C. DIFFICILE UPDATE 2012

Phyllis Flomenberg MD

Case 1

- 34 yo male presented to ED in respiratory distress due to large mediastinal mass. Patient intubated and NG tube placed
- Day 2 – Bx reveals lymphoma
- Day 3 – Chemotherapy started
- Day 5 – Abdomen distended, liquid stools

Case - continued

- Day 12 – Neutropenic and febrile. Broad spectrum IV antibiotics started.
- Day 15 – Fever persists. Increased abdominal distension, diarrhea.
  - Abdominal CT reveals diffuse colitis
  - C. difficile toxin positive

Outcome

- Day 16 – Pt taken to OR for subtotal colectomy.
  - Pt expires on OR table.

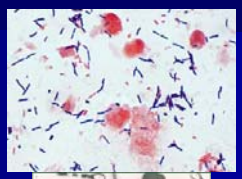
Questions

- How did this patient acquire *C. difficile* infection?
- Was this infection preventable?
- Was this patient managed appropriately?

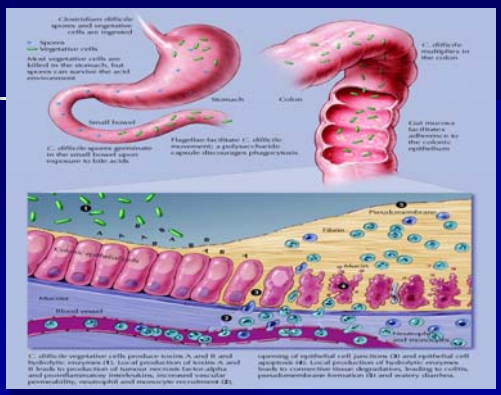
Clostridium Difficile

- Up to 20% of hospitalized patients may become colonized
  - Colonization promoted by disruption of normal flora by antibiotics
- 2/3 of colonized patients remain asymptomatic

C. Difficile and Risk Factors



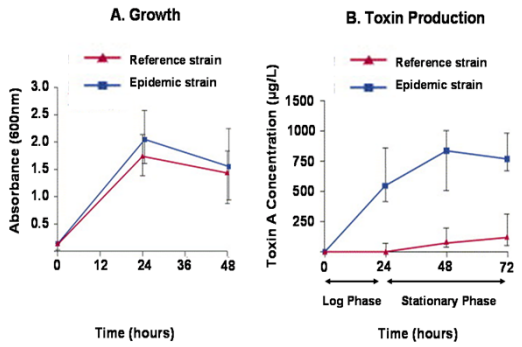
- Anaerobic gm+ rod
  - Toxins A and B
  - Spores
- Risk factors
  - Antibiotic exposure
  - Old age
  - GI surgery
  - Immunosuppression



Clostridium Difficile Update

- Increased rates of *C. difficile* globally since 2000
- Increase rates of complications associated with new epidemic strain

Increased Toxin Production



M. Warny *et al.*, *Lancet* **366**, 1079-84 (Sep 24-30, 2005)

Case 2

- 70 year old man presents with watery diarrhea, abdominal pain, and fever to 101^{0}F.
- He had recently been hospitalized with pneumonia and completed a course of Avelox 1 week ago.

Testing and Isolation

2 Blood cultures, urine culture, and *C. difficile* assay are ordered. Which of the following statements is true?

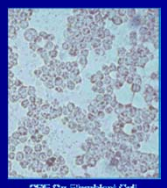
A. Send 3 stool samples for C. diff assay
B. C. diff assay usually takes 3 days
C. Wait for result to order Enteric Precautions
D. Change gloves between tasks in pt room

Diagnosis

- *C. difficile* EIAs for antigen and toxins A & B
  - Rapid
  - Antigen is sensitive but NOT specific
  - Toxin is specific but NOT sensitive

Diagnosis

- Tissue culture Cytotoxin assay for toxin B
  - More sensitive and specific
  - Labor intensive
  - Takes 48-72 hrs



CPE On Fibroblast Cell Culture

2-step Testing Protocol: Step 1

- Screen stool with rapid C. diff EIAs for antigen and toxin
  - Automatically orders Enteric precautions
- If Ag+, toxin+, confirms diagnosis in pt w compatible sx
- If Ag-, toxin-, diagnosis unlikely (high negative predictive value)
  - NO need to routinely repeat test x3

2-step Testing Protocol

Step 2:

