Campylobacter Infections

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Synonyms and related keywords: campylobacteriosis, Campylobacteraceae, Campylobacter, Campylobacter jejuni, Campylobacter fetus, Arcobacter

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Background: Family Campylobacteraceae includes 2 genera, *Campylobacter* and *Arcobacter*. There are 18 species and subspecies within the genus *Campylobacter*, 11 of which are considered pathogenic to humans, causing enteric and extraintestinal illnesses. The major pathogens are *Campylobacter jejuni* and *Campylobacter fetus*. The following *Campylobacter* species and subspecies are pathogenic to humans:

- **Enteric**
  - *C. jejuni* subspecies *jejuni*
  - *C. jejuni* subspecies *doylei*
  - *Campylobacter coli*
  - *Campylobacter upsaliensis*
  - *Campylobacter lari*
  - *C. fetus* subspecies *fetus*
  - *Campylobacter hyointestinalis*
  - *Campylobacter concisus*

- **Extraintestinal**
  - *C. jejuni* subspecies *jejuni*
  - *Campylobacter upsaliensis*
  - *C. lari*
  - *C. fetus* subspecies *fetus*
  - *C. concisus*
  - *Campylobacter sputorum*
  - *Campylobacter curvus*
  - *Campylobacter rectus*

*Campylobacter pylori* has been reclassified as *Helicobacter pylori* and will not be addressed in this chapter. (See *Helicobacter pylori Infection*.)

*Campylobacter* pathogens are small, curved, motile, microaerophilic, gram-negative rods. They vary in width from 0.2-0.9 mm and in length from 0.5-5.0 mm. They exhibit rapid, darting motility in corkscrew fashion by means of a single flagellum or 2 flagella (monotrichous.
amphitrichous). They also possess a lipopolysaccharide endotoxin.

Campylobacteriosis infects humans and animals. The animal reservoir is the gastrointestinal tract of dogs, cats, and other pets that can carry the organism. Transmission of *C. jejuni* to humans occurs by ingestion of contaminated food or water, including unpasteurized milk and undercooked poultry, or by direct contact with fecal material from infected animals or persons. The 2 types of illnesses associated with *Campylobacter* infections in humans are intestinal infection and extraintestinal infection. The prototype for intestinal infection is *C. jejuni*, and for extraintestinal infection, it is *C. fetus*.

**Pathophysiology:** Factors responsible for the diseases caused by *C. jejuni* are not well known. Based on clinical illness, researchers postulated 3 mechanisms as follows:

1. Adherence and production of heat-labile enterotoxins, inducing secretory diarrhea
2. Invasion and proliferation within the intestinal epithelium leading to cell damage and inflammatory response
3. Translocation of the organism into the intestinal mucosa and proliferation in the lamina propria and mesenteric lymph nodes, leading to extraintestinal infections such as meningitis, cholecystitis, urinary tract infection, and mesenteric adenitis

Information on the pathogenesis of *Campylobacter* infections other than *C. jejuni* is scarce. Bacteremia is more common with *C. fetus* infection. A surface protein in *C. fetus* inhibits the C3b binding responsible for both the serum and phagocytic resistance of the organism, thus making the organism resistant to the bactericidal effects of human serum. After oral ingestion, *C. fetus* may colonize the intestinal tract, resulting in portal bacteremia. In immunocompetent hosts, the organism is phagocytosed by the reticuloendothelial cells in the liver, preventing further spread. However, in patients that have predisposing factors that might serve as a local site of infection such as a gravid uterus, bacteremia can lead to severe complications. Infants may be affected hematogenously or by ascending infection during amnionitis and premature rupture of membranes.

**Frequency:**
• **In the US:** Estimated rates for symptomatic enteric *Campylobacter* infection are 2 million infections per year or 1% of the US population per year. Incidence in the rural population is 5-6 times higher because of increased consumption of raw milk. A 5-year national laboratory study from 1982-1986 showed an isolation rate of *Campylobacter* species of 5.5 per 100,000 person-years. *C jejuni* accounts for 99% of the *Campylobacter* species isolated.

