C. Difficile Infection: A Growing Threat to Public Health

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Objectives

Review of:

- mechanisms and extent of current issues with antimicrobial resistance
- risk factors for CDI
- clinical presentation of CDI
- available treatments of CDI
- action plan to control the spread of MDROs, including CDI
Principles of antibiotic therapy

- Maximize therapeutic effect and minimize unintended consequences.
Antimicrobials

- Antimicrobials are one of most commonly prescribed therapeutics in hospitalized patients.
- Some authors report in up to 50% of cases antibiotics are used inappropriately: overly broad coverage, longer duration and unnecessary treatment altogether.
Antibiotics in food and water

- Up to 80% of antibiotics sold in the US are for use in animals
- Antibiotics present in municipal water
Why should we care?

Inappropriate use of antibiotics leads to:

- Antimicrobial Resistance
- “Collateral Damage”- C.Difficile infection
- Worse health outcomes (death, longer hospital stay, prolonged recovery) and dissatisfaction of doctors and patients with care provided/received
- Increase in hospital admission and readmission rates
- Financial implications (decrease reimbursements, financial penalties)
If it doesn’t kill you it makes you stronger
Cell Wall (peptidoglycan) Synthesis
β-lactam drugs
Vancomycin
Bacitracin

Nucleic Acid Synthesis
Fluoroquinolones
Rifamycins

Cell Membrane Integrity
Polymyxin B

Metabolic Pathways (folate biosynthesis)
Sulfonamides
Trimethoprim

Protein Synthesis
Aminoglycosides
Tetracyclines
Macrolides
Chloramphenicol
Lincosamides
Oxazolidinones
Streptogramins
Response of Microorganisms to Antibiotics
Alphabet Soup

- CA-MRSA
- HA-MRSA
- VRSA
- VISA
- VRSE
- VRE
- CRE
- ESBL
- KPC
- NDM-1
- ERSP
- PRSP
- NAP1-027
- MDR-TB
- XDR-TB
Dates are based upon early reports of resistance in the literature. In the case of pan drug-resistant (PDR)-Acinetobacter and Pseudomonas, the date is based upon reports of healthcare transmission or outbreaks. Note: penicillin was in limited use prior to widespread population usage in 1943.
Clinical Impact of Resistance

<table>
<thead>
<tr>
<th>Event</th>
<th>Mortality Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA vs MSSA bacteremia</td>
<td>1.93</td>
</tr>
<tr>
<td>MRSA vs MSSA SSTI</td>
<td>3.40</td>
</tr>
<tr>
<td>VRE vs VSE bacteremia</td>
<td>2.52</td>
</tr>
<tr>
<td>Emergence of R Pseudomonas</td>
<td>3.00</td>
</tr>
<tr>
<td>MDR Acinetobacter vs non-MDR bacteremia</td>
<td>4.10</td>
</tr>
</tbody>
</table>

CID 2003:36; CID 2005:41; Arch Of Int Med 1999:159
Infect Control Hosp Epidemiol 2007:28
The Dynamics of Antibiotic Resistance

Microorganisms with a threat level **URGENT**

- **Clostridium Difficile**
  - 250,000 infections/year; 14,000 deaths
  - $1,000,000,000 healthcare cost
- **Carbapenem–resistant Enterobacteriaceae (CRE)**
  - 9,000 infections/year; 600 deaths
- **Neisseria Gonorrheae**
  - 820,000 infections/year
  - 246,000 infections are drug resistant or with decreased susceptibility (Cipro, tetracyclines, azithromycin, ceftriaxone, cefixime)
Discovery

- First discovered in 1935 in the stool of healthy infants without GI symptoms
- Gram-positive spore-forming anaerobic bacillus. Produces toxin A and B
Hardy Staff

- In spore form, C. diff can survive disinfectants and withstand drying
- It can survive up to 5 months in the environment
- It was cultured 40 days after the discharge of infected individual

*Patient Safety Advisory, Pennsylvania Patient Safety Reporting Systems, June 2005*
Pathogenesis

- Bowel flora \((10^{11}\) bact/g stool) changed by antibiotics makes the host susceptible to C. diff infection

- Two toxins produced: **Toxin A and Toxin B**
  - These toxins can work together
  - \((A+/B+, A-/B+).\) Toxin B \(\rightarrow\) alters membrane allowing A to enter the cells. Enzymatic component A enters the cells and disrupts cytoskeleton by ADP ribosylation causing cell death.
  - Both cause inflammation and production of protein-rich exudate that consists of neutrophils, monocytes and sloughed enterocytes
Pathogenesis (cont.)

