Clostridium difficile Infection
CDI

Sherif Ibrahim, MD, MPH

05/21/2013

Question

Outbreak investigation…

Threat preparedness…

Are they related?

Answer

- Two essential public health roles in emergency preparedness
  - Prevent epidemics and spread of diseases
    - Routine outbreak investigation and public health surveillance
  - Respond to disaster (disaster outbreaks) and assist community in recovery
    - What type of outbreaks after natural disaster (Derecho storm?)
    - What type of outbreaks → public health threat? Why?
- TP grant → funds → requirement → performance measures

What do you need to do?

- Routine PH surveillance & outbreak investigation
- Building relationship with your partners ….who?
- Know & communicate with your neighbors (counties/other states)
- Learn about the real public health threats
- Learn outbreak investigation steps
- Learn what measures to recommend to control outbreaks:
  - appropriate infection control measures
  - measures to control environmental contamination
- Communicate information

Objectives

- Review microbiology and epidemiology of *Clostridium difficile*
- Review risk factors for transmission
- Discuss testing methods and diagnosis
- Review surveillance for *C. difficile*
- Discuss preventive strategies

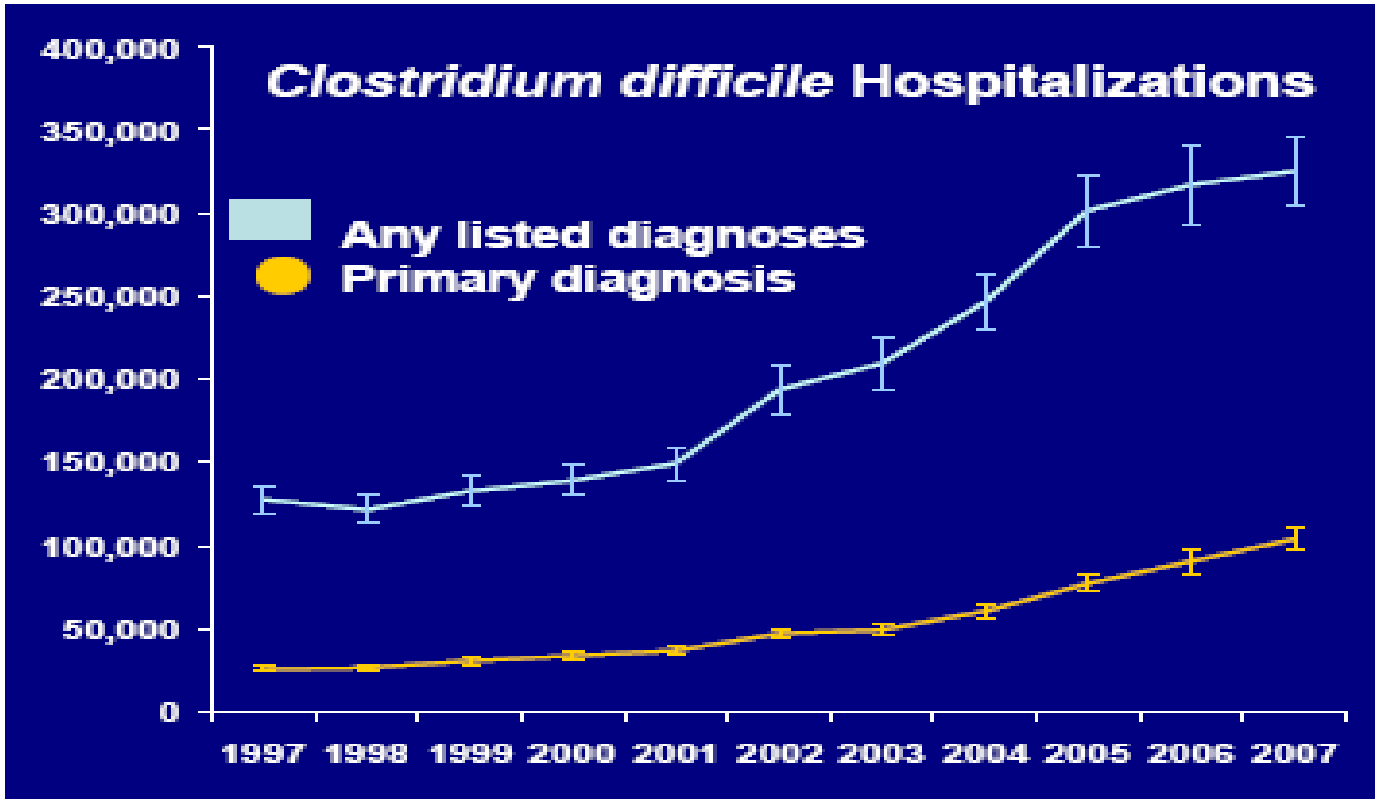
C. difficile : Microbiology

- Gram positive spore forming bacillus (rods)
- Obligate anaerobe
- Part of the GI Flora in
  - 1-3% of healthy adult
  - 70% of children < 12 months
- Some strains produce toxins A & B
- Toxins-producing strains cause *C. diff* Infection (CDI)

C. difficile: Background

- Most common cause of HAI in U.S.
- A common cause of nosocomial antibiotic-associated diarrhea (AAD) (20-30%)
- Most common infectious cause of acute diarrheal illness in healthcare settings
- The only nosocomial organism that is anaerobic and forms spores
- CDI → occur in low risk populations

