



Clostridia Difficile: An Update

2009



Clostridia Difficile

- Gram positive bacillus
- Anaerobic, difficult to grow, thus its name
- Spore forming
- Toxin producing
- Inhabits the colon



Clostridia Difficile

- Spores resistant to drying and susceptible to Clorox
- Vegetative form susceptible to drying and PH <5
- Toxins: A=enterotoxin, B=cytotoxin, Binary (new)



Clostridia Difficile

- First detected in neonates
- Colonizes 3-5% of adults; 15-70% of neonates, but not considered a pathogen in infants less than 1 year of age.



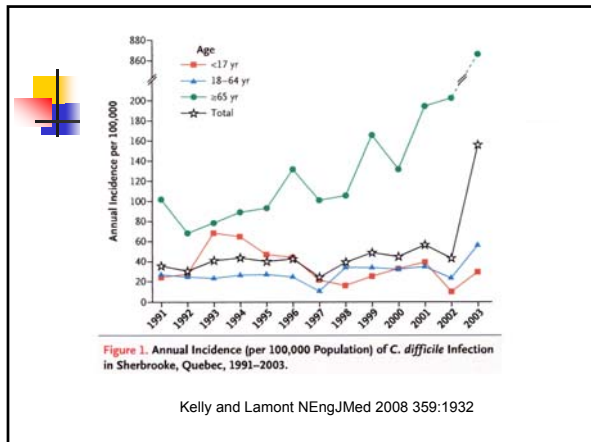
Laboratory Diagnosis of CD

- Culture: uncommon and requires 48-96 hours
- Toxin A and/or B detection by immunoenzyme assay: common and requires <24 hours
- Cytotoxic assay: gold standard, uncommon, requires 24-48 hours



Laboratory Testing for CD

- 1-2 samples sufficient to prove negative
- Do not retest positives
- Do not perform test of cure



Epidemiology in Hospitalized Children

- The incidence increased from 2001-2006, 2.6-4.0/1000 hospitalizations among children 1-11 years of age.
- 67% of children had chronic diseases.
- "Among children less than 1 year of age, the incidence increased from 2.8-5.1/1000 hospitalizations from 2000-2005".

Risk Factors for CD Associated Disease (AD)

- Antibiotic exposure
- Hospitalization
- Prolonged hospitalization
- Long term care facility
- Increasing age, especially >65 years
- Severe underlying disease
- GI surgery
- Proton pump inhibitors and H₂ blockers

Risk of CDAD by Antibiotic Class

- Fluoroquinolones 3.9
- Cephalosporins 3.8
- Clindamycin 1.6
- Macrolides 1.3

Spectrum of CDAD

- Mild
- Moderate
- Severe

Community Acquired *Clostridium difficile* (CACD) Infection in Children Undergoing Colonoscopy

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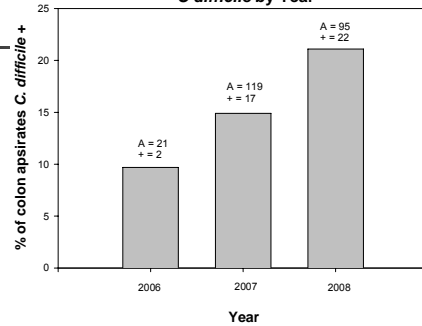
CACD

CD is associated with IBD
 CD is associated with gastric acid suppression

Noted CD positive stools in patients
 Assessed stool aspirates obtained at colonoscopy for CD



Percent of Colon Aspirates Positive for *C. difficile* by Year



Percent of colonic aspirates positive for *C. difficile* by year. A = the number of colonic aspirates, + = the number of colonic aspirates positive for *C. difficile*.



CACD

Dr. Faden reviewed procedures for colonoscopy
 Cultured 52 sites



CACD Areas Cultured

Colonoscopes X 10

Endoscopy Suite: counters and floors

Outpatient areas: counters, chairs, toilet seats, door knobs, computer key boards, table surfaces, examination tables, floors, sinks, faucet handles

Inpatient areas: beds, railings, stretchers, showers, bath areas, sinks, faucets

Total = 52



CACD

Chart review of all colonoscopies performed between September 1, 2006 and August 31, 2008

322 Total colonoscopies
 235 (73%) Colonic aspirates
 41 (17%) Positive for CD



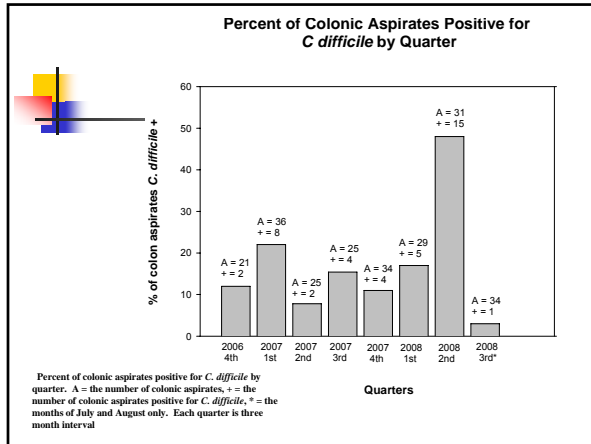
CACD

Other infections

1 pin worms (CD +)

2 *H pylori* (CD -)

1 *Y enterocolitica* (CD -)