• **Internationally:** In developing countries, *C jejuni* often is isolated from stools of healthy individuals and is especially common during the first 5 years of life. Isolation rates in children who are asymptomatic or children with diarrhea range from 8-45%, with an annual incidence as high as 2.1 episodes of *Campylobacter*-associated diarrhea per child. In developed countries, average incidence of *Campylobacter* bacteremia is estimated to be 1.5 per 1000 patients with enteritis.

**Mortality/Morbidity:**

- The vast majority of patients recover fully after *C jejuni* infection within 5 days (range 2-10 d), either spontaneously or after appropriate antimicrobial therapy. Symptomatic *Campylobacter* infection-associated mortality rate in the US is estimated as 24 per 10,000 culture-confirmed cases or 200 deaths per year.

- Infection with *C fetus* is of concern in patients who are immunocompromised, women who are pregnant, and neonates.

- Previously healthy patients usually recover without complications.

**Race:**

- No race predilection exists.

**Sex:**

- In people aged 45 years or younger, the *C jejuni* isolation rate is higher among males than among females. After age 45 years, no sexual predilection exists.
• In the adult population, the male-to-female *C fetus* ratio is 3:1.

• Among children, no sex predilection exists.

**Age:**

• Any age group can be infected with *C jejuni* enteritis. The rate of infection differs between developed and developing countries. In developed countries, the peak attack rates are in infants younger than 1 year; a second, broader peak attack rate occurs in persons aged 15-30 years. In developing countries, symptomatic infection chiefly affects children younger than 5 years and declines with age. This is likely due to the development of protective immunity secondary to a high level of exposure to the organism early in life.

• In contrast to the age-specific distribution of *Campylobacter* enteritis, the highest rate of bacteremia occurs in patients aged 65 years and older. In this age group, *Campylobacter* bacteremia occurs in 1 of 170 intestinal infections versus 1 bacteremia in 3000 intestinal infections in children younger than 14 years. Roughly 60-90% of isolates are *C jejuni* or *Campylobacter coli*; 8-15% are *C fetus*. In children from developing countries, bacteremia appears common, occurring in 45 of 1000 cases of intestinal infection. Forty-one percent of these infections consist of *C jejuni* subspecies *jejuni*, 24% *C jejuni* subspecies *doylei*, and 5.6% *Campylobacter upsaliensis*.

**History:**

• Clinical manifestations of infection by all *Campylobacter* species that cause enteric illness overlap and appear identical.

• Diarrhea
  
  o Mild episodes subside within 7 days in 60-70% of cases, last for 2 weeks in 20-30%
and persist longer in 5-10% of cases. In one third to one half of patients, initial symptoms include periumbilical cramping, intense abdominal pain that mimics appendicitis, malaise, myalgias, headache, and vomiting.

- Watery secretory diarrhea consists of more than 10 stools per day and is frequently seen in younger children. Dehydration occurs in approximately 10% of these children.

- Inflammatory diarrhea symptoms are indistinguishable from those caused by *Shigella* organisms, *Escherichia coli*, and *Salmonella* species. They are characterized by malaise, fever, abdominal cramps, tenesmus, bloody stools, and fecal leukocytes on light microscopy. Rarely, in young adults and adolescents, inflammatory diarrhea can be severe and confused with Crohn disease and ulcerative colitis. Toxic megacolon with massive bleeding may occasionally occur. In asymptomatic neonates, *C. jejuni* has been isolated from blood-streaked formed stools or hematochezia.

- Extraintestinal infections

  - Bacteremia with *C. jejuni* is uncommon, occurring most in patients with immunodeficiency, chronic illness, and at extremes of ages. Bloodstream infections and systemic infections by *C. fetus* are rare. The 3 patterns of bacteremia are as follows:
    1. Transient bacteremia in a normal host with acute *Campylobacter* enteritis: These patients usually recover completely without treatment.
    2. Secondary bacteremia or deep focus of infection such as meningitis, pneumonia, endocarditis, and thrombophlebitis in a normal host: Bacteremia usually originates from the intestinal tract and responds to antimicrobial therapy.
    3. Chronic bacteremia with relapses that can persist for several months.
occurring in an immunocompromised host: In these patients, bacteremia also can arise from an infected indwelling catheter. Many such patients do not have acute enteritis.

