What is it?
Modes of transmission?
Environmental Sources?
Control Measures?
Clostridium difficile

- *Clostridium difficile* - first described in 1935 when it was isolated from stool samples of new-born babies.
- It was not until the mid 1970’s that it became recognized as a cause of antibiotic-associated diarrhea and colitis.
Clostridium difficile

- *C. difficile* - spore forming bacteria
- Can be part of the normal intestinal flora in as many as 50% of children under age two - less frequently in individuals over two years of age.
- *C. difficile* is the major cause of pseudo-membranous colitis and antibiotic associated diarrhea.
Overview: Clostridium difficile

- Anaerobic spore-forming bacillus
- *Clostridium difficile* Infection (CDI)
- Pseudomembranous colitis, toxic megacolon, sepsis, and death
- Fecal-oral transmission through contaminated environment and hands of healthcare personnel
- Antimicrobial exposure is major risk factor for disease
  - Acquisition and growth of *C. difficile*
  - Suppression of normal flora of the colon
- Clindamycin, penicillins, and cephalosporins
New Strain of C.difficile

- NAP1 - a mutated version that produces roughly 20 times the toxins responsible for illnesses ranging from simple diarrhea to blood poisoning — and death.
- The NAP1 strain has been found in other sites and populations in recent years, infecting young adults and pregnant women with no history of antibiotic use, according to federal sources.
States with BI/NAP1/027 strain of C. difficile (N=40), October, 2008
Lethal hospital bug cases rocket, United Kingdom

- Potentially lethal cases of *C. difficile* “rocketed” from 1990s to 2004
- Cases had increased from 1,000 in 1990 to over 35,000 in 2003
- 44,488 cases of *C. difficile* in ≥ 65 year olds in 2004.

C. difficile – On the Rise

- C. difficile infections more than doubled between 2000 and 2005
- In 2005, 301,200 cases of C. difficile infection (CDI) were logged in discharge records.
- Some 28,600 people who had the infection died.
What are the risk factors for CDI?

- *C. difficile*-associated disease occurs when the normal intestinal flora is altered, allowing *C. difficile* to flourish in the intestinal tract and produce a toxin that causes a watery diarrhea.
- Antibiotic use
- Proton-pump inhibitors (antacids)
- Repeated enemas
- Prolonged nasogastric tube
- Gastrointestinal tract surgery
- Cross contamination from environment
- Food sources
Antibiotics and *C. difficile*?

- The overuse of antibiotics
  - penicillin (ampicillin)
  - Clindamycin
  - Cephalosporins
  - Fluorquinolones

alters the normal intestinal flora and increase the risk of developing *C. difficile* diarrhea.
Proton Pump Inhibitors

- Reduction of gastric acid secretion may allow *C. difficile* to be ingested and survive a "first wall of host defense" -- the acidic gastric pool.
- Reduced gastric acid facilitates survival of *C. difficile* in the upper gastrointestinal tract, leading to disease-associated sequelae.
- *C. difficile* spores are resistant to gastric acid.

Reference: Proton pump inhibitors increase significantly the risk of Clostridium difficile infection in a low-endemicity, non-outbreak hospital setting.
Aliment Pharmacol Ther. 2009; 29(6):626-34
Stomach Acid-Suppressing Medications and Community-Acquired CDAD, England

