*CAMPYLOBACTER JEJUNI &*
**RELATED ORGANISMS**

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**PHR 250**
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## Taxonomy made simple (?)

**"The Great Unknown"**

↓

**genus *Vibrio*** → (restricted)

↓

**genus *Campylobacter***

↓ ↘

**genus *Arcobacter*** **genus *Helicobacter***

## Historical aspects: the *Vibrio* days

- McFadyean & Stockman, British veterinarians, epizootic abortion in ewes (1909)
- Theobald Smith, investigating infectious abortions of U.S. cattle (1919): *Vibrio fetus*

## Historical aspects: the *Vibrio* days (2)

- Jones, Little, & Orcutt, winter dysentery in U.S. calves (1931): *Vibrio jejuni*
- Doyle, swine dysentery (1944)

## Historical aspects: the *Vibrio* days (3)

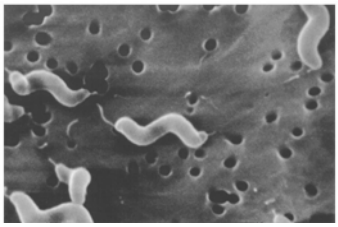
- Humans:
  - acute milkborne diarrhea, *Vibrio jejuni* (Levy, 1946)
  - abortion in two women, *Vibrio fetus* (Vinzent, 1947)
- King (1957): *Vibrio fetus* differentiated from "related vibrios"

## Historical aspects: the new genus

- Sebald and Veron (1963): differentiation from cholera and halophilic vibrios → genus ***Campylobacter*** ("curved rod")
- *C. jejuni* (+ *C. coli*) perhaps foremost bacterial causes of diarrhea in humans; a classical zoonosis—pathogen or commensal in animals

## *Campylobacter* species

- *C. coli*
- *C. concisus*
- *C. curvus*
- *C. fetus*
- *C. gracilis*
- *C. helviticus*
- *C. hominis*
- *C. hyointestinalis*
- *C. insulaenigrae*
- *C. jejuni*
- *C. lanienae*
- *C. lari*
- *C. mucosalis*
- *C. retus*
- *C. showae*
- *C. sputorum*
- *C. upsaliensis*



Scanning electron microscope image of *Campylobacter jejuni*, illustrating its corkscrew appearance and bipolar flagella (Altekruse S, 1999).

## *Background*

- **3 *Campylobacter* species account for 99% of human illnesses: *C. jejuni*, *C. coli*, and *C. lari***
- ***Campylobacter* species isolated from the intestinal tract of a wide variety of wild and domestic animals especially chicken, cattle, and pig (asymptomatic infection)**

## *Campylobacter*: present situation


- **Most commonly reported cause of bacterial gastroenteritis in the developed world, with ~2.5 million cases per year in the U.S.**
- **Foodborne outbreaks mostly associated with consumption of undercooked poultry, meats, and unpasteurized milk**

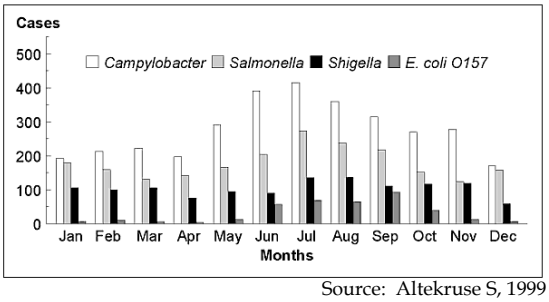
## *Campylobacter*: present situation

- U.S., 1998–2002: *Campylobacter* spp., 61 outbreaks comprising 1,440 cases (ranked #7); leader in CA FoodNet (Bay Area)
- Largest outbreak documented in the U.S. ~3,000 cases, water (city)
- Largest milkborne outbreak in U.S., ~1,600 cases, California 2006

## *Campylobacter*: present situation (2)

- CAST (1994) estimates: 170,000 to 2,100,000 cases/yr , 120–360 deaths—presumably all foodborne; average medical and productivity cost/case $920, annual total near $1 billion

