becoming increasingly more available. Sensitivity and specificity are > 90%.
- 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 (H_2) blockers, or proton pump inhibitors. therefore, follow-up testing should be delayed ≥ 4 wk after antibiotic therapy and 1 wk after proton pump inhibitor therapy.[1,2]

H pylori fecal antigen test

- This novel rapid test is based on monoclonal antibody immunochromatography of stool samples. The test has been reported to be very specific (98%) and sensitive (94%).
- The results are positive in the initial stages of infection and can be used to detect eradication after treatment.

Antibiogram

- In geographic areas with a high resistance rate against metronidazole and clarithromycin, culture for antibiotic susceptibility testing (antibiogram) seems to be useful.
- Alternatively, metronidazole and clarithromycin should not be recommended as first-line drugs in such areas.[2]

Invasive tests:

Endoscopy is used to obtain mucosal biopsy samples for a rapid urease test (RUT) or histologic staining. Bacterial culture is of limited use because of the fastidious nature of the organism. Endoscopy is not recommended solely for diagnosis of H. pylori; noninvasive tests are preferred unless endoscopy is indicated for other reasons.

The RUT, in which presence of bacterial urease in the biopsy sample causes a color change on a special medium, is the diagnostic method of choice on tissue samples. Histologic staining of biopsy samples should be done for patients with negative RUT results but suspicious clinical findings, recent antibiotic use, or treatment with proton pump inhibitors. RUT and histologic staining each have a sensitivity and specificity of > 90%.[1]

Treatments and drugs

H. pylori eradication requires multidrug therapy, typically antibiotics, proton pump inhibitors (acid suppressors), and H_2 blockers (stomach protectors). Antibiotic regimens recommended for patients may differ across regions of the world because different areas have begun to show resistance to particular antibiotics.(4)

Proton pump inhibitors suppress H. pylori, and the increased gastric pH accompanying their use can enhance tissue concentration and efficacy of antimicrobials, creating a hostile environment for H. pylori. H_2 blockers work by blocking histamine, which stimulates acid secretion. They help reduce ulcer pain after a few weeks.

Patients with complications (eg, gastritis, ulcer, cancer) should have the organism eradicated. Eradication of H. pylori can even cure some cases of MALT (mucosa-associated lymphoid tissue) lymphoma (but not other infection-related cancers).

Treatment of asymptomatic infection has been controversial, but the recognition of the role of H. pylori in cancer has led to a recommendation for treatment. Vaccines, both preventive and therapeutic (ie, as an adjunct to treatment of infected patients), are under development.(1)

Triple therapy is recommended. Oral omeprazole 20 mg bid or lansoprazole 30 mg bid, plus clarithromycin 500 mg bid, plus amoxicillin 1 g bid (or, for penicillin-allergic patients, metronidazole 500 mg bid) for 14 days, cures infection(reduces ulcer symptoms, kills the bacteria, and prevents ulcer recurrence) in > 95% of cases. This regimen has excellent tolerability. Ranitidine bismuth citrate 400 mg po bid may be substituted for the proton pump inhibitor.

Quadruple therapy with a proton pump inhibitor bid, tetracycline 500 mg and bismuth subsalicylate or subcitrate 525 mg qid, and metronidazole 500 mg tid is also effective but more cumbersome. Infected patients with duodenal or gastric ulcer require continuation of the acid suppression for at least 4 wk.

Treatment is repeated if H. pylori is not eradicated. If two courses are unsuccessful, some authorities recommend endoscopy to obtain cultures for sensitivity testing.(1)

Prevention

In areas of the world where H. pylori infection and its complications are common, doctors sometimes test healthy people for H. pylori. Whether there is a benefit to treating H. pylori when you have no signs or symptoms of infection is controversial among doctors. If you're concerned about H. pylori infection or think you may have a high risk of stomach cancer, talk to your doctor. Together you can decide whether you may benefit from H. pylori screening.(3)

References:

1)Merck Sharp & Dohme Corp. Helicobacter pylori Infection [Internet]. The Merck Manual for Health Care Professionals; January 2007 [cited Nov 2012]. Available from: http://www.merckmanuals.com/professional/gastrointestinal_disorders/gastritis_and_peptic_ulcer_disease/helicobacter_pylori_infection.html

2) Luigi Santacroce, MD. Helicobacter Pylori Infection [Internet]. Medscape Reference, Drugs, Diseases &Procedures; Sep 22, 2011 [cited Nov 25, 2012]. Available from: http://emedicine.medscape.com/article/176938-clinical

3) Mayo Clinic Staff. H. pylori infection [Internet]. Mayo Clinic, Mayo Foundation for Medical Education and Research; May24, 2011[cited Nov 24, 2012]. Available from: http://www.mayoclinic.com/health/h-pylori/DS00958/DSECTION=prevention

4) http://www.wakegastro.com/h-pylori-peptic-ulcer/

Terminology

Antrum

Antrum means a natural hollow or cavity. The maxillary antrum is now known as the maxillary SINUS. The mastoid antrum is situated in the mastoid process, the mass of bone felt behind the ear. It may become the seat of an ABSCESS in cases of suppuration of the middle ear. The pyloric antrum is the part of the stomach immediately preceding the PYLORUS.