Severe CDAD in Populations Previously at Low Risk—Four States, 2005

<table>
<thead>
<tr>
<th>Characteristic, No. (%)</th>
<th>Community (N=23)</th>
<th>Peripartum (N=10)</th>
<th>Total (N=33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aged &lt; 18 years</td>
<td>11 (48)</td>
<td>0 (0)</td>
<td>11 (33)</td>
</tr>
<tr>
<td>Female</td>
<td>15 (65)</td>
<td>10 (100)</td>
<td>25 (76)</td>
</tr>
<tr>
<td>Antimicrobial exposure</td>
<td>15 (65)</td>
<td>9 (90)</td>
<td>24 (73)</td>
</tr>
<tr>
<td>Bloody diarrhea</td>
<td>6 (26)</td>
<td>2 (20)</td>
<td>8 (24)</td>
</tr>
<tr>
<td>Hospitalization necessary</td>
<td>6 (26)</td>
<td>4 (40)</td>
<td>10 (24)</td>
</tr>
<tr>
<td>ER visit necessary</td>
<td>3 (13)</td>
<td>2 (20)</td>
<td>5 (15)</td>
</tr>
<tr>
<td>Relapse</td>
<td>8 (35)</td>
<td>5 (50)</td>
<td>13 (39)</td>
</tr>
</tbody>
</table>

Other Risk Factors

- Anticonvulsant therapy
- Antiplatelet agents
- Osteoporosis medication
- Angiotensin II receptor antagonists
- Asthma medications
- Systemic corticosteroids
- Antidiabetic agents
- Antidepressant medications
- Age
- Length of admission

The highest identified risk was actually with use of antidepressants (OR 2.99, 95% CI 2.16-4.15). By logistic regression, the number of days of PPI use was a significant predictor of *C difficile* infection (OR 1.01/day, 95% CI 1.00-1.02)

Reference: Proton pump inhibitors increase significantly the risk of Clostridium difficile infection in a low-endemicity, non-outbreak hospital setting.
Aliment Pharmacol Ther. 2009; 29(6):626-34
Some retail meats contain *C. difficile*

- Healthy adult food producing animals, such as beef and dairy cattle, may carry *C. difficile*.
- *C. difficile* has recently emerged as an important cause of disease in neonatal pigs.
- *C. difficile* may be found in healthy companion animals such as horses, dogs, and cats.
- There are no documented animal to human cases of CDI. (There has been one incident reported in the literature where a pet therapy dog was thought to have contracted the human epidemic strain of *C. difficile* while visiting a hospital, although it has not been proven that the origin of the dog’s infection was the hospital.)
1993-2005, there were 2,037,900 hospital discharges with *C. difficile*-associated infection

Average age - 68.3 years, with about two-thirds older than 65.

58.5% of those diagnosed were female.

ER admission accounted for more than 60% of CDI cases

Length of stay - 12.9 days on average and 9.5% died during their stay.

Secondary diagnosis of CDI stayed longer (14.8 days on average) and more died (11.3%).

1,100 patients in 2005 with *C. difficile*-associated disease patients received subtotal colectomy treatment for bowel perforation and peritonitis resulting from fulminant disease.
New Surveillance Definitions

Differentiating Healthcare-associated From Community associated *Clostridium difficile* Infection (CDI)

Admission

48 h

HO-HCFA

Discharge

< 4 weeks

CO-HCFA

4-12 weeks

Indeterminate

> 12 weeks

CA-CDI

* Depending upon whether patient was discharged within previous 4 weeks, CO-HA vs. CA

HO: Hospital (Healthcare) onset
CO-HA: Community Onset Healthcare-associated
CA: Community Associated

## NEBH Cases Per New Definitions

<table>
<thead>
<tr>
<th>Month</th>
<th>Hosp Onset</th>
<th>Community Onset – HAI</th>
<th>Indeterminate</th>
<th>Community-acquired</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>October</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>November</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>December</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>January</td>
<td>1</td>
<td></td>
<td>0</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>February</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>March</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>April</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>May</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>June</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>July</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Aug</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td>Sep</td>
<td>2</td>
<td></td>
<td></td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>13</strong></td>
<td><strong>8</strong></td>
<td><strong>3</strong></td>
<td><strong>10</strong></td>
<td><strong>34</strong></td>
</tr>
</tbody>
</table>
Control Measures in August 08

