

Clostridium difficile

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Bacteriology

- Gram + anaerobic spore-forming bacillus
- Spores resistant to drying
- Persists in the environment for long periods of time
- Soil, hay, mud, sand
- Animal stool: horses, dogs, cats, camels, donkeys, cattle
- Found worldwide

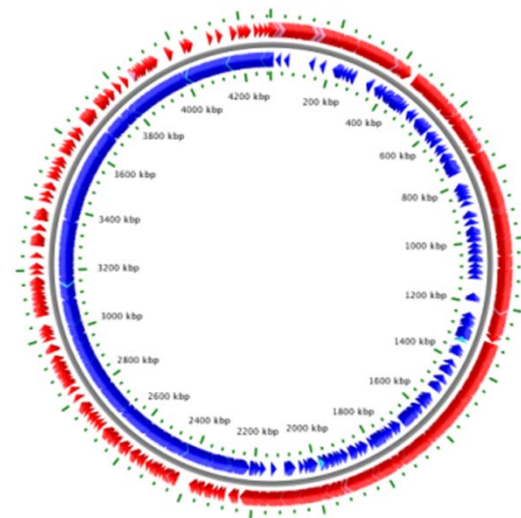


Bacteriology

- One circular chromosome and one circular plasmid.
- Conjunctive transposons = 11% of the genome.

Transposons = DNA fragments that can move from one location to another within the genome. They have the → ability to be very virulent, resist antibiotics.

Clostridium difficile 630, complete genome



Culture



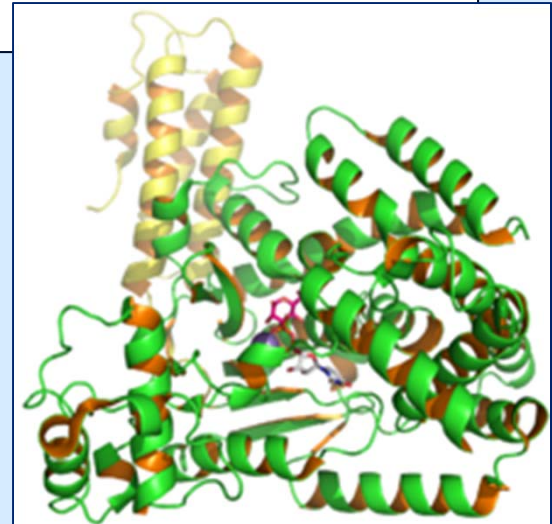
- Most sensitive test available
- Culture on cycloserine-cefoxitin-fructose agar selective medium; very sensitive but false positive due to non-toxigenic isolates.
- Most often associated with false-positive results due to presence nontoxigenic *C.difficile* strains.
- Overcome by testing isolates for toxin production
- Labor intensive
- Require an appropriate culture environment to grow anaerobic microorganisms
- Slow turn-around time (48-96 hours) → less clinically useful.
- Toxigenic cultures do serve as a gold-standard against which other test modalities are compared in clinical trials of performance.

Toxins

Disease related to the action of toxins

- Non pathogenic strains: No toxins
- Toxin A: Enterotoxic and Cytotoxic
- Toxin B: Cytotoxic
- Strain BI/NAP1/027 toxin type III
- Presence of binary toxin CDT and 18 base pair *tcdC* deletion

- Toxin degrades at room temperature
- Undetectable within two hours after collection
- Specimens should be kept at 4°C if delay is anticipated.



Characterization of the BI/NAP1/027 Strain

- Strain not new; first isolated in 1984 but more recently reported in Canadian and U.S. *C. Diff* outbreaks. Older isolates were not associated with outbreaks or exhibited fluoroquinolone resistance.
- Found to produce 16 times more toxin A and 23 times more toxin B than other *C. Diff* strains
- Resistant to Gatifloxacin and Moxifloxacin

Resistance of Current (after 2000) BI/NAP1 Isolates to Clindamycin and Fluoroquinolones Compared with Current Non-BI/NAP1 Isolates and Historic (before 2001) BI/NAP1 Isolates

No. (%) Intermediate or Resistant to:	Current BI/NAP1 Isolates n=24 (%)	Current non- BI/NAP1 Isolates n=24 (%)	<i>P-Value for BI/NAP1 vs. Non- BI/NAP1 Isolates</i>	Historic BI/NAP1 Isolates n=14 (%)	<i>P-Value for Current vs. Historic BI/NAP1 Isolates</i>
Clindamycin	19 (79)	19 (79)	1.0	10 (71)	0.7
Levofloxacin	24 (100)	23 (96)	1.0	14 (100)	1.0
Gatifloxacin	24 (100)	10 (42)	<0.001	0	<0.001
Moxifloxacin	24 (100)	10 (42)	<0.001	0	<0.001

From McDonald LC, et al. *N Engl J Med.* 2005;353:2433-2441.

Epidemic Strain

- **BI/NAP1/027, toxinotype III, aka also known as PCR ribotype 027**
- **Existed in the past, uncommon, not associated w epidemic**
- **Epidemic since 2000**
- **More resistant to fluoroquinolones**
 - **Higher MICs compared to historic strains and current non-BI/NAP1 strains**
 - **Hence a selective advantage in a high FQ environment**
- **More virulent**
 - **Increased toxin A and B production**
 - **Polymorphisms in binding domain of toxin B**
 - **Increased sporulation**

McDonald et al. N Engl J Med. 2005;353:2433-41.
Warny et al. Lancet. 2005;366:1079-84.
Stabler et al. J Med Micro. 2008;57:771-5.
Akerlund et al. J Clin Microbiol. 2008;46:1530-3.

Epidemiology

Mode of Transmission

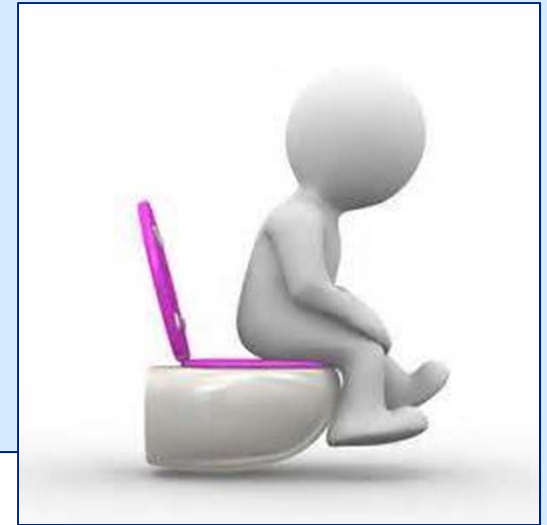
- Exact route unknown
- Believed fecal-oral (animal feces, soil)
- Healthcare Associated:
C. Difficile is most often transmitted via the hands of healthcare personnel who have had contact with contaminated feces or contaminated environmental surfaces (CDC)

Transmissibility

Difficult to assess because of:

- **Variable susceptibility of exposed persons**
- **Widespread environmental distribution of spores**
- **Variable virulence characteristics of organism**

Source



- **Oral ingestion of spores or vegetative**
- **Main source: symptomatic patients**
- **Also may be important**
 - **Asymptomatic carriers (Riggs MM Clin Inf Dis 2007; 45 e-pub)**
 - **Skin carriage common, easily transmitted**
- **Environment**

Carriers as Transmitters

- Asymptomatic carriers of *C.diff* frequently shed virus : skin & environment
- *C.diff* outbreak at LTCF (OH): 35 (51%) of 68 asymptomatic residents were carriers, 13 (37%) with epidemic strains of *C.diff*.
- Asymptomatic carriers outnumbered CDAD patients 7 to 1
- Among asymptomatic carriers, *C.diff* in:
 - skin (61%); 87% of these matched stool isolates
 - environmental sites (59%); 58% of these matched stool isolates
- Spores on skin easily transferred to investigators' hands
- Previous CDAD & previous antibiotic use associated with asymptomatic carriage
 - Combination of these two factors was predictive carriage
 - Sensitivity= 77%, specificity= 58%, PPV= 66%, NPV= 70%.
- Asymptomatic carriers = potential source for transmission of *C.diff* strains in LTCF
- Solution: Contact isolation, bleach for room disinfection

Epidemiology: Incidence

- Few community based studies:
 - 7.7 /100.000 person years;
 - 12 / 100,000 person years

Hirschhorn,LR, 1994. Epidemiology of Community Acquired CDAD, Journal of Infect Dis169:127-133
Levy 2000. Clin Therap 22:91

- Most studies in hospitals or chronic care facilities:
 - 3.2-9.9 cases per 100 patient discharges

