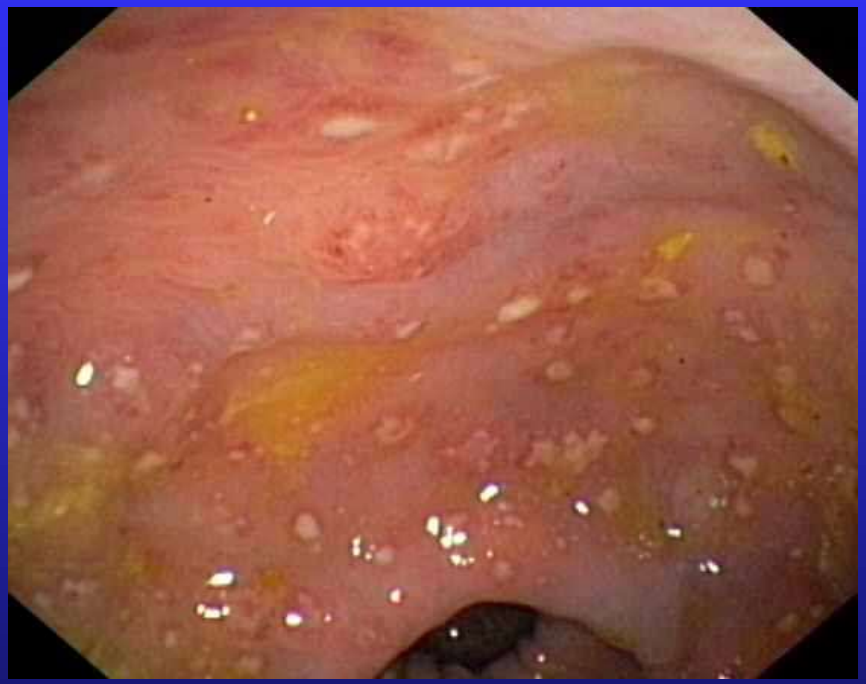
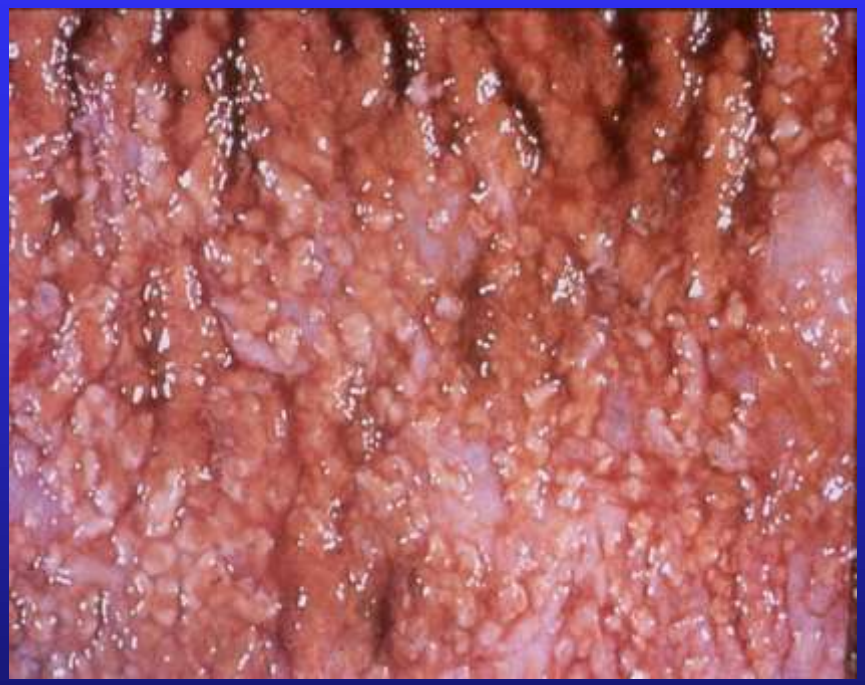
The Treatment of *Clostridium difficile* Infection





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Disclosures

I have received grants, and served as a consultant on Advisory Boards for:

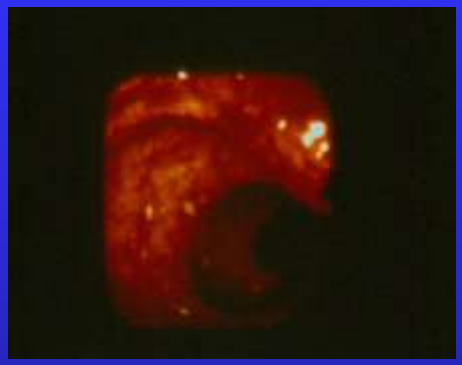
- BD GeneOhm Diagnostics
- Merck Frosst Canada Ltd
- Optimer Pharmaceuticals Canada

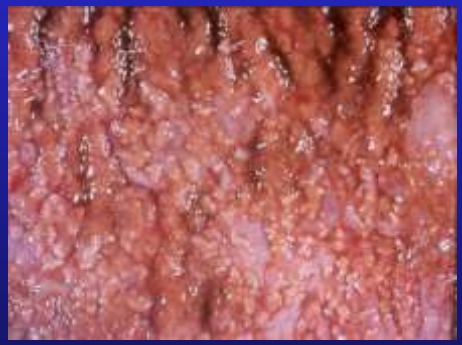
Objectives

- to review evidence-based clinical practice guidelines for the management *Clostridium difficile* infection
- to consider novel approaches for the treatment of patients with *C. difficile* infection

Clostridium difficile

- implicated in 20%-30% of antibiotic-associated diarrhea
- major cause of nosocomial infectious diarrhea
- disease caused by production of toxin A and toxin B





McFarland, NEJM 1989;
Bartlett, Clin Infect Dis 1992

C. difficile Toxins

Toxin A

- enterotoxin, causing intestinal mucosal injury and fluid secretion

Toxin B

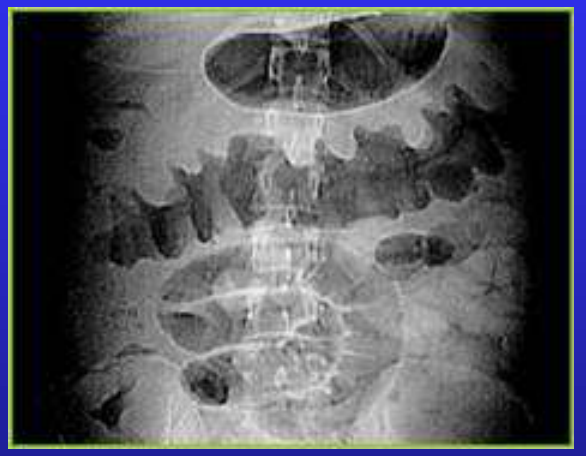
- cytotoxin, disrupts intestinal cell tight junctions

