**Clostridium difficile Infections with a Spotlight on Antimicrobial Stewardship**

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**Objectives**

- Examine the impact of antimicrobial resistance
- Assess the trends in *Clostridium difficile* infections
- Review basic principles of the diagnosis, prevention and management of *Clostridium difficile* infections
- Recognize the current status of antimicrobial stewardship programs in Florida's Long Term Care Facilities
- Integrate strategies to control *C. difficile* infections through antimicrobial stewardship

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**Stadium**  
104,000 seats
Impact of Antimicrobial Resistance (CDC: Nationally 2006)

1.7 million hospital-acquired infections
  • 3 people per minute
  • 4700 per day

100,000 deaths/year
$23 billion/year

Centers for Disease Control and Prevention

Impact of Antimicrobial Resistance

• >70% of the bacteria causing Hospital Acquired Infections are resistant to at least 1 of the drugs most commonly used to treat them

• Infected patients with drug resistant infections:
  Need treatment with 2nd or 3rd line drugs
  Increased mortality
    - MRSA bacteremia 12% vs. MSSA 5.1% (p< 0.001)
    - CRK 48% vs. CSK 20% (p< 0.001) OR 3.71 (1.97-7.01)

http://www.cdc.gov/drugresistance/healthcare/problem.htm

Costs of Antimicrobial Resistant Infections

• 188 patients with AMR infections-
  Chicago teaching hospital

• Longer hospital stay (6.4 vs. 12.7 days)
• Attributable mortality = 6.5%
• Societal costs ($18,688- $29,069) per patient

How did we get here?

- 2000 B.C. “Here, eat this root”
- 1000 A.D. “That root is heathen. Here say this prayer”
- 1850 “That prayer is superstition. Here drink this potion”
- 1940 “Miracle drug” Penicillin
- 1985 “Here take this new antibiotic! It’s bigger and better”

Fishman, N. Antimicrobial Stewardship Workshop, SHEA 2010

2012 “Here, eat this root”

Are we going back to the pre-antibiotic era?

Mr. Dificil

- A 74 year old man Nursing Home resident with history of hypertension transferred to the hospital with cough, malaise and a 1 day history of fever
- Other patients and staff have similar symptoms at the nursing home
- Chest X-Ray is negative
- He is hospitalized and started on cefepime plus azithromycin for “healthcare associated pneumonia”
**Mr. Dificil**

- After 2 days he is discharged home on an oral quinolone for 7 more days.
- The day the patient was discharged results came back positive for Influenza A.
- 2 weeks later he goes to the hospital with high WBC 34,000 and watery diarrhea (>7 BM a day).
- His roommate and 3 more residents at the Nursing Home developed severe watery diarrhea 6 days later.
- Guess the diagnosis?

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**Florida**

**Houston.. We have a problem!**

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**What can we learn from this case?**

1. Not all fevers need broad spectrum antibiotics.
2. Limit antibiotics to the shortest duration (when possible).
3. *Clostridium difficile* is a serious consequence of antimicrobial use.
4. Vaccination against Influenza (patients and healthcare workers) is very important.
5. *C. difficile* is transmissible – someone is not washing their hands and/or the environment!
What is *Clostridium difficile*?

- Anaerobic, spore-forming bacillus that causes pseudomembranous colitis, manifesting as diarrhea that often recurs and can progress to toxic megacolon, sepsis, and death.
- Infection is spread by the fecal-oral route; spores, the infective form, can persist on fomites and environmental surfaces for months.

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Pseudomembranous Ulcerative Colitis

Normal cecum vs. Pseudomembrane-bacterial overgrowth Endoscopy image

C. Difficile Pseudomembranous colitis

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*C. difficile* Infections (CDI) Incidence in the US

- CDI rates, deaths and excess healthcare costs in hospitalized patients are at historic highs
- 400% increase in CDI-related deaths between 2000 and 2007, up to 14,000 deaths annually
- Although nearly half of infections occur in people younger than 65, more than 90% of deaths occur in people 65 and older

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3/27/2012

CDC Vital Signs; March, 2012

94% of all CDI are Connected to Getting Medical Care

MMWR, March 9, 2012, 61(09);157-162

75% onset outside of hospitals
CDI Type and Location of Exposure

- 20% of hospital-onset CDIs occurred in <12 weeks residents of a nursing home
- 67% of nursing home-onset CDI occurred in patients recently discharged from an acute-care hospital

How *C. Difficile* Spreads

- George, a 68-year-old man, goes to the doctor’s office and is diagnosed with pneumonia.
- He is prescribed antibiotics, drugs that put him at risk for *C. diff.* infection for several months.