CDI: Impact



Campbell et al. Infect Control Hosp Epid. 2009:30:523-33; Dubberke et al. Emerg Infect Dis. 2008;14:1031-8; Dubberke et al. Clin Infect Dis. 2008;46:497-504; Elixhauser et al. HCUP Statistical Brief #50. 2008; Dubberke et.al CID 2012:55 (Suppl 2)
CDC/SHEA Train the Trainer

CDI: Impact

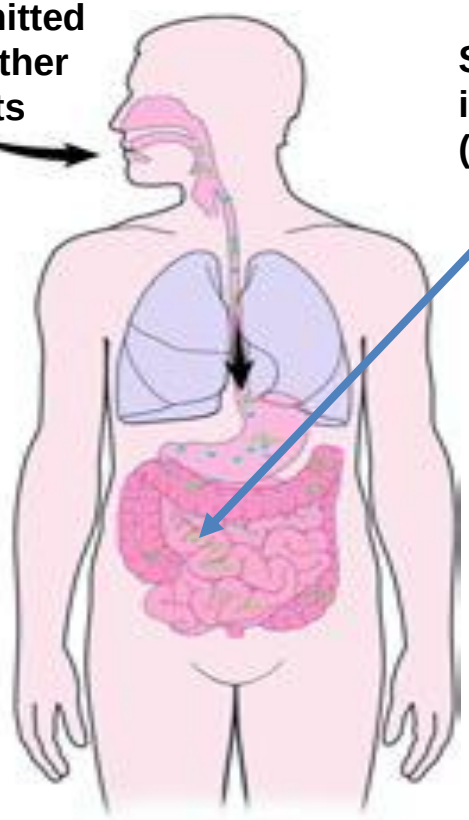
	Number of annual cases	Cost	Number of annual deaths
Hospital-onset, hospital acquired (HO-HA)	165,000	$ 1.3 B	9000
Community-onset hospital acquired (CO-HA) [4 weeks of hospitalization]	50,000	$ 0.3 B	3000
Nursing home-onset	263.000	$ 2.2 B	16,500

C. difficile : Transmission

- Fecal – oral route
  - Contaminated hands of healthcare workers
  - Contaminated environmental surfaces.
    - Survive for up 5 months on environmental surfaces
- Person to person in hospitals and LTCFs
- Reservoir:
  - Human: colonized or infected persons
  - Contaminated environment
- Infective dose is < 10 spores

CDI: Pathogenesis

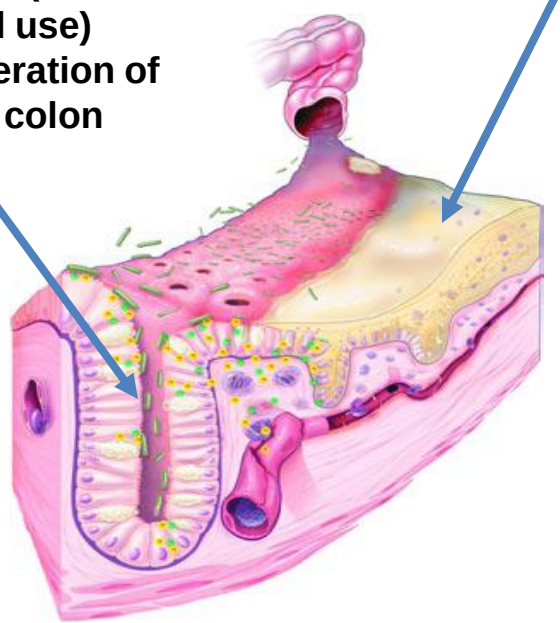
Step 1- Ingestion of spores transmitted from other patients