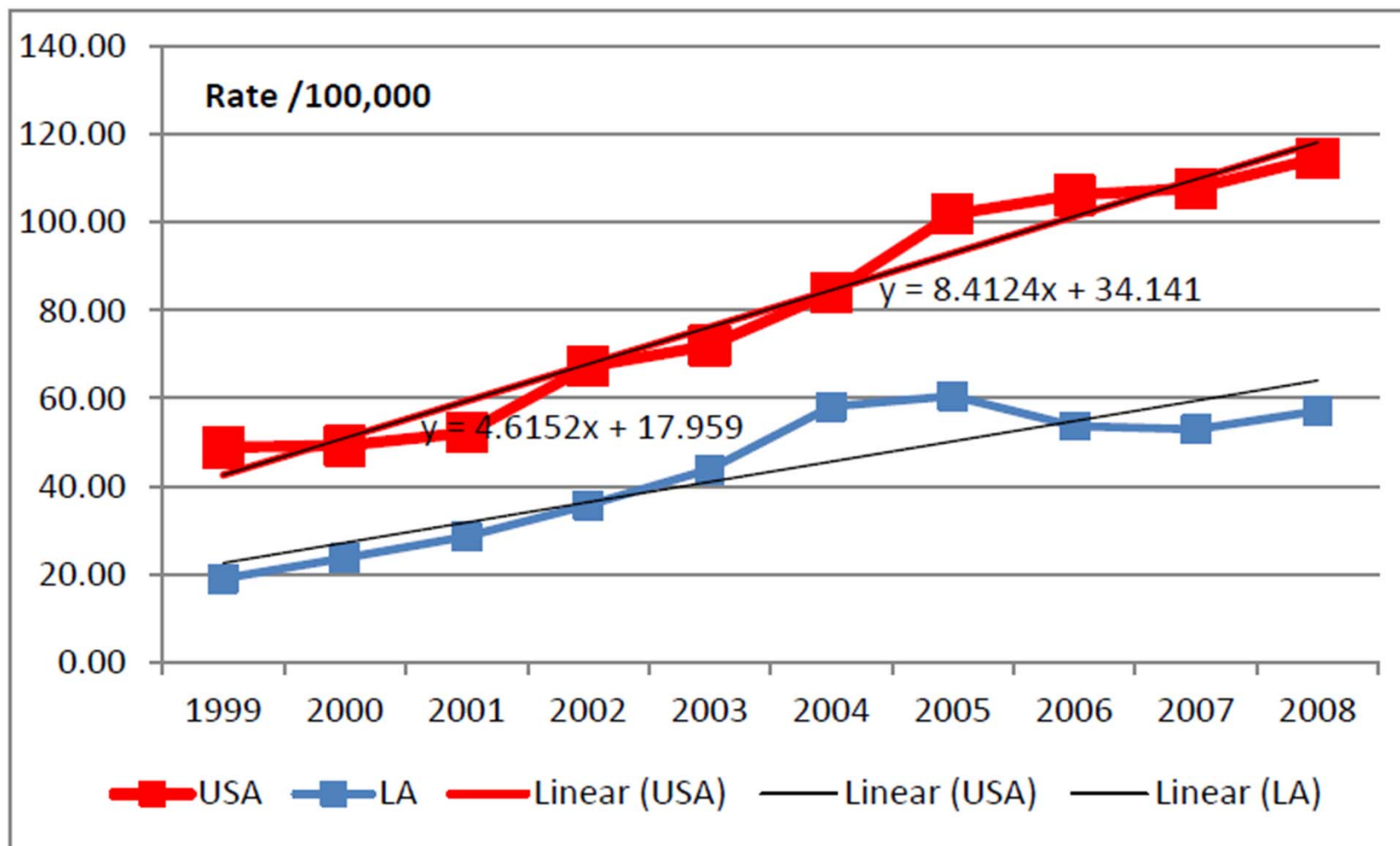
Olson,MM 1994. Ten years prospective CDAD Surveillance and tx at Minneapolis VA Medical Center. Infection Control and Hospital pidemiology 15:371-381 (1994)

- Studies in hospitals or chronic care: /1000 discharges
 - 1 to 10 Olson MM 1994 ICHE 15:371
 - 32 to 100 McFarland 1989 NEJM 320: 204



Hospitalization Rates /100,000 pop in Louisiana

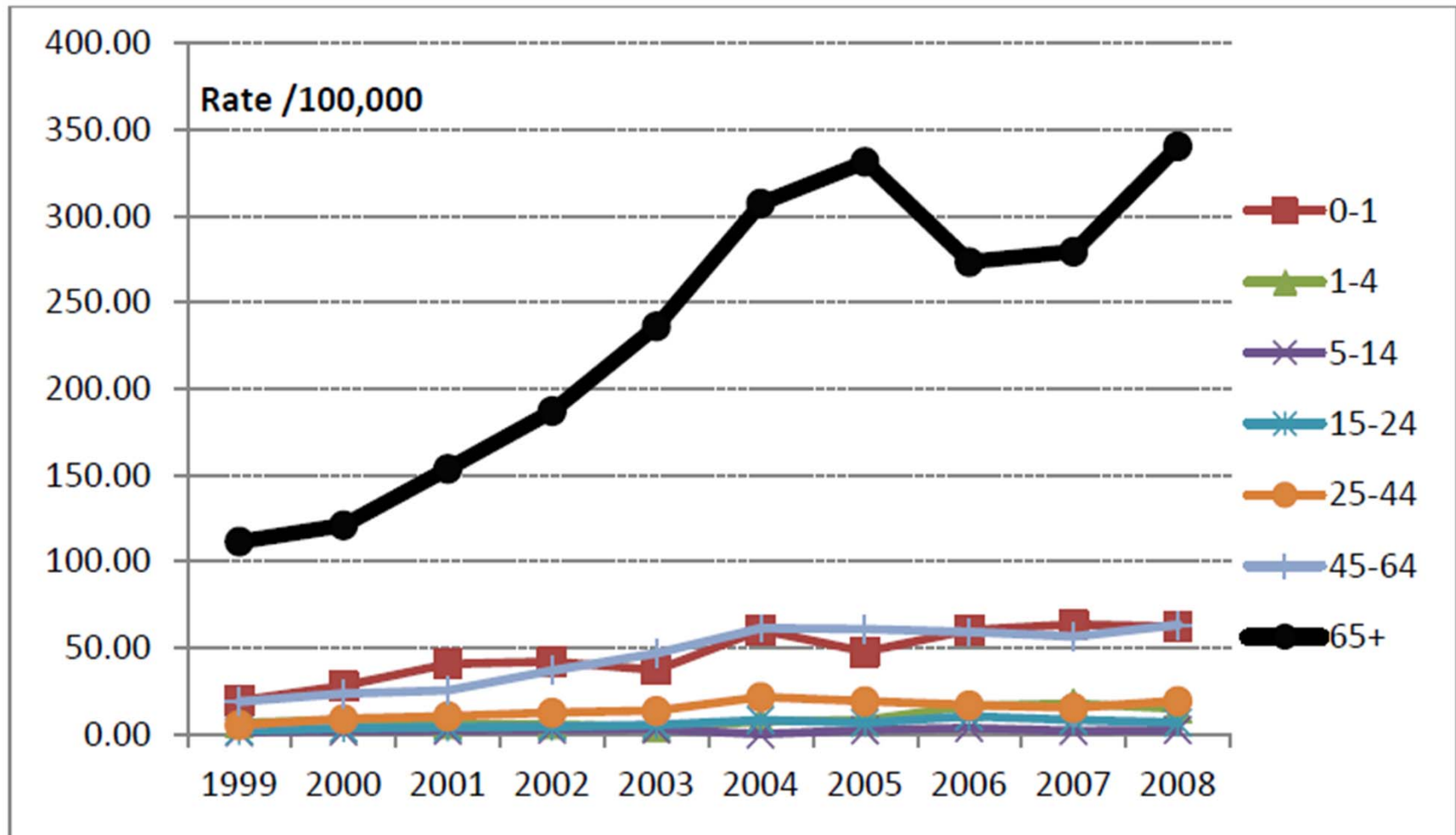
Figure 1 - CDAD Hospitalization Rates per100,000, in US and Louisiana, 1999-2008



From Smith L, Ratard RC 2011. J La State Med Soc VOL 163 (4) 192-195

Hospitalization Rates /100,000 pop in Louisiana by Age

Figure 4 - CDAD hospitalization rates per 100,000, by age Louisiana, 1999-2008,



Epidemiology: Prevalence

- Presence of *C.Difficile* in Stool specimens :

