Introduction to Microbiology

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Lecture 24

Campylobacter

- Small (0.2 to 0.5 µm wide and 0.5 to 5.0 µm long), motile, **curved, gram-negative rods**

- *Campylobacter* is the most common cause of **bacterial gastroenteritis**, with ***Campylobacter jejuni*** responsible for most infections.

- The organisms grow best in an atmosphere of reduced oxygen (5% to 7%) and increased carbon dioxide (5% to 10%) these properties are referred to as **microaerophilic. *C. jejuni* grows better at 42° C** than at 37° C.

- Express **lipooligosaccharides** (LOSs lack O-antigen in LPS)

- The organisms are killed when exposed to gastric acids, so conditions that decrease or neutralize gastric acid secretion favor disease

- *C. jejuni* GI disease characteristically produces **histologic damage to the mucosal surfaces of the jejunum** and other parts of the intestine

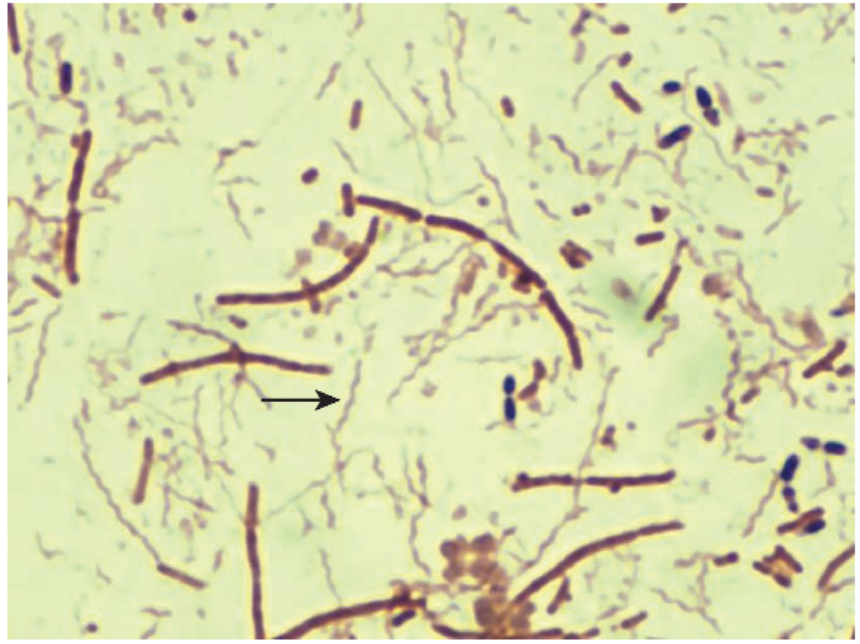


FIGURE 28-1 Mixed culture of bacteria from a fecal specimen. *Campylobacter jejuni* is the thin, curved, gram-negative bacteria *(arrow)*.

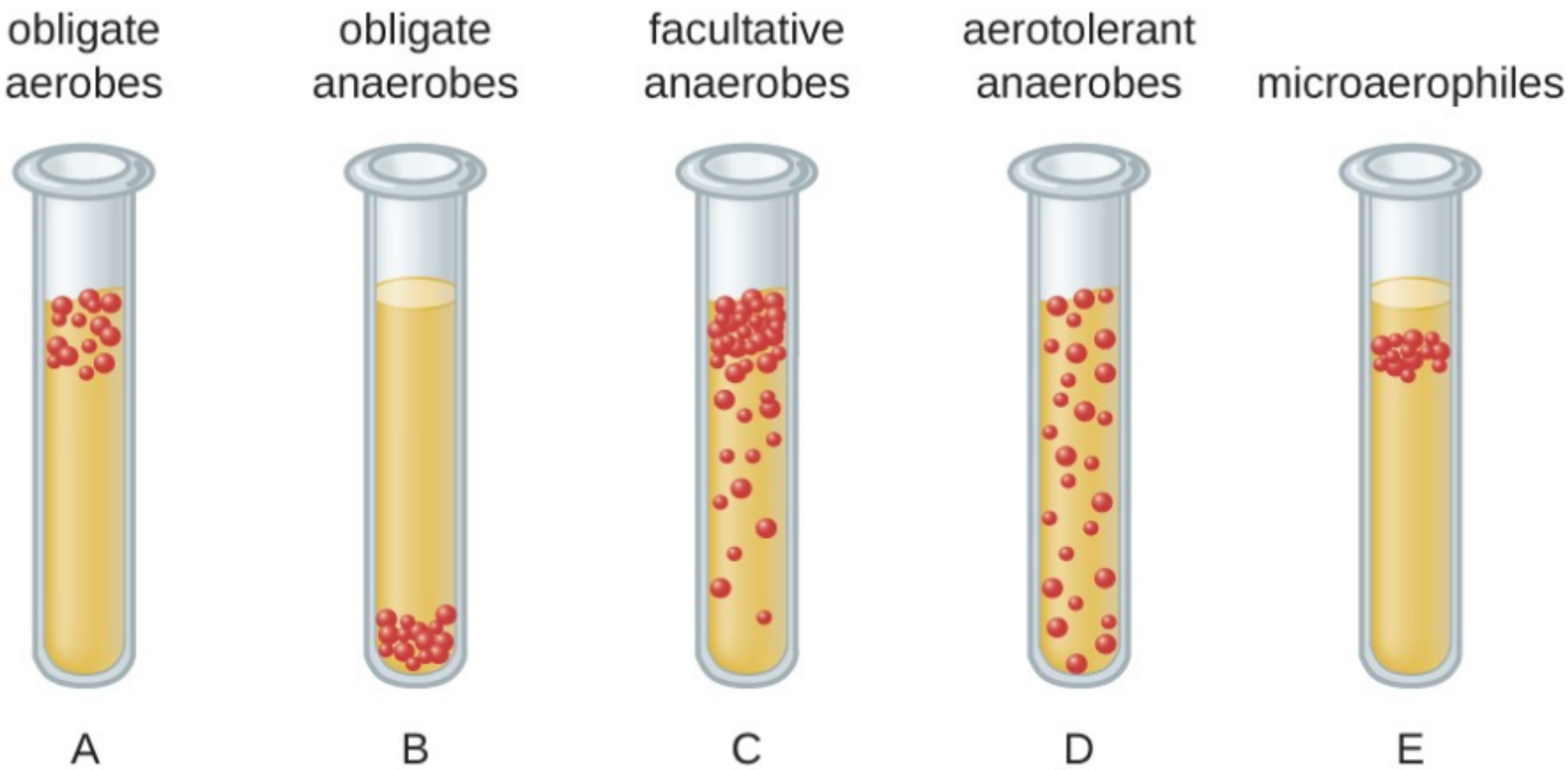


Figure 2. Diagram of bacterial cell distribution in thioglycolate tubes.