## *Cases of Campylobacter and other foodborne infections by month*




Source: Altekruse S, 1999

## *Incidence (/100,000) of Diagnosed Infections, 2002 (source: FoodNet, CDC)*

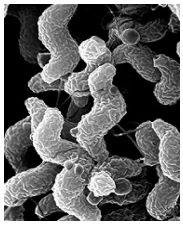
| Pathogen | All Sites | CA FN | Alameda | Contra Costa | SF |
|---|---|---|---|---|---|
| *Campylobacter* | 13.3 | 31.5 | 26.3 | 24.9 | 48.2 |
| *Cryptosporidium* | 1.3 | 1.0 | 0.7 | 0.2 | 3.0 |
| *Cyclospora* | 0.1 | 0.1 | 0 | 0 | 0.4 |
| *E. coli* O157 | 1.7 | 1.4 | 1.8 | 1.0 | 2.0 |
| *Listeria* | 0.3 | 0.4 | 0.4 | 0.3 | 0.4 |
| *Salmonella* | 16.2 | 16.1 | 17.6 | 10.8 | 19.3 |
| *Shigella* | 10.3 | 11.4 | 8.2 | 6.0 | 23.6 |
| *Vibrio* | 0.3 | 0.3 | 0.4 | 0 | 0.6 |
| *Yersinia* | 0.5 | 0.5 | 0.7 | 0.4 | 0.3 |

* Per 100,000 population

## *FoodNet data (US)*

| Organism | 1996–1998 | 2005 |
|---|---|---|
| *Campylobacter*(/$10^5$) | 21.7 | 12.7 |
| *E. coli* O157 (/$10^5$) | 2.3 | 1.1 |
| *Listeria* (/$10^6$) | 4.9 | 3.0 |
| *Salmonella* (/$10^5$) | 13.5 | 14.6 |
| *Shigella* (/$10^5$) | 7.7 | 4.7 |

## Characteristics of *Campylobacter* (classification)



- Small, nonsporeforming, gram-negative bacteria—curved, S-shaped, or spiral
- 0.5–8 µm long, 0.2–0.9 µm diameter
- Single polar flagellum at one or both ends—rapid, darting, corkscrew-like motility

## Characteristics of *Campylobacter* (classification)

- Require reduced $O_2$ for growth (microaerophilic), increased $CO_2$ (capnophilic)
- *C. jejuni* growth optimum = 42°C, minimum 30°C, maximum ca. 45°C, thermal inactivation from 48°C, survives well at 4°C in milk and water

## Characteristics of *Campylobacter*

- Many species and subspecies
- Many serotypes of *C. jejuni*, based on somatic, capsular, and flagellar antigens
- Tremendous genetic diversity ("naturally competent"): multiple molecular typing methods: PFGE, MLST, AFLP

## Survival and growth in the environment

- Labile to freezing, drying, and temperatures from 48°C up
- Stable at 4°C, dies more quickly at 25°C than at 4 or 30°C
- Some losses at atmospheric levels of O2; optimum salt level 0.5%
- Growth above pH 4.9, good at 5.5–8, optimum at 6.5–7.5

## Infections in humans

- Affects young adults as often as infants
- Human disease principally (~90%) from *C. jejuni*, also *C. coli*
- Infectious dose is apparently "small"
- Incubation 2–5 (1–10) days
- Duration 2–5 days, sometimes 10 days

## Infections in humans

- Pathogenesis is poorly understood: both enterotoxic and enteroinvasive strains may exist
- Diarrhea (watery to bloody with pus & WBC), abdominal pain, malaise, fever, nausea, and vomiting
- Rarely febrile convulsions, arthritis, Guillain-Barré syndrome, or meningitis; may mimic acute appendicitis; many infections asymptomatic

## Infections in humans

- Shedding 2–7 weeks if antibiotic treatment is not done; minor source of human infection, except for an occasional food worker contaminating food
- Lasting immunity follows infection

## *Campylobacter* in animals: Reservoirs

- Common in cattle, swine, sheep, and especially poultry (also companion animals and rodents)
- Carried in gall bladder and small and large intestines

## *Campylobacter* in animals: Transmission

- Shed in feces, which may contaminate edible portions of carcass
- Occurrence in milk may indicate shedding via the mammary gland, but mastitis is seldom involved.

## **Campylobacter insulaenigrae** ***Isolates from Northern Elephant Seals*** **(Mirounga angustirostris)** ***in California***

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## Prevalence of *Campylobacter* in foods

- Eggs—not in outbreaks
- Poultry—common at retail; fecal cross-contamination in processing
- Meat—most common on swine carcasses; sometimes on beef and lamb

## Prevalence of *Campylobacter* in foods

- Milk and milk products—readily killed by pasteurization; raw milk is a leading vehicle in U.S.
- Other foods—mainly animal products; fertilization of vegetables with manure may cause contamination

## Prevalence of *Campylobacter* in feed and water

- Animal feed—subject to contamination from bird and rodent droppings
- Water—at least two drinking water-associated outbreaks (≥130 cases), U.S., 2003–2004

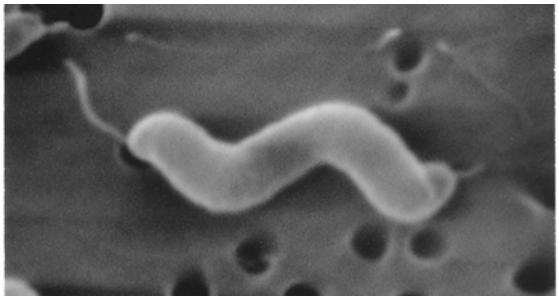
## Foods most often associated with human *Campylobacter* infections—U.S.