C. difficile Pathogenesis

Acquisition of toxigenic *C. difficile*
followed by disruption of normal bowel flora
(eg. with use of antibiotics)

C. difficile Complications

- acute abdomen, peritonitis, toxic megacolon, colon perforation
- recurrent infection



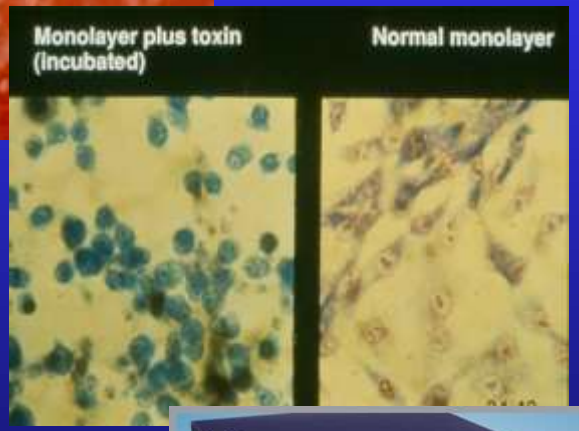
Recurrent *C. difficile*

- occurs in 20-30%; may be relapse or re-infection
- a recurrence is associated with a higher risk of repeated recurrences
- often associated with concurrent or repeat antibiotic therapy

Pépin, Clin Infect Dis 2006;
Kelly, N Engl J Med 2008

C. difficile Diagnosis

CDI should be suspected in any hospitalized patient with diarrhea who has received antibiotics in the previous 2 months (fever and leukocytosis are often present).



BMJ

BMJ 2012;345:e7396 doi: 10.1136/bmj.e7396 (Published 13 December 2012)

RESEARCH

CHRISTMAS 2012: RESEARCH

Using a dog's superior olfactory sensitivity to identify *Clostridium difficile* in stools and patients: proof of principle study

OPEN ACCESS

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Abstract

Objective To investigate whether a dog's superior olfactory sensitivity can be used to detect *Clostridium difficile* in stool samples and hospital patients.

Design Proof of principle study, using a case-control design.

Setting Two large Dutch teaching hospitals.

Participants A 2 year old beagle trained to identify the smell of *C difficile* and tested on 300 patients (30 with *C difficile* infection and 270 controls).

Intervention The dog was guided along the wards by its trainer, who was blinded to the participants' infection status. Each detection round concerned 10 patients (one case and nine controls). The dog was trained to sit or lie down when *C difficile* was detected.

Main outcome measures Sensitivity and specificity for detection of *C difficile* in stool samples and in patients.

Results The dog's sensitivity and specificity for identifying *C difficile* in stool samples were both 100% (95% confidence interval 91% to 100%). During the detection rounds, the dog correctly identified 25 of the 30 cases (sensitivity 83%, 65% to 94%) and 265 of the 270 controls (specificity 98%, 95% to 99%).

Conclusion A trained dog was able to detect *C difficile* with high estimated sensitivity and specificity, both in stool samples and in hospital patients infected with *C difficile*.

Introduction

Clostridium difficile infection is common, particularly in people in healthcare facilities who have received antimicrobials. *C difficile* causes toxin mediated intestinal disease, with symptoms ranging from mild diarrhoea to severe pseudomembranous colitis and toxic megacolon. The bacterium can be transmitted through

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Video on bmj.com (see also http://bmj.com/video)

Cliff has been trained to sniff out the bacteria clostridium difficile

The Latest in C. difficile Diagnostics

Bomers, BMJ 2012

C. difficile Diagnosis

Test	Sensitivity (%)	Specificity (%)
Culture	>90	80-90
Cytotoxin assay	75-85	>97
EIA toxin assay	70-85	95
GDH (common Ag)	85-95	96
PCR for toxin B	>90	>96

Peterson, Ann Intern Med 2009;
Eastwood, J Clin Microbiol 2009

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY MAY 2010, VOL. 31, NO. 5

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)

Stuart H. Cohen, MD; Dale N. Gerding, MD; Stuart Johnson, MD; Ciaran P. Kelly, MD; Vivian G. Loo, MD; L. Clifford McDonald, MD; Jacques Pepin, MD; Mark H. Wilcox, MD

Since publication of the Society for Healthcare Epidemiology of America position paper on *Clostridium difficile* infection in 1995, significant changes have occurred in the epidemiology and treatment of this infection. *C. difficile* remains the most important cause of healthcare-associated diarrhea and is increasingly important as a community pathogen. A more virulent strain of *C. difficile* has been identified and has been responsible for more-severe cases of disease worldwide. Data reporting the decreased effectiveness of metronidazole in the treatment of severe disease have been published. Despite the increasing quantity of data available, areas of controversy still exist. This guideline updates recommendations regarding epidemiology, diagnosis, treatment, and infection control and environmental management.

Infect Control Hosp Epidemiol 2010; 31(5):431-455

Cohen, Infect Control Hosp Epidemiol 2010

CDI Treatment Guidelines General Principles

- Discontinue inciting antibiotic(s) as soon as possible (A-II)
- If severe CDI is suspected, begin empiric treatment as soon as possible (C-III)
- Avoid anti-peristaltic agents (C-III)

SHEA/IDSA Guidelines, Infect Control Hosp Epidemiol 2010

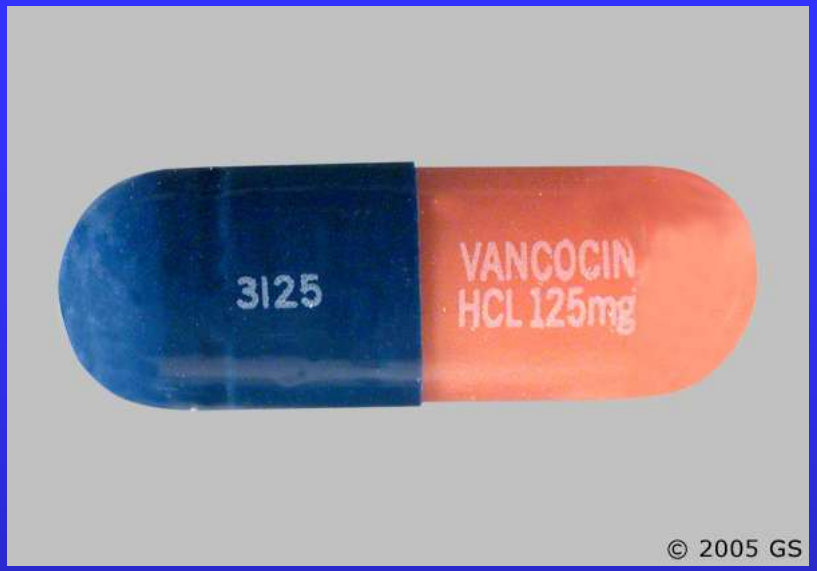
Concurrent Antibiotics and Response To Treatment for *C. difficile* Infection