Campylobacter

- *Campylobacter* infections are **zoonotic,** with a variety of animals serving as reservoirs. **Contaminated poultry** are responsible for more than half of the *Campylobacter* infections in developed countries.

- **Uncommon for the disease to be transmitted by food handlers.**

- Present most commonly as **acute enteritis** with **diarrhea** (stools may be bloody on gross examination), **fever**, and **severe** abdominal pain.

- **Guillain-Barré syndrome** and **reactive arthritis** are well-recognized complications of *Campylobacter* infections (although uncommon). Probably through molecular mimicry.

- A **presumptive identification** of isolates is based on **growth under selective conditions**, typical **microscopic morphology**, and positive oxidase and catalase tests.

Microbiological findings among US emergency department patients presenting with 549 episodes of bloody diarrhea at 11 *EMERGE*ncy ID NET sites.

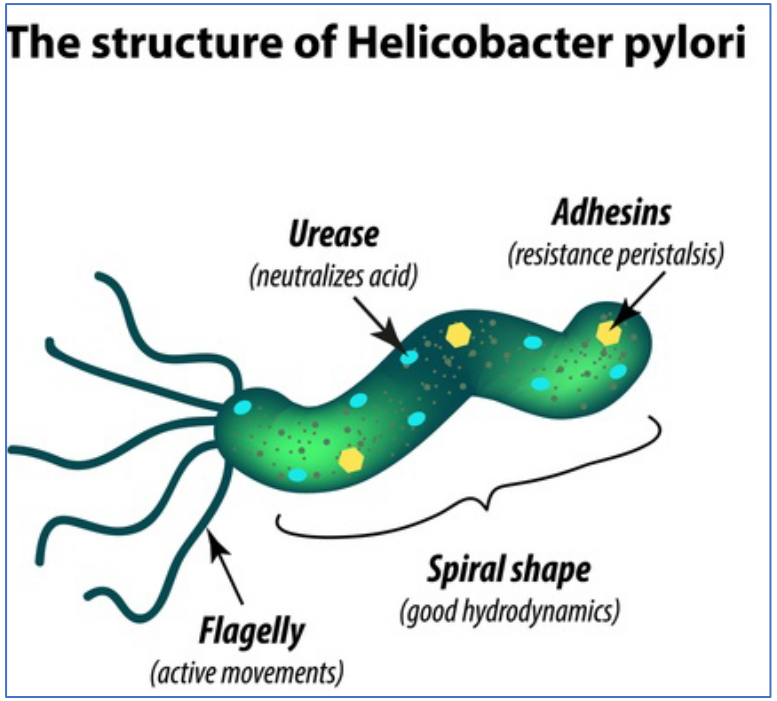
Helicobacter

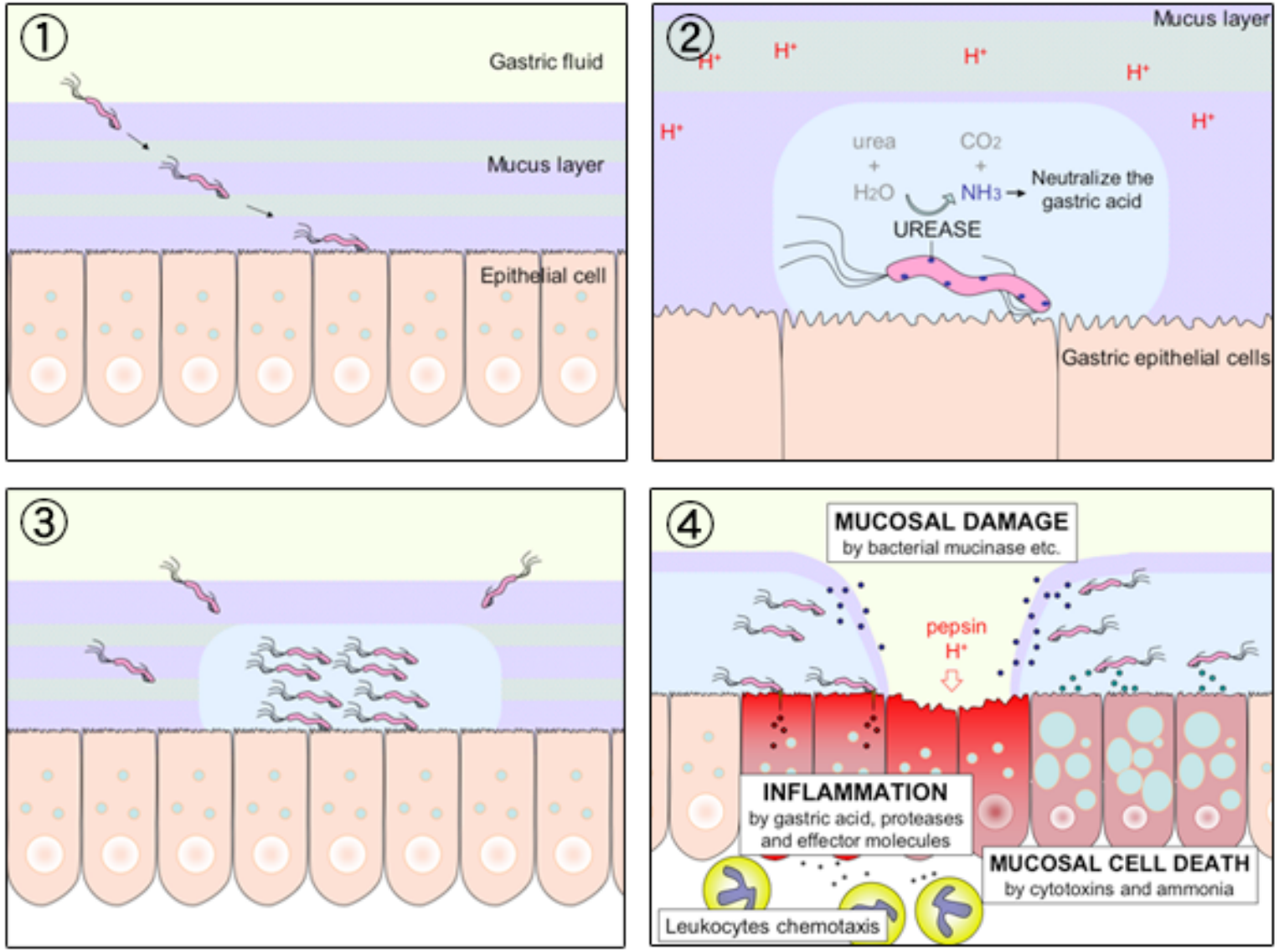
- **spiral gram-negative rods** resembling campylobacters, All gastric helicobacters, including *H. pylori,* are highly **motile** (corkscrew motility) and produce an abundance of **urease**