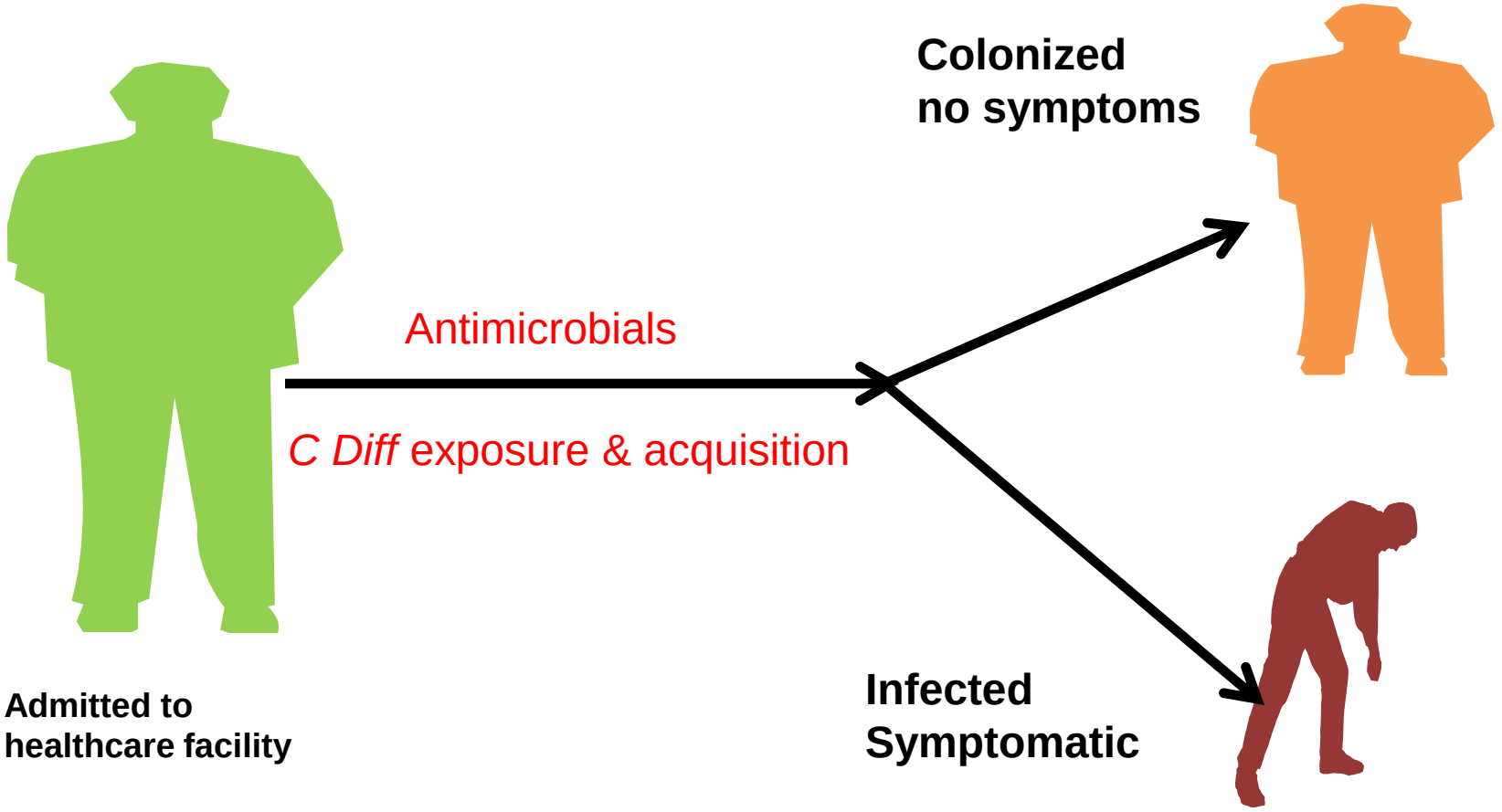
Step 2- Germination into growing (vegetative) form

Step 3 - Altered lower intestine flora (due to antimicrobial use) allows proliferation of *C. difficile* in colon

Step 4 . Toxin B & A production leads to colon damage +/- pseudomembrane



CDI Pathogenesis



CDI: Risk Factors

- Exposure to antimicrobials (prior 2-3 months)
- Exposure to healthcare (prior 2-3 months)
- Infection with toxogenic strains of C*. difficile*
- Age > 64 years
- Underlying illness
- Immunosuppression & HIV
- Chemotherapy (immunosuppression & antibiotic-like activities)
- Tube feeds and GI surgery
- Exposure to gastric acid suppression meds ??
- CDI in low risk populations

Changing CDI Epidemiology
Current Epidemic Strain of *C. difficile*

- Increase incidence and severity of CDI in the U.S.
- Emergence of CDI in low risk populations→ Severe disease
- Current epidemic Strain → BI/NAP1/027, toxinotype III
  - Historically uncommon – epidemic since 2000
- More resistant to fluoroquinolones
- Produces extra toxin called binary toxin
- More virulent
  - Increased toxin A and B production (16 and 23 times)
  - Change in binding domain of toxin B →increase adherence to the gut wall
  - Increased sporulation → increase survival

Antimicrobials Predisposing to CDI

Very commonly related	Less commonly related	Uncommonly related
Clindamycin Ampicillin Amoxicillin Cephalosporins Fluoroquinolons	Sulfa Macrolides Carbapenems Other penicillins	Aminoglycosides Rifampin Tetracycline Chloramphincol

- Among symptomatic patients with CDI:
  - 96% received antimicrobials within the 14 days before onset
  - 100% received an antimicrobial within the previous 3 months
- 20% of hospitalized patients are colonized with *C. diff*

Clinical Manifestations

- Toxin-producing strains of *C. difficile :*
  - Asymptomatic carriers = Colonized
  - Symptomatic (ill)
    - ❑ Mild or moderate diarrhea
    - ❑ Pseudo membranous colitis that can be fatal

- Exposure → **Median time of 2-3 days** → CDI

- Risk of developing CDI after exposure ranges between 5-10 days to 10 weeks

CDI: Symptoms

- Watery diarrhea (≥ 3 unformed stools in 24 or fewer consecutive hours)
- Loss of appetite
- Fever
- Nausea
- Abdominal pain and cramping

CDI: Testing

Test		Advantage	Disadvantage
Testing Toxins	Enzyme immuno-assay (EIA)	• Detects toxin A or both A & B • Rapid (same day) • Inexpensive	Less sensitive 63-94% Non specific
	Tissue culture cytotoxicity assay	Provides specific and sensitive results for *C. diff* 67-100%	-Detect toxin B -Technical expertise -Expensive -24-48 hours
Organism ID	Glutamate Dehydrogenase	Rapid, sensitive, may prove useful as a triage or screening tool	Not specific, toxin testing required to verify diagnosis
	PCR	Rapid, sensitive, detects presence of toxin gene	Expensive Special equipment
	Stool culture	Most sensitive test available when performed appropriately	False-positive results if isolate is not tested for toxin labor-intensive; requires 48–96 hours

Best Strategy for *C. difficile* Testing

- Testing should be performed only on (symptomatic patients) diarrheal stool
- Testing asymptomatic patients is not indicated
- Do not retest if the initial test was negative
- Testing for cure is not recommended