Healthy adults	2- 3 %
Elderly	2- 8 %
Chronic care facilities	7-15 %
Hospital with epidemic:	up to 50%



Epidemiologic Frequency Targets

- Case rate per 10,000 patient-days as measured in NHSN
 - National 5-Year Prevention Target: 30% reduction
- Because little baseline infection data exists, administrative data for ICD-9-CM coded *C. difficile* hospital discharges is also tracked
 - National 5-Year Prevention Target: 30% reduction

Epidemic Behavior

- **Used to be only in institutional setting**
- **Individuals that have received antimicrobial or antineoplastic agents**
- **Now cases seen in previously healthy adults, children and pregnant women**
- **Community-associated**

Epidemiology: Health Care Facility

- HCF major reservoirs for *C. difficile*
- Fecal colonization
 - 20% among adult patients hospitalized for >1 week
 - 1% to 3% among community residents
- *C.diff* Spores
 - found on environmental surfaces
 - can persist for months
 - on staff hands
- Hospital outbreaks attributed to single *C.diff* strain or multiple strains
- Transmission in HCF:
 - direct spread from staff hands (transient carriage)
 - Fomites: Contaminated commodes, telephones, and rectal thermometers ...

Epidemio: Child Care Facility

- **Child Care Facilities: major reservoirs for *C. difficile***
- **Asymptomatic fecal carriage in healthy neonates often > 50% during first 6 months**

Incubation Period

- **Exact incubation period is unknown**
- **Diarrhea may occur <1 week following acquisition of *C. Difficile***
- **Patient may be asymptomatic until exposed to antimicrobials**

Disease Burden



Disease Burden

- **In the U.S: Approximate annual burden**
 - **500,000 CDI infections / year**
 - **28,000 deaths / year from CDI;**

AHRQ: April 2008:CDAD in US hospitals 1993-2005)

- **In Louisiana: Approximate annual burden**
 - **6,000 CDI Infections /year**
 - **120 deaths / year from CDI**

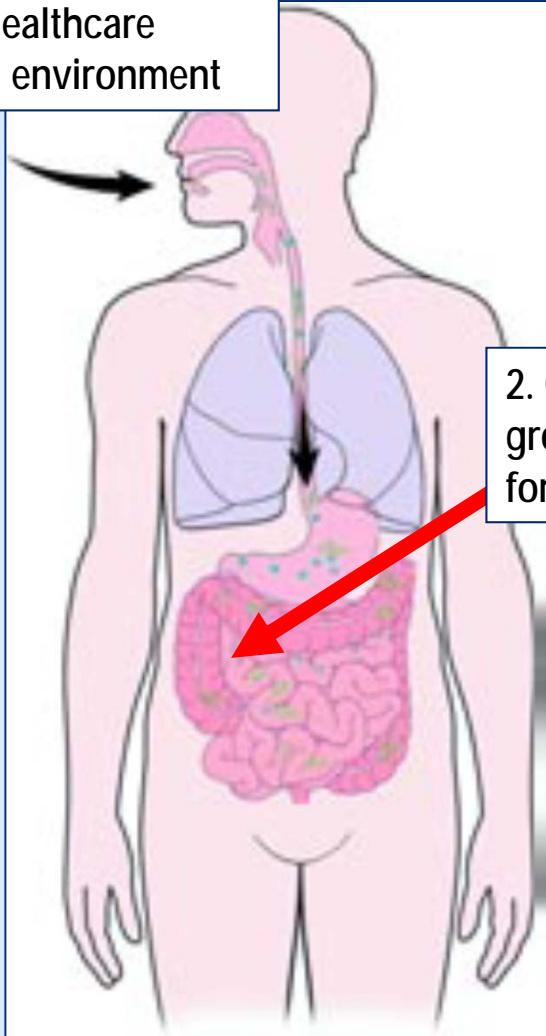
Smith L, Ratard RC 2011. J La State Med Soc VOL 163 (4) 192-195

Clinical



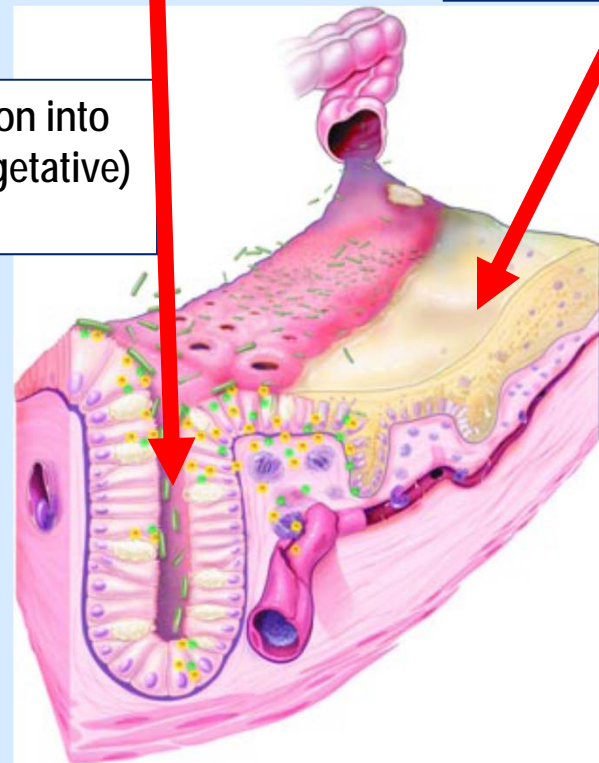
Pathogenesis of CDI

1. Ingestion of spores transmitted from other patients via the hands of healthcare personnel and environment



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

2. Germination into growing (vegetative) form

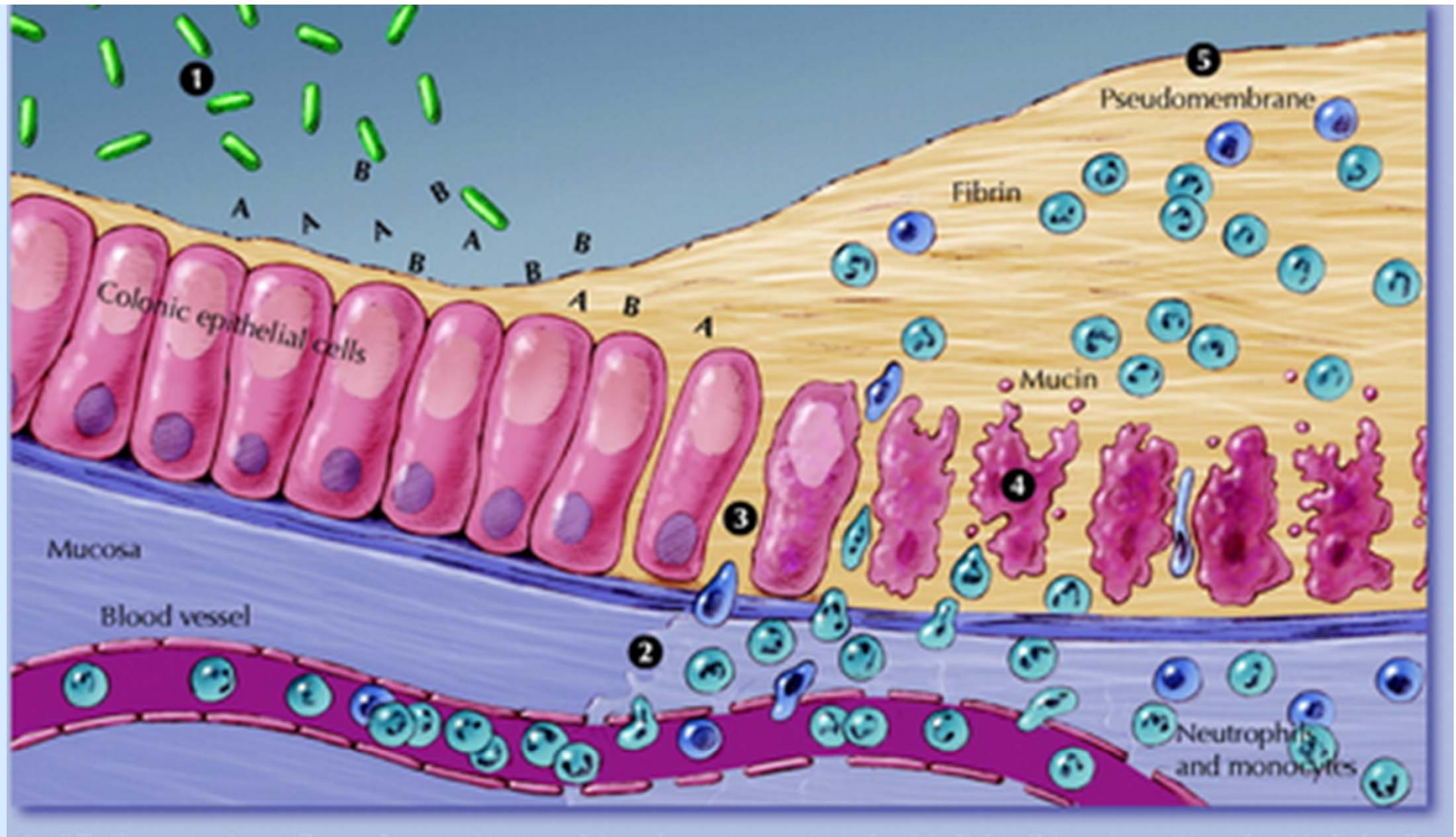


4. Toxin A & B production leads to colon damage +/- pseudo-membrane

Sunenshine et al. Cleve Clin J Med. 2006;73:187-97.

