Clostridium difficile: What Antiseptics and Disinfectants Should We Use?

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Clostridium difficile: What Antiseptics and Disinfectants Should We Use?

- Microbiology and epidemiology of *C. difficile*
- Role of the environment in disease transmission
- Prevention
  - Disinfectants for environmental disinfection
  - Disinfectants for semicritical equipment disinfection
  - Antiseptics
  - Hand hygiene

C. difficile

- Gram-positive bacillus, anaerobic, spore-forming
- *C. difficile* is responsible for 15-25% of cases of antibiotic-associated diarrhea and for virtually all cases of antibiotic-associated pseudomembranous colitis.
- Since 2000, a strain of *C. difficile* identified as NAP1 produces extra toxin and increased amounts of toxins A and B has caused increased morbidity and mortality
- Increasing incidence in U.S.
- Patients can be contaminated from environmental surfaces, shared instrumentation, hospital personnel hands and infected roommates

Clin Microbiol Infect 2001;7:405; Clin Micro Rev 2004;17:863; CID 2002;34:346

Role of Surfaces in Transmission

Pathogens implicated in transmission via contaminated noncritical surfaces. Patients C/I with these pathogens contaminate the environment and these pathogens survive in the environment.

- Bacteria
  - Methicillin-resistant *Staphylococcus aureus*
  - Vancomycin-resistant *Enterococcus spp.*
  - *Clostridium difficile*
  - *Acinetobacter* and *P. aeruginosa*
- Viruses
  - Rotavirus
  - Norovirus
  - SARS coronavirus

Environmental Contamination
C. difficile

- 9.3% (85/910) of environmental cultures positive (floors, toilets, toilet seats) for *C. difficile*. 2.6% (13/497) cultures positive in areas with no know carriers. Kim et al. J Inf Dis 1981;143:42.
- 10% (110/1086) environmental samples were positive for *C. difficile* in case-associated areas and 2.5% (14/489) in areas with no known cases. Fekety et al. Am J Med 1981;70:907.
- 31.4% of environmental cultures positive for *C. difficile*. Kaatz et al. Am J Epid 1988;127:1289.

Environmental Contamination
C. difficile

- 29% (62/216) environmental samples were positive for *C. difficile*. 29% (11/38) positive cultures in rooms occupied by asymptomatic patients and 49% (44/90) in rooms with patients who had CDAD. McFarland et al. NEJM 1989;320:204
- 25% (117/466) of cultures positive (<10 CFU) for *C. difficile*. >90% of sites positive with incontinent patients. Samore et al. Am J Med 1996;100:32.
- 27% (13/48) of samples were positive for *C. difficile*. The NAP1 epidemic strain was found in 5 of 6 facilities. Dubberke et al. AJIC 2007;35:315.

C. difficile Environmental Contamination

- Frequency ~10->50%-Stethoscopes, bed frames/rails, call buttons, sinks, hospital charts, toys, floors, windowsills, commodes, toilets, bedsheets, scales, blood pressure cuffs, phones, door handles, electronic thermometers, flow-control devices for IV catheter, feeding tube equipment, bedpan hoppers
- *C. difficile* spore load is low; 7 studies assessed the spore load and most found <10 colonies on surfaces found to be contaminated. Two studies reported >100; one reported a range of "1->200" and one study sampled several sites with a sponge and found 1,300 colonies *C. difficile*.

Role of the Environment
C. difficile

- The presence of *C. difficile* on the hands correlated with the density of environmental contamination. Samore et al. Am J Med 1996;100:32.
  - 0-25% environmental sites positive-0% hand cultures positive
  - 26-50% environmental sites positive-8% hand cultures positive
  - >50% environmental sites positive-36% hand cultures positive
- *C. difficile* incidence data correlated significantly with the prevalence of environmental *C. difficile*. Fawley et al. Epid Infect 2001;126:343.
- Environmental contamination does not play a major role in nosocomial CDAD in some endemic situations. Cohen et al. Clin Infect Dis 1997;24:889.
- 59% of 35 HCWs were *C. difficile* positive after direct contact with culture-positive patients.