- Localized extraintestinal infections are uncommon manifestations and include cholecystitis, arthritis, urinary tract infection, pancreatitis, osteomyelitis, and meningitis. These manifestations may be the initial presentation of \textit{C jejuni} infection or may occur simultaneously with bacteremia. They frequently are seen in patients who are immunocompromised or at extremes of age. Appropriate treatment is necessary.

- Because of the affinity of \textit{C fetus} for the genital tract—and by the tropism for fetal tissue—\textit{C fetus} and, rarely, \textit{C jejuni} are associated with perinatal infection. Abortion or stillbirth and premature labor have been described. Infants are often premature and develop signs and symptoms suggestive of sepsis including fever, cough, respiratory distress, vomiting, diarrhea, cyanosis, convulsions, and jaundice. Infection typically progresses to meningitis, which may be rapidly fatal or may result in serious neurologic sequelae. The source of the organism in these cases has been the mother.

**Physical:**

- The abdomen is frequently tender on palpation, especially the right lower quadrant.

- Rarely, splenomegaly may be present.

**Causes:**

- Persons at increased risk for \textit{Campylobacter} enteritis
  - Those with occupational exposure to cattle, sheep, and other farm animals
  - Laboratory workers
Those in contact with the excreta of infected persons

Homosexual men

- Underlying conditions that increase risk for *Campylobacter* bacteremia, suggesting the importance of both humoral and cell-mediated immunity

  - Hypogammaglobulinemia
  - HIV infection
  - Kwashiorkor
  - Pregnancy
  - Malignancy
  - Extremes of age
  - Alcoholism
  - Diabetes mellitus
  - Postsplenectomy status
  - Human leukocyte antigen B27 (HLA-B27) - Increases risk for immunoreactive complications, such as reactive arthritis or Reiter syndrome

Other Problems to be Considered:

Other bacterial causes of inflammatory diarrhea include the following:

- *Shigella*
- *Enteroinvasive E coli*
- *E coli* 0157: H7
Salmonella
Yersinia enterocolitica
Aeromonas species
Vibrio parahaemolyticus

Inflammatory bowel disease
Pseudomembranous enterocolitis secondary to Clostridium difficile
Intussusception in infants
Acute abdomen
Acute appendicitis

Lab Studies:

- Microbiologic studies
  - Presumptive diagnosis can be made by examination of fecal specimens by darkfield or phase-contrast microscopy, which demonstrate the characteristic darting motility, and Gram stain of the stool, which shows Vibrio forms (slim, short, curved rods). Red blood cells and neutrophils are present in stool in approximately 75% of patients with Campylobacter enteritis.
  - Definitive diagnosis of infection is based on isolation of organisms from stool culture or from another site.
  - Culture of C jejuni from stool requires special isolation techniques and special media such as Campy-BAP or Skirrow. These media contain antibiotics that reduce the emergence of other enteric microorganisms. Inoculated media should be incubated in 5% oxygen and 10% carbon dioxide at 42°C. If C fetus or other atypical enteric species are suspected, isolation from stool requires inoculation on media lacking antibiotics and at 37°C. Filtration technique may be needed. Routine media are adequate for isolation of Campylobacter from normally sterile sites such as blood, body fluids, and tissues.

- Hematology and blood chemistries
  - Peripheral white blood cell count is usually normal; however, a left
Shift may occur.

- Alanine aminotransferase and the erythrocyte sedimentation rate (ESR) may be slightly elevated.
- Other laboratory evaluations are within the reference ranges.

**Serology**

- Diagnostic rise usually occurs after symptoms have resolved. Since the median duration of fecal excretion in the convalescent phase is less than 3 weeks, serology testing may be more sensitive than culture for the diagnosis of recent *C. jejuni* infection.
- While it is also useful for epidemiological investigations, serologic testing is not recommended for routine diagnosis.

**Other Tests:**

- Deoxyribonucleic acid (DNA) probes and polymerase chain reaction are mainly research tools at this time and are not routinely performed.

**Procedures:**

- In patients who undergo proctoscopy secondary to a prolonged course of *Campylobacter* enteritis, normal mucosa is found 50% of the time. Mucosal edema, congestion, friability, and granularity are seen in the remaining half.