Pathogenesis of CDI

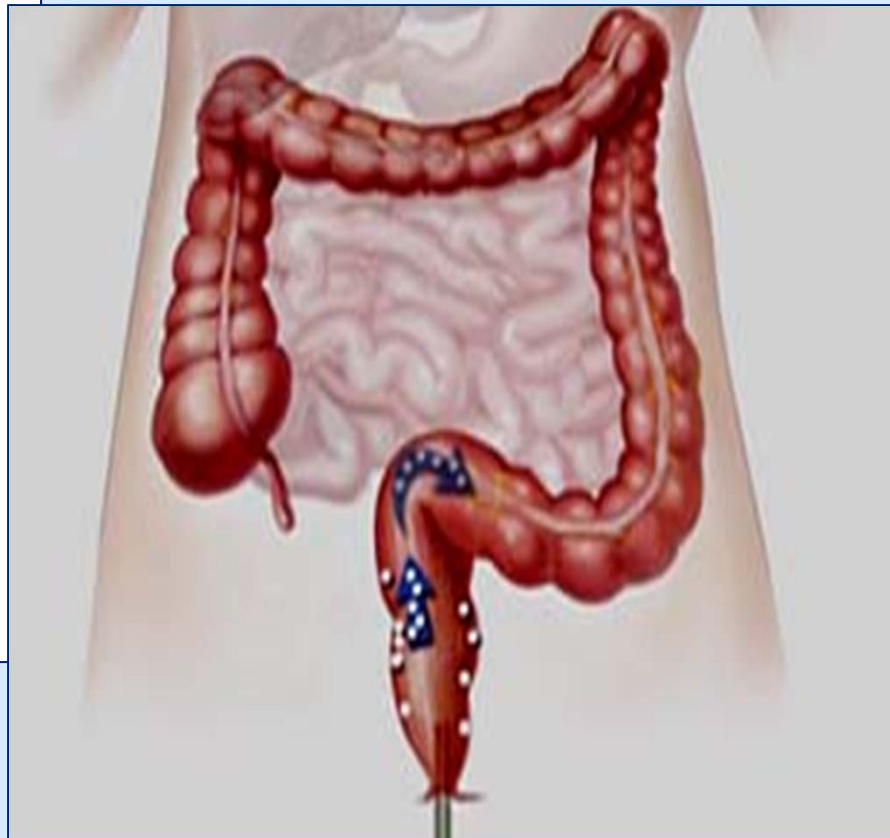
- Disruption of normal intestinal flora usually by broad spectrum antibiotic use
- Exposure to *C. Diff* generally during hospitalization
- Host Factors like co-morbidity and advanced age that can impair the immune status
- Spores of toxigenic *C. difficile* are ingested, survive gastric acidity, germinate in the small bowel, and colonize the lower intestinal tract, where they elaborate two large toxins: toxin A, an enterotoxin, and toxin B, a cytotoxin. These toxins initiate processes resulting in the disruption of epithelial-cell barrier function, diarrhea, and pseudomembrane formation.



***C.diff* vegetative cells → toxins A & B → Tumor necrosis factor- α and pro-inflammatory interleukins, increased vascular permeability, neutrophil and monocyte recruitment → opening of inter-epithelial cell junction → cell apoptosis → local connective tissue degradation**

Spectrum of Disease

- **Asymptomatic colonization**
- **Diarrhea**
- **Pseudomembranous colitis**
- **Toxic megacolon**
- **Colonic perforation**
- **Death**



Asymptomatic Colonization

- No symptoms
- More common than clinical disease
- Stool sample positive
- No antibiotic if colonization established
- In high incidence hospitals, patients become colonized 8% per week.
- In some hospitals the proportion of colonized patient reaches 50%.
- Patient who have become colonized with *C.diff* at lower risk of CDI.

From Colonization to CDI

Patients colonized with *C.diff*

- initially thought to be at high risk for CDI
- 4 prospective studies: colonized patients have a decreased risk of subsequent CDI

1.Exposure to antimicrobial agents first event establishes susceptibility to *C.diff*

2.Exposure to toxigenic *C.diff*

Most patients do not develop CDI after the first two events

3.Exposure to virulent strain, exposure to antimicrobial agents especially likely to cause CDI, inadequate host immune response.

Risk Factors for CDI

- Patient on antibiotics: Fluoroquinolone therapy
- Antimicrobial exposure
- Gastric acid suppression ?
- Proton Pump Inhibitors: Controversial?
- GI/Surgery manipulation
- Long length of stay
- Serious underlying illness
- Immunocompromised
- Tube feeds
- Advanced age



CDI Symptoms

- | | |
|-----------------------------------|---------|
| • Watery, non-bloody diarrhea, | 100% |
| • Lower abdominal pain, cramping, | 20%-33% |
| • Reduced bowel sounds, | |
| • Fever, sign of severity | 30%-50% |
| • Leukocytosis, >15,000WBC | 50%-60% |
| • Nausea, malaise, anorexia, | |
| • Hypoalbuminemia, | |
| • Occult colonic bleeding | |

Recurrence of diarrhea: 40% of patients with CDI.

Re-infection: Commonly, patient received another course of antibiotic that predisposes to second episode. Most relapses will occur within 1 month of end of therapy.

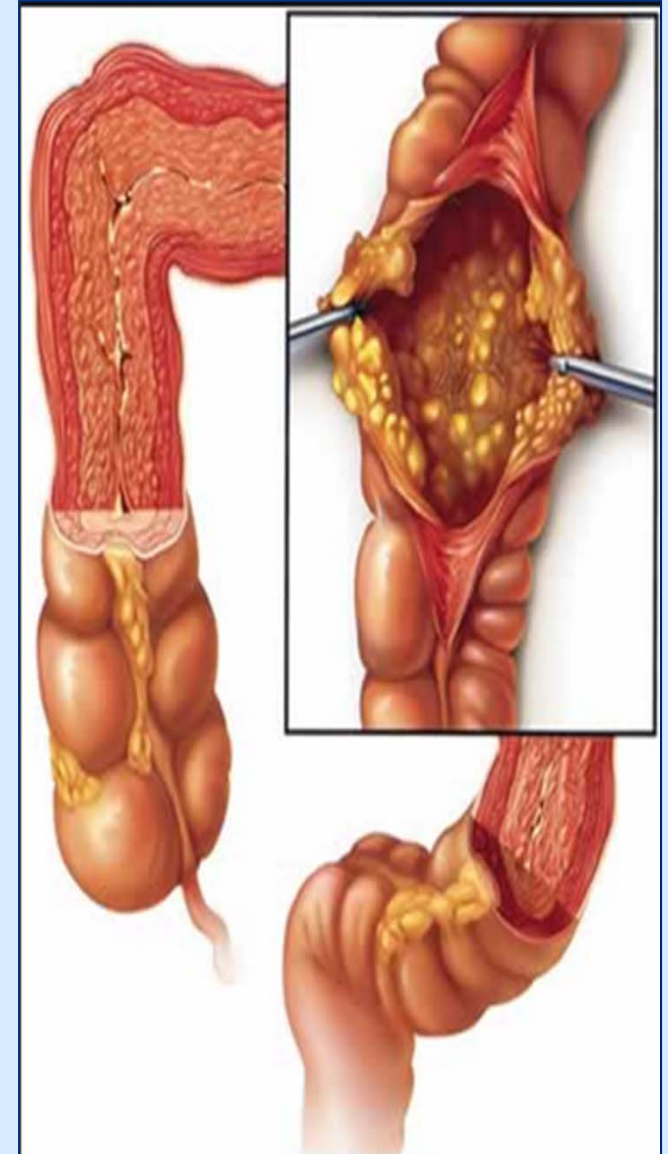
One recurrence is a risk factor for a subsequent episode.