- Growth of *H. pylori* and other helicobacters requires a **complex medium** in **microaerophilic** conditions. *H. pylori* adheres to gastric mucosa and is usually not recovered in stool or blood specimens

- *H pylori* use their motility, chemotaxis, urease production, and other mechanisms to **adapt to the acidic conditions of the stomach** and colonize a narrow protected niche near the surface of epithelial cells

- **Humans are the primary reservoir for *H. pylori,*** and colonization is believed to persist for life unless the host is specifically treated. Transmission is most likely via the **fecal-oral route.**

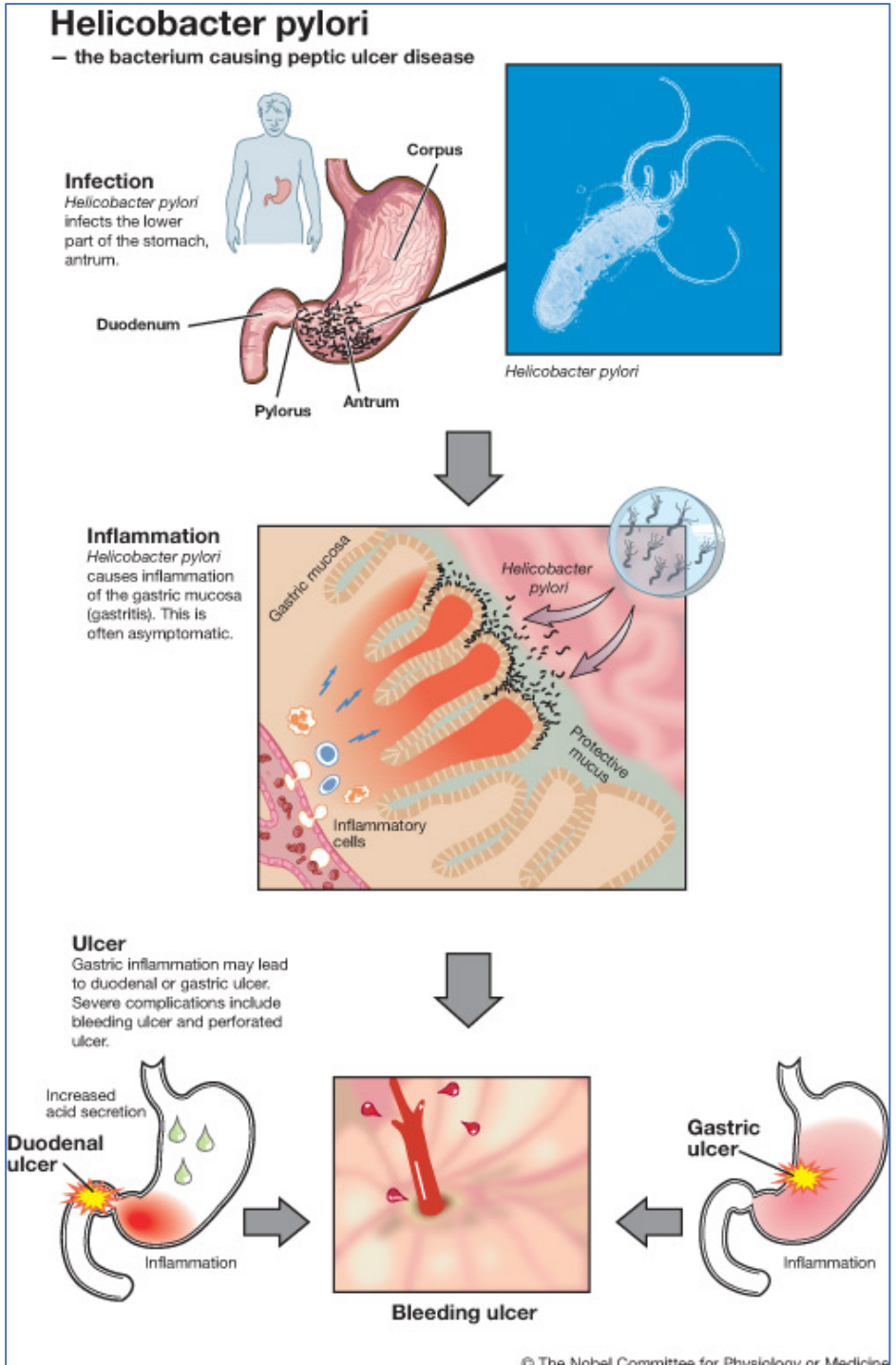




Localized tissue damage is mediated by urease byproducts, **mucinase, phospholipases,** and the activity of **vacuolating cytotoxin A (VacA),** a protein that after penetration into epithelial cells damages the cells by producing vacuoles. **cytotoxin-associated gene *(cagA)*** interferes with the normal cytoskeletal structure of the epithelial cells

Helicobacter

- Colonization with *H. pylori* invariably leads to **gastritis**
- The **acute phase** of gastritis is characterized by a **feeling of fullness**, **nausea**, vomiting, and hypochlorhydria.
- Can evolve into **chronic gastritis**, with disease confined to the gastric antrum or involve the entire stomach
- Chronic gastritis will progress to develop peptic ulcers. The ulcers develop at the sites of intense inflammation, commonly involving the junction between the corpus and antrum **(gastric ulcer)** or the proximal duodenum **(duodenal ulcer).**
- *H. pylori* is responsible for 85% of the gastric ulcers and 95% of the duodenal ulcers.
- Chronic gastritis increases the risk of **gastric cancer and MALT lymphoma (**mucosa-associated lymphoid tissue B-cell lymphomas)**.**