- If antigen+, rapid toxin-, lab automatically performs Cytotoxin assay
  - Approx. 50% of samples are Cytotoxin positive

Testing Update

- Lab switched 2nd step from Cytotoxin assay to PCR in Jan 2012
  - C Difficile Molecular DNA assay for toxin B
  - More sensitive than cytotoxin

Infection Control Issues

- *C. difficile* infection leads to extensive patient room contamination
- *C. difficile* spores survive on environment for months!
- Spores are resistant to most disinfectants
  - Use Bleach to disinfect rooms
  - Wear gloves and wash hands with soap and water – Etoh rubs are NOT active vs spores!

The Inanimate Environment Can Facilitate Transmission

~ Contaminated surfaces increase cross-transmission ~

Abstract: The Risk of Hand and Glove Contamination after Contact with a VRE (+) Patient Environment. Hayden M, ICAAC, 2001, Chicago, IL.

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Testing and Treatment

Empiric rx w oral metronidazole 500 mg q8h is prescribed. Which of the following statements is true?

A. Always give first dose STAT
B. Start first dose as routine scheduled med and send stool sample next morning
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C. Difficile Testing Caveat

- Empiric treatment for => 24 hrs can cause a false negative toxin assay
- Important to collect stool prior to rx!

Treatment of *C. Difficile* Infections

- D/c unnecessary antibiotics
- Use oral rx for *C. difficile* – need to deliver into lumen of lower GI tract
  - Oral metronidazole for mild disease
  - Oral vancomycin for moderate – severe disease

Complications of *C. difficile* infections

- Refractory infection can lead to toxic megacolon, colon perforation, death
- 15 – 25% of patients relapse
  - Risk factors include immunosuppression, continued exposure to antibiotics

How to Prevent *C. Difficile* Infections?

- LIMIT use of antibiotics
  - Antibiotic exposure is most important risk factor!
    - Esp. 3rd gen cephalosporins, clindamycin, quinolones

How to Prevent *C. Difficile* Transmission?

- Strictly adhere to Enteric Precautions
  - Must wear gloves and gown
  - Change gloves between tasks in pt room
  - Must wash hands with soap and water
  - Continue pt isolation until discharged
- Vigorously disinfect pt room and equipment

EVS Interventions

- Targeted education about *C. difficile*
- Hand hygiene observations
- AccuPoint surveillance and direct feedback
  - High-touch surface samples collected with swabs
  - Organic matter measured via bioluminescence

How can you help?

- Promptly notify EVS supervisor, IC about EVS issues
- All nursing units need to have a process to clean pt equipment that EVS does not cover e.g. MAPs, AccuChecks, code carts

New epidemic *C. Difficile* strain

- Global ↑ rates of *C. difficile* since 2000
- Assoc. with ↑ complication rate
  - Many have polymorphisms/deletions in regulatory gene *tcdC* → ↑↑ toxin production
  - Express novel binary toxin
  - No evidence of metronidazole R

Issues

- TJUH rates of *C. difficile* -associated diarrhea ↑ in 2007
- New epidemic strain present at TJUH
- *C. difficile* spores are resistant to most disinfectants, including ETOH

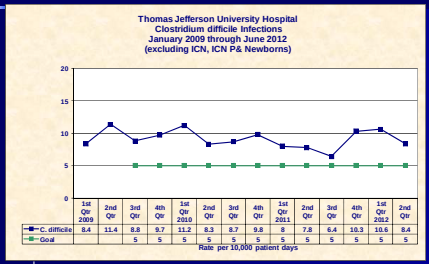
Hand Hygiene in Enteric Isolation Rooms

- 47 HCW observations Jan-Mar 2007
  - Hand hygiene prior 9 (19%)
  - Gloves used 16 (34%)
  - Hand hygiene after 16 (34%)
  - Complete adherence 9 (19%)

Interventions

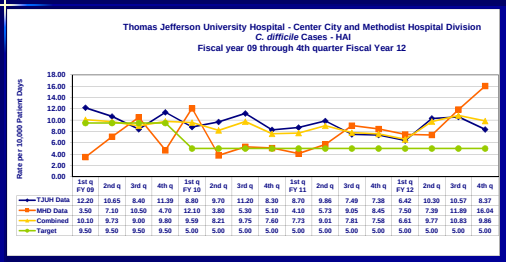
- Hand hygiene campaign
- Bleach-containing wipes to clean all patient rooms
- New yellow ENTERIC isolation signs
- Mandatory use of gowns (in addition to gloves) with Enteric Precautions
- Isolation carts
- Notify EVS about all new *C. difficile* cases

C. Difficile Rates Remain above Goal



Rate ↓ from 19.4 cases/ 10,000 patient days (365 infections) in 2007 to 9.6 in 2009 (160 infections). NO further improvement.