CDI or Plain diarrhea

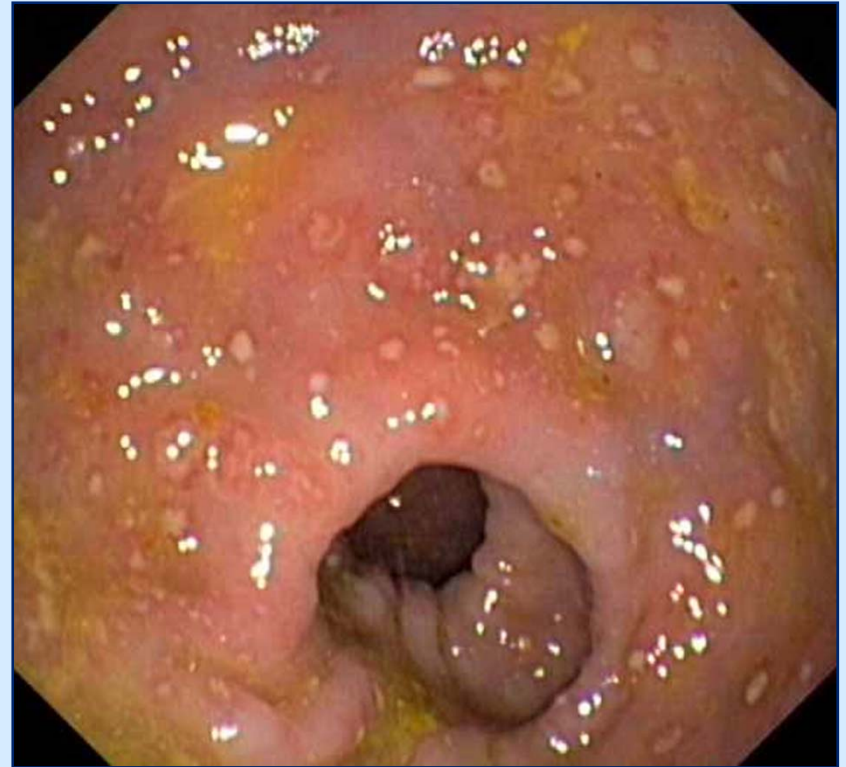
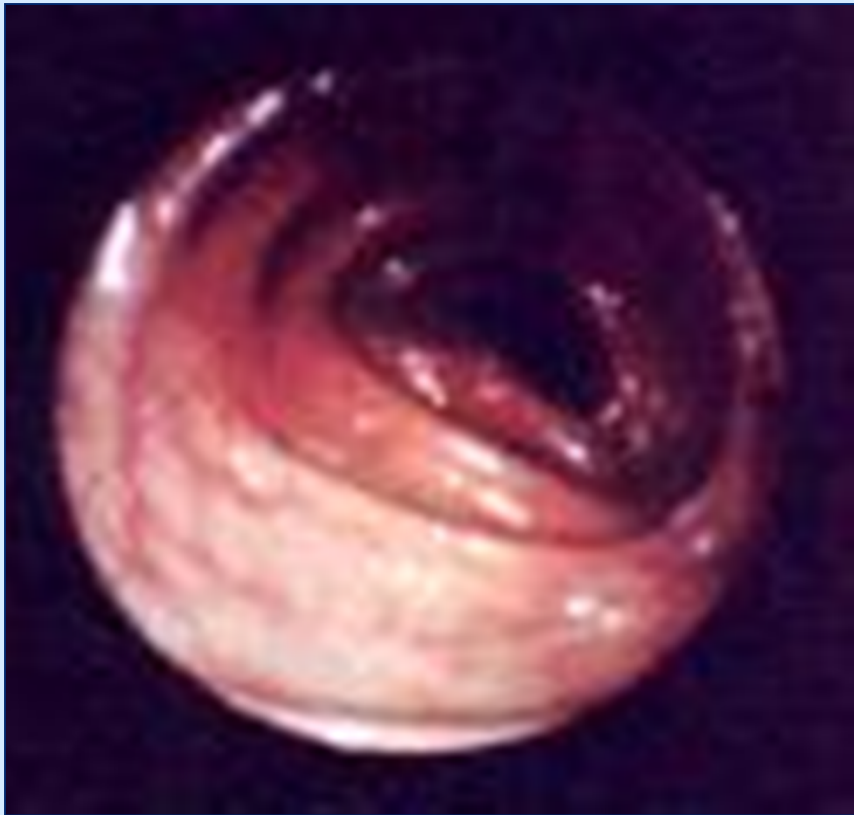
- Diagnostic stool evaluation for the presence of *C. difficile* toxins should be pursued in the setting of
 - **Clinically significant diarrhea** (usually defined as **3** or more loose stools per day for at least **2** days);
 - **Loose stool** = Stool that conforms to the shape of the container
 - High suspicion:
 - Many stools (10 to 15)
 - Fever
 - High WBC count
 - Nocturnal diarrhea even if only one day in duration

Severe Disease

- Pseudo-membranous colitis:
 - Five + episodes of diarrhea /day for >1-2 days
 - Bloody stools
 - Diffuse and severe abdominal pain, distention.
 - Toxic appearance, Fever,
 - Dehydration (dry skin, dry mouth, glassy appearance of the eyes, sunken soft spots on top of head in infants, rapid pulse, confusion, excessive tiredness)
- Toxic Megacolon
 - Life-threatening complication
 - Large intestine widening (dilation) within 1 /few days.
- Colonic perforation

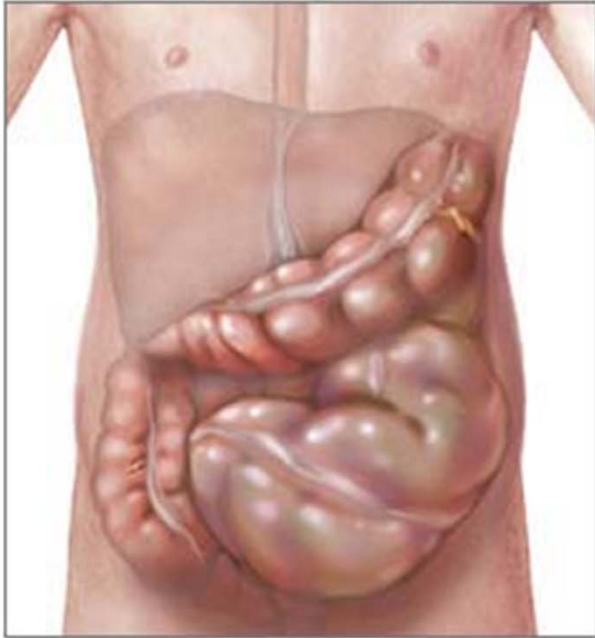


Healthy Colon Vs. Pseudomembranous Colitis



Complications

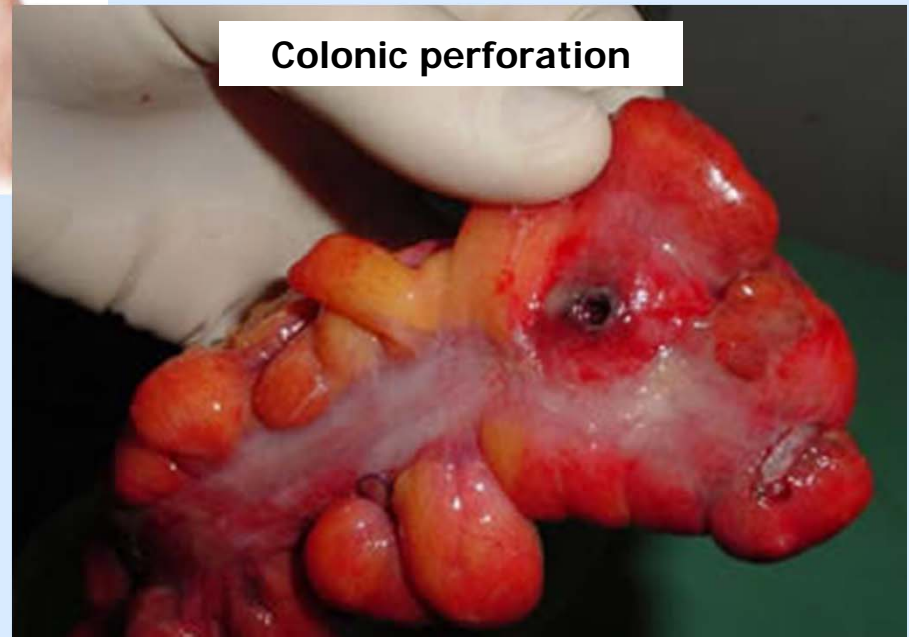
Toxic megacolon



Pseudomembranous colitis



Colonic perforation



Community-Acquired CDI

- **Becoming a greater problem**
- **Affected patients younger**
- **Do not have classic risk factors**