Survival
C. difficile

- Vegetative cells
  - Can survive for at least 24 h on inanimate surfaces
- Spores
  - Spores survive for up to 5 months. 10^6 CFU of *C. difficile* inoculated onto a floor; marked decline within 2 days. Kim et al. J Inf Dis 1981;143:42.

Decreasing Order of Resistance of Microorganisms to Disinfectants/Sterilants

Spores

Mycobacteria

Non-Enveloped Viruses

Fungi

Bacteria

Enveloped Viruses

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Environmental Surface Disinfection

Product and Practice

Low-Level Disinfection for "Noncritical" Objects

Exposure time ≥ 1 min

Germicide	Use Concentration
Ethyl or isopropyl alcohol	70-90%
Chlorine	100ppm (1:500 dilution)
Phenolic	UD
Iodophor	UD
Quaternary ammonium	UD
Accelerated hydrogen peroxide	0.5%

UD=Manufacturer's recommended use dilution

Disinfectants and Antiseptics

C. difficile spores at 20 min, Rutala et al, 2006

- No measurable activity (1 *C. difficile* strain, J9)
  - CHG
  - Vesphene (phenolic)
  - 70% isopropyl alcohol
  - 95% ethanol
  - 3% hydrogen peroxide
  - Clorox disinfecting spray (65% ethanol, 0.6% QUAT)
  - Lysol II disinfecting spray (79% ethanol, 0.1% QUAT)
  - TBQ (0.06% QUAT); QUAT may increase sporulation capacity- Lancet 2000;356:1324
  - Novaplus (10% povidone iodine)
  - Accel (0.5% accelerated hydrogen peroxide)

Disinfectants and Antiseptics

C. difficile spores at 10 and 20 min, Rutala et al, 2006

- ~4 $\log_{10}$ reduction (5 *C. difficile* strains including BI-9)
  - Clorox, 1:10, ~6,000 ppm chlorine (but not 1:50, ~1,200 ppm)
  - Clorox Clean-up, ~1,910 ppm chlorine
  - Tilex, ~25,000 ppm chlorine
  - Steris 20 sterilant, 0.2% peracetic acid
  - Cidex, 2.4% glutaraldehyde
  - Cidex-OPA, 0.55% OPA
  - Wavicide, 2.65% glutaraldehyde
  - Aldahol, 3.4% glutaraldehyde and 26% alcohol

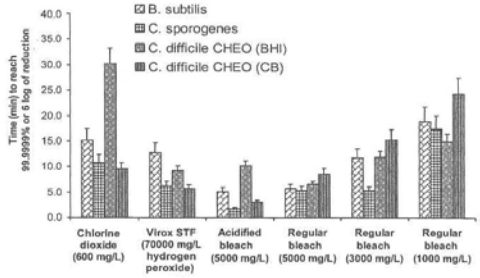

Fig 1. Times required for the microbicides to inactivate ≥6 $\log_{10}$ (99.9999%) of the spores tested.

Environmental Surface Disinfection

Product-1900-6000ppm chlorine effective (5-10m)

Epidemiological Studies with Chlorine

Effect of Hypochlorite on Environmental Contamination and Incidence of *C. difficile*

- Use of chlorine (500 [79% reduction]-1600 ppm [98%]) decreased surface contamination and the outbreak ended. Mean CFU/positive culture in outbreak 5.1, reduced to 2.0 with chlorine. Kaatz et al. Am J Epid 1988;127:1289.
- In an intervention study, the incidence of CDAD for bone marrow transplant patients decreased significantly, from 8.6 to 3.3 cases per 1000 patient days after the environmental disinfection was switched from QUAT to 1:10 hypochlorite solution in the rooms of patients with CDAD. No reduction in CDAD rates was seen among NS-ICU and medicine patients for whom baseline rates were 3.0 and 1.3 cases per 1000-patient days. Mayfield et al. Clin Inf Dis 2000;31:995.