Characteristics of patients Undergoing Colonoscopy

Parameter	CD positive	CD negative	P value
Age in years (X ± SD, range)	11.3 ± 5.3, 1-17	13.2 ± 4.0, 2-20	0.08
Male N (%)	17 (43.6%)	104 (53.1%)	0.17
Female N (%)	24 (61%)	90 (46%)	0.17
Final Diagnosis With respect to IBD			0.65
Crohn's Disease N (%)	7 (17.9%)	40 (20.6%)	
Ulcerative colitis N (%)	8 (20.5%)	24 (12.4%)	
Indeterminate colitis N (%)	1 (2.6%)	12 (6.2%)	
Other N (%)	0	4 (2.1)	
Normal N (%)	25 (64.1%)	114 (58.8%)	
Findings			
Endoscopic abnormalities N (%)	12 (30.8)	72 (37.1)	0.37
Histologic Abnormalities N (%)	13 (33.3)	72 (38.7)	0.48

Total number of colonoscopies for which aspirates were sent for CD toxin analysis = 235
 CD = *Clostridium difficile*, X = mean, SD = standard deviation, IBD = inflammatory bowel disease
 The CD positive and negative groups were compared using the Fisher exact test.

Symptoms

Symptom	CD positive N (%)	CD negative N (%)	P value
Abdominal pain	33 (84.6)	143 (73.7)	0.41
Diarrhea	25 (64.1)	121 (62.4)	0.86
Blood in stools	24 (61.5)	112 (57.7)	1
Constipation	10 (25.6)	33 (17.0)	0.06
Weight loss	8 (20.5)	60 (30.9)	0.08
Lethargy	7 (17.9)	36 (18.6)	1
Vomiting	7 (17.9)	30 (15.5)	0.82
Bloating	1 (2.6)	8 (4.1)	1

Some patients had more than one symptom
 CD = *Clostridium difficile*

CACD Symptoms

No single symptom associated with CACD

Multivariate analysis

Only abdominal pain and weight loss ($p < 0.01$) correlated with CD +

CACD

Positive correlation with the use of acid suppression ($p < 0.01$) and CD +

Too few charts to test antibiotic use and CD +, but 33% of CD + had no history of antibiotic use

CACD Outcome

41 CD +
 5 lost
 33 treated with metronidazole
 1 treated with vancomycin
 1 treated with rifaximin
 1 treated with probiotics

35 symptoms resolved
 1 symptoms continued, but follow up CD -

CACD

Summary

- Community acquired CD exists
- May be increasing in frequency
- Associated with gastric acid suppression
- Symptoms cannot be used to discriminate between CD + and CD -
- 33% had no history of antibiotic use within 3 months of procedure

CACD

What does it mean?

- Consider stool *C difficile* toxin titers for children with GI complaints in Buffalo area
- Be careful to use acid suppression only when necessary
- Consider screen for CD even if no history of antibiotic use or admission to a health care facility

Treatment of CD AD

- Mild: Stop antibiotics, Metronidazole PO or IV for 10-14 days
- Moderate: Stop antibiotics, Vancomycin PO for 10-14 days
- Severe: Stop antibiotics, Vancomycin PO for 10-14 days

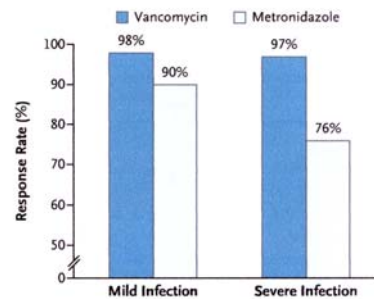


Figure 3. Response Rates to Vancomycin and Metronidazole Therapy, According to the Severity of *C. difficile* Infection.

Kelly and Lamont NEngJMed 2008 359:1932

Severe CDAD

- Fever
- Hypotension
- Sever abdominal pain and/or distention
- Ascites
- WBC >15,000
- Albumin <2.5
- Pseudomembranous colitis
- Toxic megacolon
- Perforation
- Shock

Management of Severe CDAD

- Obtain surgical consult
- Add metronidazole
- Consider rectal vancomycin
- Consider IVIG
- Consider colostomy

Recurrent CDAD

- After first episode = 20%
- After second episode/first recurrence = 45%
- After third episode/2nd recurrence = 65%

Treatment of Recurrent CDAD

1. First recurrence:
Mild: repeat metronidazole
Moderate/Severe: repeat vancomycin
2. Second recurrence: Tapering Vancomycin dosing= QID x 14 days → BID x 7days → QD x 7days → QOD x 8 days (4 doses) → Every 3 days x 19 days (5 doses)
3. Third recurrence: Vancomycin x 14 days followed by rifaximin x 14 days

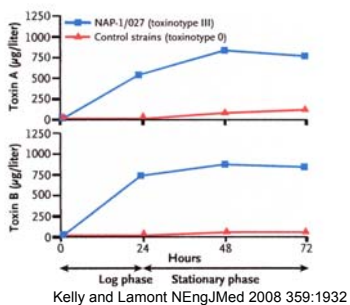
Non Proven Therapies for CDAD

- *Saccharmyces boulardii* x 28 days
- Lactobacillus GG (acidophilus)
- Rifampin

New Epidemic Strain of CDAD

- NAP 1 (North American Pulse Field Type 1)/or BI

This organism has a tcd C gene deletion which allows increase production of toxin. Also, a new toxin, the Binary toxin is produced.



References

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