- Raw milk
- Poultry
- Other foods via cross-contamination

## Detection of *Campylobacter*

- Samples ideally stored at 4°C in $N_2$ atmosphere, with 0.01% sodium bisulfite added
- Expect low contamination levels: pre-enrichment likely to be necessary
- Slow-growing organism—isolation medium must be selective, to inhibit competitors.

## *Campylobacter jejuni*



## Detection of *Campylobacter*

- Optimum atmosphere is 5% $O_2$, 10% $CO_2$, 85% $N_2$; candle jars are marginally useful
- Incubation generally 42°C
- Antibiotics used in some selective media may inhibit some strains of *C. jejuni*, also *C. coli*; cefaperazone is presently recommended, not cephalothin

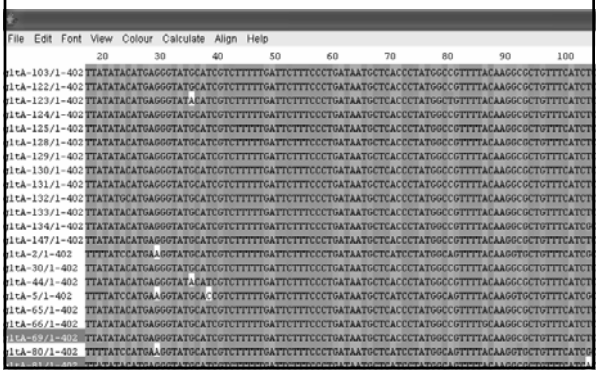
## Identification of *Campylobacter*

- Gram-negative, appropriate appearance, growth temperature and atmosphere; oxidase and catalase positive; hydrolyzes hippurate and indoxyl acetate; reduces nitrate; produces $H_2S$; some tests require special precautions
- Nonculture detection methods and epidemiologic typing systems available

## *Multilocus Sequence Typing*

- **Approach takes advantage of information from sequenced genomes of pathogenic bacteria**
- **Exploits the genetic variation present in 7 housekeeping loci to determine the genetic relatedness between isolates: *aspA, glyA, gltA, glnA, pgm, tkt, uncA***

## *Multilocus Sequence Typing*




## *Multilocus sequence typing*




## *Arcobacter* (1991,1992)

- "Aerotolerant *Campylobacter*"
- Grow at 15, 25, and 30°C, but variably at 37 and 42°C
- Similar appearance : Gram-negative, curved, S-shaped, or helical; single polar flagellum, 1–3 µm long, 0.2–0.9 µm diameter
- May grow aerobically at 30°C and anaerobically at 35–37°C

## *Arcobacter*

- "Frequently isolated from cattle and pigs suffering from abortion and enteritis"
- Human illnesses from two of the species include bacteremia, endocarditis, peritonitis, and diarrhea

## *Arcobacter Species in Humans*

- During an 8-year study period, *Arcobacter butzleri* was the fourth most common *Campylobacter*-like organism isolated from 67,599 stool specimens in Belgium
- Observations suggest that *A. butzleri* displays microbiologic and clinical features similar to those of *Campylobacter jejuni*
- *A. butzleri* was more frequently associated with a persistent, watery diarrhea
- Emerging infection?

Source: Vandenberg O, 2004

## *Helicobacter pylori*

- Discovered in 1982, separated from genus *Campylobacter* in 1989
- Looks like *Campylobacter*, microaerophilic, optimum growth at 37°C
- Culture characteristics, etc., need not be discussed here

## *Helicobacter pylori*

- Clinically important as a probable cause of chronic gastritis and peptic and duodenal ulcer in humans
- Human infection is widespread (nonhuman reservoirs of this species unknown); shed with feces and may contaminate food, but foodborne transmission is not clearly established

## Summary: three genera

- *Campylobacter*: a leading bacterial cause of foodborne disease in U.S.
- *Arcobacter*: also can cause foodborne disease.
- *Helicobacter*: causes ulcers; may not be foodborne.