Effect of Hypochlorite on Environmental Contamination and Incidence of *C. difficile*

- 35% of 1128 environmental cultures were positive for *C. difficile.* To determine how best to decontaminate, a cross-over study conducted. There was a significant decrease of *C. difficile* on one of two medicine wards (8.9 to 5.3 per 100 admissions) using hypochlorite (1,000 ppm) vs. detergent. Wilcox et al. J Hosp Infect 2003;54:109.
- Acidified bleach (5,000 ppm) and the highest concentration of regular bleach tested (5,000 ppm) could inactivate all the spores in <10 minutes. Perez et al. AJIC 2005;33:320

Control Measures
C. difficile

- Handwashing (soap and water) , contact precautions, and meticulous environmental cleaning with an EPA-registered disinfectant should be effective in preventing the spread of the organism. McFarland et al. NEJM 1989;320:204.
- In units with high endemic *C. difficile* infection rates or in an outbreak setting, use dilute solutions of 5.25-6.15% sodium hypochlorite (e.g., 1:10 dilution of bleach) for routine disinfection. (Category II)
- For semicritial equipment, glutaraldehyde (20m), OPA (12m) and peracetic acid (12m) reliably kills *C. difficile* spores using normal exposure times

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- In units with high endemic *C. difficile* infection rates or in an outbreak setting, use dilute solutions of 5.25-6.15% sodium hypochlorite (e.g., 1:10 dilution of bleach) for routine disinfection. (Category II). One application of an effective product covering all surfaces to allow a sufficient wetness for > 1 minute contact time. Chlorine solution normally takes 1-3 minutes to dry. We use QUAT for disinfection of patient rooms with sporadic CDI.
- For semicritial equipment, glutaraldehyde (20m), OPA (12m) and peracetic acid (12m) reliably kills *C. difficile* spores using normal exposure times

Environmental Surface Disinfection

Poor Product and/or Poor Practice

Risk of Acquiring MRSA, VRE, and *C. difficile* from Prior Room Occupants

- Admission to a room previously occupied by an MRSA-positive patient or VRE-positive patient significantly increased the odds of acquisition for MRSA and VRE (although this route is a minor contributor to overall transmission). Arch Intern Med 2006;166:1945.
- Prior environmental contamination, whether measured via environmental cultures or prior room occupancy by VRE-colonized patients, increases the risk of acquisition of VRE. Clin Infect Dis 2008;46:678.
- Prior room occupant with CDAD is a significant risk for CDAD acquisition. ICACC (K-4194) 2008. Shaughnessy et al.

Current Issues

Clostridium difficile

- Improve cleaning/disinfecting patient care areas
- Hydrogen peroxide vapor
- Ultraviolet light

Patient Area Cleaning/Disinfecting

PC Carling et al, ICHE 2008;29:1 and ICHE 2008;29:1035

- Monitor cleaning performance using an invisible fluorescent targeting method. Rooms (14 high-risk objects) were marked and evaluated after terminal cleaning.
- Results: 1,605 rooms and 20,646 objects were evaluated in 36 hospitals. Mean proportion of objects cleaned was 48%. Following education and process improvement feedback, cleaning improved to 77%
- Conclusion: Substantial opportunity for improving terminal cleaning/disinfecting activities.

TABLE. Rates of Cleaning for 14 Types of High-Risk Objects

Object	Percentage cleaned		95% CI
	Mean ± SD	Range	
Sink	82 ± 12	57-97	77-88
Toilet seat	76 ± 18	40-98	68-84
Tray table	77 ± 15	53-100	71-84
Bedside table	64 ± 22	23-100	54-73
Toilet handle	60 ± 22	23-89	50-69
Side rail	60 ± 21	25-96	51-69
Call box	50 ± 19	9-90	42-58
Telephone	49 ± 16	18-86	42-56
Chair	48 ± 28	11-100	35-61
Toilet door knobs	28 ± 22	0-82	18-37
Toilet hand hold	28 ± 23	0-90	18-38
Bedpan cleaner	25 ± 18	0-79	17-33
Room door knobs	23 ± 19	2-73	15-31
Bathroom light switch	20 ± 21	0-81	11-30

NOTE. CI, confidence interval.

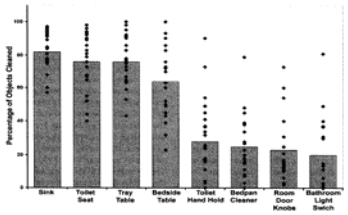

FIGURE 2. Rates of cleaning for the 4 types of object with the highest cleaning rates and the 4 types of object with the lowest rates. *Shaded bar*, mean value; *filled diamond*, value for a single hospital.