Table 2. Effect of Concomitant Antibiotic (CA) Therapy During Treatment and/or Follow-up Periods

Endpoint study period	No CA	≥1 CA	Difference, % (95% CI)	*P*
Clinical cure (*n* = 999)				
Treatment (days 1–10)	92.57 (747/807)	84.38 (162/192)	8.19 (2.98–13.89)	<.001
Recurrence (*n* = 794)				
Treatment (days 1–10)	17.88 (118/660)	23.88 (32/134)	−6.00 (−14.04 to 1.46)	.11
Follow-up (days 11–40)	17.74 (118/665)	24.81 (32/129)	−7.06 (−15.3 to 0.60)	.06
At any time (days 1–40)	17.57 (107/609)	23.24 (43/185)	−5.67 (−12.63 to 0.92)	.08
Global cure (*n* = 999)				
At any time (days 1–40)	74.72 (541/724)	65.82 (181/275)	8.91 (2.54–15.37)	.005

NOTE. Data are % (proportion) of subjects unless otherwise specified.

Mullane, Clin Infect Dis 2011



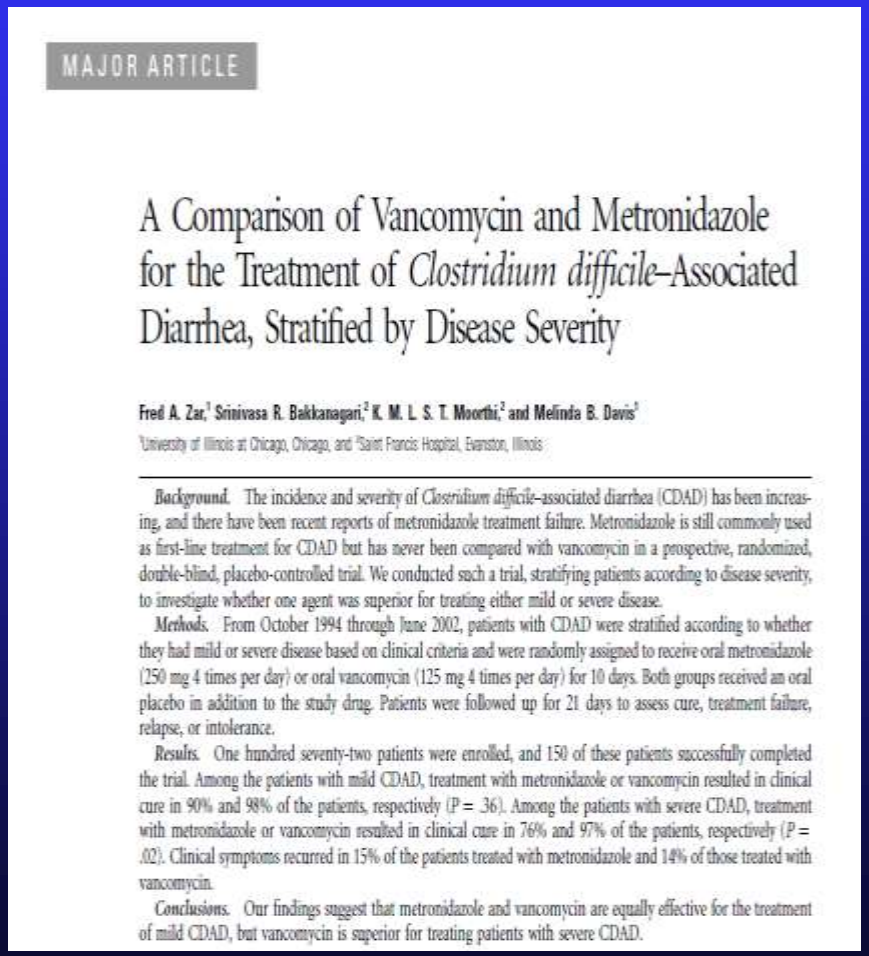
Vancomycin or Metronidazole?

Vancomycin vs Metronidazole (early studies)

Study	Antibiotic	No. patients	Initial cure (%)	Recurrence (%)
1	Vanco	52	100	11
	Metro	42	95	5
2	Vanco	31	94	16
	Metro	31	94	16

[1] Teasley, Lancet 1983; [2] Wenisch, Clin Infect Dis 1996

Efficacy of Vancomycin and Metronidazole for Treatment of *C. difficile* Infection



MAJOR ARTICLE

A Comparison of Vancomycin and Metronidazole for the Treatment of *Clostridium difficile*–Associated Diarrhea, Stratified by Disease Severity

Fred A. Zar,[1] Srinivasa R. Bakkanagari,[2] K. M. L. S. T. Moorthi,[2] and Melinda B. Davis[1]

[1]University of Illinois at Chicago, Chicago, and [2]Saint Francis Hospital, Evanston, Illinois

Background. The incidence and severity of *Clostridium difficile*–associated diarrhea (CDAD) has been increasing, and there have been recent reports of metronidazole treatment failure. Metronidazole is still commonly used as first-line treatment for CDAD but has never been compared with vancomycin in a prospective, randomized, double-blind, placebo-controlled trial. We conducted such a trial, stratifying patients according to disease severity, to investigate whether one agent was superior for treating either mild or severe disease.

Methods. From October 1994 through June 2002, patients with CDAD were stratified according to whether they had mild or severe disease based on clinical criteria and were randomly assigned to receive oral metronidazole (250 mg 4 times per day) or oral vancomycin (125 mg 4 times per day) for 10 days. Both groups received an oral placebo in addition to the study drug. Patients were followed up for 21 days to assess cure, treatment failure, relapse, or intolerance.

Results. One hundred seventy-two patients were enrolled, and 150 of these patients successfully completed the trial. Among the patients with mild CDAD, treatment with metronidazole or vancomycin resulted in clinical cure in 90% and 98% of the patients, respectively ($P = .36$). Among the patients with severe CDAD, treatment with metronidazole or vancomycin resulted in clinical cure in 76% and 97% of the patients, respectively ($P = .02$). Clinical symptoms recurred in 15% of the patients treated with metronidazole and 14% of those treated with vancomycin.

Conclusions. Our findings suggest that metronidazole and vancomycin are equally effective for the treatment of mild CDAD, but vancomycin is superior for treating patients with severe CDAD.

