**Campylobacter**

**Helicobacter**

**Arcobacter**

**General**
- Gram-negative
- Short, curved (comma shaped), spiral or S forms ➔ May turn coccoid in old cultures
- Oxidase +
- Urease negative
cf. *Helicobacter* – mostly urease positive
- Microaerophilic (3% - 15% O₂)
- Slow growing (2 – 6 days)
- Formerly in the genus *Vibrio* ➔ Still called “vibriosis” by many

**Difference from Vibrio**
- Vibrio: monotrichous flagella
- Campylobacter: amphitrichous flagella

**Difference from Vibrio**
- Glucose fermentation
  - Vibrio: Glucose (+)
  - Campylobacter: Glucose (−) (lack of phosphofructokinase)
**Campylobacter & Diseases**

- **Reproductive Diseases**
- **Gastrointestinal Diseases**

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**C. fetus subsp. venerealis**

- Obligate parasite of the genitalia of male and female cattle
  - The male is an asymptomatic carrier
- **Disease:** early embryonic death & occasional abortions in cattle
- **Pathogenesis**
  - Colonize the prepuce of bulls
    - Transmitted venereally
  - Localizes in the anterior vagina and cervix
    - Then invade the uterus and oviducts (ascending infection)
  - Infertility and occasional abortions
- **Diagnosis**
  - Culture: possible but difficult
  - Direct exam of fetal membranes: with darkfield microscopy
- **Vaccination:** killed-vaccines are effective

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**C. fetus subsp. fetus**

- Formerly *C. intestinalis*
- **Habitat:** Intestinal tract and reproductive tract of sheep and cattle
- **Transmission:** by "ingestion" of contaminated food or water
  - Not "venereally"
- **Disease**
  - Colonize host's intestines
    - A transient bacteremia
    - Spread to the placentas of pregnant animals
    - Placentitis and abortions
  - Cause of abortion in sheep and occasionally cattle
    - But does not cause infertility
- **Treatment**
  - Susceptible to some antibiotics (tetracycline)
  - Probably best to try controlling with vaccination

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**C. fetus: S-layer**

- S-layer (Surface layer)
  - Located external to bacterial outer membrane
  - Consisting of proteins
- **Possessed by two Campylobacter species:** *C. fetus & C. rectus*
- **Roles in pathogenesis**
  - Resistance to serum
  - Resistance to phagocytosis
  - Important for colonization and translocation to the placenta

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**Summary of C. fetus**

<table>
<thead>
<tr>
<th>Species</th>
<th>Host(s)</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. fetus ssp. venerealis</td>
<td>Cattle</td>
<td>Bovine genital campylobacteriosis, infertility, early embryonic death, Occasional abortions</td>
</tr>
<tr>
<td>C. fetus ssp. fetus</td>
<td>Sheep/Cattle</td>
<td>Ovine genital campylobacteriosis, abortions Sporadic abortions</td>
</tr>
</tbody>
</table>

**Story of C. fetus**

- *C. fetus ssp. fetus*
  - Oral ingestion
  - Fecal-oral
  - Ovine genital campylobacteriosis - abortion

- *C. fetus ssp. venerealis*
  - Venereal transmission
  - Bovine genital campylobacteriosis - infertility - occasional abortion

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**C. jejuni and C. coli**

- **Habitat**: Intestinal tract of various wild and domestic animals including poultry, cattle, pigs, cats, and dogs
- **Reservoir**: *C. jejuni* – chicken  
  *C. coli* – turkey and pigs
- **Transmission**: Oral ingestion
- **Disease in humans**
  - Enteritis: "C. jejuni" is major (92–95%)
  - *C. jejuni ssp. jejuni & C. jejuni ssp. doylei*
  - A major cause of human gastroenteritis worldwide  
    annually 0.6 M (Canada) and 400-500 M (worldwide)
  - A primary cause of Guillain-Barré syndrome
- **Disease in animals**
  - Often found in fecal samples from dogs and cats with diarrhea
  - *C. jejuni*: sheep abortion
- **Treatment**: Susceptible to some antibiotics (macrolides)

**Human infection by C. jejuni**

- Enteritis: "C. jejuni" is major (92–95%)
- *C. jejuni ssp. jejuni & C. jejuni ssp. doylei*
- A major cause of human gastroenteritis worldwide  
  annually 0.6 M (Canada) and 400-500 M (worldwide)
- A primary cause of Guillain-Barré syndrome
- Often found in fecal samples from dogs and cats with diarrhea
- *C. jejuni*: sheep abortion
- Susceptible to some antibiotics (macrolides)
Guillain-Barré syndrome

- An acute autoimmune disease causing muscular paralysis
- Molecular similarity between *C. jejuni* LOS and human ganglioside

Ovine abortion by *C. jejuni*

- *C. fetus* was the major cause of ovine abortion
- Ovine abortion caused by *C. jejuni* is increasing
- An identical single clone has been isolated, causing sheep abortions in several states in the US
- Tet resistant

Other Campylobacter species

- *C. concisus*
  - implicated in human gastrointestinal diseases

- *C. upsaliensis*
  - isolated from feces of dogs and cats with diarrhea
  - associated with human enteric disease