Mean proportion of surfaces disinfected at terminal cleaning is ~50%

Environmental Surface Disinfection

Poor Practice

Disinfection of Patient Area: *C. difficile*

Eckstein et al. BMC Infect Dis 2007:7;61

- Assessed adequacy of cleaning practices in rooms of patients with CDI
- Cultured commonly touched surfaces (bedrails, phones, call buttons, door knobs, bedside tables) in rooms of patients with CDI
- Of 9 rooms of patients with CDI, 100% positive cultures prior to cleaning versus 7 (78%) after cleaning, whereas only 1 had positive cultures after bleach disinfection by research staff
- After educational intervention (stressed high touch objects to be disinfected) , rates of environmental contamination after housekeeping cleaning were significantly reduced (90%→20%)

Room Decontamination Units

Hydrogen Peroxide Vapor Decontamination

- Bartels MD et al. J Hosp Infect 2008;70:35. MRSA/Sterinis
- Boyce JM et al. ICHE 2008;29:723. *C. difficile*/Bioquell
- Shapey S et al. J Hosp Infect 2008;70:136. *C. difficile*/Sterinis
- Hardy KJ et al. J Hosp Infect 2007;66:360. MRSA/Bioquell
- Hall L et al. J Clin Microbiol 2007;45: 810. *M. tuberculosis*/Bioquell
- Bates CJ, Pearse R. J Hosp Infect 2005;61:364. *S. marcescens*/Bioquell
- Johnston MD et al. J Microbiol Methods 2005;60:403. *C. botulinum*/Bioquell
- French GL et al. J Hosp Infect 2004;57:31. MRSA/Bioquell
- Heckert RA et al. Appl Environ Microbiol 1997;63:3916. Viruses/Steris VHP
- Klapes NA et al. Appl Environ Microbiol 1990;56;503. *Bacillus* spores/Prototype HPV generator

Decontamination with Hydrogen Peroxide Vapor

Boyce et al: ICHE 2008;29:723

- 5 wards with a high incidence of *C. difficile*
- HPV was injected into sealed wards and individual patient rooms using generators until approx 1 micron film of HP was achieved on the surface
- 11/43 (25.6%) surface samples yielded *C. difficile* compared to 0/27 (0%) after HPV decontamination
- The incidence of nosocomial CDAD was significantly lower during the intervention period
- Conclusion: HPV was efficacious in eradicating *C. difficile* from contaminated surfaces

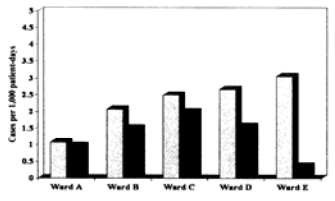

FIGURE 2. Incidence of nosocomial *Clostridium difficile*–associated disease on 5 wards (A–E) that underwent intensive hydrogen peroxide vapor decontamination, during the preintervention period (*gray bars*; June 2004 through March 2005) and the intervention period (*black bars*; June 2005 through March 2006).

Feasibility of Routinely Using HPV

Boyce et al: ICHE 2009: 30:574

- Used HPV to decontaminate selected rooms (e.g., MRSA, VRE, *C. difficile*)
- HPV requires room be vacated, cleaned of dirt, and sealed
- 1656 rooms decontaminated with HPV
- Total time from room vacated until ready for the next patient was 270min for HPV and 67min for bleach cleaning
- Despite the greater time for decontamination, HPV decontamination is feasible in a busy hospital

Comparison of HP and Chlorine with *C. difficile*

(Barbut et al. *Infect Control Hosp Epidemiol* 2009;30:507)

Treatment	Before Treatment	After Treatment	% Reduction
Hydrogen peroxide mist	19% (34/180)	2% (2/180)	91% (p<.005)
Chlorine	24% (46/194)	12% (23/194)	50%