Best Strategy for *C. difficile* Testing

- For clinical use: two-step testing
  - ❑ Screen → EIA detection of GDH
  - ❑ Follow → cytotoxicity assay or toxigenic culture to confirm
- Gold standard → stool culture → toxigenic culture assay
- Toxin is very unstable, degrades at room temperature, and undetectable within 2 hours (false negative results)

CDI Surveillance: Case Definition

Commonly used case definitions

- CDC (NHSN)
  - Infection Surveillance
  - Lab surveillance (ID or event)
- Case definition (SHEA/IDSA)
  - Clinical: presence of diarrhea 3 or more unformed stools in 24 or fewer consecutive hours)

AND

  - Laboratory: A stool test result positive for toxigenic *C. diff or* its toxins **OR** colonoscopic / histopathologic findings demonstrating evidence of pseudomembranes

SHEA- ADSA, 2010

CDI Surveillance: Case Definition

McGeer case definition for LTCFs

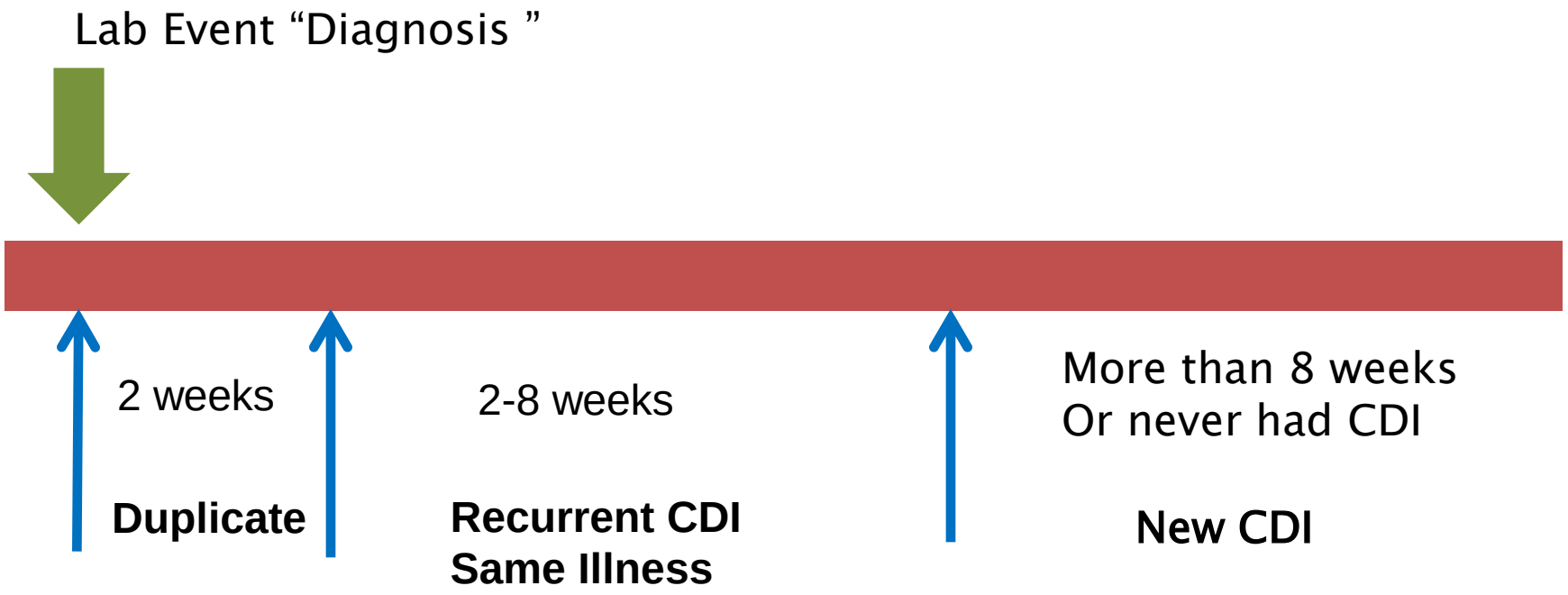
- Both 1 & 2 should be present
  1. GI sub criteria
     - Diarrhea: 3 or more liquid or watery stools above what is normal for the resident within a 24-h period
     - Presence of toxic megacolon (abnormal dilatation of the large bowel, documented radiologically)
  2. One of the following diagnostic subcriteria
     - Positive stool sample yields a positive laboratory test result for
     - Pseudomembranous colitis is identified during

- It is important to differentiate primary from recurrent episode of CDI

Lab Event (ID) - CDC

- A case of CDI = positive test result that is not duplicate for *C. difficile* toxin A and/or B, or a *toxin-producing C. difficile* organism detected by culture or other laboratory means performed on a stool sample
- A duplicate→ positive test from the same patient and location within the past two weeks
- Recurrent CDI: Any Lab ID → >2 weeks ≤8 weeks after the most recent one
- New CDI: Any Lab ID Event >8 weeks after the most recent one or with no previous Lab ID Event documented for that patient.
- Uses: time , location, new cases, recurrence, prevention strategies