Diagnosis

Diagnostic Definition of CDI includes:

1. Diarrhea

- 3 watery stools in 36 hours,
- 3 unformed stools in 24 hours for 2 days or 8 unformed stools in 48 hours

2. Pseudo Membranous Colitis detected by endoscopy or Toxin A ,B detected in stool ,or + stool culture for Cdiff.

3. No other recognized etiology for the diarrhea

Example of Lab Guidelines

- **Test only diarrheal stool:** that which assumes the shape of the container.
- **Do not perform tests of cure.** (Cure is cessation of symptoms since the toxin tests can remain positive for long periods after treatment.)
- Test only specimens from patients who are **older than one year** due to the high carriage rate in infants.
- Test diarrhea that develops after three days of hospitalization for *C. difficile*. (Stool for culture and ova and parasites are not recommended because of the low yield. Other stool tests should be ordered as clinically indicated.)

Vanderbilt UMC Guidelines 2011

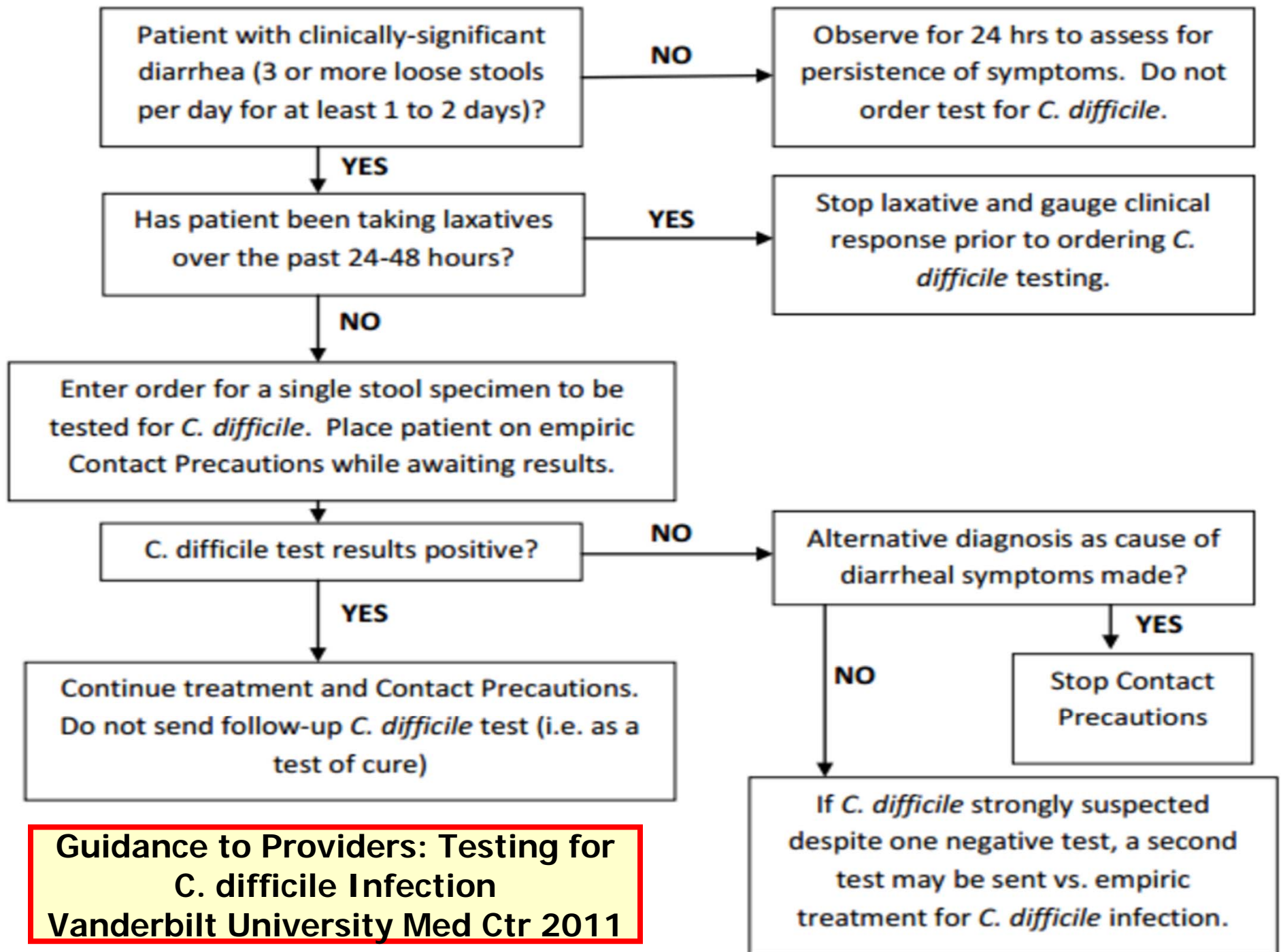
- Testing for *C. difficile* should be performed on patients **with clinically-significant diarrhea**, defined as
 - 3 or more loose stools per day for at least 1 to 2 days.
 - Ensure that patient has not received laxatives in the prior 24-48 hrs as a possible explanation of diarrheal symptoms.
- Testing is only performed on **loose or watery stool specimens**. VUMC microbiology lab will reject any formed stools sent for testing. On the rare occasion where an ileus due to *C. difficile* (which occurs in less than 1% of CDI cases) is suspected, the provider must specifically request testing on a formed stool specimen via verbal communication with lab personnel prior to specimen submission.
- **NO Repeat Testing to Diagnose CDI**: Multiple studies have demonstrated that repeat stool testing is
 - Ineffective for the diagnosis of CDI
 - With rare exception, **only one test** should be ordered to rule in or out CDI, given the test's very high negative predictive value. When repeat testing is performed for CDI within a 7-day period, the pre-test probability for the second assay is so low that the ratio of true-positive results to false-positive results becomes very unfavorable; this could result in misdiagnosis for some patients.

Vanderbilt UMC Guidelines 2011 cont.

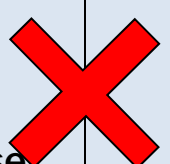
- **Do not order multiple tests for *C. difficile* on a single patient** (i.e. "*C. diff* x 3") but instead wait for the results of a single test to return before considering whether to test again.
- **DO NOT repeat stool testing for test of cure:** *C. difficile* toxin may persist despite a clinical response to treatment. In addition, a positive test at the end of a course of therapy **does not predict** who will develop a recurrence or relapse.
- Patients for whom a *C. difficile* test is ordered are placed on empiric **Contact Precautions**. If the test is negative and an alternative diagnosis for the diarrheal symptoms is documented by the patient's provider, Contact Precautions can be discontinued.
- **DO NOT require negative test for removal from isolation.** Patients placed on Contact Precautions for *C. difficile* infection stay on isolation until the following has occurred:
 - Resolution of symptoms for 48 hours AND
 - Discharge or transfer from room so that all surfaces in room may be cleaned thoroughly
 - Approval by IP
 - Patient must be bathed, placed in a clean gown, and placed in a clean bed if transferred to new room) AND

Vanderbilt UMC Guidelines 2011 cont.

