Vibrios

The vibrios are **Rapidly motile curved rods,** are found in seawater (**marine and surface waters**) All *Vibrio* species are able to survive and replicate in contaminated waters with increased **salinity** and among the most common bacteria to be found there.
Pathogenic vibrios can also **flourish** in **waters with chitinous shellfish** (e.g., oysters, clams, mussels)—hence the association between *Vibrio* infections and the consumption of shellfish. Asymptomatically infected humans can also be an important reservoir for this organism in areas where *V. cholerae* disease is endemic.

Currently the genus is composed of more than 200 species of **curved rods.** Three species are particularly **important human pathogens *Vibrio cholerae, Vibrio parahaemolyticus,*** and ***Vibrio vulnificus.***

-*V. cholerae* O1 and O139 produce **cholera toxin** and are associated with **epidemics of cholera**. **Other strains of *V. cholerae (Non-* O1 and O139 *V. cholerae) generally* do not produce cholera toxin** and do not cause epidemic disease.
V. cholerae serogroup **O1 is further subdivided** into serotypes **(Inaba, Ogawa,** and **Hikojima)** and biotypes **(Classical** and **El Tor).**
V. cholerae O1 does not produce a capsule, so infections with this organism do not spread beyond the confines of the intestine.

-Vibrio parahaemolyticus, Non- O1, O139 Vibrio causes **acute gastroenteritis** after ingestion of contaminated **seafood** such as raw fish or shellfish. It is **the most common cause of Sea-foodborne acute gastroenteritis.**

-V vulnificus a cause of severe sepsis in patients with cirrhosis and primary wound infection (Vulnificus is Latin for "wound maker." *V. vulnificus* and non-O1 *V. cholerae* produce acidic **polysaccharide capsules** that are important for disseminated infections.

Morphology

-Gram stain of Vibrio cholerae Often, they are **comma shaped or slightly curved.** Most vibrios have **polar flagella** (important for motility) as well as various pili that are important for virulence (e.g., **toxin co-regulated pilus** in epidemic strains of *V. cholera*). The cell wall structure of vibrios is also important. 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:** There are more than 200 serogroups of *V. cholerae* plus multiple serogroups of *V. vulnificus* and *V. parahaemolyticus.*

-Vibrio cholerae has a low tolerance for acid, but grows under alkaline (pH 8.0-9.5) conditions that inhibit many other Gram-negative bacteria. So, in areas where cholera is endemic, direct cultures of stool on selective media, such as **TCBS**, and enrichment cultures in alkaline peptone water are appropriate.

Colonies of Vibrio cholerae growing on thiosulfate, citrate, bile salts, and sucrose agar. **The glistening yellow colonies** are 2–3 mm in diameter and are surrounded by a **diffuse yellowing of the indicator in the agar up to 1 cm in diameter**.

-Vibrios are **oxidase positive**, which differentiates them from **enteric gram-negative bacteria**.
-O/129 is a pteridine derivative that shows protective effects in mice infected with Vibrio cholerae. which differentiates them from Aeromonas species, which are resistant to O/129.
-Halotolerance is the adaptation of living organisms to conditions of high salinity.
-Another difference **between vibrios and aeromonas is that vibrios grow on media containing 6% NaCl.**

Pathogenesis

-In the final analysis, **cholera is a toxin-mediated disease** by the elaboration of a heat-labile enterotoxin that has **the classic A-B toxin structure**. The B segment binds to GM1 ganglioside receptors, and the active A subunit induces **cAMP**, causing secretion of sodium chloride while at the same time preventing the reabsorption by the microvilli.
Cholera enterotoxin is antigenically related to LT of Escherichia coli ETEC and can stimulate the production of neutralizing antibodies.