- Zar, Clin Infect Dis 2007
- Tolevamer studies (Louie, ICAAC, Washington, 2007; Bouza, ESCMID, Barcelona, Spain, 2008)

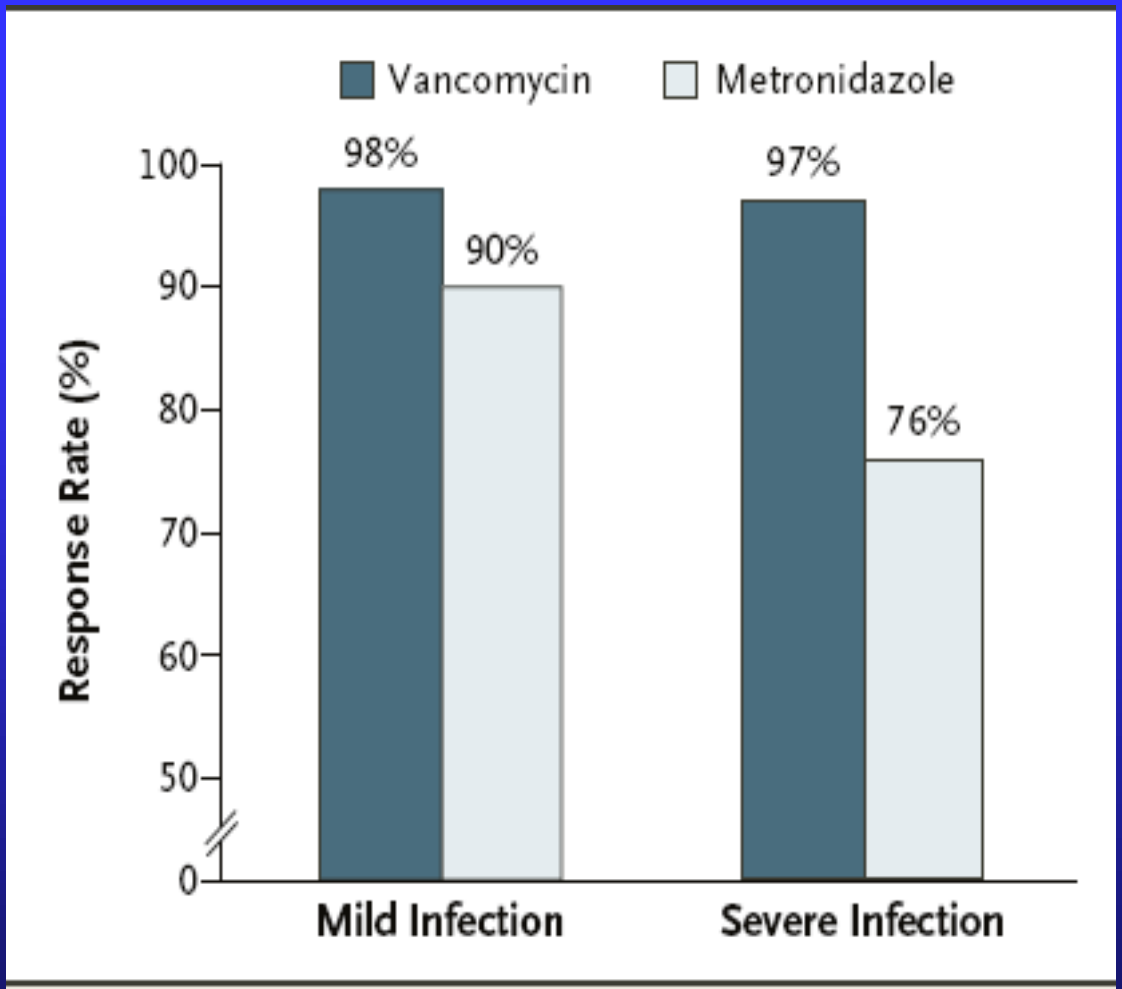


Figure 3. Response Rates to Vancomycin and Metronidazole Therapy, According to the Severity of *C. difficile* Infection.

C. difficile Treatment Response Rates

Zar, Clin Infect Dis 2007

Criteria for Severe *C. difficile* Infection

- Pseudomembranous colitis
- Treatment in an ICU
- Any two of:
  - Age > 60 yrs
  - Temp > 38.3°C
  - WBC > 15,000
  - Albumin < 2.5 mg/dL

Zar, Clin Infect Dis 2007

C.difficile Treatment

- **Treatment guidelines stratified:**
  - **first episode or recurrence**
  - **disease severity**

SHEA/IDSA Guidelines, Infect Control Hosp Epidemiol 2010

C. difficile Infection (CDI) Definitions

- **Mild-Moderate CDI**
- **Severe CDI**

  WBC ≥ 15,000/mm^3 or rising creatinine > 50% higher than before
- **Severe complicated CDI**

  criteria as above plus hypotension, ileus, perforation, toxic megacolon

Cohen, Infect Control Hosp Epidemiol 2010

CDI Treatment Guidelines
First Episode

CDI	Treatment
1st episode, mild-moderate	metronidazole 500 mg PO tid X 10-14 days
1st episode, severe	vancomycin 125 mg PO qid X 10-14 days

Cohen, Infect Control Hosp Epidemiol 2010

CDI Treatment Guidelines
First Episode

CDI	Treatment
1st episode, severe, complicated	vancomycin 500 mg PO qid + IV metronidazole ± vancomycin rectal instillation

Cohen, Infect Control Hosp Epidemiol 2010

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

Comparison of treatment outcomes with vancomycin alone versus combination therapy in severe *Clostridium difficile* infection

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Metronidazole
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SUMMARY

Background: The recommended treatment for severe *Clostridium difficile* infection (CDI) is oral vancomycin alone. Combination therapy with metronidazole is only recommended in cases complicated by shock, ileus, or toxic megacolon. However, patients with severe infection are often treated with combination therapy despite a lack of data supporting this practice.

Aim: To evaluate differences in outcomes for patients with severe CDI treated with oral vancomycin alone versus combination therapy.

Methods: Medical records of 78 patients with severe CDI receiving either oral vancomycin alone or combination therapy for ≥72 h were retrospectively reviewed. The primary outcome was time to clinical cure of CDI, defined as the first day of resolution of diarrhoea for ≥48 h without development of a complication. Other endpoints included cure rates, complication rates, and recurrence rates.

Findings: There was no difference in the incidence of clinical cure between monotherapy and combination therapy (57.1% vs 65.1%, $P = 0.49$). Median time to clinical cure was 7.0 days for the monotherapy group and 8.0 days for combination therapy ($P = 0.19$). After adjustment for potential confounders, the hazard ratio of the time to clinical cure for combination therapy compared with monotherapy was 0.58 ($P = 0.10$). There was no difference in recurrence rate or rates of individual complications between groups; however, there was a significantly higher composite complication rate in the combination therapy group.