Phenotype Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th><em>C. fetus</em> ssp. fetus</th>
<th><em>C. jejuni</em> ssp. venerealis</th>
<th><em>C. coli</em> ssp. fetus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxidase</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Catalase</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Urease</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nitrate reductase</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>A,5 from TisA</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Growth at 25°C</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Growth at 42°C</td>
<td>(-)</td>
<td>(+)</td>
<td>+</td>
</tr>
<tr>
<td>Growth in 1% glycine</td>
<td>+</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Growth in 3.5% NaCl</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Hippurate hydrolysis</td>
<td>+</td>
<td>(+)</td>
<td>+</td>
</tr>
<tr>
<td>Nalidixic acid sensitivity</td>
<td>R</td>
<td>R</td>
<td>(S)</td>
</tr>
<tr>
<td>Cephalosporin sensitivity</td>
<td>S</td>
<td>S</td>
<td>R</td>
</tr>
<tr>
<td>Acyl acetate production</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
**Hippurate test**

- Important test to identify *Campylobacter* infecting humans (*C. jejuni*)
- Hippurate – (hippuricase) $\rightarrow$ glycine + benzoic acid

**General**

- Gram-negative
- Formerly considered as *Campylobacter*
- Microaerophilic
- Helical and curved rod
  -> As culture gets old, forms coccoid shapes
- Motile via 2 to 6 unipolar flagella

**Discovery**

- Marshall and Warren, 1982
  - Described a spiral or curved bacilli in 60% of biopsy specimens (histology, microscopic)
  - Microaerophilic, Gram-negative, *Campylobacter*-like
- In order to verify the virulent nature, Warren drank the culture!
  -> Developed acute gastritis
  -> Proved gastritis is caused by infection

Robin Warren  Barry Marshall  Nobel Prize 2005
Helicobacter Species & Disease

- **Disease**: Gastritis, gastric cancer, hepatic cancer
- **High level of organ specificity**: subdividing into two lineages
  1. Gastric *Helicobacter* species
  2. Enterohepatic (nongastric) *Helicobacter* species

Selected *Helicobacter* Species

<table>
<thead>
<tr>
<th>Gastric <em>Helicobacter</em> spp.</th>
<th>Human, primate</th>
<th>Gastritis, peptic ulcer disease, gastric adenocarcinoma, MALT lymphoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>H. pylori</em></td>
<td>Cat, dog, mouse</td>
<td>Gastritis in natural host; may cause peptic ulcers or gastric adenocarcinoma in mouse</td>
</tr>
<tr>
<td><em>H. felis</em></td>
<td>Ferret</td>
<td>Gastritis, peptic ulcer disease, gastric adenocarcinoma, MALT lymphoma</td>
</tr>
<tr>
<td><em>H. mustelae</em></td>
<td>Ferret</td>
<td>Gastritis, peptic ulcer disease, gastric adenocarcinoma, MALT lymphoma</td>
</tr>
<tr>
<td><em>H. acinonychis</em></td>
<td>Cheetah, tiger, other big cats</td>
<td>Gastritis, peptic ulcer disease</td>
</tr>
<tr>
<td><em>H. heilmannii</em></td>
<td>Human, dog, cat, monkey, cheetah, rat</td>
<td>Gastritis, dyspeptic symptoms, MALT lymphoma</td>
</tr>
</tbody>
</table>

Enterohepatic *Helicobacter* spp.

| *H. hepaticus* | Mouse, other rodents | Hepatitis, hepatocellular carcinoma |

H. pylori

- **Habitat**: unknown, perhaps carried by humans
- **Disease**
  - 50% of world’s population infected
  - Acute or chronic gastritis
  - 90-95% of people with duodenal ulcers
  - 70-90% with gastric ulcers infected with *H. pylori*
  - Gastric cancer (classified as a “carcinogen”)
- **Pathogenesis**
  - Survive in the deeper layers of mucus
  - Virulence factors: Urease, CagA, VacA
- **Treatment**: antibiotic cocktails
  - Metronidazole, amoxicillin, tetracycline or clarithromycin in combination with a proton pump inhibitor
Detection

- **Bacterial Culture**
  - Brucella or Columbia agar supplemented with antibiotics (Trimethoprim, Vancomycin, Polymyxin B)

- **Biopsy**
  - Isolation or observance of bacteria in endoscopy biopsy specimens
  - Invasive, false negatives (stomach is huge)

- **Urea Breath Test**
  - Uses $^{13}$C or $^{14}$C to test for urease enzyme
  - $(NH_2)_2C*O + H_2O \rightarrow 2NH_3 + C*O_2$
  - Non-invasive

Campylobacter

Helicobacter

Arcobacter

General

- Gram-negative, curved to spiral shaped

- Optimal growth under microaerobic
  - "Aerotolerant" → Grows aerobically

- Grow at 15-30 °C, not at 4 °C

- Difference from *Campylobacter*

<table>
<thead>
<tr>
<th>Arcobacter</th>
<th>Campylobacter</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen</td>
<td>Aerotolerant</td>
</tr>
<tr>
<td>Optimal Growth Temperature</td>
<td>Low (25-30 °C)</td>
</tr>
</tbody>
</table>

General

- Energy is obtained from amino acids and TCA cycle intermediates, not carbohydrates

- Various habitats:
  - Reproductive organs
  - Aborted fetuses of various animals
  - Intestinal tract of animals and humans

- **A. cryaerophilus**
  - Abortion in swine, cattle, horses, sheep, and dogs

- **A. butzleri**
  - Causes diarrhea, nausea, vomiting and fever in humans

- **A. skirrowii**
  - Isolated from cases of diarrhea in humans, lambs, and calves