UV Room Decontamination

- Fully automated, self calibrates, activated by hand-held remote
- Room ventilation does not need to be modified
- Uses UV-C (254 nm range) to decontaminate surfaces
- Measures UV reflected from walls, ceilings, floors or other treated areas and calculates the operation time to deliver the programmed lethal dose for pathogens.
- UV sensors determines and targets highly-shadowed areas to deliver measured dose of UV energy
- After UV dose delivered, will power-down and audibly notify the operator
- Reduces colony counts of pathogens by >99.9% within 20 minutes

Room Decontamination with UV

(Rutala, Gergen, Weber, 2009, Unpublished Results)

Organism	Dose Reading (time)	Log_{10} Reduction (10 sites, 5 replicates)
MRSA	~470 mj/cm^2 (~15m)	3.91
VRE	~660 mj/cm^2 (~15m)	3.36
Acinetobacter	~630 mj/cm^2 (~14m)	3.77
C. difficile	~2120 mj/cm^2 (~50m)	2.67

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Disinfection and Sterilization

EH Spaulding believed that how an object will be disinfected depended on the object's intended use.

CRITICAL - objects which enter normally sterile tissue or the vascular system or through which blood flows should be sterile.

SEMICRITICAL - objects that touch mucous membranes or skin that is not intact require a disinfection process (high-level disinfection[HLD]) that kills all microorganisms but high numbers of bacterial spores.

NONCRITICAL -objects that touch only intact skin require low-level disinfection.

High Level Disinfection of "Semicritical Objects"

Exposure Time ≥ 12 m-30m (US), 20°C

Germicide	Concentration
Glutaraldehyde	≥ 2.0%
Ortho-phthalaldehyde (12 m US)	0.55%
Hydrogen peroxide*	7.5%
Accelerated hydrogen peroxide	2.0%
Hydrogen peroxide and peracetic acid*	1.0%/0.08%
Hydrogen peroxide and peracetic acid*	≥7.35%/≥0.23%
Hypochlorite (free chlorine)*	650-675 ppm
Glut and phenol/phenate	1.21%/1.93%
Glut and alcohol	3.4%/26% IPA

*May cause cosmetic and functional damage

High-Level Disinfection
C. difficile spores

- 2% glutaraldehyde for 5 min resulted in 99% or more killing of *C. difficile* spores. Hughes et al.Gastro Endo 1986;32:7.
- 2% glutaraldehyde for 10 or 20 min inactivated *C. difficile* spores using the AOAC test. Rutala et al. ICHE 1993;14:36
- 2% glutaraldehyde and peracetyl ions inactivated *C. difficile* spores. Wullt et al. ICHE 2003;24:765.

Disinfectants and Antiseptics
C. difficile spores at 10 and 20 min, Rutala et al, 2006

- ~4 $\log_{10}$ reduction (3 *C. difficile* strains including BI-9)
  - Clorox, 1:10, ~6,000 ppm chlorine (but not 1:50)
  - Clorox Clean-up, ~1,910 ppm chlorine
  - Tilex, ~25,000 ppm chlorine
  - Steris 20 sterilant, 0.35% peracetic acid
  - Cidex, 2.4% glutaraldehyde
  - Cidex-OPA, 0.55% OPA
  - Wavicide, 2.65% glutaraldehyde
  - Aldahol, 3.4% glutaraldehyde and 26% alcohol

High-Level Disinfection
C. difficile spores

- 2% glutaraldehyde is effective against *C. difficile* at 20 minutes
- 0.55% ortho-phthalaldehyde is effective against *C. difficile* at 12 minutes
- Steris 20 is effective against *C. difficile* at 10 and 20 minutes

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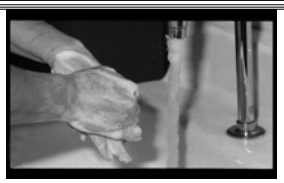
C. difficile spores at 20 min, Rutala et al, 2006

- No measurable activity (1 *C. difficile* strain, J9)
  - CHG-chlorhexidine gluconate
  - Vesphene (phenolic)
  - 70% isopropyl alcohol
  - 95% ethanol
  - 3% hydrogen peroxide
  - Clorox disinfecting spray (65% ethanol, 0.6% QUAT)
  - Lysol II disinfecting spray (79% ethanol, 0.1% QUAT)
  - TBQ (0.06% QUAT); QUAT may increase sporulation capacity- Lancet 2000;356:1324
  - Novaplus (10% povidone iodine)
  - Accel (0.5% hydrogen peroxide)

HAND HYGIENE



Either soap or CHG works as a handwash for removal of *C. difficile.*
ICHE 1994;15:697.