Conclusion: These data suggest that there is no difference in treatment outcomes between monotherapy and combination therapy for severe CDI.

In severe CDI, addition of metronidazole to vancomycin had no benefit.

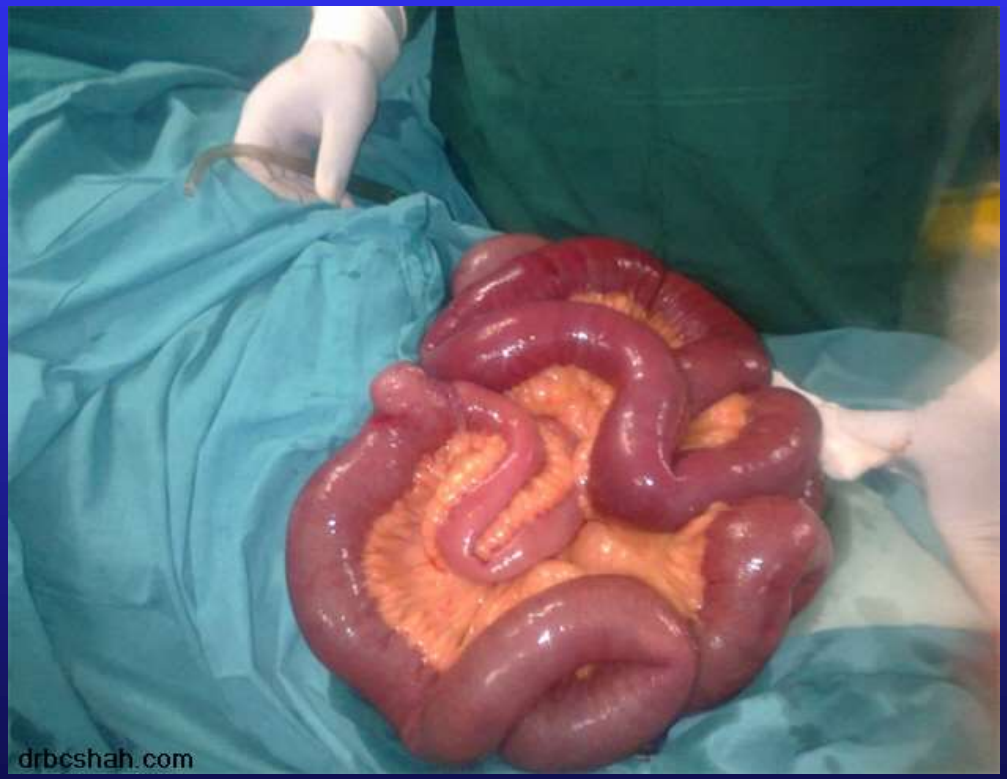
Bass, J Hosp Infect 2013

Severe, Complicated CDI

- Surgery (colectomy) may be life-saving
- Consider colectomy if toxic megacolon, colonic perforation, septic shock
- Serum lactate >5 mmol/L, postoperative mortality > 75%

Lamontagne, Ann Surg 2007

Surgical Management of Severe CDI



Diverting loop ileostomy with colonic lavage may be an alternative to colectomy

Neal, Ann Surg 2011

CDI Treatment Guidelines
Recurrent Disease

CDI	Treatment
1st recurrence	same as for initial episode
2nd recurrence	vancomycin, pulsed/tapered

Cohen, Infect Control Hosp Epidemiol 2010

Treatment of Recurrent CDI

- **“Tapered” vancomycin: 500 mg qid X 14 days and then slowly tapered over 6-12 wks**
- **“Pulsed” vancomycin: 500 mg qid X 14 days and then 500 mg very 2- 3 days X 6-12 wks (± subsequent taper)**

McFarland, Am J Gastroenterol 2002

Other Antimicrobial Agents for the Treatment of CDI

- **teicoplanin, fusidic acid, bacitracin have all had equal efficacy to Vanco/Metronidazole in small RCTs (equal response to treatment and recurrence rates)**

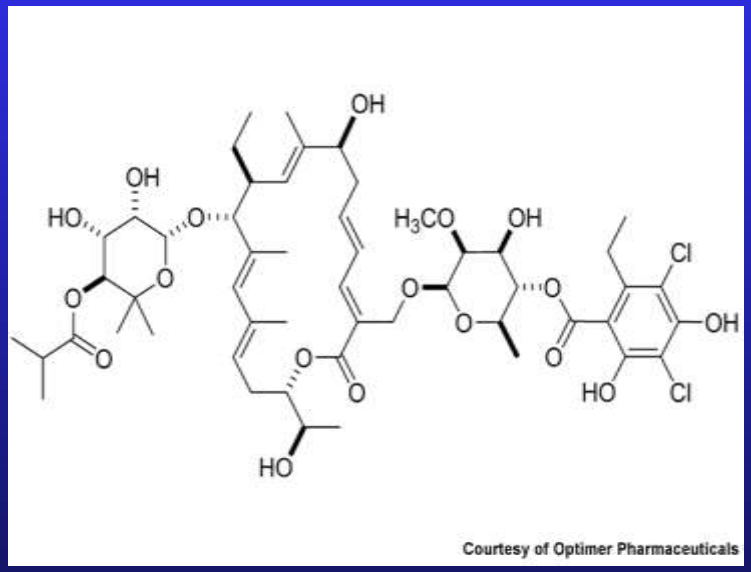
McFarland, J Med Microbiol 2005

for the treatment of *C. difficile* infection?

New Treatment Strategies for *C. difficile*

- new drugs
- immune modulation
- non-toxigenic *C. difficile*
- restoration of fecal microbiota

Fidaxomicin (Dificid™)



- macrocyclic antibiotic
- inhibits RNA synthesis
- inhibits *C. difficile* sporulation and toxin production
- minimal absorption; fecal concentrations >MIC_{90} (0.125 µg/ml)
- usual dose: 200 mg. BID

Fidaxomicin versus vancomycin for infection with *Clostridium difficile* in Europe, Canada, and the USA: a double-blind, non-inferiority, randomised controlled trial

Oliver A Cornely, Derrick W Crook, Roberto Esposito, André Poirier, Michael S Somero, Karl Weiss, Pamela Sears, Sherwood Gorbach, for the OPT-80-004 Clinical Study Group

Summary

Background Infection with *Clostridium difficile* is the primary infective cause of antibiotic-associated diarrhoea. We aimed to compare efficacy and safety of fidaxomicin and vancomycin to treat patients with *C difficile* infection in Europe, Canada, and the USA.