CC and MHD *C. Difficile* Rates



Treatment of *C. Difficile* Disease

- Stop unnecessary antibiotics
- Start po metronidazole 500 mg tid
- Closely monitor patient
  - Epidemic strain may respond less well
  - Increased risk of complications such as toxic megacolon

Treatment Issues

- If poor response at 48 -72 hr, switch to po vancomycin 125 mg qid
- If severe disease, START with po vancomycin

IDSA C. Difficile Treatment Guidelines 2010

- Mild-to-moderate disease
  - Metronidazole 500 mg po tid for 10 -14 d
- Severe (WBC >15k or >1.5x ↑ creatinine)
  - Vancomycin 125 mg po qid for 10 -14 d
- Severe, complicated (↓BP, ileus, megacolon)*
  - Vancomycin 500 mg po qid +/- metronidazole 500 mg IV q8h
  - Give Vancomycin enema if ileus present

*Consider colectomy, especially if WBC >50k, lactate >5

Complications of *C. difficile* infections

- 15 – 25% of patients relapse
  - Risk factors include immunosuppression, continued exposure to antibiotics
- Re-treatment with po metronidazole or vancomycin is usually successful

Some patients have multiple relapses

- Treat with po vancomycin for prolonged course
- Prolonged vancomycin with slow taper
- Vancomycin plus rifampin
- Vancomycin followed by Rifaximin
- Adjuncts
  - Bile acid resins
  - IV immunoglobulin

Treatment Update 1

- Prior studies suggest that antibody response to toxin helps protect against disease
- Investigational monoclonal antibodies vs toxins A and B in combination w vancomycin compared to vancomycin alone[1]
  - Response rates noninferior
  - Combination rx ↓ relapse rate compared to vancomycin alone

[1]Lowy I et al, NEJM 2010;362:197

Treatment Update 2

- New nonabsorbable antibiotic fidaxomycin
  - Limited activity vs normal gut flora
- Randomized over 600 patients to treatment with either fidaxomycin or vancomycin alone[1]
  - Response rates comparable
  - Fidaxomycin ↓ relapse rate compared to vancomycin (13% vs 24%, P=0.005)

[1]Louie TJ et al, NEJM 2011;364:422.

Fidaxomicin vs Vancomycin Outcomes*

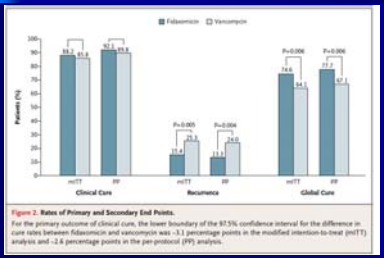


Figure 2. Rates of Primary and Secondary End Points.
For the primary outcome of clinical cure, the lower boundary of the 97.5% confidence interval for the difference in cure rates between fidaxomicin and vancomycin was −3.1 percentage points in the modified intention-to-treat (mITT) analysis and −2.4 percentage points in the per-protocol (PP) analysis.

*Caveat: NO difference in recurrence rate among patients with epidemic strain (24% each)!

Other Interventions under Investigation

- Probiotics
  - Studies inconclusive
  - Small risk of bacteremia (Lactobacillus) or fungemia (Saccharomyces) so avoid use in immunosuppressed pts, ICU pts
- Toxin vaccines
- Fecal transplant
  - Case reports showing benefit in pts with multiple relapses

Prevention of *C. difficile* Disease

- Antibiotic exposure is most important risk factor!
  - Old age, GI surgery, immunosuppression increase risk for disease
- Recommend LIMIT use of antibiotics
  - Esp. 3rd gen cephalosporins, clindamycin, quinolones

Back to Case 1

- 34 yo male presented to ED in respiratory distress due to large mediastinal mass. Patient intubated and transferred to ICU. NG tube placed.
  - Past medical hx - none
- Day 3 – Chemotherapy started for lymphoma
- Day 5 – Abdominal distention, liquid stool
- Day 12 – IV Abx started for neutropenic fever

Case - continued

- Day 15 – Fever persists. Increased abdominal distension, diarrhea.
  - C. difficile toxin positive
  - Oral vancomycin and IV metronizadole started
- Day 16 – Pt taken to OR for subtotal colectomy. Expires on table.