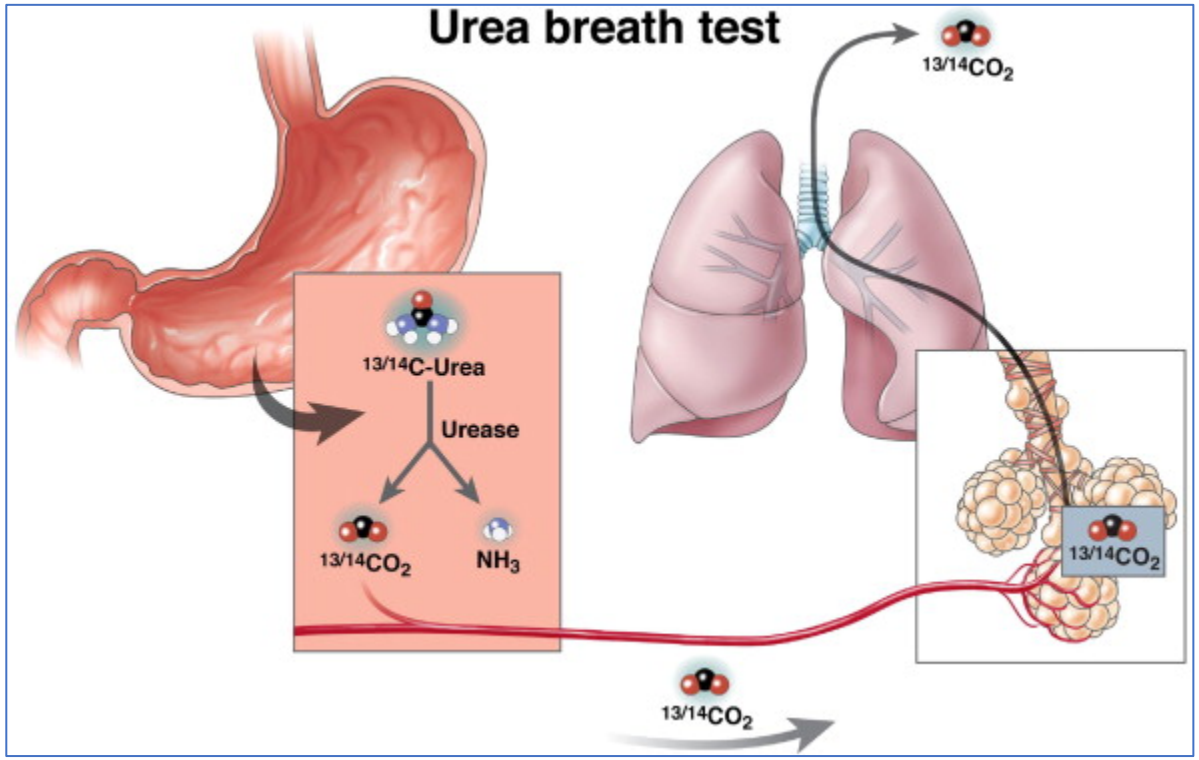


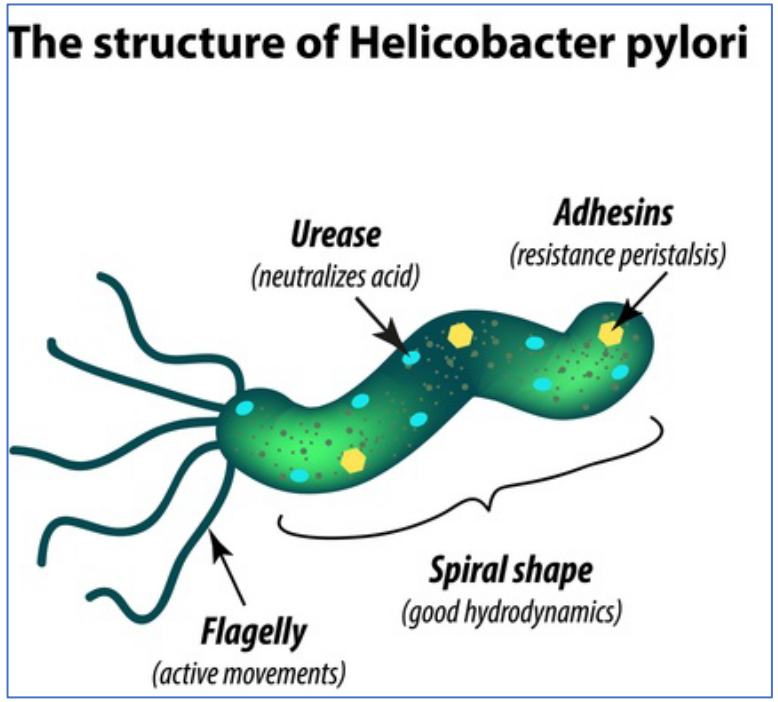
Helicobacter

- *Since H. pylori* adheres to gastric mucosa , *H. pylori* can be detected by **histologic examination of gastric biopsy** specimens, but identification is usually done by non-invasive methods, A number of **polyclonal and monoclonal immunoassays for *H. pylori* antigens excreted in stool** have been developed and demonstrated to have sensitivities and specificities exceeding 95%.

Serology	Widely available Least expensive of available tests	Positive results may reflect previous rather than current infection Not recommended for confirming eradication
Urea breath test	High negative and positive predictive values Useful before and after treatment	False-negative results possible in the presence of proton pump inhibitors or with recent use of antibiotics or bismuth preparations Considerable resources and personnel required to perform test
Stool antigen test	High negative and positive predictive values with monoclonal antibody test Useful before and after treatment	Process of stool collection may be distasteful to patient False-negative results possible in the presence of proton-pump inhibitors or with recent use of antibiotics or bismuth preparation

Data from McColl KE. *N Engl J Med.* 2010;362:1597-1604.[15]





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Letters to the Editor

UNIDENTIFIED CURVED BACILLI ON GASTRIC EPITHELIUM IN ACTIVE CHRONIC GASTRITIS

J Robin Warren [a], Barry Marshall [b]

In 2005, the Karolinska Institute in Stockholm awarded the Nobel Prize in Physiology or Medicine to Marshall and Robin Warren, his long-time collaborator, "**for their discovery of the bacterium Helicobacter pylori and its role in gastritis and peptic ulcer disease**"

Vibrio

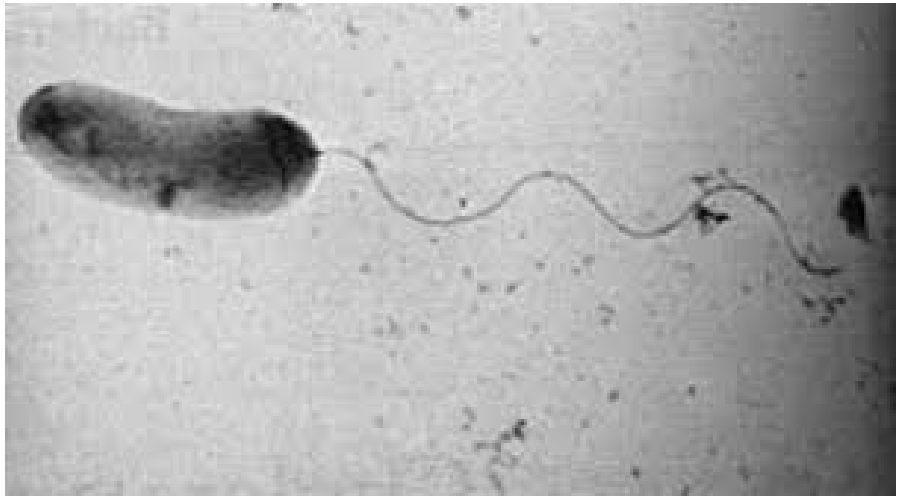
- **Gram-negative, facultatively anaerobic, fermentative rods,** characterized by a **positive oxidase reaction** and the presence of **polar flagella .**

