Case 28
The Bacterium *Helicobacter pylori* and Peptic Ulcers

Focus concept
The entire genome of *Helicobacter pylori* has recently been sequenced. This will allow biochemists to examine the organism’s proteins in detail. In this case, mechanisms employed by *Helicobacter pylori* that allow it to survive in the acidic environment of the stomach will be examined.

Prerequisites
- Protein structure and function.
- Basic metabolic pathways up through amino acid metabolism.

Background
For the past hundred years or so, the cause of peptic ulcers has been attributed to excess acid production by stomach parietal cells. The production of acid was thought to be influenced by environmental factors such as diet and stress. But in 1983, Australian physician Robin Warren described a spiral-shaped bacterium that he had observed on the gastric epithelium of his peptic ulcer patients, and the following year, he and biochemist Barry Marshall put forth the hypothesis that this as-yet unidentified spiral-shaped bacterium was the causative agent of peptic ulcers. Although the scientific community was initially skeptical, further study of the bacterium identified subsequently as *Helicobacter pylori* (or *Campylobacter pylori*) supported this hypothesis. The complete genome sequence of *H. pylori*, reported by Tomb et al. in 1997, will allow further detailed studies of the proteins of this bacterium and will provide information that can be used to develop drugs to treat peptic ulcers.

*H. pylori* has the unusual ability to colonize host cells in the extremely acidic environment of the gastric mucosa, where the pH is typically around 2. *H. pylori* probably employs several different mechanisms to ensure its survival in this environment:

- The bacterium has the ability to establish a positive inside-membrane potential.
- The bacterium may release factors that decrease the secretion of acid by gastric parietal cells.
- The protein urease is essential to the *H. pylori*’s ability to survive in the gastric environment.
Questions

1. The proteins found in *H. pylori* have different characteristics than those of bacteria that colonize cells in the usual physiological environment where pH = 7.4. Describe these proteins—what kinds of amino acids would you expect to find in abundance? What would the pI of these proteins be?

2. *H. pylori* synthesizes the enzyme urease, which converts urea to carbon dioxide and ammonia in the aqueous medium of the cell. Write a balanced equation for this reaction. How would the products of this reaction contribute to the survival of *H. pylori* in an acidic environment?

3. A current hypothesis is that *H. pylori* has the ability to establish a *positive inside-membrane potential*. This means that the interior of the bacterium is more positively charged than its exterior. What kinds of mechanisms might *H. pylori* employ in order to accomplish this? List as many as you can think of.

4. The following information concerning the metabolism of *H. pylori* was obtained from the complete genomic sequence:
   - Glucose is the sole source of carbohydrate.
   - Glycolysis, gluconeogenesis, and the pentose phosphate pathway are all active. Lactate dehydrogenase is present.
   - Peptidoglycans (for cell walls) are synthesized from fructose-6-phosphate, phospholipids from glyceraldehyde-3-phosphate and aromatic amino acids from phosphoenolpyruvate.
   - The conversion of pyruvate to acetyl CoA is accomplished by the enzyme pyruvate ferredoxin oxidoreductase (POR) instead of pyruvate dehydrogenase.
   - The glyoxylate cycle is absent.
   - The tricarboxylic acid cycle is incomplete, ending at isocitrate, which is converted to glutamate in a two-step process.
   - Fatty acid synthetic processes are present.
   - Glutamine synthetase and glutamate dehydrogenase are present.
   - Glutamine is the nitrogen donor in pyrimidine biosynthesis.

Using the above information, construct a diagram which integrates the major metabolic pathways found in *H. pylori*.

References