- Decontaminated 19 rooms on J4East with the Zimek machine (kills spores)
- Instituted Use of Chlorox Bleach Wipes
- Education for Staff
- Monitoring for New Cases
- Formation of C. Difficile Team:
  - Dr. Camer (Chief of Surgery) Dr. Lui (Chief of Gastroenterology), Sharon Connolly, RN – Nurse Manager, Sue Cohen, MT (ASCP) Microbiology Supervisor, Pam Dejoie, Maureen Spencer, RN – Infection Control
- Retrospective Case Review of all CDI cases
Zimek Decontamination Unit

- ZIMEK is a Room and Vehicle Decontamination System
- Dri-Mist® Micro-Particle Generator breaks down disinfectant solution into microscopic, negatively charged ion particulates.
- These particulates are so small (smaller than one micron in diameter) that they can access ALL surfaces of a room.
- Because these particulates are negatively charged, they stick to positively charged contaminants and kills them.
<table>
<thead>
<tr>
<th>Month</th>
<th>Hosp Onset</th>
<th>Community Onset – HAI</th>
<th>Indeterminate</th>
<th>Community-acquired</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>October</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>November</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>December</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>January</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>February</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>March</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>April</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>May</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>June</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>July</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Aug</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Sep</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10</strong></td>
<td><strong>3</strong></td>
<td><strong>3</strong></td>
<td><strong>4</strong></td>
<td><strong>20</strong></td>
</tr>
<tr>
<td></td>
<td>FY08</td>
<td>FY09</td>
<td>FY10 1&lt;sup&gt;st&lt;/sup&gt; Qtr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
<td>-------------</td>
<td>------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total HAI</td>
<td>21</td>
<td>13</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Days</td>
<td>28914</td>
<td>28382</td>
<td>6911</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate/PtDays</td>
<td>0.73</td>
<td>0.46</td>
<td>0.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital Onset</td>
<td>13</td>
<td>10</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate/PtDays</td>
<td>0.45</td>
<td>0.35</td>
<td>0.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comm Onset HA</td>
<td>8</td>
<td>3</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rate/PtDays</td>
<td>0.28</td>
<td>0.11</td>
<td>0.0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Outbreak Situations

BACKGROUND AND OBJECTIVE:
- Fluoroquinolones have not been frequently implicated as a cause of Clostridium difficile outbreaks
- Nosocomial C. difficile infections increased from 2.7 to 6.8 cases per 1000 discharges (P < .001)
- During the first 2 years of the outbreak, there were 253 nosocomial C. difficile infections; of these, 26 (10%) resulted in colectomy and 18 resulted in death (7%)

METHODS: A retrospective case-control study of case-patients with C. difficile infection from January 2000 through April 2001 and control-patients matched by date of hospital admission, type of medical service, and length of stay; an analysis of inpatient antibiotic use; and antibiotic susceptibility testing and molecular subtyping of isolates were performed.

RESULTS:
• Fluoroquinolone use increased before the onset of the outbreak (P < .001); 59% of case-patients and 41% of control-patients had received this antibiotic class.
• The outbreak was polyclonal, although 52% of isolates belonged to two highly related molecular subtypes.

CONCLUSIONS:
• Exposure to levofloxacin was an independent risk factor for C. difficile-associated diarrhea and appeared to contribute substantially to the outbreak.
• Restricted use of levofloxacin and the other implicated antibiotics may be required to control the outbreak.
Bacteria That Strikes Elderly Spreads in Canadian Hospitals

August 9, 2004

- Two hospitals in Montreal and one in Sherbrooke, Quebec
- The rate had increased from 2.1 cases per 1,000 admissions in 2002 to 10 per 1,000 in 2003
- University of Sherbrooke's medical center in southern Quebec, 54 deaths in 2003 and 46 more during the first half of 2004.
- The bacteria were also found to have contributed to the deaths of 81 patients in Montreal.
Clinical Manifestation

- Mild colitis, or simple diarrhea that is watery and contains mucus but not blood.
- Examination by sigmoidoscopy usually reveals normal colonic tissue.
- General symptoms are commonly absent and diarrhea usually stops when antibiotics are discontinued.
Antidiarrheal Agents