Reference: Marcovitch H. 2005. Black's Medical Dictionary. 41th ed. London: A&C Black Publishers Limited. p 48.

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Drug- Drug Interaction

Orlistat + Vitamins

Orlistat decreases the absorption of supplemental beta-carotene and vitamin E. There is some evidence to suggest that some patients may have low vitamin D levels while taking orlistat, even if they are also taking multivitamins.It is recommended that multivitamin preparations should be taken at least 2 hours after orlistat, or at bedtime. The US manufacturers suggest that patients taking orlistat should be advised to take multivitamins, because of the possibility of reduced vitamin levels. Note that it has been suggested that monitoring of vitamin D may be required, even if multivitamins are given.

Source: Baxter K. 2009: Stockley's Drug Interactions Pocket companion, 1st ed., Page 354. UK, London, Pharmaceutical Press.

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FDA News

New Sleeping Pill May Help Insomnia

Nov. 28, 2012 -- Merck's experimental sleep drug **suvorexant** helps insomniacs fall asleep faster and stay asleep longer, early data suggest.

Later studies reported at a sleep conference last June confirmed the findings. Those studies are not yet published, but they've been sent to the FDA in Merck's filing for approval of **suvorexant**. It is effective over the long term and well tolerated.

The published study tested whether a range of doses, each given in a sleep lab to about 60 people suffering from insomnia, improved sleep better than an inactive placebo pill. Without knowing which was which, each study participant took either suvorexant or the placebo for four weeks, and then switched to the other for another four weeks.

The main study measure was sleep efficiency -- that is, the percentage of an eight-hour night people slept. At the beginning of the study, participants' average sleep efficiency was 66%. After falling asleep, they woke for an average 101 minutes during the night.

There was a range of results, but generally sleep efficiency improved 5% to 13% compared to placebo. They also found that patients have 21 to 37 minutes less time awake during the night.

That may not seem like a lot. But it could mean a lot to a person suffering from insomnia, as insomnia patients seem to feel better and function better when they get 15 to 20 minutes more sleep.

What they find particularly exciting is that **suvorexant** doesn't work like other sleeping pills. Current sleep drugs enhance brain functions that increase sleepiness. **Suvorexant** inhibits orexin, a hormone that acts on the brain to increase wakefulness.

Brain levels of orexin are naturally lower during the night. While Merck has focused on developing **suvorexant** specifically for people with insomnia, it's suggested that it might be particularly helpful for shift workers, who need to sleep during the day when orexin levels are high.

Although Merck has not disclosed the date by which the FDA must decide on **suvorexant**'s approval, financial analysts suggest the decision is likely to come in the late summer of 2013.

Source: http://www.emedicinehealth.com/script/main/art.asp?articlekey=165475

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Test Your Knowledge

1. Which one of the following body areas usually has the lowest (most acidic) pH?
(A) blood
(B) lacrimal fluid
(C) oral cavity
(D) intestinal fluid
(E) vagina

2. Patients with phenylketonuria (PKU) should avoid food products containing
(A) unsaturated fats
(B) medium-chain triglycerides
(C) soy protein
(D) sodium chloride
(E) aspartame

3. A patient with an abnormally elevated number of erythrocytes is said to have
(A) macrocytic anemia
(B) polycythemia
(C) sickle cell anemia
(D) aplastic anemia
(E) microcytic anemia

4. A patient is using benazepril (Lotensin) for the treatment of hypertension. This patient should not receive
(A) potassium supplementation
(B) antihistamines
(C) aluminum-containing antacids
(D) folic acid supplementation
(E) tricyclic antidepressants

Real Enquiries

At the "Drug Information Center", we respond to enquiries from the professional health team as well as from others. Here's one of the enquiries received at the center!

Enquiry received from Dr. Naglaa Hassan, Assiut Univ. Pediatrics' Hospital

Enquiry: Are Paracetamol and NSAIDs safe to use in patients with liver disease?

Summary of Answer:

Preventive care can play an important role in patients with chronic liver diseases. Based on the existing data, the preventive strategies of avoidance of NSAIDs are prudent in such patients

It has been advised to avoid liver toxic medications, most common to be used is over-the-counter pain killers (aspirin-like medications), and Acetaminophen in less than 2 grams per day is safest (one extra-strength every 6 hours).