- Once a patient tests positive for *C. difficile*, the laboratory
 - **will not perform repeat testing for *C. difficile* for the subsequent 7 days**
 - **only two (2) tests will be allowed per patient in a 7 day period**
- **NO NEED FOR NEGATIVE STOOL PRIOR TO TRANSFER:**
 - External Transfer of *C. difficile* Infected Patients: On occasion, accepting facilities (e.g. nursing homes, rehabilitation centers) will request 1 or more negative stool tests for *C. difficile* prior to allowing transfer. As infectivity is guided primarily by the presence of symptoms, and many individuals with carriage of *C. difficile* are not at risk for transmission to other persons, such testing is not recommended.
 - Case managers have been provided with a letter from VUMC leadership outlining our stance on this issue that will be distributed to facility leaders when follow-up *C. difficile* testing is requested.
 - In addition, members of the VUMC Department of Infection Control and Prevention team are available to discuss such requests with the referring facility. perform repeat testing for *C. difficile* for the subsequent 7 days.
- **NO MULTIPLE REPEAT TESTING FOR NEGATIVE PATIENTS:** Patients who have not tested positive for CDI, only two (2) tests will be allowed per patient in a 7 day period



Laboratory Diagnosis

Test	Sensitivity (%)	Specificity (%)	Advantages	Disadvantages
Cytotoxin assay	80-90	99-100	Standard highly sensitive and specific; considered as gold standard	Takes 24-48 hr to complete; requires tissue culture facility; cost; detects only toxin B
ELISA toxin test	65-85	95-100	Fast (2-6 hr), easy to perform, high specificity	Not as sensitive as cytotoxin assay
Stool culture	90-100	98-100	Allows strain typing in epidemics	Takes 2-5 days to complete; labor intensive; not specific for toxin-producing bacteria
Latex agglutination assay for glutamate dehydrogenase 	58-68	80-96	Fast, inexpensive, easy to perform	Poor sensitivity and specificity needed to establish diagnosis; requires confirmatory test
PCR assay toxin gene detection	92-97	100	Excellent sensitivity and specificity compared with cytotoxin assay	Research test only; no commercial assays available
Endoscopy	51	~ 100	Diagnostic of pseudomembranous colitis; can be used without need to collect stool sample	Cost; invasive test; risk of perforation

Laboratory Diagnosis

- Most lab use Toxin A/B enzyme immunoassays
 - Low sensitivities (70-80%) lead to low negative predictive value
- Poor test ordering practices:
 - Testing formed stool
 - Repeat testing negative patients
 - Restrict testing to unformed stool only
 - Focus testing on patients with ≥ 3 unformed stools within 24 hours
 - Require expert consultation for repeat testing within 5 days
 - Employ a highly sensitive screen with confirmatory test or a PCR-based molecular assay

Too many False
Positive

Risk Factors for CDI

- Patient on antibiotics
- GI/Surgery manipulation
- Long length of stay
- Serious underlying illness
- Immunocompromised
- Advanced age



Antibiotics as Risk Factors

- Clindamycin: first recognized as cause
 - Penicillins, ampicillin,
 - Cephalosporins (third-generation cephalosporins, particularly cefotaxime, ceftriaxone, ceftazidime),
 - Trimethoprim–sulfamethoxazole
- most frequently associated with Cdiff colitis**
- ALSO, almost every antimicrobial agent
 - Penicillin/-lactamase-inhibitor combinations such as ticarcillin/clavulanate and piperacillin/tazobactam significantly less risk.
 - In general broad-spectrum antibiotics are more likely than narrow spectrum antibiotics



Treatment

- **Metronidazole and vancomycin**
 - 7 to 10 days
 - NO drugs that decrease intestinal motility
 - Average time to resolution of diarrhea with tx 3 days, up to 6-7 days
- **First line: oral metronidazole 500mg every 6-8 hours for 10 days; if oral therapy is not tolerated, IV therapy is indicated until oral ingestion becomes possible. Contra-indications are allergy, pregnancy or verified resistance**
- **Second line: Oral vancomycin 125mg every 6 hours or nitazoxanide.**

Treatment

- **Discontinue antimicrobial therapy ASAP in patients w clinically significant diarrhea or colitis**
- **Antimicrobial tx for Cdiff indicated for:**
 - **severe toxic effects**
 - **diarrhea persists after antimicrobial tx discontinued.**
- **If treatment with antibiotics is still indicated**
 - **Use metronidazole, vancomycin, amino-glycosides**
 - **Nitazoxanide, bacitracin, teicoplanin, fusidic acid**

Recurrences

- Recurrences in 10-20% of cases
 - Early recurrences within 30 days, same strains
 - Later recurrences, new strains.
- Asymptomatic persistence and toxins in stools following treatment common (McFarland LV 2002. Am J Gastroenterol 97:1769)
- NOT recommended to repeat stool testing or re-treatment.
Only symptomatic patients should be treated

Non Response

- **If tests for *C. difficile* are negative and the patient has persistent symptoms:**
 - Repeat the EIA A/B test.
 - Use an alternative test, such as cytotoxin B tissue culture.
 - **Expand the diagnostic evaluation to include other causes.**
 - Treat empirically for *C.diff* disease.
 - If the patient fails to respond to metronidazole therapy and his or her tests remain negative, the patient probably does not have CDI.
 - Ileus without prior diarrhea. This may be secondary to antiperistaltic agents or opiates that were administered postoperatively. Making the diagnosis is difficult in these cases and may require endoscopy. An infectious disease or gastroenterology consult may aid diagnosis.

Control

Current Infection Prevention Recommendations

- **Surveillance for *C. Diff* isolates rates**
- **Contact precautions according to institutional policies; Heightened IP practices during outbreaks**
- **Discontinue alcohol based antiseptics not effective in eradicating *C. Diff* spores**
- **Isolation or cohorting during outbreaks**
- **Hypochlorite disinfectant**
- **Review of severe CDI cases**
- **Identification of specific strains**
- **Antibiotic stewardship programs**



Surveillance

Surveillance

- **Performance improvement in hospitals**
- **Outbreak detection**
- **Inter-hospital comparisons**
- **Public reporting**
- **Pay for performance**
- **Community-associated CDI**
- **NHSN MDRO and CDAD module**

Surveillance Definitions

- **Hospital-onset (HO):** Onset occurs > 2 calendar days after the day of admission
- **Community-Onset/HCF-Associated (CO-HCFA):** Onset occurs < 4 weeks after discharge
- **Indeterminate:** Onset occurs from 4-12 weeks after discharge
- **Community-Associated (CA):** Onset occurs > 12 weeks,

Incidence Definitions

- **Healthcare Facility-Onset Incidence Rate = Number of all Incident HO CDI LabID Events per patient per month / Number of patient days for the facility x 10,000**
- **Combined Incidence Rate = Number of all Incident HO and CO-HCFA CDI LabID Events per patient per month / Number of patient days for the facility x 10,000**

No testing of Asymptomatic Patients

- **Identification of carriers (Tx of carrier futile)**
- **Not indicated for test of cure: toxin may persist in stools after successful tx**
- **May be recovered from neonates and infants w no GI tract illness. This finding confounds the interpretation of positive toxin assays in patients younger than 12 to 24 months.**

Not Recommended

- Routine stool culture in asymptomatic patients or health care providers, even during outbreaks but...
- Isolation of suspects has been considered based on
 - 1. History of previous CDI
 - 2. Antibiotic use in previous 3 months
 - 3. Fecal incontinence
 - 1&2 sensitivity 77%; 1,2&3 sensitivity 83%
- Culturing hands of health care providers
- Treating empirically before completion of toxin results unless the patient is very sick with a compatible syndrome or there is hospital-wide high prevalence of Cdiff

Carriers

- Resistant to acquisition of outbreak-associated strains
- No more likely to develop CDI than those with negative stool cultures.
- Metronidazole not effective in eradicating carriage
- Oral vancomycin only transient elimination of fecal carriage



Do Not Treat Carriers (I)

- Johnson S, Homann SR, et al, Ann Intern Med. 1992 Aug 15;117(4):297-302.
- **Treatment of asymptomatic *Clostridium difficile* carriers (fecal excretors) with vancomycin or metronidazole. A randomized, placebo-controlled trial.**
- To compare the efficacy of vancomycin and metronidazole for eradication of asymptomatic *Clostridium difficile* fecal excretion as a means of controlling nosocomial outbreaks of *C. difficile* diarrhea.
- Randomized, placebo-controlled, non-blinded trial.
- VA 600 beds, 30 patients excreting *C. difficile* without diarrhea or abdominal symptoms.
- Randomized: oral vancomycin, 125 mg qid, 10 days
- or metronidazole, 500 mg bid; or placebo, tid.
- Stool cultures during tx and for 2 months after. All *C. difficile* isolates typed by restriction endonuclease analysis (REA).

Do Not Treat Carriers (II)

RESULTS:

- Immediately: *C.diff* not detected in
 - 90% patients vancomycin tx; [Vanc] in stools 1406 +/- 1164 ug/g feces
 - 30% patients metronidazole tx; [Metronidazole] ND in 90%
 - 20% placebo group
- Later:
 - After 20+/- days 88% of Vanc pts began to excrete *C.diff*

CONCLUSIONS:

- Asymptomatic fecal excretion of *C.diff* is transient in most patients,
- Tx with metronidazole is not effective.
- Tx with vancomycin is temporarily effective, it is associated with a significantly higher rate of *C. difficile* carriage 2 months after treatment and is not recommended.