- Antidiarrheal agents such as Lomotil® or Imodium® have been shown to increase the severity of symptoms and should **NOT be taken.**
Non-Specific Colitis

- C. difficile can also cause non-specific colitis quite reminiscent of other intestinal bacterial infections such as *Shigella* or *Campylobacter*

- This is a more serious illness than simple antibiotic-associated diarrhea
- Patients experience watery diarrhea **10 to 20 times** a day and lower
- Crampy abdominal pain, low-grade fever, dehydration, and non-specific colitis are common manifestations.
Fulminant Colitis

- Fulminant colitis (severe sudden inflammation of the colon), is frequently associated with very serious complications.
- This can be a life-threatening form of C. difficile infection and occurs in ~ 3% of patients.
How can *C. difficile* spores be spread?
How can *C. difficile*-associated disease be spread?

- CDI - shed spores in the stool that can be spread from person to person.
- Spores can survive up to 70 days in the environment
- Transported on the hands of health care personnel who have direct contact with infected patients
- Transferred from touching contaminated environmental surfaces (floors, bedpans, toilets, stretchers, electronic thermometers, etc.)
Hands and Gloved Hands as Sources for Spread

- Scientists cultured the imprint of a health care worker's gloved hand after examining a patient infected with Clostridium difficile.
- The larger yellow colonies outlining the fingers are clusters of Clostridium difficile.
- The patient had showered an hour before the specimen was collected.

Clinical Infectious Diseases, February 2008

- Contamination of blood pressure cuffs at a rate similar to that for bedside commodes (10% and 11.5%, respectively).
- An observational survey revealed that healthcare workers in the patient care areas not infrequently failed to remove their potentially stool-contaminated gloves prior to touching clean surfaces, which might have contributed to contamination of blood pressure cuffs.
Transmission Factors

- High prevalence among hospitalized patients.
- Some elderly adults experience chronic diarrhea (eg from tube feedings, medications, IBS)
- Other serious co-morbidities
Transmission

- One study demonstrated that 20% of patients admitted to a hospital for various reasons were either positive for C. difficile on admission or acquired the microorganism during hospitalization.

- Interestingly, only one-third of these patients developed diarrhea while the remainder were asymptomatic carriers serving as a reservoir of C. difficile infection.
Reservoirs for Spores

- The organism and its spores were also demonstrated in the hospital environment, including toilets, telephones, BP cuffs, stethoscopes, commodes, bathrooms, electronic thermometers, and especially hands of healthcare personnel.
PURPOSE:
A prospective clinical and molecular epidemiologic study was conducted to define the frequency of nosocomial Clostridium difficile patient-to-patient transmission in an urban tertiary referral hospital.

FINDINGS
- Environmental contamination was detected in 58% of rooms and often involved wide dispersed areas.
- Among 99 prospectively identified patient contacts, C. difficile was cultured from the stool of 31 (31%), including 12 with diarrhea and 19 who were asymptomatic.
Environmental Sources

- Even after cleaning, studies show that C. diff spores linger on virtually every hospital surface, including bedrails, telephones, call buttons and toilets.
- C. diff spores cling to patient skin
- 40% of patients diagnosed with CDI infections tested positive for C. diff on their hands
- 20% had the bacteria on their forearms
- 60% had C. diff detected on their chest and abdomen.
How is *C. difficile*-associated disease diagnosed?