While hepatotoxicity related to NSAIDS is an uncommon adverse effect, it is important to be vigilant to the hepatotoxic potential of any NSAID, as increased awareness, surveillance and reporting of these events will lead to a better understanding of the risk factors and the pathophysiology of NSAID-related hepatotoxicity. Idiosyncratic reactions due to hypersensitivity or metabolic aberration are responsible for toxicity in the vast majority of cases and at-risk groups for idiosyncratic hepatotoxicity have been identified. Although hepatotoxicity is listed as a class warning for NSAIDs, diclofenac and sulindac seem most commonly associated with the problem.

References:

1) Thomas R. Riley, Milton S.: Preventive Care in Chronic Liver Diseases. JGIM, Vol.14, pages 699-704, Nov.1999.

2) rxlist.com/ibuprofen-drug/warnings-precautions.htm

3) N. O'connor , P.I. Dargan and A.L. Jones: Hepatocellular damage from non-steroidal anti-inflammatory drugs. QJM: An International Journal of Medicine, Volume 96, No. 11 Pp. 787-791

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Complementary Medicine

Evening primrose oil

Common Names: evening primrose oil, EPO

Latin Name: Oenothera biennis

Evening primrose is a plant native to North America, but it grows in Europe and parts of the Southern Hemisphere as well. It has yellow flowers that bloom in the evening. Evening primrose oil contains gamma-li nolenic acid (GLA), an essential fatty acid. Essential fatty acids are required by the body for growth and development, and must be obtained from the diet.

What It Is Used For

Evening primrose oil has been used since the 1930s for eczema (a condition in which the skin becomes inflamed, itchy, or scaly because of allergies or other irritation).

More recently it has been used for other conditions involving inflammation, such as rheumatoid arthritis. Evening primrose oil is used for conditions affecting women's health, such as breast pain associated with the menstrual cycle, menopausal symptoms, and

premenstrual syndrome. Other conditions for which evening primrose oil is used include cancer and diabetes

How It Is Used

Evening primrose oil is extracted from the seeds of the evening primrose. The oil is usually put into capsules for use.

What the Science Says

Evening primrose oil may have modest benefits for eczema, and it may be useful for rheumatoid arthritis and breast pain. However, study results are mixed, and most studies have been small and not well designed.

Reference: *U.S. Department Of Health And Human Services, National Institutes of Health,National Center for Complementary and Alternative Medicine, herbs at aglance.2009. p38.*

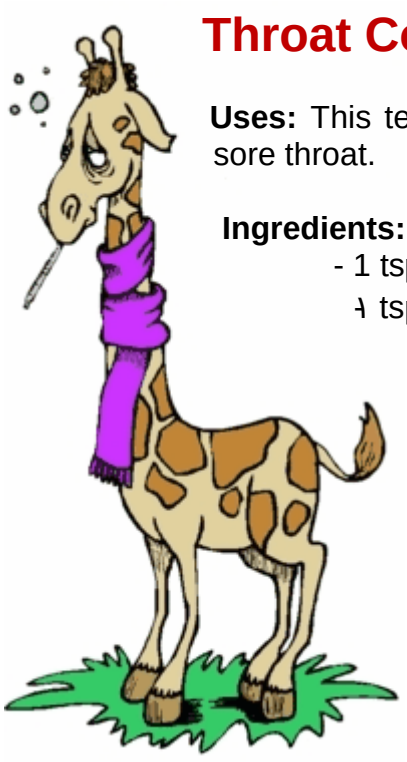
Answers:

Q1: E) vagina has the lowest (most acidic) pH.

Q2: E) Patients with phenylketonuria (PKU) should avoid food products containing aspartame.

Q3: B) patient with an abnormally elevated number of erythrocytes is said to have polycythemia

Q4: A) patient is using benazepril (Lotensin) for the treatment of hypertension. This patient should not receive potassium supplementation



Throat Coating Tea

Uses: This tea can be used for infection, colds, cough, throat dryness, or sore throat.

Ingredients:

- 1 tsp . Fenugreek **الحلبة**
- ١ tsp. Marshmallow root **الخبيز أو الختمية الطبية**
- 1/2 tsp. Myrrh gum **لبان المر**
- 1/2 tsp. Licorice powder **العرقسوس**
- ١ tbsp. Honey
- ٣ cups water

Place the herbs and the water in a pot. Bring the mixture to a boil, and then reduce the heat to a low simmer, cover. Let simmer for 15 minutes. Remove from heat and strain the herbs. Add honey to taste. Drink 3-4 cups throughout the day.

Source: *The Herbal Pharmacy CD, By Hale Software, Inc 1997.*

BEST WISHES FROM ALL OF US AT THE DIC FOR A BLESSED & A JOYOUS NEW YEAR 2013!!!

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Tel.088/2357399 & 088/2411556
E-mail: clinipharm_assiut@yahoo.com, website: www.clinpharm.aun.edu.eg

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