Questions

- How did this patient acquire *C. difficile* infection?
- Was this infection preventable?
- Was this patient managed appropriately?

Question 1

How did patient most likely acquire C. difficile infection?

A. Colonized prior to admission
B. Direct contact w contaminated ED room
C. Direct contact w contaminated ICU room
D. Direct contact w contaminated hands of HCW

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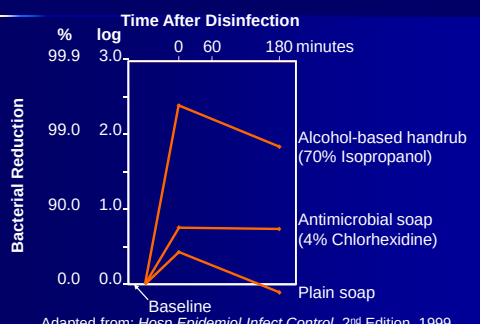
D. Direct contact w contaminated hands of HCW

Other Questions

- Was this preventable?
  - YES!
- Was this patient managed appropriately?
  - Yes, likely acute fulminant disease. Colectomy indicated.

The most common mode of transmission of pathogens is via hands!

Ability of Hand Hygiene Agents to Reduce Bacteria on Hands



Adapted from: *Hosp Epidemiol Infect Control*, 2nd Edition, 1999.

Hand Hygiene Products

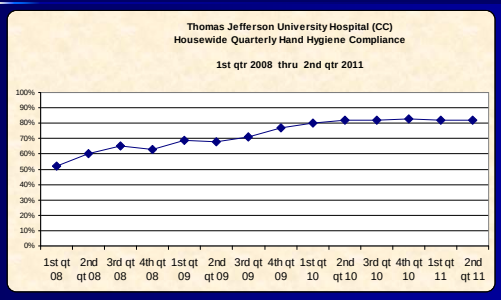
- When hands are visibly dirty, wash with soap and water.
- If hands are not visibly soiled, use an alcohol-based handrub for routinely decontaminating hands.
- Exception: Use soap and water after contact with C. difficile.

Guideline for Hand Hygiene in Health-care Settings. *MMWR 2002*; vol. 51, no. RR-16.

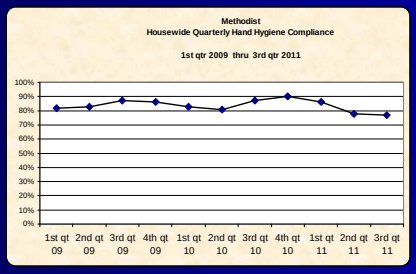
Hand Hygiene Interventions

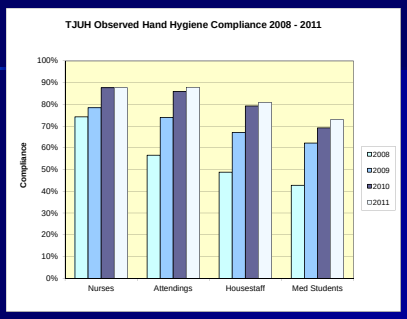
- Volunteers perform observations and enter data on IntraNet website
  - Only physicians reported by name
- Hand hygiene video
  - Pts can watch on GetWell network
  - Nearly 100,000 You-tube hits to date!
- Blue "Wash your hands" (with soap and water) signs for Enteric rms

Overall Hand Hygiene Compliance has hit a Plateau



MHD Hand Hygiene Compliance





Compliance: Performs hand hygiene BEFORE and AFTER patient and/or environment contact. Uses soap and water AFTER contact with patient / pt room on Enteric precautions. Gloves are not a substitute for hand hygiene.

Reducing C. Difficile Infections is New Balanced Scorecard Project

- Reduce environmental contamination
- Improve hand hygiene compliance
- Reduce inappropriate antibiotic use

Speak Up!

- Remind other HCWs to adhere to hand hygiene and isolation precautions
- Educate patients and visitors about MDRO infections and isolation precautions

Educate!

- Counsel patients about benefits and risks of antibiotics