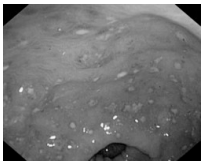
Clostridium difficile - A Challenge in Long Term Care

Dr. Andrew Simor, University of Toronto

A Webber Training Teleclass

Clostridium difficile – A Challenge in Long-Term Care



Andrew E. Simor, MD, FRCPC
Sunnybrook Health Sciences Centre
University of Toronto

Hosted by Paul Webber
paul@webbertraining.com

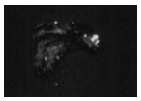
www.webbertraining.com

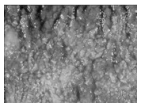
Objectives

- to understand the changing epidemiology and outcome of *C. difficile*-associated diarrhea
- to appreciate the unique features of *C. difficile* in long-term care facilities
- to identify evidence-based strategies for the management and prevention of *C. difficile* infection

Clostridium difficile

- implicated in 20%-30% of antibiotic-associated diarrhea
- major cause of nosocomial infectious diarrhea
- fecal-oral transmission via hands of HCWs and contact with contaminated environment

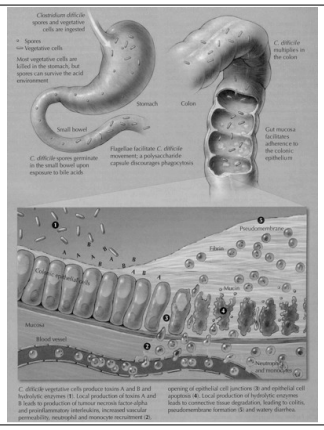




McFarland, NEJM 1989;
Bartlett, Clin Infect Dis 1992

C. difficile-Associated Diarrhea

Clinical Feature	Frequency (%)
Watery diarrhea	>90
Bloody diarrhea	<10
Abdominal pain	60-90
Peritoneal signs	10-20
Fever	70-80



C. difficile Pathogenesis

Disruption of normal enteric flora (eg. by antibiotics) with acquisition of toxigenic *C. difficile*

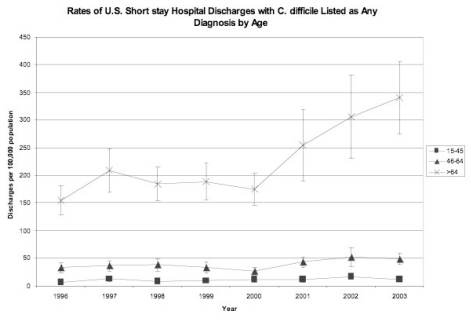
- **Toxin A Ab present** → **asymptomatic *C. difficile* colonization**
- **No toxin A Ab** → ***C. difficile*-associated diarrhea**

C. difficile-Associated Diarrhea

- >80% onset during antibiotic therapy
- may occur with single dose of antibiotic
- may occur after antibiotics discontinued (up to 6 wks later)

C. difficile in the Elderly

- increasing age is a risk factor for acquiring *C. difficile* and for CDAD
  (McFarland, J Infect Dis 1990; Brown, ICHE 1990)
- most patients > 60 yrs of age
  (Aronsson, J Infect Dis 1985; Wilcox, J Antimicrob Chemother 1998)
- 5-10 fold higher rates of CDAD in older adults; 228/100,000 pop'n. in US in those >65 yrs (McDonald, Emerg Infect Dis 2006; Pépin, Can Med Assoc J 2004)



McDonald, Emerg Infect Dis 2006

C. difficile in LTCFs

- ***C. difficile*** **prevalence in LTCFs up to 15%** (Simor, Clin Infect Dis 1993; Walker, J Am Geriatr Soc 1993)
- **incidence of *C. difficile* acquisition in LTCFs: 0.2-2.6/1,000 resident-days** (Simor, Clin Infect Dis 1993; Laffan, J Am Geriatr Soc 2006)
- **in state-wide surveillance (Ohio), approx 50% of CDAD acquired in a LTCF; rate: 2-3/10,000 resident-days** (Ohio Dept. of Health; www.odh.state.oh.us/)

Risk Factors for *C. difficile* in LTCFs

Risk factor	O.R. (p value)
Antibiotics (prior 4 wks)	3.3 (0.03)
Cephalosporin use	4.7 (0.04)
Presence of >3 comorbidities	2.0 (0.03)
Presence of feeding tube	6.5 (0.006)
Fecal incontinence	2.5 (0.03)

Simor, Clin Infect Dis 1993; Walker, JAGS 1993

Why are the elderly at risk?

- **impaired *C. difficile* phagocytosis and toxin neutralizing Ab** (Bassaris, Med Microbiol Immunol 1984; Viscidi, J Infect Dis 1983)
- **presence of underlying diseases, use of H2-antagonists, PPIs** (Simor, Clin Infect Dis 1993; Walker, J Am Geriatr Soc 1993)
- **residence in a closed environment, with limited infection control and housekeeping resources**

Why are the elderly at risk?