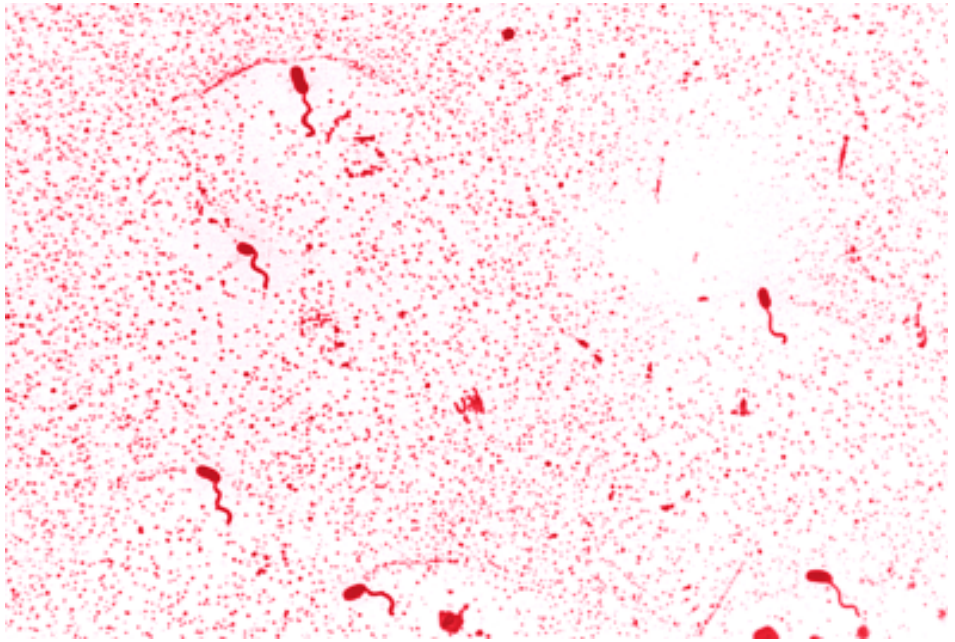
- *Vibrio* species can grow on a variety of simple media within a broad temperature range (from 14° C to 40° C). And tolerate a wide range of pH (e.g., pH of 6.5 to 9.0) but are **susceptible to stomach acids.**

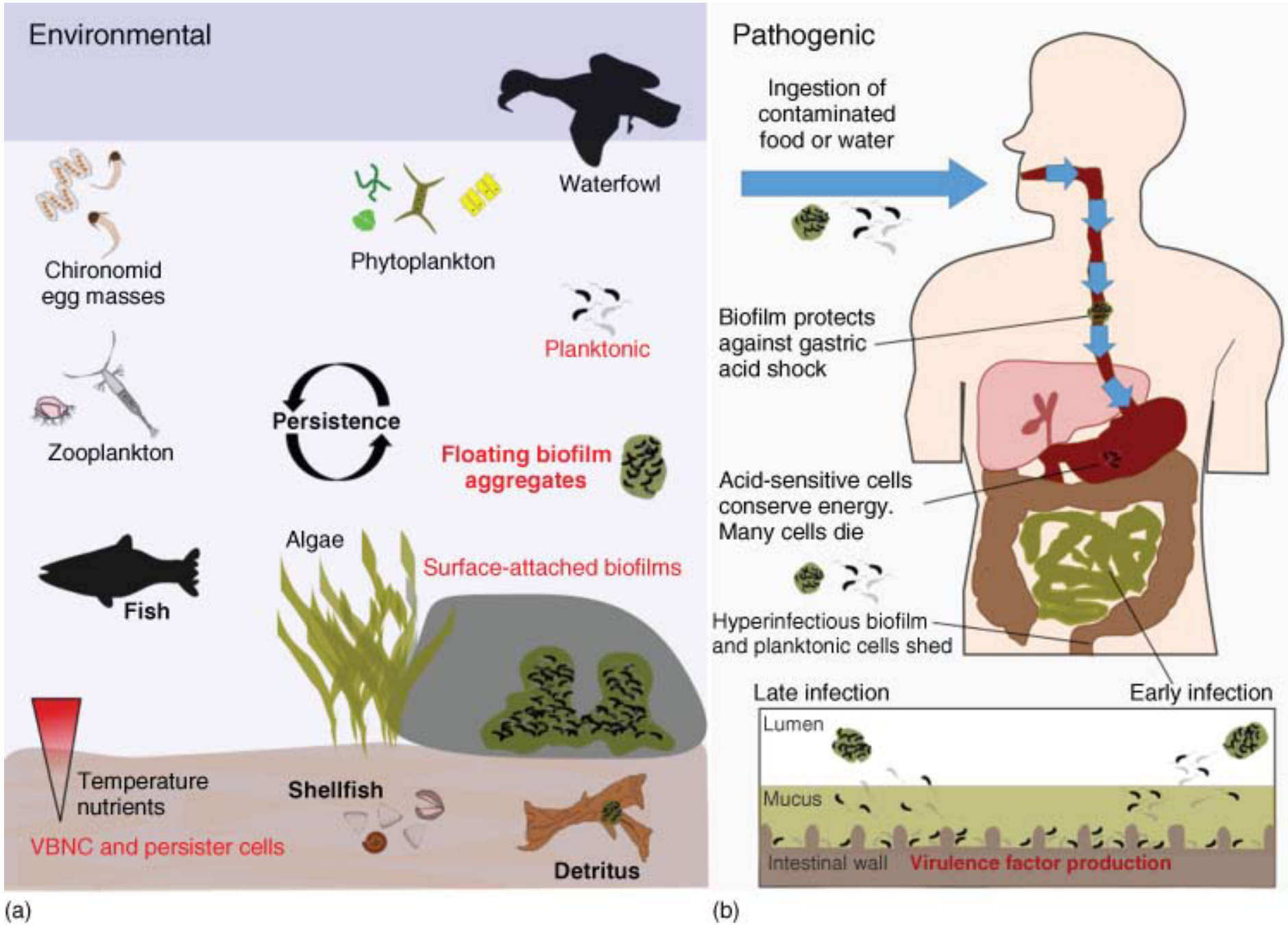
- All species of *Vibrio* **require sodium chloride (NaCl)** for growth. Most species are halophilic ("salt-loving").

- *Vibrio* species, including *V. cholerae,* grow naturally in **estuarine and marine environments** worldwide.