Lab Event (ID) - CDC

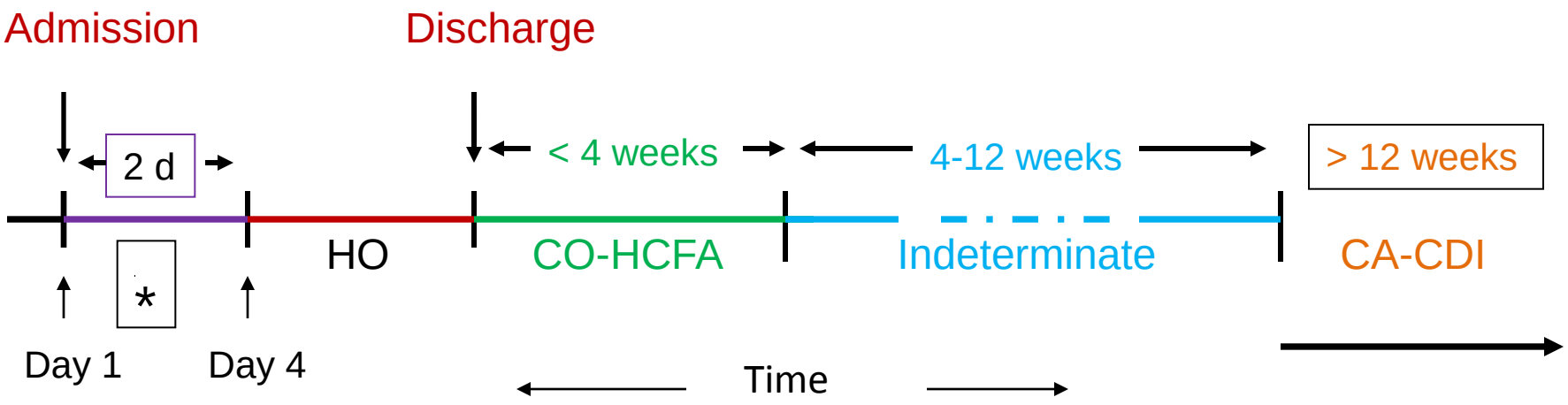


CDI Surveillance

- **Surveillance definitions of CDI by time of onset:**

Case Classification	Case Definition
Healthcare facility (HCF)-onset, HCF-associated CDI	Onset > 3 days of admission (on or after the 4th day)
Community-onset, HCF-associated CDI	Community onset or within 48 hours of admission and within < 4 weeks of the last discharge
Community-associated CDI	Onset in the community but within more that 12 weeks of last discharge

Time Line for Surveillance Definitions of CDI



HO: Hospital (Healthcare)-Onset
CO-HCFA: Community-Onset , Healthcare Facility-Associated
CA: Community-Associated

* Depending upon whether patient was discharged within previous 4 weeks. Onset defined in NHSN by specimen collection date

CDI Surveillance: Recommendations

- Minimum: surveillance→ HCF-onset, HCF-associated to
    - Detect outbreaks
    - Monitor patient safety

- Rate of HCF-associated CDI (number of cases per 10,000 patient-days

- Compare your rates with other facilities

- In outbreaks → stratify rates by patient location in order to target control measures

CDI Outbreaks

Outbreak definition:

- Three or more epidemiologically linked CDI cases occurring in the same area/unit of the facility within a period of seven days or less

OR

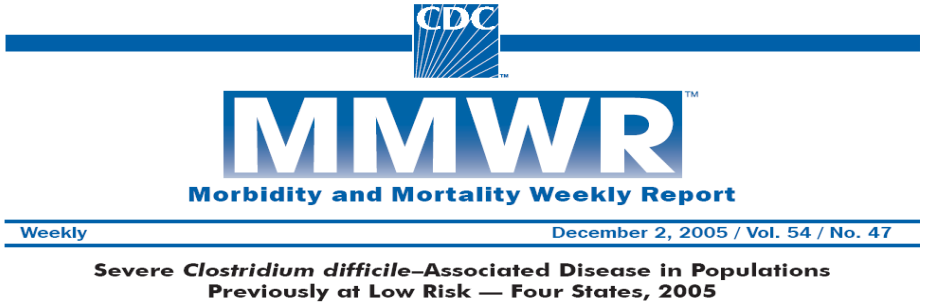
- Occurrence of facility-acquired CDI in excess of what is normally expected

- What do you want to know?
  - Date of onset
  - Facility acquired
  - Meet case definition
    - Clinical picture
    - Lab confirmation
  - Infection control measures

Is CDI Reportable in WV?