- colonization pressure
  (Dubberke, Arch Intern Med 2007)
- antimicrobial utilization: 8-33% of LTCF residents treated with an antibiotic acquire *C. difficile*
  (Thomas, J Am Geriatr Soc 1990; Simor, Clin Infect Dis 1993)

Clostridium difficile Changing Epidemiology

- increasing incidence and severity in US, Canada, UK, and Europe
- rates doubled in US hospitals 1996-2003: 3.1 to 6.1/100,000 pop'n (p=0.01)
- associated with a hypervirulent epidemic strain (NAP1; PCR ribotype O27; toxinotype III)

McDonald, NEJM 2005; Loo NEJM 2005; Warny, Lancet 2005; McDonald, Emerg Infect Dis 2006

C. difficile – Increasing Burden of Disease in U.S. Hospitals

Year	Rate per 1,000 admissions
2001	4.3
2004-2005	6.9
2005-2006	7.3

McDonald, IDSA 2007

C. difficile-Associated Diarrhea Increasing Incidence/Severity

- Centre Hospitalier Universitaire de Sherbrooke:
  2.1/1,000 admissions in 2002
  10/1,000 admissions in 2003
  18/1,000 admissions early 2004
  (Valiquette, CMAJ 2004)
- Sherbrooke rates increased:
  35.6/100,000 pop'n in 1991
  156/100,000 pop'n in 2003
  866/100,000 pop'n in those ≥65 yrs
  (Pépin, CMAJ 2004)

Nosocomial *C. difficile* in Canadian Hospitals

Region	Rate	
	per 1,000 admissions	per 10,000 patient-days
East	3.4	5.2
Central	5.6	8.1
West	4.5	7.3
Overall	4.7	7.3

Canadian Nosocomial Infection Surveillance Program, 2007

Why is there a problem with *C. difficile* now?

- more virulent strain
  - clonal outbreak
  - less susceptible strain
  - toxin genes; other virulence factors
- changes in how antibiotics are used
- changes in infection control practices or environmental cleaning

Epidemic *C. difficile*

- Quebec strain:
  NAP1/027, toxinotype III
  N. Amer. PFGE type 1
- 67% of healthcare facility isolates
  37% of community isolates

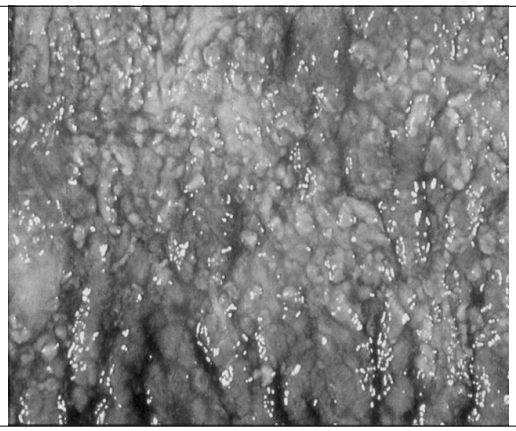
Warny, Lancet 2005

Epidemic *C. difficile*

- binary toxin (significance uncertain, as binary toxin does not cause disease in animal models)
- deletions in *tcdC* gene (associated with higher levels of toxins A and B)
  (Warny, Lancet 2005)
- high-level fluoroquinolone and clindamycin resistance

C. difficile Complications

- acute abdomen, peritonitis
- toxic megacolon
- colonic perforation
- dehydration, hypokalemia, GI bleeding



C. difficile Mortality

- 161 cases/656 controls matched by age, sex, Charlson Comorbidity Index; Sherbrooke Que., 2003-04

	Mortality (%)	
	30-day	12-month
Cases	23	37
Controls	7	21

Attributable mortality: 16%

Pépin, CMAJ 2005

C. difficile Impact

- attributable mortality, as high as 16% (Pépin, CMAJ 2005)
- 3 to 11 excess days of hospital stay; $3,700 to $13,675 incremental costs
  (Kyne, Clin Infect Dis 2002; O'Brien, ICHE 2007)

C. difficile Diagnosis

- CDAD should be suspected in any hospitalized/LTCF patient with diarrhea who has received antibiotics in the previous 2 months
- fever is typically present
- leukocytosis (WBC >20,000) is associated with more severe disease

C. difficile colitis: thumbprinting

C. difficile Diagnosis

Test	Sensitivity (%)	Specificity (%)
Culture	89-100	84-99
Cytotoxin assay in cell culture	67-100	85-100
EIA toxin assay	63-99	75-100

C. difficile Diagnosis

- only diarrheal (unformed) stools should be tested, unless ileus is suspected
- no value to testing stools of patients without symptoms (including "test of cure"), unless investigating an outbreak

C. difficile Treatment

- stop antibiotic, if possible
- avoid anti-peristaltic agents (may precipitate toxic megacolon)
- treat only symptomatic patients