- Pathogenic vibrios can also flourish in waters with chitinous **shellfish**






Environmental
Waterfowl
Chironomid egg masses
Phytoplankton
Planktonic
Zooplankton
Persistence
Floating biofilm aggregates
Fish
Algae
Surface-attached biofilms
Temperature nutrients
Shellfish
VBNC and persister cells
Detritus
(a)
Pathogenic
Ingestion of contaminated food or water
Biofilm protects against gastric acid shock
Acid-sensitive cells conserve energy. Many cells die
Hyperinfectious biofilm and planktonic cells shed
Late infection
Early infection
Lumen
Mucus
Intestinal wall
Virulence factor production
(b)

Vibrio

- All strains possess **lipopolysaccharides** consisting of lipid A (endotoxin), core polysaccharide, and an **O polysaccharide** side chain.

- The O polysaccharide is used to subdivide *Vibrio* species into **serogroups, *V. cholerae* O1 and O139** produce **cholera toxin** and are associated with epidemics of cholera. Other strains of *V. cholerae* generally do not produce cholera toxin and do not cause epidemic disease.

- Cholera is spread by **contaminated water and food** rather than direct person-to-person spread, because a **high inoculum** (e.g., $>10^8$ organisms) is required to establish infection in a person with normal gastric acidity.

- Cholera is usually seen in communities with **poor sanitation. Immunoassays** for the detection of cholera toxin or the O1 and O139 lipopolysaccharides are used for the diagnosis of cholera in endemic areas.

- It is estimated that **3 to 5 million cases** of cholera and 120,000 deaths occur worldwide **each year**. Seven major pandemics of cholera have occurred since 1817, resulting in thousands of deaths and major socioeconomic changes.

Countries reporting cholera, 2010–2015

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: World Health Organization
Map Production: Information Evidence and Research (IER)
World Health Organization

World Health Organization

Vibrio

- The majority of individuals exposed to toxigenic ***V. cholerae* O1** have asymptomatic infections or self-limited diarrhea; however, some individuals develop severe, rapidly fatal diarrhea. *V. cholerae* O1 does not produce a capsule, so infections with this organism do not spread beyond the confines of the intestine.

- The clinical manifestations of cholera begin an average of 2 to 3 days after ingestion of the bacteria (can be <12 hours), with the abrupt onset of watery diarrhea and vomiting. Fever is rare.

- The feces-streaked stool specimens become colorless and odorless, free of protein, and speckled with mucus **("rice-water" stools).**

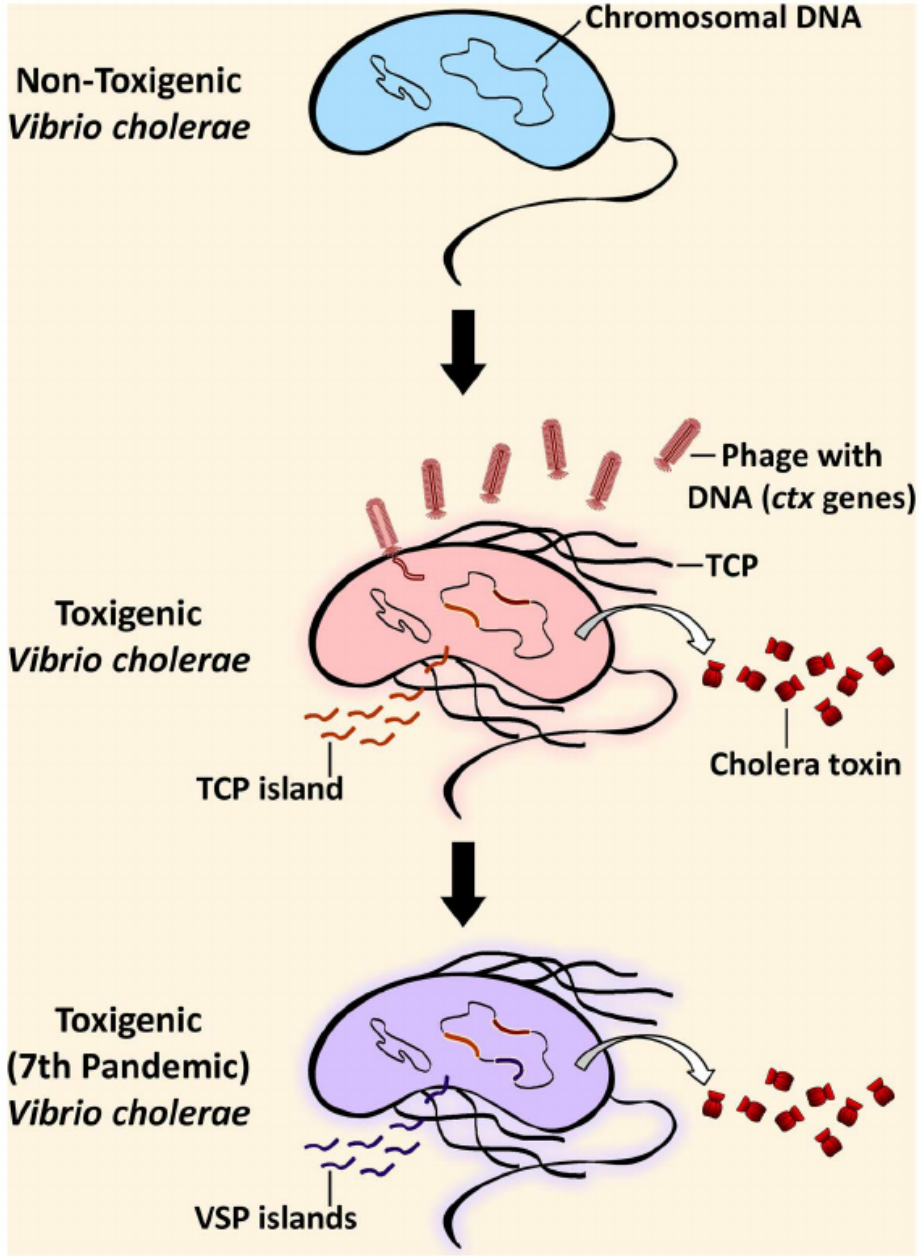
- Patients with cholera must be promptly treated with **fluid and electrolyte replacement** before the resultant massive fluid loss leads to hypovolemic shock.

Species	Virulence Factor	Biological Effect
V. cholerae	Cholera toxin	Hypersecretion of electrolytes and water
	Toxin co-regulated pilus	Surface binding site receptor for bacteriophage CTXΦ; mediates bacterial adherence to intestinal mucosal cells
	Chemotaxis protein	Adhesin factor
	Accessory cholera enterotoxin	Increases intestinal fluid secretion
	Zonula occludens toxin	Increases intestinal permeability
	Neuraminidase	Modifies cell surface to increase GM_1 binding sites for cholera toxin

Vibrio cholera

- Virulence of *V. cholerae* involved acquisition of first a sequence of genes including the **toxin co-regulated pilus (TCP)** on what is termed the **vibrio pathogenicity island (VPI-1),** followed by infection with the **bacteriophage CTXΦ** that encodes the genes for the two subunits of **cholera toxin** (*ctxA* and *ctxB*).