**Histologic Findings:** The spectrum of histologic findings in the intestinal tract ranges from minimal edema with acute and chronic inflammatory cells without vascular congestion, to moderate inflammation and cryptitis, to crypt abscess formation. For perinatal infections secondary to *C. jejuni* and *C. fetus*, the placenta may have areas of necrosis, infarction, microabscesses, and inflammation.

**Medical Care:**

- Evaluation usually can be performed on an outpatient basis.
- For patients who are severely dehydrated and cannot tolerate oral hydration, intravenous hydration and inpatient care may be necessary.

**Surgical Care:**

- Occasionally, acute abdominal pain may be the only presenting
symptom, often mimicking acute appendicitis and resulting in immediate laparotomy.

**Consultations:**

- Consultation with an infectious disease specialist and a gastroenterologist may be necessary for complicated cases.

**Diet:**

- Because rehydration and electrolyte replacement are the mainstays for treating diarrheal disease, oral rehydration with an electrolyte and glucose solution is necessary.

**Activity:**

- Permit activity as tolerated.

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Most *C. jejuni* infections are mild and self-limited; therefore, they do not usually require antibiotic therapy. Correction of electrolyte abnormalities and rehydration are usually sufficient. Treatment often is reserved for compromised hosts or persons with fever, increasing bloody diarrhea, or symptoms that last longer than 1 week.

*C. jejuni* is usually sensitive to erythromycin, gentamicin, tetracycline, ciprofloxacin, and clindamycin. Reports of erythromycin- and ciprofloxacin-resistant strains are increasing. In adults, placebo-controlled studies of erythromycin demonstrate no improvement in the clinical symptoms if given late in the course of illness but have resulted in decreased fecal shedding. If an appropriate antibiotic therapy was initiated within the first 4 days of illness, there was a reduction in the excretion of the organism; however, results regarding the resolution of symptoms were controversial. In contrast, early erythromycin treatment for children with bloody diarrhea shortened both the duration of diarrhea and excretion of microbes in the stool.

Recommended duration for antibiotic treatment given for gastroenteritis is 5-7 days. Antimicrobial therapy for all bacteremic and immunocompromised patients with *C. jejuni* should be selected based on a laboratory susceptibility test. Begin therapy with gentamicin, imipenem, third-generation cephalosporins, or chloramphenicol until susceptibility test results are available. Because infections with *C. fetus* usually are systemic, IV antibiotics usually are required. Aminoglycosides, such as gentamicin, are usually the DOC.
Alternatives for *C fetus* bacteremia include ampicillin, imipenem, chloramphenicol, and third-generation cephalosporins. Reported synergistic combinations include ampicillin with gentamicin and imipenem with gentamicin. Duration of therapy is empiric.

Patients with central nervous system infection require treatment for 2-3 weeks with a third-generation cephalosporin, ampicillin, or chloramphenicol. Those with endovascular infection should be treated for at least 4 weeks with gentamicin as the DOC. Treatment with ampicillin or third-generation cephalosporins are other alternatives. Erythromycin is the DOC for patients with diarrheal illness secondary to *C fetus*.

Drug Category: *Macrolide antibiotics* -- Ease of administration, lack of serious adverse effect, and fewer propensities to select for plasmid-mediated antibiotic resistance make erythromycin the DOC.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Erythromycin (E.E.S., E-Mycin, Eryc, Ery-Tab) -- Inhibits bacterial growth, possibly by blocking dissociation of peptidyl t-RNA from ribosomes causing RNA-dependent protein synthesis to arrest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>800 mg (EES) PO qid; not to exceed 4 g/d 250-500 mg (base, stearate, or estolate) PO qid; not to exceed 4 g/d 15-20 mg/kg/d IV divided q6h; not to exceed 4 g/d</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>30-50 mg/kg/d PO divided q6h; not to exceed 2 g/d 20-50 mg/kg/d IV divided q6h; not to exceed 2 g/d</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; hepatic impairment; concomitant administration of terfenadine (<em>recalled from US market</em>), cisapride, and astemizole (<em>recalled from US market</em>)</td>
</tr>
<tr>
<td>Interactions</td>
<td>Inhibits CYP450 isoenzyme 3A4; decreases clearance of terfenadine, cisapride, and astemizole, which may result in serious cardiac arrhythmias; may potentiate carbamazepine, methylprednisolone, cyclosporine,</td>
</tr>
</tbody>
</table>
may potentiate carbamazepine, methylprednisolone, cyclosporine, digoxin, theophylline, warfarin, ergotamine, triazolam, and others; avoid lovastatin; monitor phenytoin, hexobarbital