-A large inoculum is needed to establish infection depending if you ingest or drink Any medication or condition that decreases stomach acidity makes a person more susceptible to infection with V cholerae.
Cholera is not an invasive infection. The toxin-coregulated pilus (**TCP**), is **essentia**l for V. cholerae to survive and multiply in **(colonize) the small intestine**.
There they **multiply and liberate cholera toxin** and perhaps mucinases and endotoxin.

Clinically

-In many instances, **only 1–5% of exposed susceptible persons develop disease.** The carrier state seldom **exceeds 3–4 weeks**, and the importance of carriers in transmission is unclear.
Vibrio survive in water for up to 3 weeks.
-Most infection are asymptomatic and **the burden of disease is often greatest during "cholera seasons"** associated with **high temperatures, heavy rainfall, and flooding, Wars and earthquakes but cholera can occur year-round.**

-Cholera is the most dramatic diarrhea disease .1L/h--as much as 20–30 L/day—with resulting dehydration, shock, acidosis, and death characterized by Rice water stool with floating mucus and gray watery appearance.
-The mortality rate without treatment is between 25% and 50%.

Diagnosis

-The initial suspicion of cholera depends on recognition of the typical clinical features in an appropriate epidemiologic setting.
-A bacteriologic diagnosis is accomplished by isolation of V cholerae from the stool.

For enrichment, a few drops of stool can be incubated for 6–8 hours in taurocholate peptone broth (pH, 8.0–9.0); organisms from this culture can be stained or subcultured **by a selective medium (thiosulfate– citrate–bile salt–sucrose agar)**. Once isolated, the organism is readily identified by biochemical reactions.

-The diagnosis of cholera under field conditions has been reported to be facilitated by a sensitive and **specific immuno-chromatographic dipstick test.**

Treatment

In light of the level of dehydration and the patient's age and weight, euvolemia should first be rapidly restored, and adequate hydration should then be maintained to replace ongoing fluid losses
Antibiotics play a secondary role in cholera patient management, tetracyclines are drug of choice, Erythromycins are alternatives for pregnant and child patients.

Prevention &Control

-Improvement of sanitation, particularly of food and water. Patients should be isolated, their excreta disinfected, and contacts followed up.

-Repeated injection of a **vaccine** containing either lipopolysaccharides extracted from vibrios or dense Vibrio suspensions **can confer limited protection** to heavily exposed persons (eg, family contacts) but is not effective as an epidemic control measure.
The oral vaccines are generally of two forms: **inactivated (Killed) and attenuated.**

- killed cholera vaccines have been prequalified by the WHO and are available internationally:
- WC-rBS (Dukoral.; Crucell, Stockholm, Sweden) contains several biotypes and serotypes of V. cholerae O1 supplemented **with** recombinant **cholera toxin B subunit.**
- BivWC (Shanchol™; Shantha Biotechnics–Sanofi Pasteur, Mumbai, India) contains several biotypes and serotypes of V. cholerae O1 and V. cholerae O139 **without** supplemental **cholera toxin B subunit**.

- **A live, attenuated oral vaccine (CVD 103-HgR or Vaxchora), derived from a serogroup O1 classical Inaba strain, was approved by the US FDA in 2016**

CAMPYLOBACTER

Campylobacter Greek for "**curved rod**". Originally known as Vibrio fetus These species are currently divided into three genera: Campylobacter, Arcobacter, and Helicobacter.
Campylobacter enteritis resembles other acute bacterial diarrheas, particularly shigella dysentery.
- Oxidase-positive

-Campylobacter jejuni , and Campylobacter Coli are the prototype organism in this group and are a very common cause of diarrhea in humans. **C jejuni and C coli cause infections that are clinically indistinguishable, and laboratories generally do not differentiate between the two species.**
- **The most common cause of bacterial enteritis in the developed world.**

-Campylobacter fetus has two subspecies, **fetus and venerealis causes systemic infections in immunocompromised patients. It may occasionally cause diarrhea.** Campylobacter lari - seagulls Campylobacter upsaliensis from dogs
- C fetus is not a thermophilic organism and has been primarily recovered from the blood and other extraintestinal sites of immunocompromised patients.
-Note that Helicobacter cinaedi, and Helicobacter fennelliae are part of the Campylobacter genus can cause diarrheal diseases but mainly cause bacteremia and cellulitis.