1 Month Later

- George breaks his leg and goes to a hospital.
- A health care worker spreads *C. difficile* to him after forgetting to wear gloves when treating a *C. difficile* infected patient in the next room.
**2 Days Later**

- George transfers to a rehabilitation facility for his leg and gets diarrhea.
- He is not tested for *C. diff*
- The health care worker doesn’t wear gloves and infects other patients.

**3 Days Later**

- George goes back to the hospital for treatment of diarrhea and tests positive for *C. difficile*.
- He is started on specific antibiotics to treat it. Health care workers wear gloves and do not spread *C. difficile*.
- George recovers.

Hospitalization related to CDI adds **$1.3 billion** in extra costs to the national healthcare system

Antimicrobial Prescribing Facts

- Inappropriate and excessive use leads to resistance, *C. difficile* & other ecological consequences, increased morbidity, mortality, increased cost, increased litigation and reduce quality of life.

- In acute care facilities up to 50% of antimicrobial use is either unnecessary or inappropriate.

Magnitude of Antimicrobial Use

- 8.5 billion dollars spent on antimicrobials annually.
- 30-50% of all hospitalized patients receive antibiotics.

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>2008 Expenditures ($ Thousands)</th>
<th>Percent Change From 2007</th>
<th>2008 Expenditures (% Total)</th>
<th>Percent Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimicrobials</td>
<td>3,975,342</td>
<td>-3.4</td>
<td>2,110,810,183</td>
<td>19.4</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>2,105,624</td>
<td>-0.9</td>
<td>1,154,446,172</td>
<td>10.9</td>
</tr>
<tr>
<td>Antifungals</td>
<td>794,917</td>
<td>-2.2</td>
<td>794,917,912</td>
<td>7.0</td>
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<tr>
<td>Antivirals</td>
<td>695,974</td>
<td>1.8</td>
<td>695,974,926</td>
<td>6.2</td>
</tr>
<tr>
<td>Others</td>
<td>1,959,205</td>
<td>0.4</td>
<td>1,959,205,598</td>
<td>1.8</td>
</tr>
<tr>
<td>Respiratory</td>
<td>792,613</td>
<td>6.9</td>
<td>621,175,038</td>
<td>5.7</td>
</tr>
<tr>
<td>Anti-infectives</td>
<td>1,256,337</td>
<td>4.3</td>
<td>1,256,337,000</td>
<td>3.6</td>
</tr>
<tr>
<td>Total</td>
<td>8,505,577</td>
<td>4.7</td>
<td>8,505,577,000</td>
<td>4.7</td>
</tr>
</tbody>
</table>

Antimicrobial use in LTCF

- On average, residents of long-term care facilities (LTCF) receive one course of antimicrobials each year.
- 25-75% of these antimicrobials are not necessary.

- Jump, et al: Cleveland VA LTCF.
Unnecessary Antibiotics
Cleveland VA LTCF

Study Population
100 Abx Regimens
1,351 days of therapy

Abx Unnecessary
42 regimens
334 days of therapy

Abx Necessary
58 regimens
1,017 days of therapy

Part of Regimen Unnecessary
22 regimens
494 days of therapy

All of Regimen Necessary
36 regimens
523 days of therapy

Unnecessary Days
241 days of therapy

Necessary Days
253 days of therapy

42% of regimens were wholly unnecessary
43% of antibiotic days were unnecessary

Peron et al. ICAAC 2010 (Courtesy of Dr. Robin Jump)

What is Stewardship?

Wikipedia
“A responsibility to take care of something owned by someone else”
Antimicrobial Stewardship

- Ongoing effort by a health care institution to optimize antimicrobial use among patients to...
  - Improve patient outcomes
  - Ensure cost-effective therapy
  - Reduce adverse effects of antimicrobial use (including antimicrobial resistance)

- Antimicrobial Stewardship programs can save up to 10% of pharmacy budgets

Antimicrobial Stewardship in Florida's LTCF

Grant Support
Florida Department of Health
Bureau of Epidemiology

Methods

- July through November 2011
- 2 electronic surveys
  - Acute care facilities (ACF)
  - Nursing Homes/Skilled Nursing Facilities (NH/SNF)
- Facilities were contacted via Email through professional associations (FADONA) and Florida DOH
- No incentives were given for participation
Methods and Limitations