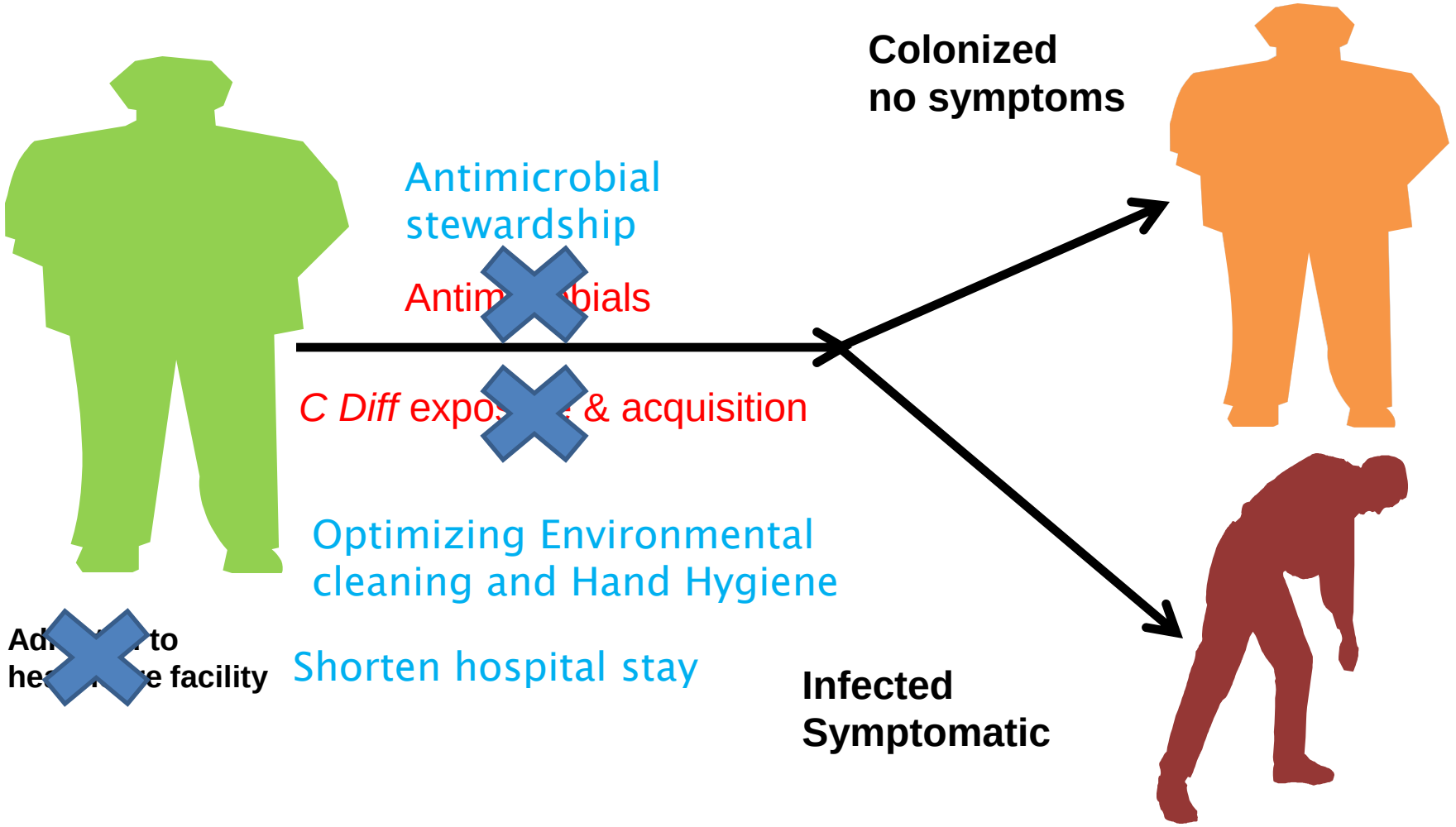
- Currently
  - Individual cases are not reportable
  - Outbreaks of CDI are reportable

- New reportable disease rules → effective in July, 2013
  - CDI → Lab event → reportable to NHSN
  - Outbreaks of CDI are reportable



- A 31 YO 14 weeks pregnant with twins →ED → 3 weeks of intermittent diarrhea, then 3 days of cramping and watery, black stools 4-5 times/day
- Hx of trimethoprim-sulfamethoxazole exposure for a UTI 3 months ago
- Stool → positive for *C. difficile* toxin → admitted, treated metronidazole and discharged
- Readmitted the next day for 18 days with severe colitis and was treated with metronidazole, cholestyramine, and oral vancomycin, improved and discharged
- 4 days later she was readmitted with diarrhea and hypotension, had a spontaneous abortion
- Aggressive resuscitation and subtotal colectomy, patient died→ the 3rd day
- Histopathologic exam of the colon → megacolon & pseudomembranous colitis.

CDI Pathogenesis



Antimicrobial Stewardship

- Regardless of setting, ~ 50% antibiotic use is "inappropriate"


Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship

Timothy H. Dellit,[1] Robert C. Owens,[2] John E. McGowan, Jr.,[3] Dale N. Gerding,[4] Robert A. Weinstein,[5] John P. Burke,[6] W. Charles Huskins,[7] David L. Paterson,[8] Neil O. Fishman,[9] Christopher F. Carpenter,[10] P. J. Brennan,[9] Marianne Billeter,[11] and Thomas M. Hooton[12]

Antimicrobial Stewardship

- Recommendations:
  - Minimize →frequency and duration of antimicrobial therapy
  - Decrease the number of antimicrobial prescriptions
  - Targeted antimicrobials should be based on the local epidemiology and the *C. difficile* strains
  - Restrict the use of cephalosporin and clindamycin
  - Audit and feedback targeting broad-spectrum antibiotics

Prevention Strategies

Core

- High level of scientific evidence
- Demonstrated feasibility

Supplementary

- Some scientific evidence
- Variable level of feasibility

Prevention Strategies: Core

- Contact Precautions for duration of diarrhea
- Hand hygiene (HH) in compliance with CDC/WHO
- Cleaning and disinfection of equipment and environment
- Laboratory-based alert system for immediate notification of positive test results
- Educate HCP, housekeeping, admin staff, patients, families, visitors, about CDI

Tip: Routine identification of colonized patients for infection control purposes is not recommended and treatment of such identified patients is not effective

Prevention Strategies: Supplemental

- Extend contact precautions beyond duration of diarrhea (48 hours)
- Presumptive isolation for symptomatic patients
- Implement soap and water for hand hygiene before exiting room of a patient with CDI
- Implement universal glove use on units with high CDI rates
- Use sodium hypochlorite (bleach) - containing agents for environmental cleaning
- Implement an antimicrobial stewardship program