-The source of infection may be food (eg, milk, undercooked fowl) or contact with infected animals or humans and their excreta. Outbreaks arising from a common source, eg, unpasteurized milk, may require public health control measures. The bacterium's main natural reservoir is poultry
-In many developing countries, C. jejuni infections are hyperendemic, with the highest rates among children <2 years old. **Infection rates fall with age, as does the illness-to-infection ratio. These observations suggest that frequent exposure to C. jejuni leads to the acquisition of immunity.**

Morphology

-Gram stain of Campylobacter jejuni showing "comma"- or "gull wing"–shaped gram-negative bacilli.
-Campylobacter jejuni and other thermophilic campylobacters grow well at 42°C in a microaerophilic environment of 5% oxygen and 10% CO_2.
-Campylobacters do not oxidize or ferment carbohydrates.
-The inoculum is similar to that required for Salmonella and Shigella infection but less than that for Vibrio infection.

Pathogenesis

The organisms multiply in the small intestine, invade the epithelium, and produce inflammation that results in the appearance of red and white blood cells in the stools. (although they have been described and include classic enterotoxins, cytolethal distending toxin, or CDT) appear **not to play substantial roles** in tissue injury or disease production.
-Intracellular movement is associated with microtubules.
-Reiter's syndrome with the classic triad of conjunctivitis, urethritis, and arthritis may be occurring after an infection.
- Guillain-Barré syndrome (acute demyelinating neuropathy) may follow infection, Anti-LOS antibodies cross-react with neural gangliosides.(30% of the GBS in the U.S. Serotype O:19, antigenic cross-reactivity between Campylobacter oligosaccharides and glycosphingolipids on neural tissues)

Clinically

-The illness typically begins 1 to 7 days after ingestion, with fever and lower abdominal pain that may be severe enough to mimic acute appendicitis. These are followed within hours by dysenteric stools that usually contain blood and pus. The illness is typically self-limiting after 3 to 5 days but may last 1 to 2 weeks.
-Invasion may lead to Local suppurative complications of infection include cholecystitis, pancreatitis, and cystitis; distant complications include meningitis, endocarditis, arthritis, peritonitis, cellulitis, and septic abortion. All these complications are rare, **except in immunocompromised hosts.**

Diagnosis

-Campylobacters are thin and not easily seen when specimens are Gram stained. Despite the low sensitivity of a Gram stain, observation of the characteristic **thin, S-shaped organisms** in a stool specimen showing the typical **darting motility** is diagnostic.
-*C. jejuni, C. coli,* their isolation requires growth in a **microaerophilic atmosphere** (i.e., 5% to 7% oxygen, 5% to 10% carbon dioxide), at an **elevated incubation temperature** (i.e., 42° C), and on **selective agar media** to suppress nonpathogenic enteric bacteria. (**Skirrow's, Butzler's, Blaser's, Campy-BAP and Preston media**)
-A commercial immunoassay for detection of *C. jejuni* and *C. coli* is available

Treatment

-*Campylobacter* gastroenteritis **is typically a self-limited infection** managed by the replacement of lost fluids and electrolytes.
-Even among patients presenting for medical attention with Campylobacter enteritis, not all clearly benefit from specific antimicrobial therapy but the regimen of choice is Macrolides and fluoroquinolones. Antibiotic therapy may be used in **patients with severe**

infections or septicemia. **Erythromycin** or **azithromycin** are the antibiotics of choice for the treatment of enteritis

Prevention & control

-Exposure to enteric campylobacters is prevented by proper food preparation (particularly poultry), avoidance of unpasteurized dairy products, and implementation of safeguards to prevent contamination of water supplies.
-No vaccines