- TCP serves as the cell surface receptor for the bacteriophage, permitting it to move into the bacterial cell, where it becomes integrated into the *V. cholerae* genome.

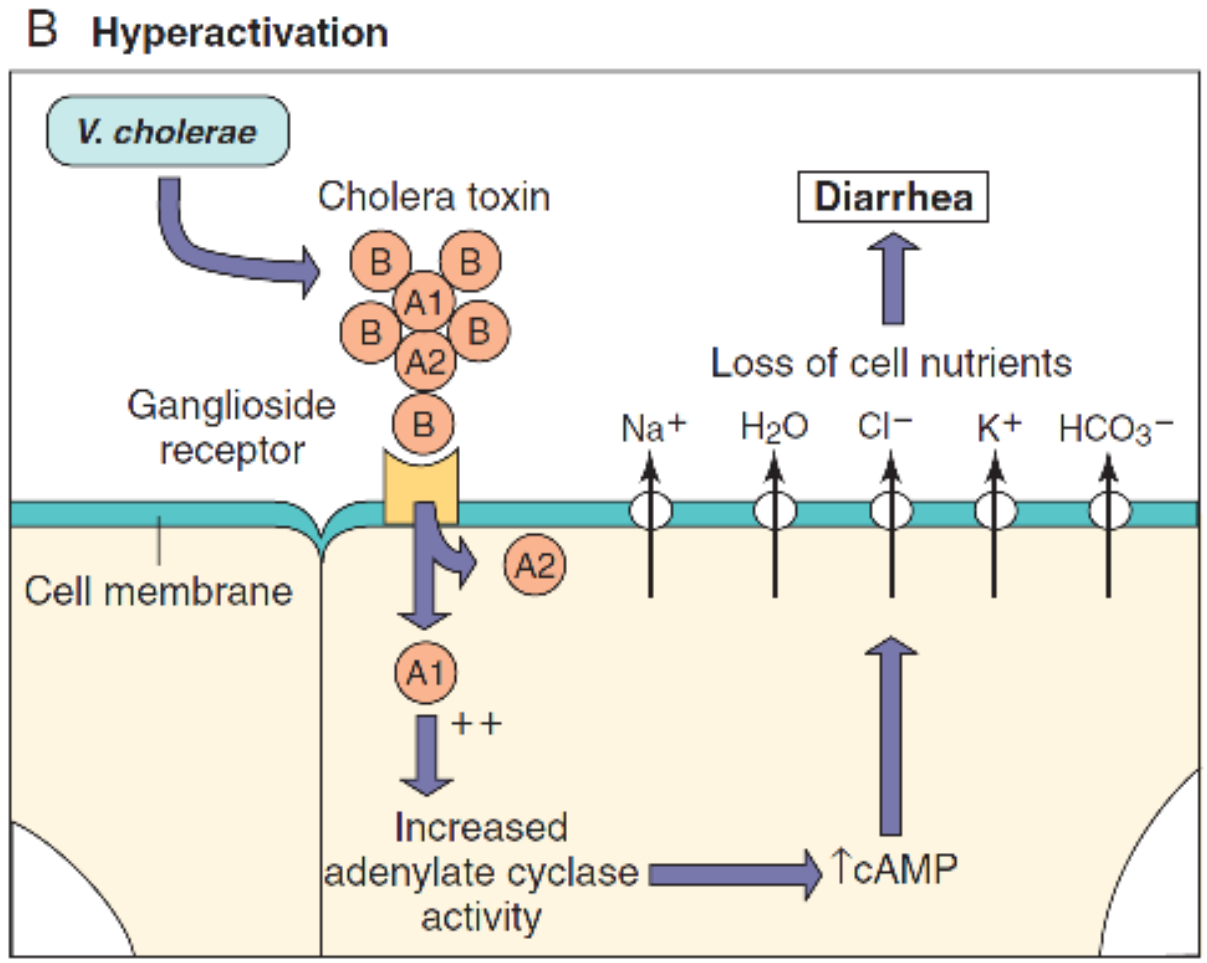


Vibrio cholera

- The cholera toxin is a **complex A-B toxin.** The active portion of the A subunit is internalized and interacts with G proteins that control adenylate cyclase, leading to the catabolic conversion of adenosine triphosphate (ATP) to cyclic adenosine monophosphate (cAMP). This results in a hypersecretion of water and electrolytes.

- The resulting severe fluid and electrolyte loss can lead to dehydration, painful muscle cramps, metabolic acidosis (bicarbonate loss), and hypokalemia and hypovolemic shock (potassium loss), with cardiac arrhythmia and renal failure.

- The mortality rate is as high as 70% in untreated patients but less than 1% in patients who are promptly treated with replacement of lost fluids and electrolytes