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>B - Usually safe but benefits must outweigh the risks.</th>
</tr>
</thead>
</table>

**Precautions**

Caution in liver disease; estolate formulation may cause cholestatic jaundice; GI adverse effects are common (give doses pc); discontinue use if nausea, vomiting, malaise, abdominal colic, or fever occur

Drug Category: *Fluoroquinolone antibiotics* -- Ciprofloxacin and other fluoroquinolones are alternative agents to erythromycin but are not approved for persons younger than 18 years.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Ciprofloxacin (Cipro) -- Inhibits bacterial DNA synthesis and, consequently, growth. Continue treatment for at least 2 d after signs and symptoms have disappeared.</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Adult Dose</th>
<th>250-750 mg/dose PO q12h; not to exceed 2 g/d 200-400 mg/dose IV q12h; not to exceed 800 mg/d</th>
</tr>
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</table>

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<thead>
<tr>
<th>Pediatric Dose</th>
<th>20-30 mg/kg/d PO divided bid; not to exceed 1.5 g/d 10-20 mg/kg/d IV divided q12h; not to exceed 800 mg/d</th>
</tr>
</thead>
</table>

**Contraindications**

Documented hypersensitivity

**Interactions**

May increase theophylline levels; avoid oral forms with antacids, calcium, iron, zinc, and sucralfate; avoid urinary alkalinizers; potentiated by probenecid; interferes with caffeine metabolism; severe hypoglycemia with glyburide (rare); increased serum creatinine with cyclosporine; monitor oral anticoagulants (potentiation), phenytoin (variable effects)

<table>
<thead>
<tr>
<th>Pregnancy</th>
<th>C - Safety for use during pregnancy has not been established.</th>
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<tr>
<th>Renal (creatinine clearance &lt;29</th>
<th></th>
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</table>
mL/min) or hepatic dysfunction, reduce dose; discontinue if tendon pain, inflammation, or rupture occur; discontinue if rash, phototoxicity, or other sign of hypersensitivity occurs; may cause CNS or convulsive disorders; maintain hydration, avoid alkaline urine to avoid crystalluria; avoid excessive sun and UV light; not recommended for nursing mothers

Drug Category: *Tetracyclines* -- May be used in children but are not approved for children younger than 9 years because of the risk of dental staining.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Tetracycline (Sumycin) -- Inhibits bacterial protein synthesis by binding with 30S and possibly 50S ribosomal subunit(s).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>250-500 mg/dose PO divided q6h; not to exceed 2 g/d</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>&lt;8 years: Not recommended &gt;8 years: 25-50 mg/kg/d PO divided q6h; not to exceed 2 g/d</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; severe hepatic dysfunction</td>
</tr>
<tr>
<td>Interactions</td>
<td>May increase serum digoxin levels; antacids, iron, zinc, calcium, magnesium, dairy products, urinary alkalinizers, and food reduce absorption; avoid concomitant methoxyflurane; monitor prothrombin time with oral anticoagulant</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>D - Unsafe in pregnancy</td>
</tr>
<tr>
<td>Precautions</td>
<td>Renal impairment; monitor blood, renal, and liver function in long-term use; sun or UV light; not recommended for nursing mothers; use of tetracyclines during tooth development (last half of pregnancy through age 8 y) can cause permanent discoloration of the teeth; never administer outdated tetracyclines; degradation products of tetracyclines are highly nephrotoxic and can cause a Fanconilike</td>
</tr>
</tbody>
</table>
Drug Category: **Lincosamide antibiotics** -- Alternative to tetracycline.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Clindamycin (Cleocin) -- Inhibits bacterial growth, possibly by blocking dissociation of peptidyl tRNA from ribosomes, causing RNA-dependent protein synthesis to arrest.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>150-450 mg/dose PO q6-8h; not to exceed 1.8 g/24h 600-2700 mg/d IM/IV divided q6-12h; not to exceed 4.8 g/24h</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>20-30 mg/kg/d PO divided q6h 25-40 mg/kg/d IM/IV divided q6-8h</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity to preparations containing clindamycin or lincomycin; pseudomembranous colitis; hepatic impairment</td>
</tr>
<tr>
<td>Interactions</td>
<td>May potentiate neuromuscular blocking agents; may antagonize erythromycin; antiperistaltic agent may worsen colitis</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>B - Usually safe but benefits must outweigh the risks.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Not for treatment of meningitis; discontinue if colitis occurs and treat; monitor neonates and those with gastrointestinal disease; monitor blood, renal, and hepatic function in long-term use and in children; use with caution in patients with renal or hepatic disease with metabolic aberrations; nursing mothers</td>
</tr>
</tbody>
</table>

Drug Category: **Aminoglycoside antibiotics** -- Reserve these drugs for treatment of infections caused by organisms not sensitive to less toxic agents.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Gentamicin (Garamycin, Pediatric Gentamicin Sulfate) -- Aminoglycoside antibiotic for gram-negative coverage.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug Name</td>
<td>Used in combination with both an agent against gram-positive organisms and one that covers anaerobes</td>
</tr>
<tr>
<td><strong>Adult Dose</strong></td>
<td>1 mg/kg/dose IM/IV q8h or total dose once a day; not to exceed 5 mg/kg/d Dosing intervals based on CrCl: &gt;60 mL/min: Administer every 8 h 40-60 mL/min: Administer every 12 h 20-40 mL/min: Administer every 24 h 10-20 mL/min: Administer every 48 h &lt;10 mL/min: Administer every 72 h</td>
</tr>
<tr>
<td>---------------</td>
<td>-------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>Neonates/Infants: &lt;29 weeks postconception, 0-28 days postnatal: 2.5 mg/kg/dose IM/IV qd &lt;29 weeks postconception, &gt;28 days postnatal: 3 mg/kg/dose IM/IV qd 30-36 weeks postconception, 0-14 days postnatal: 3 mg/kg/dose IM/IV qd 30-36 weeks postconception, &gt;14 days postnatal: 2.5 mg/kg/dose IM/IV q12h &gt;37 weeks postconception, 0-7 days postnatal: 2.5 mg/kg/dose IM/IV q12h &gt;37 weeks postconception, &gt;7 days postnatal: 2.5 mg/kg/dose IM/IV q8h Children: 2-2.5 mg/kg/dose IM/IV q8h</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity to gentamicin or another aminoglycoside</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Avoid concomitant furosemide, ethacrynic acid, other nephrotoxic or neurotoxic drugs including cephalosporins; may potentiate neuromuscular blockade</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>Monitor for nephrotoxicity and neurotoxicity; avoid peak serum levels &gt;12 mcg/mL and trough levels &gt;2 mcg/mL; for renal impairment, reduce dose, maintain adequate hydration; prolonged use or excessive doses; asthma; neuromuscular disorders</td>
</tr>
</tbody>
</table>