- In addition to toxins TcdA and TcdB, which belong to group of Large Clostridial Toxins (LCT), *C. difficile* strains produce a third toxin CDT, belonging to the group of clostridial binary toxins (Perelle et al., 1997).
  - Binary toxin is encoded by two genes: *cdtA* for catalytic component and *cdtB* for binding component. Up to now all strains tested had both genes.
Spectrum of Disease

Table 1: Patients with Clostridium difficile-associated diarrhea (CDAD) in the Estrie region of Quebec who died within 30 days after diagnosis or who had complicated CDAD, 1991–2003

<table>
<thead>
<tr>
<th>Period</th>
<th>No. of patients with CDAD*</th>
<th>No. (% who died within 30 days after diagnosis)</th>
<th>Adjusted OR (95% CI)†</th>
<th>No. (% who had complicated CDAD)</th>
<th>Adjusted OR (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991–1992</td>
<td>169</td>
<td>8 (4.7)</td>
<td>1.0</td>
<td>12 (7.1)</td>
<td>1.0</td>
</tr>
<tr>
<td>1993–1994</td>
<td>217</td>
<td>11 (5.1)</td>
<td>1.7 (0.5–5.3)</td>
<td>14 (6.5)</td>
<td>1.0 (0.4–2.7)</td>
</tr>
<tr>
<td>1995–1996</td>
<td>215</td>
<td>13 (6.0)</td>
<td>1.6 (0.5–5.0)</td>
<td>17 (7.9)</td>
<td>0.9 (0.3–2.2)</td>
</tr>
<tr>
<td>1997–1998</td>
<td>192</td>
<td>11 (5.7)</td>
<td>1.1 (0.4–3.7)</td>
<td>13 (6.8)</td>
<td>0.6 (0.3–1.7)</td>
</tr>
<tr>
<td>1999–2000</td>
<td>248</td>
<td>19 (7.7)</td>
<td>1.5 (0.5–4.6)</td>
<td>28 (11.3)</td>
<td>1.2 (0.5–2.9)</td>
</tr>
<tr>
<td>2001–2002</td>
<td>244</td>
<td>21 (8.6)</td>
<td>1.6 (0.5–4.7)</td>
<td>28 (11.5)</td>
<td>1.1 (0.5–2.5)</td>
</tr>
<tr>
<td>2003</td>
<td>390</td>
<td>54 (13.8)</td>
<td>3.0 (1.1–8.4)</td>
<td>71 (18.2)</td>
<td>2.2 (1.0–4.9)</td>
</tr>
</tbody>
</table>

Note: OR = odds ratio, CI = confidence interval.
*Includes only patients for whom enough information was available to assess these outcomes.
†Adjusted for age, sex, initial treatment, immune status, and tube feeding and surgery in the 2 months preceding diagnosis; 1991–1992 was used as the baseline period.

Table 2: Factors associated with complicated CDAD

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>% (no.) of patients with complicated CDAD†</th>
<th>Unadjusted OR (95% CI)†</th>
<th>Adjusted OR (95% CI)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>8.7 (82/940)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Male</td>
<td>13.7 (101/735)</td>
<td>1.7 (1.2–2.3)</td>
<td></td>
</tr>
<tr>
<td>Age, yr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 17</td>
<td>1.3 (4/301)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>18–64</td>
<td>6.0 (38/635)</td>
<td>4.7 (1.7–13.4)</td>
<td>1.6 (0.5–5.1)</td>
</tr>
<tr>
<td>≥ 65</td>
<td>19.1 (141/739)</td>
<td>17.5 (6.4–47.8)</td>
<td>3.4 (1.1–10.3)</td>
</tr>
<tr>
<td>Place CDAD acquired</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Community</td>
<td>2.0 (15/76)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Hospital</td>
<td>18.7 (168/900)</td>
<td>11.5 (6.7–19.7)</td>
<td>4.6 (2.4–8.6)</td>
</tr>
<tr>
<td>Surgery in 2 mo preceding diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>10.8 (123/1141)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Yes</td>
<td>13.4 (60/448)</td>
<td>1.3 (0.9–1.8)</td>
<td>0.6 (0.4–0.9)</td>
</tr>
<tr>
<td>Tube feeding in 2 mo preceding diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>9.5 (135/1416)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Yes</td>
<td>28.5 (43/151)</td>
<td>3.8 (2.5–5.6)</td>
<td>2.4 (1.5–3.9)</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>9.4 (128/1358)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Yes</td>
<td>21.7 (54/249)</td>
<td>2.7 (1.9–3.8)</td>
<td>2.3 (1.5–3.6)</td>
</tr>
<tr>
<td>Fever (temperature &gt; 38.0°C)</td>
<td></td>
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<tr>
<td>No</td>
<td>8.8 (52/592)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17.1 (123/718)</td>
<td>2.1 (1.5–3.0)</td>
<td></td>
</tr>
<tr>
<td>Peak leukocyte count, × 10⁹/L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 10.0</td>
<td>5.4 (23/423)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>10.1–19.9</td>
<td>9.8 (62/633)</td>
<td>1.9 (1.2–3.1)</td>
<td>1.3 (0.8–2.3)</td>
</tr>
<tr>
<td>≥ 20.0</td>
<td>33.4 (96/287)</td>
<td>8.7 (5.4–14.2)</td>
<td>4.6 (2.8–8.4)</td>
</tr>
<tr>
<td>Peak creatinine level, μmol/L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 100</td>
<td>6.8 (54/797)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>100–199</td>
<td>24.1 (78/324)</td>
<td>4.4 (3.0–6.4)</td>
<td>2.2 (1.4–3.5)</td>
</tr>
<tr>
<td>≥ 200</td>
<td>32.2 (46/143)</td>
<td>6.5 (4.2–10.2)</td>
<td>3.1 (1.8–5.2)</td>
</tr>
<tr>
<td>Initial antibiotic treatment§</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>10.4 (41/394)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>13.1 (125/951)</td>
<td>1.3 (0.9–1.9)</td>
<td>1.0 (0.6–1.6)</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>5.9 (5/85)</td>
<td>0.5 (0.2–1.4)</td>
<td>0.2 (0.05–0.8)</td>
</tr>
<tr>
<td>Metronidazole and vancomycin</td>
<td>60.0 (9/15)</td>
<td>12.9 (4.4–38.1)</td>
<td>3.7 (0.9–14.1)</td>
</tr>
</tbody>
</table>
Hypervirulent C. Difficile-BI/NAP1/027—
restriction enzyme analysis BI, North American Pulse Field type 1 or PCR ribotype 027

- Increased Incidence
- Increased Severity
- Increased Recurrence
- Increased Mortality
Community Acquired-C. diff and Peripartum C. diff

- CDI impacts populations previously thought to be at low-risk, including young adults and children, and those who lack the traditional risk factors of hospitalization or antibiotic exposure. In this cohort, community-acquired CDI was common in younger patients (61% of younger patients acquired infection in the community), the majority of patients were females, and many of them (22%) were not exposed to antibiotics in the 90-day period before acquiring CDI. Am J Gastro 2012.

- Ten peripartum cases were reported from four states during May-June 2005 with onset dates ranging from February 26, 2003, to June 28, 2005. All but one of the cases occurred during 2004--2005. Baseline-1 state reported 3 cases of C. diff in 10 years. MMWR 2005.
Rate of hospital stays associated with *Clostridium difficile* infections (CDI), per 100,000 population, 1993–2009

**Figure 2**

- **Principal Diagnosis**
- **All-listed Diagnoses**

**Source:** Center for Delivery, Organization and Markets, Healthcare costs and Utilization Project, Nationwide Inpatient sample
C. diff rates for hospitalized persons aged ≥65 years increased 200%, with increases of 175% for those aged 65-74 years, 198% for those aged 75-84 years, and 201% for those aged ≥85 years.

National Hospital Discharge Survey, United States, 1996--2009
Figure 3. Rate of principal and secondary diagnosis Clostridium difficile infection (CDI) stays per 100,000 population, by region, income quartile, age group, and sex, 2009

Source: AHRQ, Center for Delivery, Organization, and Markets, Healthcare Cost and Utilization Project, Nationwide Inpatient Sample, 2009

*Income quartile is based on the median income of the patient’s ZIP Code. Differences between income quartile group rates are not statistically significant.
Mortality from C. difficile

Deaths caused by C. difficile infections*

*Age-adjusted rate of C. difficile as the primary (underlying) cause of death.
SOURCE: CDC National Center for Health Statistics, 2012
C. Diff Risk Factors

- Age
- Hospitalization
- Antibiotic exposure
- GI procedures
- Immunosuppression
- Antacids
- IBD
Where is it lurking?
1. **Special** Contact Precautions (soap and water + gloves).
2. Send stool for testing.
3. Stop all unnecessary antibiotics or change them to more gut friendly options.
4. Stop all a/motility agents.
7. Barrier creams for incontinent patients.
8. Clean with bleach.
Contact Precautions

- Private room. If not available cohort with patient with CDI (for patients with the same infection!).
- If private room or cohorting are not available, place patient with a roommate who is immunocompetent, doesn’t share bathroom, doesn’t have indwelling catheters (IV, feeding tube, Foley), follows directions on hygiene.
- Continue precautions until patient returns to his/her “normal stooling pattern.”
## Testing Methods

### Table 1: Diagnosis of *C. diff*

<table>
<thead>
<tr>
<th>Diagnostic Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Turn around time</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Toxin detection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Cytotoxin assay</td>
<td>+++ (94-100%)</td>
<td>+++ (99%)</td>
<td>48 hrs</td>
<td>High</td>
</tr>
<tr>
<td>2. Enzyme Immunoassay (EIA)</td>
<td>+ (60-95%)</td>
<td>++ (75-100%)</td>
<td>&lt;24 hrs</td>
<td>Low</td>
</tr>
<tr>
<td>3. PCR of stool</td>
<td>++ (93%)</td>
<td>+++ (97%)</td>
<td>&lt;1 hr</td>
<td>High</td>
</tr>
<tr>
<td><strong>B. Organism detection</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Common antigen testing (GDH antigen)</td>
<td>+++ (96-100%)</td>
<td>Low</td>
<td>15-45 min</td>
<td>Low</td>
</tr>
<tr>
<td>2. Stool culture</td>
<td>+++</td>
<td>Low (asymptomatic carriage)</td>
<td>72 hrs</td>
<td>Labour intensive</td>
</tr>
</tbody>
</table>
Testing

- GDH ag
  - Positive
  - Negative
- Toxin EIA
  - Positive
  - Negative
## Treatment Guidelines

### TABLE 3. Recommendations for the Treatment of *Clostridium difficile* Infection (CDI)

<table>
<thead>
<tr>
<th>Clinical definition</th>
<th>Supportive clinical data</th>
<th>Recommended treatment</th>
<th>Strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial episode, mild or moderate</td>
<td>Leukocytosis with a white blood cell count of 15,000 cells/µL or lower and a serum creatinine level less than 1.5 times the premorbid level</td>
<td>Metronidazole, 500 mg 3 times per day by mouth for 10–14 days</td>
<td>A-I</td>
</tr>
<tr>
<td>Initial episode, severe*</td>
<td>Leukocytosis with a white blood cell count of 15,000 cells/µL or higher or a serum creatinine level greater than or equal to 1.5 times the premorbid level</td>
<td>Vancomycin, 125 mg 4 times per day by mouth for 10–14 days</td>
<td>B-I</td>
</tr>
<tr>
<td>Initial episode, severe, complicated</td>
<td>Hypotension or shock, ileus, megacolon</td>
<td>Vancomycin, 500 mg 4 times per day by mouth or by nasogastric tube, plus metronidazole, 500 mg every 8 hours intravenously. If complete ileus, consider adding rectal instillation of vancomycin</td>
<td>C-III</td>
</tr>
<tr>
<td>First recurrence</td>
<td>...</td>
<td>Same as for initial episode</td>
<td>A-II</td>
</tr>
<tr>
<td>Second recurrence</td>
<td>...</td>
<td>Vancomycin in a tapered and/or pulsed regimen</td>
<td>B-III</td>
</tr>
</tbody>
</table>

*IDSA guidelines, 2010*
A Comparison of Vancomycin and Metronidazole for the Treatment of *Clostridium difficile*–Associated Diarrhea, Stratified by Disease Severity.


**Conclusion:**

Metronidazole and Vancomycin are equally effective for the treatment of mild CDAD, but Vancomycin is superior for treating patients with severe CDAD.
Treatment of *Clostridium difficile*-associated disease: old therapies and new strategies.


- Metronidazole (Flagyl) vs PO Vancomycin-
- Similar recurrence but higher failure rates
- Over time more studies show decrease in response rates of C.diff to Flagyl
DIFICID

Indications and Usage

- DIFICID is a macrolide antibacterial drug indicated in adults ≥18 years of age for treatment of *Clostridium difficile*-associated diarrhea.

Safety Information

- The most common adverse reactions reported in clinical trials are nausea (11%), vomiting (7%), abdominal pain (6%), gastrointestinal hemorrhage (4%), anemia (2%), and neutropenia (2%).
DIFICID vs Oral Vancomycin

- Prospective, double-blind, randomized, parallel-group study.
- 629 adults with non-severe infection, with no h/o CDAD or 1 prior episode.
- For 10 days, patients received either vancomycin 125 mg four times daily (n = 327) or fidaxomicin 200 mg twice daily with intervening placebo for the other two doses (n = 302).
- During the 4 weeks following therapy, significantly lower recurrence rates were noted with fidaxomicin than with vancomycin in the per-protocol group (13.3% vs. 24.0%, respectively; P = 0.004). Significantly fewer recurrences were also observed with fidaxomicin, compared with vancomycin (15.4% vs. 25.3%, respectively; P = 0.005).
- No significant difference between fidaxomicin and vancomycin in the rate of recurrence in patients infected with the hypervirulent NAP1/B1/027 strain of C. difficile. Fidaxomicin, however, provided a 69% relative reduction in the risk of recurrence of non-NAP1/B1/027 strains compared with vancomycin.

Both Oral Metronidazole and Oral Vancomycin Promote Persistent Overgrowth of Vancomycin-Resistant Enterococci during Treatment of Clostridium difficile-Associated Disease

Wafa N. Al-Nassir, Ajay K. Sethi, Yuejin Li, Michael J. Pultz, Michelle M. Riggs and Curtis J. Donskey, 2008

Conclusion:
New CDAD treatments are needed that are less likely to disrupt the intestinal microflora and promote overgrowth of healthcare-associated pathogens.
Probiotics vs. Antibiotics

- 31 trials with a total of 4492 participants
- Trials assessed effectiveness of probiotics in preventing CDAD in participants taking antibiotics
- Results suggested that when probiotics were implemented during antibiotic therapy, CDAD was reduced by 64%.

Saccharomyces boulardii

- Saccharomyces boulardii is a tropical strain of yeast first isolated from lychee & mangosteen fruit in 1923 by French scientist Henri Boulard.
- Boulard first isolated this yeast after he observed natives of SE Asia chewing on the skin of lychee and mangosteen to control symptoms of cholera.
Action of S. Boulardii

- Inhibits toxin A mediated diarrhea and inflammation
- Produces an enzyme that cleaves toxin and toxin receptors
- Stimulates antitoxin A immunoglobulins
- Inhibits IL-8 production and activation
- In animal studies of C. diff it was associated with improved survival

Combination of standard antibiotics and S. boulardii was shown to be effective and safe therapy for patients with recurrent CDD; no benefit of S. boulardii demonstrated for those with initial CDD episode.

Significant relative reduction in recurrent CDI in adults taking S. boulardii ranged between 19% and 33.3% [McFarland et al. 1994; Surawicz et al. 2000].

Guidelines: no compelling evidence exists to support routine use of probiotics for prevention or treatment of CDI. 2010
Non-conventional treatments

- Vancomycin enema
- FMT

<table>
<thead>
<tr>
<th>Study/year</th>
<th>Number of patients</th>
<th>*Success rate %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arkkila et al., 2010</td>
<td>37</td>
<td>34/37 92</td>
</tr>
<tr>
<td>Khoruts et al., 2010</td>
<td>1</td>
<td>1/1 100</td>
</tr>
<tr>
<td>Yoon et al., 2010</td>
<td>12</td>
<td>12/12 100</td>
</tr>
<tr>
<td>Rohlke et al., 2010</td>
<td>19</td>
<td>18/19 95</td>
</tr>
<tr>
<td>Silverman et al., 2010</td>
<td>7</td>
<td>7/7 100</td>
</tr>
<tr>
<td>Garborg et al., 2010</td>
<td>40</td>
<td>33/40 83</td>
</tr>
<tr>
<td>Russell et al., 2010</td>
<td>1</td>
<td>1/1 100</td>
</tr>
<tr>
<td>Kelly et al., 2010</td>
<td>12</td>
<td>12/12 100</td>
</tr>
<tr>
<td>Mellow et al., 2010</td>
<td>13</td>
<td>12/13 92</td>
</tr>
<tr>
<td>Kassam et al., 2010</td>
<td>14</td>
<td>14/14 100</td>
</tr>
<tr>
<td>Kelly et al., 2011</td>
<td>26</td>
<td>24/26 92</td>
</tr>
</tbody>
</table>