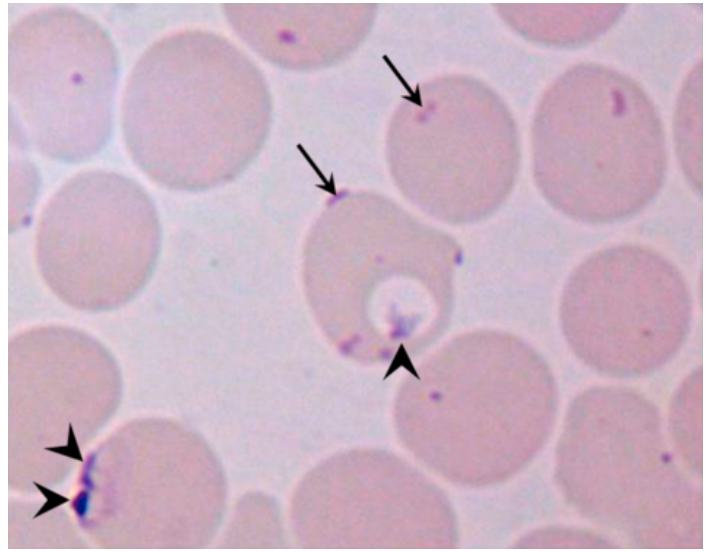


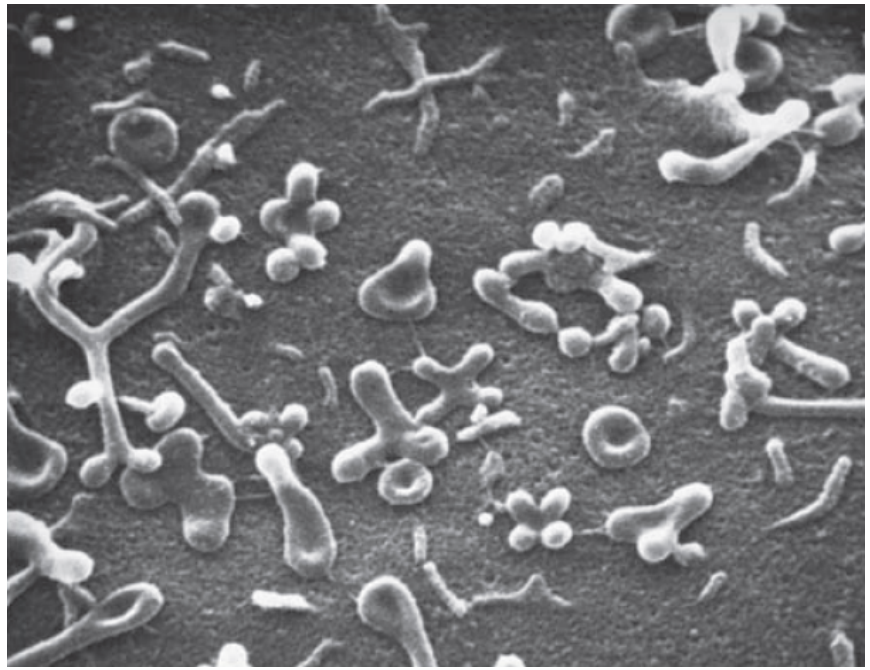
Mycoplasma

- *Mycoplasma* and *Ureaplasma* organisms are the **smallest free-living bacteria.** They are unique among bacteria because they **do not have a cell wall** and their cell membrane contains **sterols.**

- The mycoplasmas form **pleomorphic shapes** varying from 0.2 to 0.3 µm coccoid forms to rods 0.1 to 0.2 µm in width and 1 to 2 µm long.

- ***M. pneumoniae*** is a **strict human pathogen**.





Mycoplasma

- **Respiratory disease** (e.g., tracheobronchitis, pneumonia) caused by *M. pneumoniae* occurs worldwide throughout the year.

- Exposure to ***M. pneumoniae*** typically results in **asymptomatic carriage.** The most common clinical presentation of *M. pneumoniae* infection is **tracheobronchitis.**

- Pneumonia (referred to as primary **atypical pneumonia** can also develop, with a patchy bronchopneumonia seen on chest radiographs.

- ***M. genitalium*** can cause **nongonococcal urethritis** (NGU) and **pelvic inflammatory disease**.

Organism	Site	Human Disease
Mycoplasma pneumoniae	Respiratory tract	Tracheobronchitis, pharyngitis, pneumonia, secondary complications (neurologic, pericarditis, hemolytic anemia, arthritis, mucocutaneous lesions)
Mycoplasma genitalium	Genitourinary tract	Nongonococcal urethritis, pelvic inflammatory disease

Mycoplasma

- **Microscopy** is of **no diagnostic value** because mycoplasmas stain poorly with the Gram stain. Likewise, antigen tests have poor sensitivity and specificity and are not recommended.

- The most sensitive diagnostic tests are **PCR amplification** tests of species-specific gene targets.

- Absence of the cell wall renders the mycoplasmas resistant to penicillins, cephalosporins, vancomycin, and other antibiotics that interfere with synthesis of the cell wall.

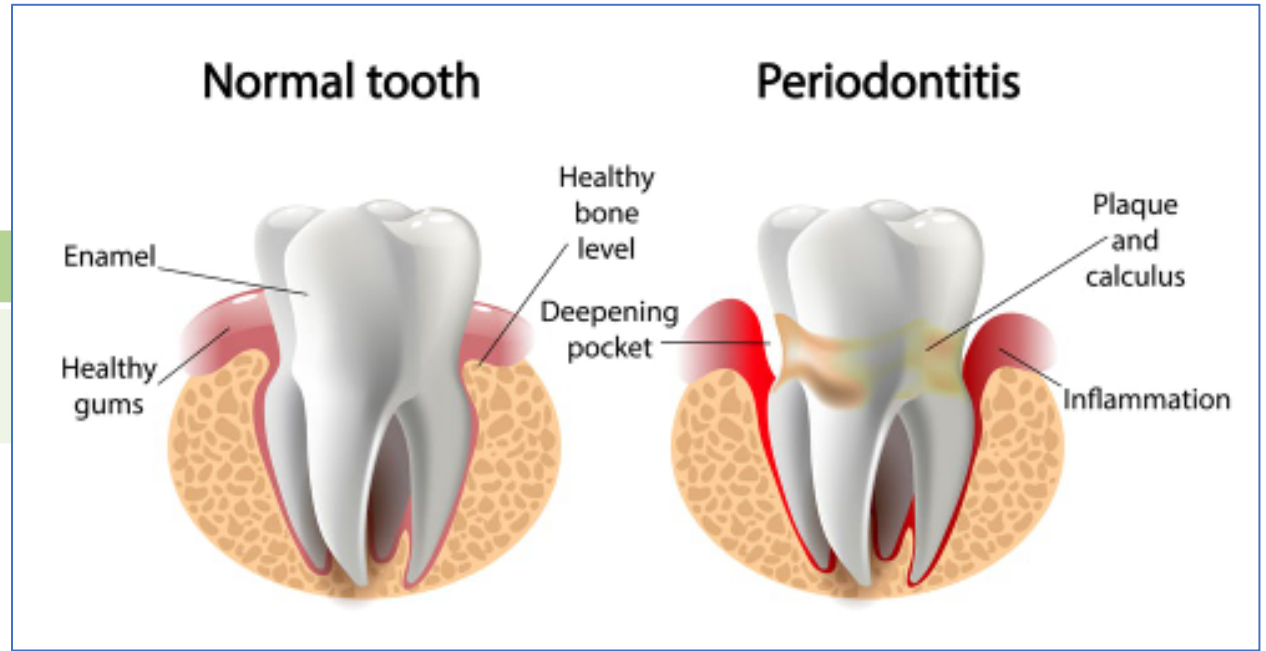
Aggregatibacter

- Two members of this genus are important human pathogens: ***A. actinomycetemcomitans*** and ***A. aphrophilus***

- ***A. actinomycetemcomitans*** is a Gram-negative, facultative anaerobe, non-motile bacterium that is often found in association with localized aggressive periodontitis

- Both species colonize the human mouth and can spread from the mouth into the blood and then stick to a previously damaged heart valve or artificial valve, leading to the development of **endocarditis**.

Species	Primary Diseases	Frequency
A. actinomycetemcomitans	Periodontitis, endocarditis, bite wound infections	Common



Further reading:

- Murray - Medical Microbiology 8th Edition
  Section 4: Bacteriology
    Chapter 26:
    Chapter 28:
    Chapter 33: