Management of Patients with Bacterial Gastroenteritis

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Topics to be Covered

- Salmonellosis
- Shigellosis
- Campylobacteriosis
- Cholera
- CDI (*C. difficile* infection)
- Shiga toxin producing *E. coli*
Background

- Infectious diarrhea is most dangerous in infants and the elderly- dehydration is acute threat.
- Infectious diarrhea in children is associated with malnutrition. Study of diarrhea from Bangladesh showed that “Factors significantly associated with overall malnutrition were disease severity, age (24–59 months), mother's schooling, and monthly household income (< $100 US)....”
- Infectious diseases often coexist with micronutrient deficiencies and exhibit complex interactions leading to the vicious cycle of malnutrition and infections.
Global burden of childhood pneumonia and diarrhea

Christa L Fischer  Walker et al The Lancet Volume 381, 2013 1405 - 1416
Background

• Most people do not bother to see a healthcare provider for diarrhea because they expect it to be self-limited.

• When they do, usually treated empirically with a fluoroquinolone and an anti-motility drug.

• Stool cultures are rarely done; mostly during recognized outbreaks or in hospitalized patients.
Can Clinicians predict Etiology?

• Cholera in its extreme form is easily recognized - vomiting plus copious “rise water” diarrhea. Patients usually have muscle cramps from electrolyte imbalance and may already be in shock.

• Dysentery- small volumes of bloody, mucusy diarrhea with abdominal pain, tenesmus, and fever. In US most cases due to ulcerative colitis (UC). *Shigella* sp. are most common bacterial causes but *Campylobacter* and *Salmonella* can do it. Guess UC and you will be right ~90% of time but you will the miss treatable diseases.
Clinical recognition

• Febrile gastroenteritis
  - Nearly impossible to guess the etiology, and often no etiological diagnosis is made (will change with molecular diagnosis). Fever, cramping abdominal pain, and non-bloody diarrhea. Could be due to viruses or several different bacteria. *Salmonella* and *Campylobacter* are most common bacterial pathogens in the U.S. Sea food associated likely to be from a non-cholera *Vibrio*. 
Salmonellosis

• Almost always foodborne in U.S. but can be spread person-to-person or be waterborne. Water is probably the culprit in Africa where Salmonella bacteremia is extraordinarily common in infants and in adults with AIDS.

• Infectious dose uncertain but lower in food.
Salmonellosis

No evidence that antibiotics shorten the course of *Salmonella* gastroenteritis and they definitely prolong the convalescent excretion of *Salmonella*. 
Who should be treated?

• AIDS
• Other T cell disorders, e.g., lymphoma, transplantation
• Sickle cell anemia and other hemolytic anemias
• Colitis
• Bacteremia
  – In absence of severe diarrhea, non-typhoid *Salmonella* bacteremia indicates immunosuppression or an intravascular site of infection.
Salmonellosis- what if treatment is needed?

• Aminoglycoside antibiotics are ineffective even if the bacteria are susceptible *in vitro*.

• Potentially effective drugs:
  – co-trimoxazole
  – amoxicillin/ampicillin
  – fluoroquinolones
  – third generation cephalosporins

• But acquired resistance is increasingly common.
Shigellosis

• A human infection spread person to person
• Due to one of four species of Shigella.
• In Europe and US most common isolate is S. sonnei, while in Asia and Africa S. flexneri and S. dysenteriae predominate.
• Antibiotic treatment shortens the illness, saves lives, reduces excretion so reduces risk of transmission.
Shigellosis

• Possibly effective drugs
  – Ampicillin*
  – Co-trimoxazole**
  – Naladixic Acid- 85% of *S. flexneri and sonnei* R in Asia/Africa
  – Fluoroquinolone**- 3-7% resistance
  – Azithromycin**- rare but no *in vitro* standard.
• 5 days
• ** Can use a single large dose.
Treatment of Shigellosis: Azithromycin vs. Ciprofloxacin: A Double-Blind, Randomized, Controlled Trial

5 day treatments while under observation

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Treatment Group*</th>
<th>Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Azithromycin (n = 34)</td>
<td>Ciprofloxacin (n = 36)</td>
<td></td>
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<tr>
<td>Clinical success, n (%)</td>
<td>28 (82 [70–95])</td>
<td>32 (89 [74–97])</td>
<td>-7% (-23% to 10%)</td>
</tr>
<tr>
<td>Bacteriologic success, n (%)</td>
<td>32 (94 [80–99])</td>
<td>36 (100 [90–100])</td>
<td>-6% (-14% to 2%)</td>
</tr>
<tr>
<td>Fever &gt;24 h, n (%)</td>
<td>1 (3 [&lt;1–15])</td>
<td>0 [0–10]</td>
<td>-3% (-3% to 9%)</td>
</tr>
<tr>
<td>Tenesmus &gt;72 h, n (%)</td>
<td>8 (24 [9–38])</td>
<td>2 (6 [1–19])</td>
<td>18% (2% to 34%)</td>
</tr>
<tr>
<td>Median total stools during study, n</td>
<td>29 [25–38]</td>
<td>24 [22–32]</td>
<td>2 (-3 to 9)</td>
</tr>
</tbody>
</table>

* Values in brackets are 95% CIs.
Campylobacteriosis

- Foodbourne
- Chickens most common food source; raw milk
- Infectious dose uncertain
- *C. jejuni* and *C. coli* most common etiologies
- Febrile gastroenteritis most common; dysentery
- Self-limited unless immunoglobulin or T cell deficient
- Recurrences are possible; LPS varies but some people do not make antibodies and relapse even after antibiotic treatment
Complications

• Guillain-Barré syndrome- molecular mimicry between LOS and neuronal gangliosides
• Irritable bowel syndrome- more likely if diarrhea lasts > 7 days. Swedish study estimated 3X> risk after *Campylobacter* infection. ? If Rx prevents
• Reactive arthritis- true of all causes of bacterial gastroenteritis; associated with HLA B27
• Small intestinal lymphoma- “Koch’s” postulates
Resolution of Immunoproliferative Small Intestinal Disease in the Index Patient after Antimicrobial Therapy

CDI

• Mostly in hospitalized or institutionalized patients.
• Antibiotics and chemotherapy are major risks.
• Caused by toxigenic *C. difficile*.
• Symptoms vary from mild chronic diarrhea to fulminant colitis with mega-colon and death.
• BI/NAP1/027 ribotype causes more severe illness.
• Relapses are common.
• Advanced age is a major risk factor for severe disease.
Treatments

• Stop antibiotics- mild case may resolve
• Metronidazole- oral or i.v.
• Oral vancomycin- sometimes enemas
• Fidaxomycin
• Rifaximin- only one with acquired resistance. Prior exposure to a rifamycin predicts resistance.
Treatment

Can decrease diarrhea by ~ 1 day if started within 3 days of onset.

• Ciprofloxacin- no resistance in 1995 up to 25% in 2007. 80% in Spain, Thailand, Hong Kong

• Azithromycin- resistance ~5%. Not much used because by time diagnosis is made patients are better. Will change with molecular techniques.
Shiga Toxin + *E. coli* (STEC)

- Acquired from bovines in whom it is normal flora, via contaminated food or water.
- Symptoms vary from mild diarrhea to bloody stool.
- Usually afebrile
- Complication- hemolytic uremic syndrome (HUS), especially in children. Can lead to permanent renal failure.
STEC

• Etiology- most common is serotype O157:H7 in U.S.
• *E. coli* serotype O104:H4 epidemic in northern Germany affected >3,842 patients, 22% of whom developed HUS. Was an EAEC strain with a toxigenic phage.
• Neurological symptoms occurred in 48%; 67.3% presented with cognitive impairment or aphasia. During the course of the disease, 20% of the patients developed epileptic seizures. Full recovery occurred. ? Toxin mediated.
Treatment

• Not ciprofloxacin or co-trimoxazole. Toxin synthesis by Shiga toxin-producing STEC appears to be co-regulated through induction of the integrated bacteriophage that encodes the toxin gene. Phage production is linked to induction of the bacterial SOS response, a ubiquitous response to DNA damage.

• Probably not true for protein synthesis inhibitors. Treatment with azithromycin was associated with a lower frequency of long-term STEC O104:H4 carriage and did not increase HUS.