70% isopropyl showed no inactivation of *C. difficile* spores at exposure times of 5m, 15m, and 30m.
Wullt et al. ICHE 2003;24:765.

What are the data for soap and water versus alcohol-based hand rubs for *C. difficile* spores?

Hand Hygiene

- Evaluated effectiveness of liquid soap vs. CHG for removal of *C. difficile*. Two agents did not differ significantly in counts of *C. difficile* on bare hands. Use either soap or CHG as a handwash for removal of *C. difficile.* Study did not evaluate alcohol-based hand rubs. Bettin et al. ICHE 1994;15:697.
- 70% isopropyl showed no inactivation of *C. difficile* spores at exposure times of 5m, 15m, and 30m. Wullt et al. ICHE 2003;24:765.

Hand Hygiene with Soap and Water Is Superior to Alcohol Rub and Antiseptic Wipes for Removal of *C. difficile*

(Oughton et al. Infect Control Hosp Epidemiol 2009; 30:939)

Objective: Evaluate HH methods for efficacy in removing *C. difficile*

Design: Randomized crossover comparison among 10 volunteers experimentally contaminated by 1.4×10^5 *C. difficile* (62% spores)

Methods: Interventions were evaluated for mean reduction

Conclusion: Handwashing with soap and water showed the greatest efficacy in removing *C. difficile* and should be performed preferentially over the use of alcohol-based hand rubs when contact with *C. difficile* is suspected or likely

C. difficile after Hand Hygiene Interventions

(Oughton et al. Infect Control Hosp Epidemiol 2009; 30:939)

Intervention	Mean Count, $\log_{10}$ CFU/ml
Warm water and plain soap, 10s	1.99
Cold water and plain soap, 10s	1.90
Warm water and antibacterial (CHG) soap, 10s	2.31
Antiseptic (PCMX) hand wipe, 15s	3.25
Alcohol-based handrub, 15s	3.74
No intervention	3.82

Antisepsis to Prevent *C. difficile* Infections

YES!!

NO!!

Conclusions

C. difficile

Clostridium difficile

- Have been found in abundance in the environment of individuals with disease
- Have been found on the hands of healthcare workers providing care to affected patients or touching the contaminated environment
- Survive in the environment (months [spores])
- Are relatively resistant to chemical disinfection (including alcohol)
- Have caused outbreaks in hospitals
- Are transmitted by either ingestion or direct inoculation of the GI tract
- Have epidemiological evidence that environmental surface contamination may be a source for infections

Conclusions

C. difficile

- Environmental control
  - In general, changes in disinfectants to eliminate specific pathogens not required.
  - Because *C. difficile* spores are resistant to many surface disinfectants, care must be taken to use agents with evidence of efficacy (e.g., hypochlorite-based products). Ensure all surfaces are disinfected and all equipment is assigned.
  - Current high-level disinfection recommendations are adequate to prevent healthcare-associated infections via semicritical items such as endoscopes
  - Areas with high endemic or epidemic *C. difficile* (e.g., 3 cases/1000 patient days) warrant hypochlorite-based products or room decontamination units (HPV or UV)
  - Soap and water should be used preferentially to alcohol-based hands rubs for *C. difficile*.

Clostridium difficile: What Antiseptics and Disinfectants Should We Use?

- Microbiology and epidemiology of *C. difficile*
- Role of the environment in transmission
- Prevention
  - Disinfectants for environmental disinfection (chlorine, HPV, UV)
  - Disinfectants for semicritical equipment disinfection (HLD such as glut, OPA, PA)
  - Antiseptics (not active against *C. difficile* spores [soap and water removal])
  - Hand hygiene (soap and water (removal] not alcohol-based hand rubs)

disinfectionandsterilization.org

Thank you