C. difficile Response to treatment

Disease severity	No. cured/No. treated(%) Mtz	Vanco	p value
Mild	37/41 (90)	39/40 (98)	0.36
Severe	29/38 (76)	30/31 (97)	0.02
	Relapse rate (%)		
	9/66 (14)	5/69 (7)	0.27

Zar, Clin Infect Dis 2007

C. difficile
Treatment

Typical response to treatment with Vanco/Flagyl is 3-5 days, and up to 10 days for complete resolution of symptoms

C. difficile
Relapse

- relapse occurs in 5-30% of patients (persistence of spores or re-infection)
- most respond to repeat of initial therapy; 92% will have no further recurrence (Olson, 1994)

C. difficile
Relapsing Disease

- *Saccharomyces boulardii*
- *Lactobacillus* GG
- Vancomycin + rifampin

C. difficile - New Agents

- tolevamer (resin that binds toxins)
- macrocyclic antibiotics:
  ramoplanin
  OPT-80 (tiacumicin)
- nitazoxamide
- IVIG
- ingestion of non-toxigenic *C. difficile*; donor stool replacement (enema/NG tube)

Is the most important factor affecting the emergence and spread of *C. difficile*:

antibiotic utilization?

infection control practices?

Antimicrobial Utilization and *C. difficile*

- decreasing use of broad-spectrum cephalosporins associated with decreased CDAD
  (McNulty, JAC 1997; Khan, J Hosp Infect 2003; Thomas, CID 2005)
- reduced use of clindamycin associated with decreased CDAD
  (Brown, ICHE 1990; Pear, Ann Int Med 1994; Climo, Ann Int Med 1998)
- change in fluoroquinolones associated with change in CDAD rates (Gaynes, CID 2004)

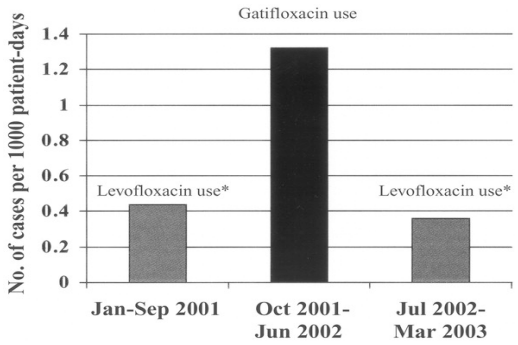


Figure 1. Rate of *Clostridium difficile*-associated diarrhea at a long-term care facility. **P*< .002 for either period of levofloxacin use versus period of gatifloxacin use.

(Gaynes, CID 2004)

Hand Hygiene

- **4% chlorhexidine gluconate equivalent to soap/water for removing *C. difficile* from hands** (Bettin, ICHE 1994)
- **alcohol-based products are not reliably sporocidal** (Larson, AJIC 1995)

Clostridium difficile

Intervention	Effectiveness
Barriers	
Handwashing	probable
Gloves	proven (Johnson, AJM 1990)
Gown	no data
Cohorting	probable

Gerding, ICHE 1995

Clostridium difficile

Intervention	Effectiveness
<u>Environment</u>	
Disinfection of room (hypochlorite)	proven (Mayfield, CID 2000)
Use of disposable thermometers	proven (Brooks, ICHE 1992)
Endoscope disinfection	probable

Gerding, ICHE 1995

Environmental Cleaning

- hypochlorite solutions effective in reducing bacterial load and sporulation
- quaternary ammonium compounds, hydrogen peroxide, and other non-chlorine-containing agents less effective for inactivating spores

Kaatz, Am J Epidemiol 1988; Mayfield, Clin Infect Dis 2000; Fawley, Infect Control Hosp Epidemiol 2007

Clostridium difficile

Intervention	Effectiveness
Antibiotic use restriction	proven (Pears, Ann Int Med 1994)
Use of probiotics	ineffective
Gut "decontamination" to eradicate *C. difficile*	ineffective

C. difficile in LTCFs

Recommendation	Strength and Quality of Evidence
CDAD surveillance	*BIII*
Antimicrobial use surveillance	*BIII*
Prudent use of antibiotics	*AII*
Hand hygiene (soap or alcohol gel)	*BIII*

SHEA Position Paper,
Infect Control Hosp Epidemiol 2002

C. difficile in LTCFs

Recommendation	Strength/Quality of Evidence
Isolation, private room, commode (if feasible)	*BIII*
Glove use	*AI*
Use of disposable thermometers	*AII*
Dedicated patient care items, equipment (if feasible)	*BIII*
Environmental cleaning, disinfection with a sporocidal agent (diluted hypochlorite solution)	*BII*

SHEA Position Paper,
Infect Control Hosp Epidemiol 2002

References

Gerding, Infect Control Hosp Epidemiol 1995; 16:459-77

Simor, Infect Control Hosp Epidemiol 2002; 23:696-703

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