Interrupt Transmission from Person-to-Person

- **Hand-washing preferred**
- **Alcohol-based hand sanitizers not as effective against the spore**
- **Contact precautions**
 - **Gloving whenever touching the patient or areas possibly contaminated,**
 - **Emphasize gloving**
 - **Gown whenever coming in contact with areas possibly contaminated**

Interrupt Transmission from Person-to-Person

- **Isolation and cohorting of CDAD patients until asymptomatic and able to maintain good bowel hygiene**
Maybe reasonable to extend isolation until discharge
- **Increased spacing of hospital beds**
- **Proper handling of contaminated waste (diapers) and fomites**
- **Private room**
- **Avoid rectal thermometers**
- **Thorough cleaning of hospital rooms and bathrooms**
 - **Environmental cleaning with solutions containing hypochlorite**
 - **Detergents not as effective**

Infection Control Measures: Contact Precautions

- Strict hand hygiene and isolation
- Private room or cohorting
- Gowns and gloves when entering room
- Alcohol not effective
- ONLY soap and water for handwashing
- Bleach for environmental disinfection
- Single-use patient care items

Consider
presumptive
isolation for patients
with ≥ 3 unformed
stools within 24
hours

Universal Glove Use in High Risk Unit

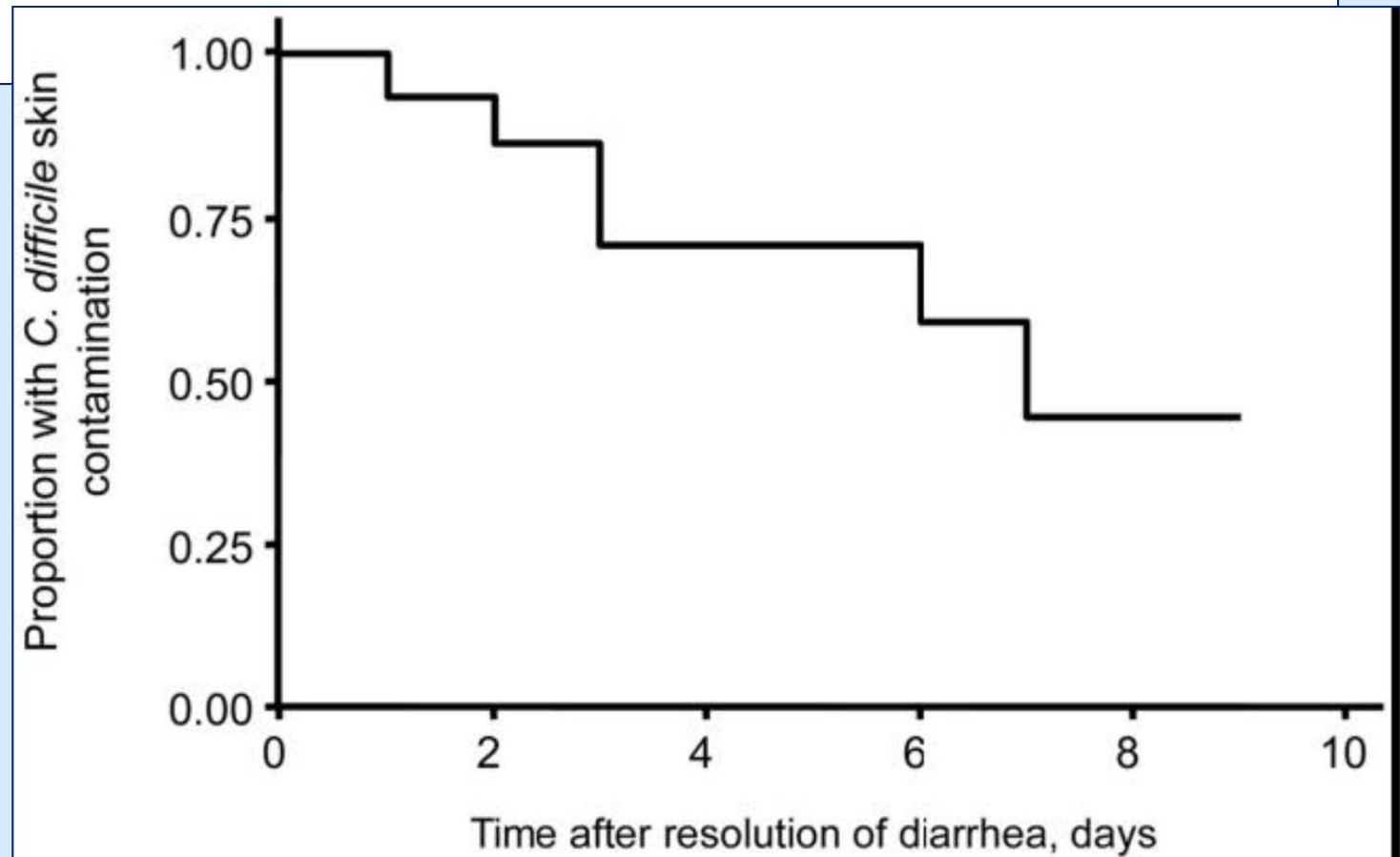
Rationale for considering universal glove use (in addition to Contact Precautions for patients with known CDI) on units with high CDI rates

- **Although the magnitude of their contribution is uncertain, asymptomatic carriers have a role in transmission**
- **Practical screening tests are not available**
- **There may be a role for universal glove use as a special approach to reducing transmission on units with longer lengths of stay and high endemic CDI rates**
- **Focus enhanced environmental cleaning strategies and avoid shared medical equipment on such units as well**



Extending Isolation

- Although not supported by direct evidence, the rationale for extending the duration of isolation beyond resolution of diarrhea is that skin contamination of patients with *C. diff* spores may persist after resolution of diarrhea for many days.



Alcohol Sanitizers

- Alcohol not effective in eradicating *C. difficile* spores
- However, one hospital study found that from 2000-2003, despite increasing use of alcohol hand rub, there was no concomitant increase in CDI rates
- Discouraging alcohol gel use may undermine overall hand hygiene program with untoward consequences for HAIs in general



Disinfection



Spore Removal

Product	Log10 Reduction
Tap Water	0.76
4% CHG antimicrobial hand wash	0.77
Non-antimicrobial hand wash	0.78
Non-antimicrobial body wash	0.86
0.3% triclosan antimicrobial hand wash	0.99
Heavy duty hand cleaner	1.21*

Data suggest that

- Spores may be very difficult to remove despite hand washing
- Lower log reductions of spore contamination with all hand washing products
- Most effective agent is heavy-duty hand cleaner (not practical for frequent use.
- Hence importance of GLOVE use when caring for CDI patients and reducing the environmental spore burden

Restrict Antibiotic Use

- Only Clindamycin restriction has shown effectiveness with other antibiotics; few reports show success of this approach
- Judicious Antibiotic Use: reduction of unnecessary antimicrobials in general will reduce the risk of disease

From: Sunenshine R.H, McDonald L.C. Cleveland Clinic
Journal of Medicine 73, 2 187-197



Environmental Cleaning

- Use EPA approved hospital disinfectant for environmental cleaning
- **BLEACH** can kill spores, whereas other standard disinfectants cannot
- Limited data suggest cleaning with bleach (1:10 dilution prepared fresh daily) reduces *C. difficile* transmission
- Two before-after intervention studies demonstrated benefit of bleach cleaning in units with high endemic CDI rates

Mayfield et al. Clin Infect Dis 2000;31:995-1000.
Wilcox et al. J Hosp Infect 2003;54:109-14.

- Follow manufacturer's instructions for endoscopic and other device disinfection

Making Sure Cleaning is Thorough

Assess adequacy of cleaning before changing to new cleaning product such as bleach

- **Ensure that environmental cleaning is adequate and high-touch surfaces are not being overlooked**
- **One study using a fluorescent environmental marker to assess cleaning showed:**
 - **only 47% of high-touch surfaces in 3 hospitals were cleaned**
 - **sustained improvement in cleaning of all objects, especially in previously poorly cleaned objects, following educational interventions with the environmental services staff**
- **The use of environmental markers is a promising method to improve cleaning in hospitals.**

Carling et al. Clin Infect Dis 2006;42:385-8.

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