Preventive Strategies: Contact Precautions

Core

- Gloves/gowns on room entry
- Private room (preferred) or cohort with dedicated commodes
- Dedicated equipment
- Maintain for duration of diarrhea
- Measure compliance

Supplemental

- Extend use of contact precautions beyond duration of diarrhea
- Presumptive isolation
- Universal glove use on units with high CDI rates
- Intensify assessment of compliance

Preventive Strategies: Hand Hygiene

Core

- HH based on CDC or WHO guidelines
- Soap and water preferentially in outbreak or endemic settings
- Measure compliance

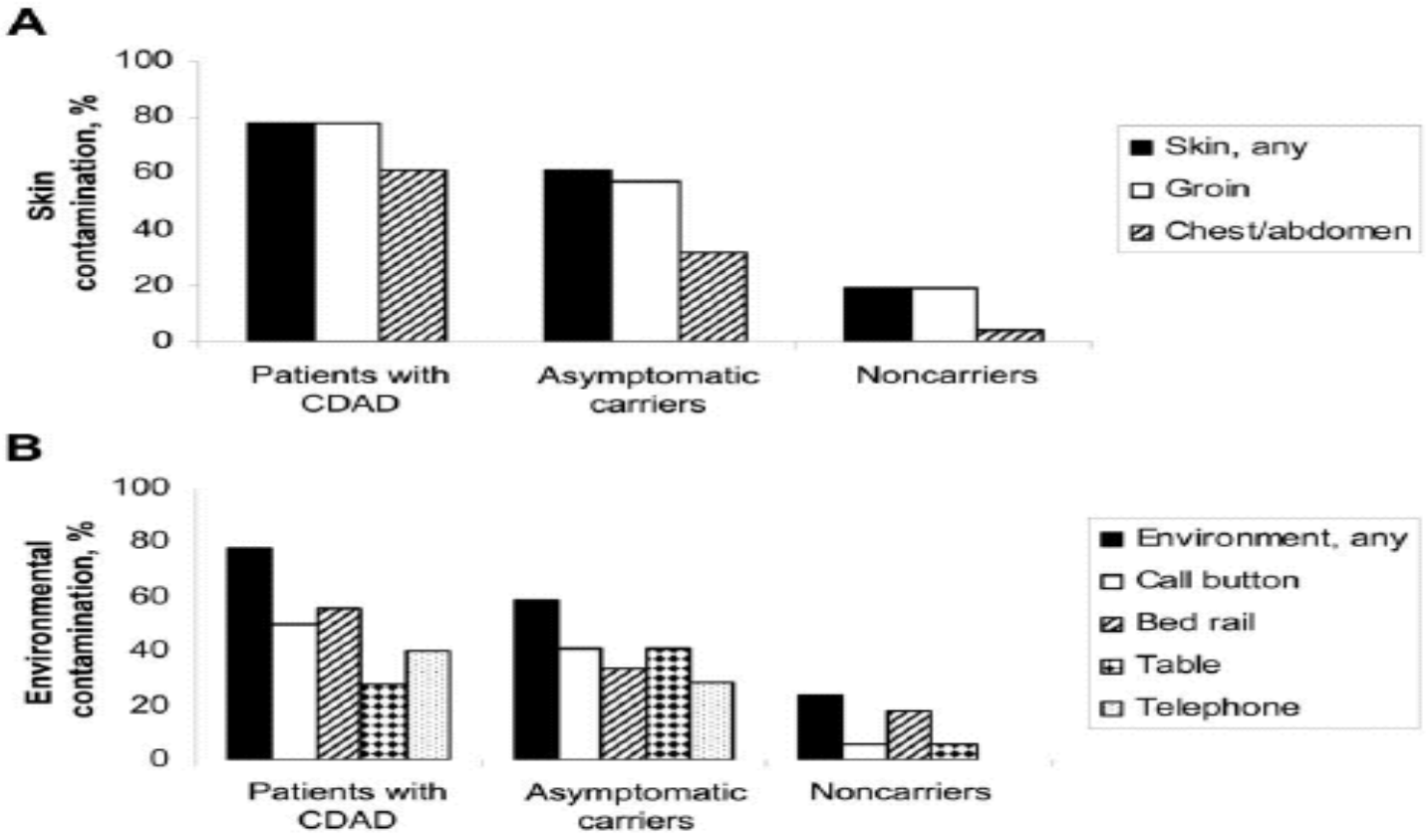
Supplemental

- Soap and water for HH before exiting room of a patient with CDI
- Intensify assessment of compliance

Conclusion: Spores may be difficult to eradicate even with HH

absolute adherence with glove use

Environmental Contamination Rationale for Universal Glove Use



Riggs et al. Clin Infect Dis2007;45:992–8.