Helicobacter Pylori

-Helicobacter species are also curved or spiral-shaped gram-negative rod.
All gastric helicobacters, including *H. pylori,* are highly **motile** (corkscrew motility) and produce an abundance of **urease.**
-Oxidase positive
-H pylori are associated with upper gastrointestinal diseases such as gastric and duodenal ulcers, gastric adenocarcinoma, and MALT lymphomas. (Now classed by WHO as type I carcinogen)
-H. cinaedi and H. fennelliae, are intestinal rather than gastric organisms; in terms of the clinical features of the illnesses they cause, these species most closely resemble Campylobacter rather than Helicobacter pylori.
-The organism is urease positive, which protects it against gastric acidity.
-*H. pylori* is a remarkable bacterium in its ability to establish lifelong colonization in the stomach of untreated humans.
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.**

Pathogenesis

-Initial colonization is facilitated by blockage of acid production by a **bacterial acid–inhibitory protein** and neutralization of gastric acids with the ammonia **produced by bacterial urease activity.**
-motile helicobacters can then pass through the gastric mucus and adhere to the gastric epithelial cells by multiple surface adhesion proteins.On contrast to the lumen side of the mucus (pH is low (1.0–2.0)) the epithelial side, (the pH is about 7.4).
-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**. Another important virulence factor of *H. pylori* is the **cytotoxin-associated gene *(cagA)*** that resides on a **pathogenicity island**. **These genes encode a structure (type VI secretion system)**

H. pylori is associated with gastritis,. Colonization with *H. pylori* invariably leads to histologic evidence of **gastritis** (i.e**., infiltration of neutrophils and mononuclear cells into the gastric mucosa**). **The acute phase of gastritis is characterized by a feeling of fullness, nausea, vomiting, and hypochlorhydria (decreased acid production in the stomach).**
This can evolve into chronic gastritis, with disease confined to the gastric antrum (where few acid-secreting parietal cells are present) in individuals with normal acid secretion, or involve the entire stomach (pangastritis) if acid secretion is suppressed.
H. pylori is responsible for 85% of the gastric ulcers and 95% of the duodenal ulcers.
C**hronic gastritis eventually leads to replacement of the normal gastric mucosa with fibrosis and proliferation of intestinal-type epithelium. This process increases the patient's risk for gastric cancer by almost 100-fold.**

-increasing evidence indicates that lifelong H. pylori colonization may offer some protection against complications of gastroesophageal reflux disease (GERD), including esophageal adenocarcinoma.

Diagnosis

-H. pylori is detected by histologic examination of gastric biopsy specimens which can show the **curved or spiral-shaped organisms**. The microscopic examination of stool specimens for helicobacters is not reliable, because the organisms are difficult to see and nonpathogenic helicobacters may be present.

-Culture can be used as well However, diagnosis of H. pylori infections is most commonly by **noninvasive methods** (e.g. Urea breath test, immunoassays), with culture reserved for antibiotic susceptibility tests.
- Urea breath test : Patients swallow urea labelled with an uncommon isotope, either radioactive carbon-14 or non-radioactive carbon-13. In the subsequent 10–30 minutes, the detection of isotope-labelled carbon dioxide in exhaled breath indicates that the urea was split; this indicates that urease (the enzyme that H. pylori uses to metabolize urea) is present in the stomach, and hence that H. pylori bacteria are present.
-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
-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.

Treatment

-The greatest success in curing gastritis or peptic ulcer disease has been accomplished with the combination of a **proton pump inhibitor** (e.g., omeprazole), a **macrolide** (e.g., clarithromycin), and a **β-lactam** (e.g., amoxicillin), with administration for 7 to 10 days initially.
- Quadruple therapy is used in areas where clarithromycin resistance is ≥15%, e.g., PPI + bismuth + 2 antibiotics (metronidazole + tetracycline).