- Prior to any analysis duplicate responses were cleaned
- Demographic information was confirmed with the database from Florida Hospital Association (Acute) and Florida Healthcare Association (NH/SNF) to ensure correct information
- The response rate is underestimated, we are not able to obtain an exact number of facilities that received the surveys (sent by organizations)
- No information available on “non respondents”

Results

Nursing Homes/ Skilled Nursing Facilities (SNF)

- 1465 NH/SNF in Florida (FHA’s website)
- Approximately reached 300 facilities “FADONA”
- 48 responses, 30 included in the analysis
- Underestimated 10% response rate (30/300)

- Survey sent again by FADONA (February 2012) anonymous = 35 responses
  we cannot accurately estimate the number of duplicates

Florida’s NH/ SNF

Antimicrobial Stewardship Respondents by Region (n=30)

Abbo L, et al FASS 2011
### Florida’s NH/SNF Antimicrobial Stewardship Related Activities Performed by Respondents (n=30)

- Tracking when a new antibiotic starts: 100%
- Assess antibiotic appropriateness (right bug/drug combination): 97%
- Assess appropriate duration of antibiotic therapy: 97%
- Staff education about appropriate antibiotic usage: 97%
- Tracking antibiotic resistance patterns: 97%
- Restrict antibiotic use/antibiotic protocols: 97%
- Dose optimization: automatic dose adjustments: 97%
- Parenteral to oral conversion protocols: 97%
- Formulary restrictions: 97%
- Post-prescription review with prescriber feedback: 97%
- Streamlining or de-escalation of therapy: 97%
- Antibiotics order forms: 97%
- Antibiotic cycling: 97%

### Proportion of Respondents Reported Access to Support at NH/ SNF (n=28)

- **Pharmacy support services**
  - Outside consulting pharmacist: 64%
  - Contract services: 32%
  - In house pharmacist: 4%

- **Availability of Pharmacy support**
  - Anytime/as needed: 75%
  - Monthly/Daily: 25%

- **Infectious Diseases support**
  - ID physician on site: 4%
  - ID consult upon request: 71%
  - None: 25%

### Most Challenging Hospital Acquired Infection reported by respondents NH/SNF (n=28)

- **Clostridium difficile associated diarrhea**
- Methicillin-resistant S. aureus infections
- Multidrug resistant gram negative bacteria (Acinetobacter spp, Klebsiella spp, etc)
- Catheter associated urinary tract infections
- Vancomycin resistant enterococcus
- Influenza
- Norovirus
- Central-line associated blood stream infections

*Other: Non CAUTI*
Impact of Antibiotic Stewardship Programs on C. difficile Infections

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Setting</th>
<th>Key staff</th>
<th>Intervention</th>
<th>Impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valiquette, L, et al (2007)</td>
<td>488-bed secondary/tertiary care hospital, Quebec, Canada</td>
<td>ID physician, PharmD, infection control</td>
<td>Guidelines for decreasing use of antibiotics associated with C. difficile infections, education to shorten course of antibiotic therapy based on IDSA guidelines</td>
<td>C. difficile incidence decreased by 60% between 2003-2006, total antibiotic consumption decreased by 54%</td>
</tr>
<tr>
<td>Muto CA, et al (2007)</td>
<td>834-bed tertiary care, urban teaching hospital, Pittsburgh, PA, USA</td>
<td>ID physicians</td>
<td>Active surveillance for C. difficile, expanded infection control audits (i.e., observing handwashing), targeted antimicrobial restriction and pharmacist approval.</td>
<td>Antibiotic use decreased by 41% (2003-2005) (clindamycin 69% and Fluoroquinolones 54%), rate of C. difficile infections decreased from 7.2 per 1000 discharges to 4.8 (2001-06)</td>
</tr>
<tr>
<td>Carling, et al (2003)</td>
<td>174-bed, university-affiliated community teaching hospital during 7 years, Boston, MA, USA</td>
<td>ID physician and pharmacist</td>
<td>Emphasis on inappropriate parenteral antibiotic use, guidelines, pharmacy intervention, feedback to individual prescribers.</td>
<td>22% decrease in parenteral antibiotic use 7 years, incidence of C. difficile infections per 1000 patient-days was 4.14 cases per 100,000 days (p&lt;0.001)</td>
</tr>
</tbody>
</table>