Preventive Strategies: Environmental Cleaning

Core

- Cleaning and disinfection of equipment and environment
- Consider sodium hypochlorite in outbreak or endemic settings
- Routinely assess adherence to protocols and adequacy of cleaning

Supplemental

- Reassess adequacy of room cleaning and address issues
- Use sodium hypochlorite (bleach) – containing agents

Preventive Strategies: Environmental Cleaning

- Identify and remove environmental sources of *C. diff*
- Routine environmental screening for *C. diff is* not recommended
- Ensure that environmental cleaning is adequate and high-touch surfaces are not being overlooked
- If possible, use the environmental markers to assess cleaning after education

Infection Prevention and Control Isolation Compliance Checklist

Date and Time of Observation_____ Observer_____

Precaution/Isolation Type _____

Unit	Room #	Compliance with Hand Hygiene Practices		Person Observed (HCW or visitor) Please check appropriate box. KEY: 1 = Physician; 2 = RN; 3 = Transporter; 4 = PA; 5 = Respiratory RX; 6 = Nursing assistant; 7 = Rehab; 8 = Lab; 9 = Dietary; 10 = Housekeeping; 11 = Other HCW; 12 = Visitor												100% Compliant with isolation? Yes or No Identify variance by PPE or Signage				
																YES	NO Check Observed Variance			
		ABHR	Soap + H_20	1	2	3	4	5	6	7	8	9	10	11	12		Gloves	Gown	Mask	Signs

Figure 8.1. Infection Prevention and Control Isolation Compliance Checklist. Source: Loretta Litz Fauerbach, Shands at the University of Florida.

Table 10.2. Environmental checklist using sodium hypochlorite for daily cleaning when *C. difficile* is involved.

Clostridium difficile ENVIRONMENTAL CHECKLIST USING SODIUM HYPOCHLORITE

FOR DAILY CLEANING - ROOM OBSERVATIONS: Please review a sample of 5 patients per week (1 patient per day) with known or suspected *C. difficile*.

Hospital: _____
Date: _____
Unit: _____
Room: _____
Time: _____

Instruction	Component	Yes	No	N/A
At start, perform hand hygiene.	N/A			
Put on PPE.	N/A			
Disinfect w/ hypochlorite-based disinfectant, high-touch surfaces.	Door knobs/handles			
	Door surface			
	Bed rails			
	Call button			
	Phone			
	Overbed table & drawer			
	Countertop			
	Light switches			
	Furniture			
	Arms of patien' chair			
	Seat of patient chair			
	All other miscellaneous horizontal surfaces			
	Window sills			
	Bedside commode			
	Medical equipment (e.g., IV controls)			
	Spot clean walls with disinfectant cloth			
Disinfect w/ hypochlorite-based disinfectant:	BATHROOM, including:			
	Bathroom door knob			
	Toilet horizontal surface/seat			
	Toilet lever/flush			
	Faucets (at sink)			
	Bathroom handrails			
	Sink			
	Tub/shower			
	Mirror			
Damp dust:	Overhead light (if the bed is empty)			
	TV & stand			
Clean:	Lights			
Clean floor:	Dust mop tile			
	Wet mop tile			
Replace as needed:	Hand sanitizer			
	Paper towels			
	Soiled curtains			
For terminal cleaning, damp dust:	Bed frame			
	Mattress			
	Remake bed with clean linen			
	Replace as needed: Pillows, mattresses, pillow covers, mattress covers			
Other:	Empty trash & replace liner			
Discard dust cloths.	N/A			
Change mop heads after each isolation room.	N/A			
Remove PPE before exit.	N/A			
Perform hand hygiene.	N/A			

Any significant areas not mentioned above (please describe):

This room looks clean and ready for use:
Sign-off by Environmental Services employee cleaning the room: _____

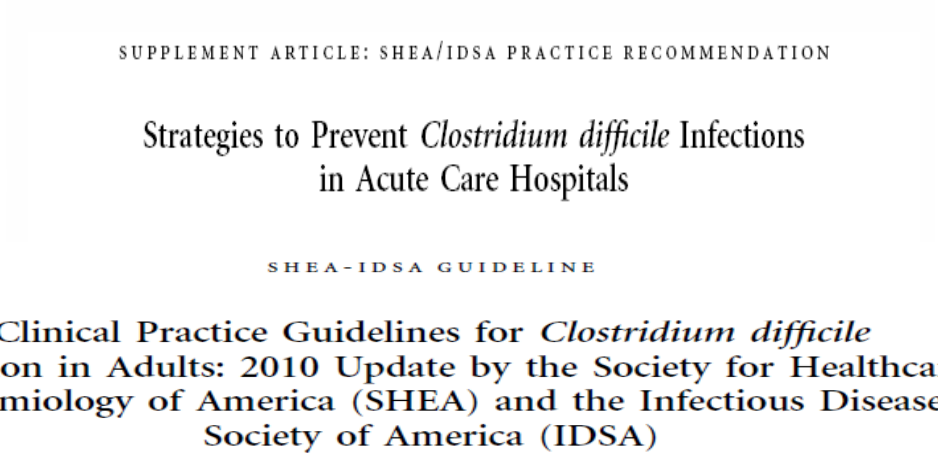
Sign-off by TBD, based on your hospital process for cleaning room: _____

Preventive Strategies: Summary

- Surveillance
- Microbiologic identification
- Contact precautions
- Hand hygiene
- Environmental cleaning
- Antimicrobial stewardship
- Education → HCWs, patients, visitors, families
- Administrative support

Resources

- APIC: Guide to Preventing *Clostridium difficile* Infections (2013)
- SHEA/IDSA Compendium of Recommendations



SUPPLEMENT ARTICLE: SHEA/IDSA PRACTICE RECOMMENDATION

Strategies to Prevent *Clostridium difficile* Infections in Acute Care Hospitals

SHEA-IDSA GUIDELINE

Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults: 2010 Update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA)

Prevention of *Clostridium difficile* Infection (CDI) Massachusetts CDI Prevention Collaborative; Carolyn Gould, MD MSCR; L. Cliff McDonald, MD

SHEA HAI training program, May 2011

Questions / Discussion