Methods In this multicentre, double-blind, randomised, non-inferiority trial, we enrolled patients from 45 sites in Europe and 41 sites in the USA and Canada between April 19, 2007, and Dec 11, 2009. Eligible patients were aged 16 years or older with acute, toxin-positive *C difficile* infection. Patients were randomly allocated (1:1) to receive oral fidaxomicin (200 mg every 12 h) or oral vancomycin (125 mg every 6 h) for 10 days. The primary endpoint was clinical cure, defined as resolution of diarrhoea and no further need for treatment. An interactive voice-response system and computer-generated randomisation schedule gave a randomisation number and medication kit number for each patient. Participants and investigators were masked to treatment allocation. Non-inferiority was prespecified with a margin of 10%. Modified intention-to-treat and per-protocol populations were analysed. This study is registered with ClinicalTrials.gov, number NCT00468728.

Findings Of 535 patients enrolled, 270 were assigned fidaxomicin and 265 vancomycin. After 26 patients were excluded, 509 were included in the modified intention-to-treat (mITT) population. 198 (91·7%) of 216 patients in the per-protocol population given fidaxomicin achieved clinical cure, compared with 213 (90·6%) of 235 given vancomycin, meeting the criterion for non-inferiority (one-sided 97·5% CI −4·3%). Non-inferiority was also shown for clinical cure in the mITT population, with 221 (87·7%) of 252 patients given fidaxomicin and 223 (86·8%) of 257 given vancomycin cured (one-sided 97·5% CI −4·9%). In most subgroup analyses of the primary endpoint in the mITT population, outcomes in the two treatment groups did not differ significantly; although patients receiving concomitant antibiotics for other infections had a higher cure rate with fidaxomicin (46 [90·2%] of 51) than with vancomycin (33 [73·3%] of 45; p=0·031). Occurrence of treatment-emergent adverse events did not differ between groups. 20 (7·6%) of 264 patients given at least one dose of fidaxomicin and 17 (6·5%) of 260 given vancomycin died.

Interpretation Fidaxomicin could be an alternative treatment for infection with *C difficile*, with similar efficacy and safety to vancomycin.

Lancet Infect Dis 2012; 12: 281–89

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See Comment page 256

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Fidaxomicin versus Vancomycin for *Clostridium difficile* Infection

Thomas J. Louie, M.D., Mark A. Miller, M.D., Kathleen M. Mullane, D.O., Karl Weiss, M.D., Arnold Lentnek, M.D., Yoav Golan, M.D., Sherwood Gorbach, M.D., Pamela Sears, Ph.D., and Youe-Kong Shue, Ph.D., for the OPT-80-003 Clinical Study Group*

ABSTRACT

BACKGROUND

Clostridium difficile infection is a serious diarrheal illness associated with substantial morbidity and mortality. Patients generally have a response to oral vancomycin or metronidazole; however, the rate of recurrence is high. This phase 3 clinical trial compared the efficacy and safety of fidaxomicin with those of vancomycin in treating *C. difficile* infection.

METHODS

Adults with acute symptoms of *C. difficile* infection and a positive result on a stool toxin test were eligible for study entry. We randomly assigned patients to receive fidaxomicin (200 mg twice daily) or vancomycin (125 mg four times daily) orally for 10 days. The primary end point was clinical cure (resolution of symptoms and no need for further therapy for *C. difficile* infection as of the second day after the end of the course of therapy). The secondary end points were recurrence of *C. difficile* infection (diarrhea and a positive result on a stool toxin test within 4 weeks after treatment) and global cure (i.e., cure with no recurrence).

RESULTS

A total of 629 patients were enrolled, of whom 548 (87.1%) could be evaluated for the per-protocol analysis. The rates of clinical cure with fidaxomicin were noninferior to those with vancomycin in both the modified intention-to-treat analysis (88.2% with fidaxomicin and 85.8% with vancomycin) and the per-protocol analysis (92.1%

From the University of Calgary, Calgary, AB, Canada (T.J.L.); McGill University (M.A.M.) and the University of Montreal (K.W.) — both in Montreal; the University of Chicago, Chicago (K.M.M.); Wellstar Infectious Disease, Marietta, GA (A.L.); Tufts Medical Center, Boston (Y.G., S.G.); and Optimer Pharmaceuticals, San Diego, CA (S.G., P.S., Y.-K.S.). Address reprint requests to Dr. Louie at the Division of Infectious Diseases, Departments of Medicine and Microbiology and Infectious Diseases, University of Calgary, Foothills Hospital, 1403 29 St. NW, Calgary, AB T2N 4J8, Canada, or at thomas.louie@albertahealthservices.ca.

*Additional investigators in the OPT-80-003 Clinical Study Group are listed in the Supplementary Appendix, available at NEJM.org.

N Engl J Med 2011;364:422-31.

Cornely, Lancet Infect Dis 2012

Louie, New Engl J Med 2011

Fidaxomicin vs Vancomycin for *C. difficile* Infection

- 2 large international double-blind RCTs
- fidaxomicin and vancomycin had similar cure rates (88% vs 86%)
- lower recurrence rates with fidaxomicin (15% vs 25%, esp. non-NAP-1 strains; *P*=0.005)