**Weekly Infectious Disease Consult Service at LTCF**

**Total Antimicrobial Use**

![Graph showing Total Antimicrobial Use](image)

*Courtesy slide: Jump R, et al. ICAAC 2011*

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**Diagnosis of CDI**

**EIA's (toxin detection)**
- Rapid turn-around
- Poor sensitivity—false negatives

**Glutamate dehydrogenase (GDH)**
- More sensitive than enzyme immunoscassays (EIA)
- Less specific (great screening tool)
- Will always be present if patient is colonized (asymptomatic)
- Lab will only accept unformed stool sample

**Nucleic acid amplification test (NAAT)/ PCR**
- Quick turn-around time
- More sensitive than toxin EIA's (90% vs. 40-80%)
- More specific—detects genes associated with toxigenic C. difficile in the stool

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**Diagnosis of CDI**

1. **Step 1**
   - Enzyme immunoscassay GDH and Toxin (A, B) Kew
     - GDH Positive: Toxin Negative
     - GDH Positive: Toxin Positive
     - GDH Negative: Toxin Positive

2. **Step 2**
   - Polymerase chain reaction (PCR)
     - GDH Negative: Toxin Negative
     - GDH Negative: Toxin Positive
     - GDH Positive: Toxin Positive

**Note:** Repeat stool assays are NOT recommended during or following treatment in patients who are asymptomatic or are symptom-free. Up to 50% of patients have positive stool assay for as long as six weeks after the completion of therapy.
Prevention of CDI
Key Players

- Hospitals, providers are pivotal players
  - the majority of all CDIs are related to healthcare exposure

- Potentially preventable
  - focusing on reducing unnecessary antibiotic use and interrupting patient-to-patient spread within a facility

- Coordinated prevention strategies are needed
  - community, LTCF, NH and Acute Care Facilities upon patient transfer

Urgency To Expand Antimicrobial Stewardship Efforts

- A greater emphasis is needed on expanding antibiotic stewardship and prevention strategies across the entire spectrum of healthcare delivery

- Collaboration among all healthcare-related organizations and federal, state and public health agencies
Required electronic reporting of CDI in 2013

- Beginning in 2013, all hospitals participating in the Centers for Medicare & Medicaid Services’ Inpatient Prospective Payment System Quality Reporting Program will be required to report facility-wide laboratory-identified \textit{C. difficile} (LABID-DCI) events using NHSN to qualify for their 2015 annual payment update.

- Public reporting of hospital rates will begin in 2014 at the Hospital Compare website.

Recommendations to Control CDI

- \textbf{Prescribe and use antibiotics only when necessary!}

- \textbf{Identify patients with CDI:}
  - Test for \textit{C. difficile} when patients have diarrhea.
  - Suspect CDI while on antibiotics or within several months of taking them.
  - Use of the more sensitive nucleic acid amplification tests in detecting \textit{C. diff}.

- \textbf{Isolate patients with \textit{C. difficile} immediately - wear gloves and gowns when treating patients even during short visits.}

Infection Control for CDI

- \textbf{When a patient transfers, notify the new facility if the patient has a \textit{C. difficile} infection.}

- \textbf{Hand sanitizer does not kill \textit{C. difficile}, hand washing may not be sufficient.}

- \textbf{Clean room surfaces with bleach or another EPA-approved, spore-killing disinfectant after a patient with \textit{C. difficile} has been there.}
Avoid unnecessary antibiotics!!

CDI Prevention
Not Just a Maid Service

- 15 min YouTube video developed by the Chicago DOH
  - challenged 20 hospitals to decrease their C.diff rates in 18 months
  - 2 Chicago hospitals demonstrating how they implemented efficient environmental cleaning with black light program
- 22% decrease in CDI rates since implementation
- Engagement and Feedback to the environmental services personnel is extremely important

www.youtube.com/watch?v=nIZtqBELsA

Public Health Impact

Every time we prescribe antimicrobials (appropriately or inappropriately) we contribute to the problem
Take Home Points

1. Antimicrobial Resistance doesn't seem an issue until we have no options… we are getting there
2. *C. difficile* infections are an important cause of morbidity and mortality
3. CDI is associated with previous antibiotic exposure
4. Use antibiotics judiciously: de-escalate or stop whenever possible
5. The best treatment for CDI is **PREVENTION**

Vancopime Video

[http://www.youtube.com/watch?v=N1R94X0JeMs](http://www.youtube.com/watch?v=N1R94X0JeMs)

Thank You