*Eradication by negative culture or toxin assay and/or clinical response
FMT in a pill
Secret Weapon


Test of Cure???

- After resolution of symptoms, testing stool for C. difficile or its toxins as a test of cure for CDI is NOT recommended
  - Patients may shed the organism or toxin for several weeks after the cessation of treatment

- Asymptomatic carriers (without h/o CDI) are not at increased risk for disease
In LTCF make decisions regarding patient placement on a case by case basis, balancing infection risk to other patients in the room, factors that increase transmission, and potential adverse psychological impact on the infected patient. (CDC, 2007)

If patient completed treatment for CDI, has stable frequency of stooling without worsening, is not incontinent of stool, clinically stable, tolerates PO, you can consider stopping isolation.

Evaluate this type of scenario on case-by-case basis
In cases of suspected C. difficile...

- Contact Isolation/Soap and water hand washing
- Stop all unnecessary antibiotics and change therapy to “C.Diff friendly” if possible
- Start Treatment
- Avoid all anti-peristaltics when CDI is suspected or patient is receiving antibiotics or patient just finished treatment for C.diff
- Aggressive fluid management
- NPO→parenteral nutrition if needed with transition to Low residue, Low fat, Lactose free
- Consider consultation with ID, especially if first line treatment failed or patient has recurrent symptoms
Figure 1
Confirmed and non-confirmed *Clostridium difficile* infection with ribotype 027 in northern France, 2006-2009 (n=602 cases)
What can change the trajectory of C. diff rates?

- Antibiotic stewardship programs in hospitals, extended care facilities, outpatient facilities
- National campaigns to educate public on risks of unrestricted/unnecessary antibiotic use
- Encourage development of new treatments
- Limit use of antimicrobials in agriculture
Antibiotic Stewardship - Optimize Benefit, Reduce Damage and Cut Costs

1. Infection Prevention (hand hygiene, vaccination, environmental cleaning, track and trend transmissible pathogens and employ methods to decrease transmission)
2. Rapid diagnostics and prompt treatment
3. Consider local susceptibility patterns when choosing the treatment
4. Use of antibiotics at the right dose, interval and indications
5. De-escalate antibiotics when culture results become available
Antimicrobial Stewardship- Infection Prevention

- Hand Hygiene
- Vaccination
- Environmental cleaning
- Tracking and trending of transmissible pathogens
- Using various policies to decrease transmission of pathogens in healthcare setting
Monitoring of susceptibility patterns: Antibiogram

- Susceptibility patterns
- Choice in empiric therapy
- Trends in resistance
- Directs plan of action
Clinical Challenges with CDI

- Prevention of acquisition in high risk settings
- Rapid and accurate diagnosis, which is not price prohibitive
- Treatment options that are effective and prevent recurrences
- Data on probiotic use: quantity, brand, duration.
- Treatment of fulminant C. difficile
What You Can Do

A. Improve Hand-Hygiene!

B. Avoid ALL Unnecessary antibiotics!
   - Develop algorithms of evaluating residents with asymptomatic bacteriuria/UTI, fevers, respiratory symptoms, wounds
   - Question MD if necessary

C. Use proper isolation methods

D. Educate staff, patients and their families on dangers of antibiotics

E. Do not hesitate to call ID about difficult patients especially with h/o MDRO organisms, including C. diff.
In Summary:

- Antibiotics are a limited resource
- They are overused, leading to dangerous antibacterial resistance and C. difficile
- CDI reached epidemic scale and can be life-altering and life-threatening
- Flagyl, PO Vancomycin are mainstay treatments
- FMT is a ground-breaking option
- Proper isolation, limiting antibiotic use by developing of treatment guidelines for ECF residents and robust hand washing programs will help staff and residents decrease the risk of unexpected/unwanted complications
- We are all in it together!
Thank You!