Louie, N Engl J Med 2011;
Cornely, Lancet Infect Dis 2012

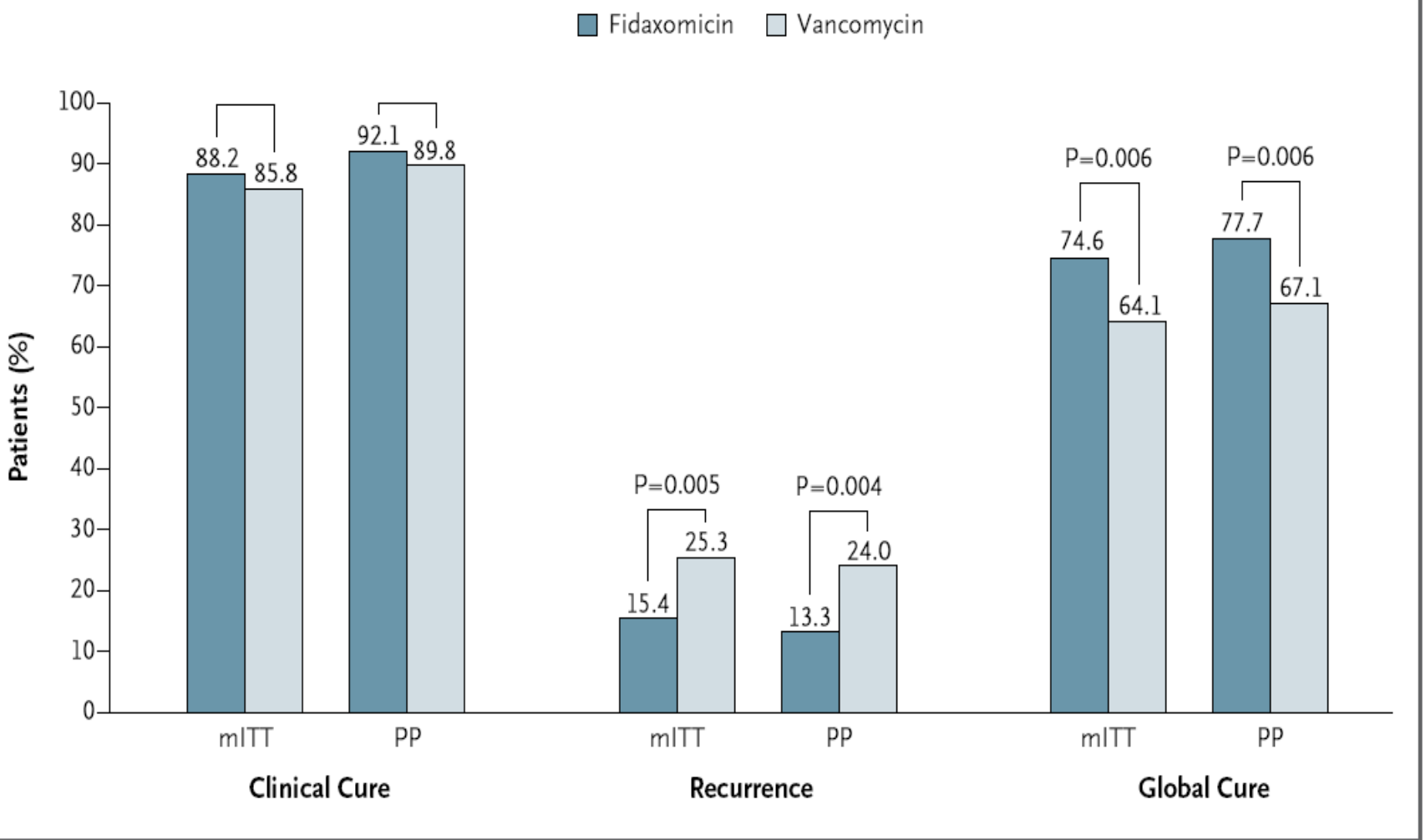


Figure 2. Rates of Primary and Secondary End Points.

Louie, N Engl J Med 2011

Fidaxomicin vs Vancomycin: Sustained Clinical Response

Drug	Response rates (%)	
	End of treatment	25 days after end of treatment
Vancomycin	86	57
Fidaxomicin	88	71*

*p<0.001

Louie, N Engl J Med 2011; Cornely, Lancet Infect Dis 2012; Johnson, Antimicrob Agents Chemother 2012

Response to Therapy and Recurrence Rates in Patients with Epidemic (BI) *C. difficile*

Outcome	Vancomycin (n=363)	Fidaxomicin (n=356)
REA Group		
BI (NAP1)	127 (35)	120 (34)
Other	236 (65)	236 (66)
Cure rate		
BI (NAP1)	109 (86)	105 (88)
Other	220 (93)*	225 (95)*
Recurrence rate (%)		
Overall	99 (25)	51 (13)*
BI (NAP1)	30 (31)	21 (23)
Other	69 (25)	30 (13)*

Petrella, Clin Infect Dis 2012

* $P < 0.001$

Fidaxomicin vs Vancomycin for *C. difficile* Infection

- **subset analysis suggests fidaxomicin more effective than vancomycin in patients taking concurrent antibiotics** (Mullane, Clin Infect Dis 2011)
- **subset analysis suggests in patients with a 1st recurrence, fidaxomicin had similar clinical response as vancomcyin, but was superior in preventing another recurrence within 28 days** (Cornely, Clin Infect Dis 2012)

Why Might Fidaxomicin Reduce Rates of Recurrent CDI?

- fidaxomicin preserves normal intestinal bacterial flora[1]
- fidaxomicin inhibits *C. difficile* sporulation[2]

[1]Louie, Clin Infect Dis 2012; [2]Babakhani, Clin Infect Dis 2012

Other "New" Drugs for the Treatment of CDI

- **Rifamixin:** in a series of 8 patients with recurrent CDI, Vanco followed by rifamixin effective (Johnson, Clin Infect Dis 2007)
- **Nitazoxanide:** in a small RCT, equivalent to metronidazole (Musher, Clin Infect Dis 2006)
- **Tigecycline:** effective in a small series of patients with severe refractory CDI (Herpers, Clin Infect Dis 2009)