**Drug Category: Antibiotics** -- Alternatives for C fetus bacteremia include ampicillin, imipenem, chloramphenicol, and third-generation cephalosporins.
Reported synergistic combinations include ampicillin with gentamicin and imipenem with gentamicin. Duration of therapy is empiric.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Ampicillin (Marcillin, Omnipen) --</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Dose</td>
<td>500-3000 mg IV q4-6h; not to exceed 12 g/d IV</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Neonates &lt;7 days: &lt;2 kg: 50-100 mg/kg/d IV divided</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity; also contraindicated in infections caused</td>
</tr>
<tr>
<td>Interactions</td>
<td>May cause false-positive Clinitest; potentiated by probenecid</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>B - Usually safe but benefits must outweigh the risks</td>
</tr>
<tr>
<td>Precautions</td>
<td>May have cross-sensitivity with</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Imipenem and cilastatin sodium</th>
</tr>
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<tbody>
<tr>
<td>Adult Dose</td>
<td>Based on imipenem component, 250-1000 mg/dose IV q6-8h; not to exceed</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>50-100 mg/kg/d IV divided q6-8h; not to exceed 4 g/d</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>50-100 mg/kg/d IV divided q6-8h; not to exceed 4 g/d</td>
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<td>-------------------</td>
<td>---------------------------------------------------</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Coadministration with cyclosporine may increase CNS adverse effects of both agents; coadministration with ganciclovir may result in generalized seizures</td>
</tr>
<tr>
<td><strong>Pregnancy</strong></td>
<td>C - Safety for use during pregnancy has not been established.</td>
</tr>
<tr>
<td><strong>Precautions</strong></td>
<td>Penicillin, cephalosporin, or other allergy; CNS disorders, especially brain lesions or seizures; reduce dose for renal impairment</td>
</tr>
<tr>
<td><strong>Drug Name</strong></td>
<td>Chloramphenicol (Chloromycetin) -- Binds to 50 S bacterial-ribosomal subunits and inhibits bacterial growth by inhibiting protein synthesis. Effective against gram-negative and gram-positive bacteria.</td>
</tr>
<tr>
<td><strong>Adult Dose</strong></td>
<td>50-100 mg/kg/d IV divided q6h; not to exceed 4 g/d</td>
</tr>
<tr>
<td><strong>Pediatric Dose</strong></td>
<td>Neonates: Loading dose: 20 mg/kg IV Maintenance dose: Administer first maintenance dose 12h after loading dose &lt;7 days: 25 mg/kg/d IV qd &gt;7 days: &lt;2 kg: 25 mg/kg/d IV qd &gt;2 kg: 50 mg/kg/d IV divided q12h Infants/children: 50-100 mg/kg/d IV divided q6h; not to exceed 4 g/d</td>
</tr>
<tr>
<td><strong>Contraindications</strong></td>
<td>Trivial infections or prophylaxis; previous toxic reactions to chloramphenicol; G-6-PD deficiency</td>
</tr>
<tr>
<td><strong>Interactions</strong></td>
<td>Avoid other agents that cause bone marrow depression; may increase effects of hydantoins or sulfonylureas; may increase serum iron levels, decrease response to iron, vitamin B-12 Administered concurrently with barbiturates, chloramphenicol serum levels may decrease while barbiturate levels may increase causing toxicity; rifampin may reduce serum</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>D - Unsafe in pregnancy</td>
</tr>
<tr>
<td>-----------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Precautions</td>
<td>Caution in pregnancy at term or during labor because of potential toxic effects on fetus (gray baby syndrome) Perform blood tests at baseline and q2d during therapy; discontinue if blood dyscrasias, optic neuritis, or peripheral neuritis develops; avoid repeat therapy; monitor serum levels; breastfeeding women</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Ceftriaxone (Rocephin) -- Third generation cephalosporin. Arrests bacterial growth by binding to one or more penicillin binding proteins.</td>
</tr>
<tr>
<td>Adult Dose</td>
<td>1-4 g/d IV divided q12-24h; not to exceed 4 g/d</td>
</tr>
<tr>
<td>Pediatric Dose</td>
<td>Infants and children: 50-75 mg/kg/d IM/IV divided q12-24h Meningitis: 100 mg/kg/d IV/IM divided q12-24h; not to exceed 4 g/d</td>
</tr>
<tr>
<td>Contraindications</td>
<td>Documented hypersensitivity</td>
</tr>
<tr>
<td>Interactions</td>
<td>May cause false-positive Clinitest results; potentiated by probenecid</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>B - Usually safe but benefits must outweigh the risks.</td>
</tr>
<tr>
<td>Precautions</td>
<td>Penicillin or other allergy; concomitant renal and hepatic impairment, (not to exceed 2 g/d); chronic hepatic disease or malnutrition, monitor prothrombin time; gastrointestinal disease</td>
</tr>
</tbody>
</table>

**Further Inpatient Care:**

- Evaluate protracted cases further to rule out other causes of fever, diarrhea, and sepsis.

- Provide close monitoring and support in the intensive care unit for immunoreactive complications such as Guillain-Barré syndrome (GBS).
Further Outpatient Care:

- Assess the resolution of illness and patient compliance with medication.