- *C. difficile* diarrhea is confirmed by the presence of a **toxin** in a stool specimen.
- Enzyme immunoassay detects toxin A & B
- *C. difficile* toxin is very unstable. The toxin degrades at room temperature and may be undetectable within 2 hrs after collecting the specimen.
- Laboratory requests the specimen be immediately brought to the lab within ½ hr.
- Refrigeration does not stabilize the toxin.
Hand Hygiene Key Prevention Measure to Prevent Spread

• Practice good hygiene often

• Keep your hands clean by washing thoroughly with soap and water – especially important with C. difficile to remove spores

• Keep cuts and abrasions clean and covered with a proper dressing (e.g. transparent bandage) until healed
ALCOHOL-BASED HAND RUB
Not Effective Against C. difficile

- Alcohol sanitizer does not kill spores
- **Hand washing** is imperative following contact with a C. difficile patient to get rid of spores.
- You may still use alcohol after hand washing
SPECIAL CONTACT PRECAUTIONS

- Appropriate sign visibly posted at the room entrance describing what to do; read before entering room
- Isolation cart or materials outside of room stocked with gowns, masks, gloves, red bags, etc.
- Designated equipment in room (e.g., stethoscope, designated commode, oximeter sensor and electronic thermometer)
- Red lined trash & linen containers kept inside patient room
Special Contact Precautions

- Gowns upon entering room – contamination can occur from touching patient, up against the bed, changing a dressing, sitting in the chair next to the bed, moving the patient, changing bed linen
- Most contaminated area is within 3 feet of patient’s bed
- Mask with faceshield if irrigating wounds, suctioning, splashing of blood or body fluids to prevent blood/body fluid exposure
Protocol to Discontinue Contact Precautions

- Continue until discharge – asymptomatic carriage can occur

- **No need to retest if diarrhea and symptoms are gone after treatment**
Environmental Disinfection

- Intermediate level disinfection is used for C. difficile
- Use bleach for environmental cleaning (10 min contact time)
- Bleach wipes for superficial surfaces and equipment
- Physical removal of spores will occur with cleaning procedures
- Change cloth frequently – after each piece of equipment is cleaned
Consider “GloGerm” Studies

- Glo-germ fluorescent powder can be used in bathrooms, on room surfaces and on shared patient equipment and monitoring with a black light to ascertain if adequate cleaning is being done.
- www.glogerm.com
Environmental Cleaning Study


- Method:
  A transparent stable solution that fluoresces when exposed to ultraviolet light was applied to various environmental surfaces in patient rooms

- Results:
  Overall thoroughness of terminal cleaning was 49%
  Patient telephones, nurse call devices and bedside rails were inconsistently cleaned

- Conclusion:
  Suboptimal cleaning is being done in hospitals
Therapy for C. difficile

- Directed against eradication of the microorganism from the colonic microflora.
- No therapy is required for asymptomatic carriers.
- Discontinuation of antibiotics (if possible) in noncomplicated patients with mild diarrhea, no fever, and modest lower abdominal pain, is often enough to alleviate symptoms and stop diarrhea.
- 23% of patients will resolve within 2-3 days of discontinuing the antibiotic.
Therapy continued.....

- Severe diarrhea and colitis:
  - *metronidazole* or *oral vancomycin*, for 10 to 14 days.
- Several clinical trials have shown that these antibiotics are equally effective in cases of mild to moderate *C. difficile* infection and more than 95% of patients respond very well to this treatment.
- Diarrhea following treatment with either *vancomycin* or *metronidazole* is expected to improve after 1 to 4 days with complete resolution within 2 weeks.
Relapse of C. Difficile

- Approximately 15 to 20% of patients will experience re-appearance of diarrhea and other symptoms weeks or even months after initial therapy has been discontinued.
Relapse

- Repeat the 10 to 14 day course of either metronidazole or vancomycin.
- However, a subset of patients continues to relapse whenever antibiotics are discontinued and this represents a therapeutic challenge.
- Some authorities recommend switching to the alternative antibiotic from the one used initially.
In Summary.....

- Clostridium difficile infections are a newly emerging outbreak problem in hospitals
- Resulting in increased morbidity and mortality
- Infection control measures, such as Special Contact Precaution techniques and excellent hand hygiene have been shown to prevent the spread of Clostridium difficile
- Thorough cleaning of the environment with bleach is vital to prevent cross-contamination of spores
- Judicious use of antibiotics is an important prevention measure.