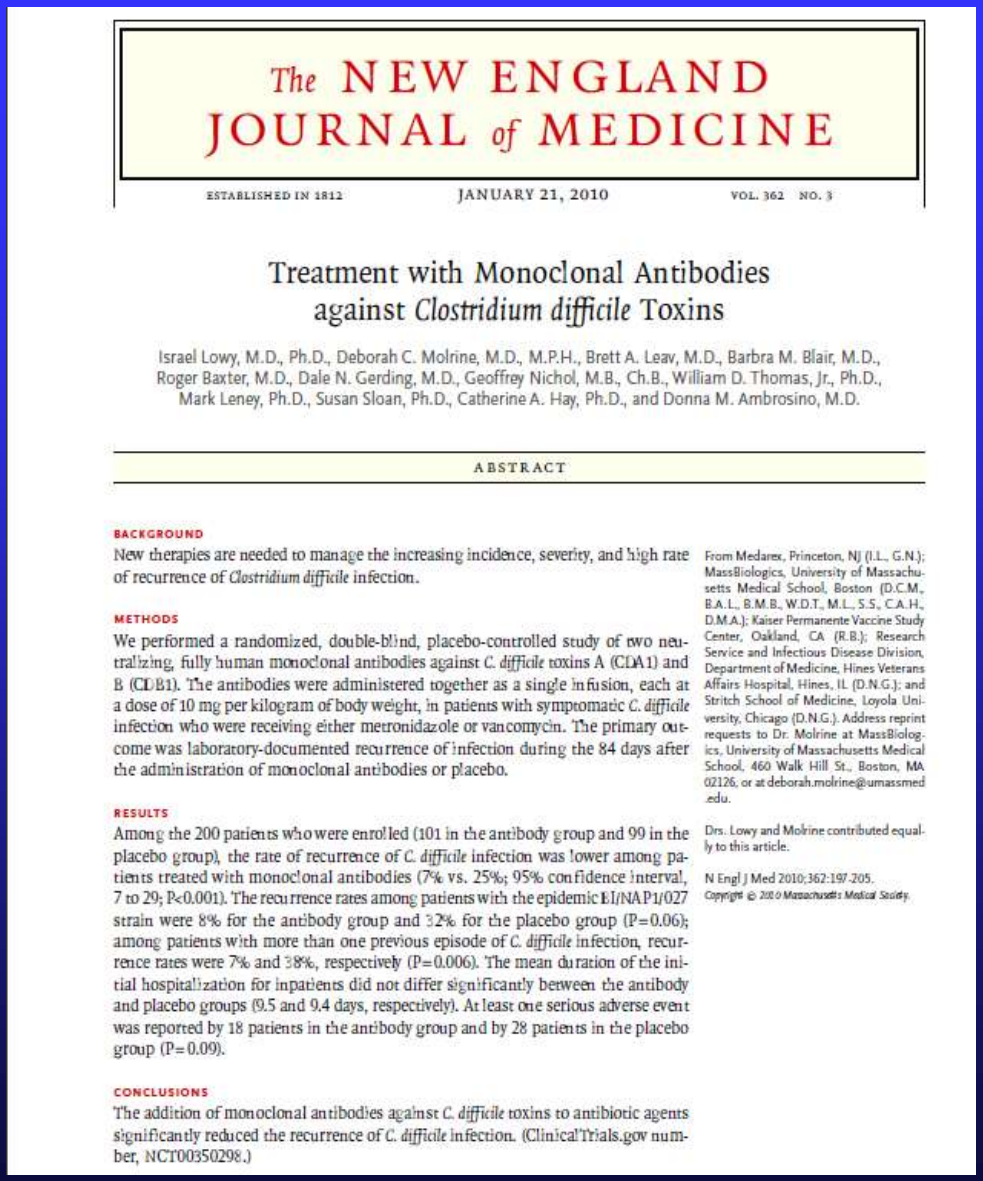
Immune Modulation as Treatment for *C. difficile* Infection

- IVIG
- Anti-toxin monoclonal antibodies
- Vaccine (toxoid)

IVIG for Treatment of *C. difficile* Infection

- anecdotal reports, case series in patients with severe or recurrent CDI
- some studies show benefit, but others do not

Wilcox, J Antimicrob Chemother 2004; McPherson, Dis Colon Rectum 2006; Juang, Am J Infect Control 2007



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Treatment with Monoclonal Antibodies against *Clostridium difficile* Toxins

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ABSTRACT

BACKGROUND

New therapies are needed to manage the increasing incidence, severity, and high rate of recurrence of *Clostridium difficile* infection.

METHODS

We performed a randomized, double-blind, placebo-controlled study of two neutralizing, fully human monoclonal antibodies against *C. difficile* toxins A (CDA1) and B (CDB1). The antibodies were administered together as a single infusion, each at a dose of 10 mg per kilogram of body weight, in patients with symptomatic *C. difficile* infection who were receiving either metronidazole or vancomycin. The primary outcome was laboratory-documented recurrence of infection during the 84 days after the administration of monoclonal antibodies or placebo.

RESULTS

Among the 200 patients who were enrolled (101 in the antibody group and 99 in the placebo group), the rate of recurrence of *C. difficile* infection was lower among patients treated with monoclonal antibodies (7% vs. 25%; 95% confidence interval, 7 to 29; P<0.001). The recurrence rates among patients with the epidemic BI/NAP1/027 strain were 8% for the antibody group and 32% for the placebo group (P=0.06); among patients with more than one previous episode of *C. difficile* infection, recurrence rates were 7% and 38%, respectively (P=0.006). The mean duration of the initial hospitalization for inpatients did not differ significantly between the antibody and placebo groups (9.5 and 9.4 days, respectively). At least one serious adverse event was reported by 18 patients in the antibody group and by 28 patients in the placebo group (P=0.09).

CONCLUSIONS

The addition of monoclonal antibodies against *C. difficile* toxins to antibiotic agents significantly reduced the recurrence of *C. difficile* infection. (ClinicalTrials.gov number, NCT00350298.)

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Drs. Lowy and Molrine contributed equally to this article.

N Engl J Med 2010;362:197-205.

Addition of human monoclonal antibodies against toxin A & toxin B to standard therapy reduced risk of recurrence (7% vs 25%; *P*<0.001) in phase II clinical trial

Lowy, N Engl J Med 2010

Other Approaches for *C. difficile* Treatment

- **CamSA**
  (bile salt analog, inhibits *C. difficile* sporulation)
- **Non-toxigenic *C. difficile***
- **Fecal transplant**
  (“the only time you should take crap from a spouse”)


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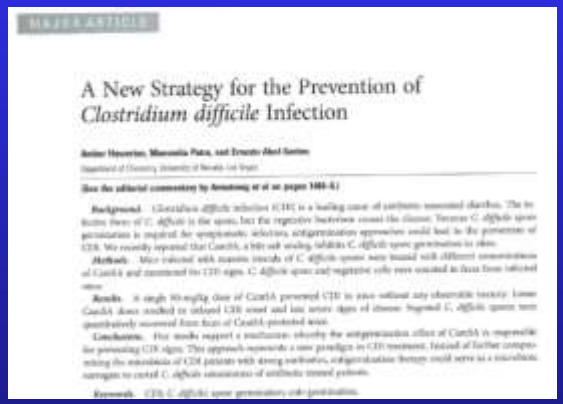
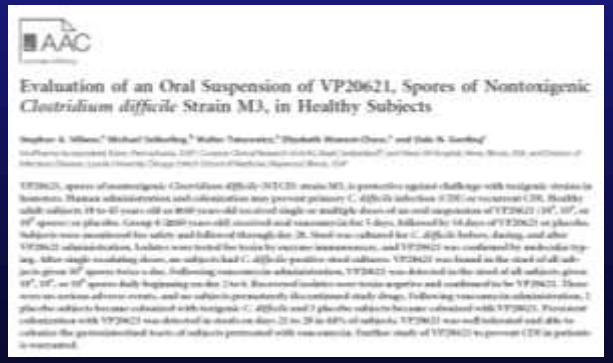
Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*


A New Strategy for the Prevention of *Clostridium difficile* Infection


AAC

Evaluation of an Oral Suspension of VP20621, Spores of Nontoxigenic *Clostridium difficile* Strain M3, in Healthy Subjects

Summary

- Treatment of CDI with metronidazole or vancomycin should be based on disease severity.
- Fidaxomicin has equivalent response rate to vancomycin, but is associated with fewer recurrent infections.
- Other treatment strategies are being investigated.

The End