In/Out Patient Meds:

- Rehydrate intravenously or orally.
- Administer antibiotics as indicated.

Transfer:

- Patients with immunoreactive complications such as GBS may require transfer to a chronic care facility for rehabilitation after their condition stabilizes.

Complications:

- Guillain-Barré syndrome
  - GBS is a disorder of peripheral nerves and is characterized by ascending paralysis.
  - It occurs more often in males (male-to-female ratio of 3:1), during summertime, and in adults.
  - A disproportionate amount of GBS-associated *C jejuni* belongs to a rare serotype called Penner (lipopolysaccharide) type 0:19. Other variants of GBS include the following:
    - Acute motor axonal neuropathy (AMAN) or Chinese paralytic syndrome: This syndrome is characterized by a rapid onset of paralysis with progression to tetraplegia and respiratory failure, occurring among children in northern China during summer and fall.
    - Fisher syndrome is characterized by ophthalmoplegia, areflexia, and cerebellar ataxia.
  - Strong evidence exists on the association between preceding *C jejuni* infection and GBS. The antigenic similarity between specific regions (terminal tetrasaccharide) of lipopolysaccharide (LPS) of *C jejuni* and human gangliosides (GM1) led to the concept of "molecular mimicry." This concept implies the sharing of homologous epitopes between the bacterial LPS and ganglioside surface components of the peripheral nerve. Immune response from simple *C jejuni* infection could induce antibodies that cross-react to the gangliosides and trigger GBS.

- Reactive arthritis
Sixty percent of patients are positive for HLA-B27; this is more common in young men.

Arthritis starts a few days to several weeks after the episode of diarrhea. Joint involvement is usually monoarticular and affects the knees. The course is self-limited, ranging from 1 week to several months.

Synovial fluid is sterile, fever and leukocytosis are absent, and ESR is elevated.

Other infrequently reported complications are as follows:

- Reiter syndrome
- Erythema nodosum
- Hepatitis
- Intestinal nephritis
- Hemolytic-uremic syndrome
- Immunoglobulin A (IgA) nephropathy

**Prognosis:**

- The majority of patients fully recover after *C jejuni* infection, with or without antibiotics.

- *Campylobacter* septicemia in patients with immune deficiencies (including congenital hypogammaglobulinemia, acquired hypogammaglobulinemia, malnutrition, HIV) and in neonates is associated with a high mortality rate.

- Even with plasmapheresis and intravenous immunoglobulin, up to 20% of patients with GBS may require mechanical ventilation. Between 15-20% of all patients may be left with severe neurologic deficit. Between 5-10% of all patients may die as a consequence of GBS disease. Since GBS secondary to *C jejuni* may be more severe, the percentages of patients who require mechanical ventilation, experience severe neurologic sequelae, and die may also be higher.

- Previously healthy persons infected with *C fetus* usually recover without sequelae. This infection may be lethal to patients with altered immune status and neonates. Prognosis for these patients depends on the early administration of fluids and appropriate antimicrobial therapy.

**Patient Education:**

- Tips for preventing campylobacteriosis
  - Cook all poultry products thoroughly. If served undercooked poultry in a restaurant, return it for further cooking.
- Wash hands with soap before and after handling raw foods of animal origin.

- Prevent cross-contamination in the kitchen
  - Use separate cutting boards for foods of animal origin and other foods.
  - Carefully clean all cutting boards, countertops, and utensils with soap and hot water after preparing raw food of animal origin.

- Avoid consuming unpasteurized milk and untreated surface water.

- Make sure that persons with diarrhea, especially children, wash their hands carefully and frequently with soap to reduce the risk of spreading infection.

- Wash hands with soap after contact with pet feces.

### Medical/Legal Pitfalls:

- Failure by physicians and clinical laboratories to report diagnosis of campylobacteriosis to local health departments to further prevent possible outbreaks.

### Special Concerns:

- Because of the widespread use of antibiotics, especially quinolones, in humans and animal food, increasing resistance to these agents is reported.

### Bibliography

- Feigin. et al: Textbook of Pediatric Infectious Diseases. 4th ed. WB


NOTE:

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