1252. CD4+ T Cells Specific for C. difficile Toxins are a Marker of Patients with Active Relapsing Disease

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Background. The bacterial pathogen *Clostridium difficile* is the leading cause of nosocomial infectious diarrhea. Although *C. difficile* infection (CDI) can be treated with antibiotics, approximately 25% of patients relapse after treatment. The pathogenicity of CDI requires the activities of its toxins, TcdA and TcdB, but T cell-mediated responses to these toxins remain uncharacterized.

Methods. We enrolled two cohorts of patients, one with newly acquired CDI (n = 14) and the other with relapsing CDI (n = 25); and healthy volunteers with no history of CDI (n = 12). We measured peripheral blood $CD4^+$ T cell responses to the toxins using a whole blood flow cytometry assay that identifies antigen-specific $CD4^+$ T cells by co-expression of CD25 and OX40 following 44h incubation with antigen (**Fig 1**).

Results. We found that in patients with recurring CDI, T cell responses to TcdB were significantly higher than in healthy controls (median 1.04% vs. 0.18%; P = 0.003, **Fig 2**). In contrast, TcdA T cell responses and anti-TcdA/TcdB IgG titres were not different between recurring patients and controls. TcdB, but not TcdA, T cell responses were significantly higher in recurring CDI compared with newly acquired CDI (median 1.04% vs. 0.44%; P = 0.032). In both patient cohorts TcdB-specific CD4+ T cells were functionally heterogeneous, on average: 25% expressed the gut homing marker integrin β7; there was a 1:1 ratio of Tregs to T effectors; and T effectors contained Th1, Th2 and Th17 cells at a 1.5:1:3 ratio. The proportion of Th1 and Th17 cells within TcdB-specific CD4+ T cells was also significantly reduced in recurring, compared with newly acquired, CDI (**Fig 3**). Analysis of sorted TcdB-specific CD25+OX40+ cells confirmed specificity for TcdB and polarization towards Th17 cells, which are important for intestinal anti-pathogen immunity.

Conclusion. This is the first investigation of T cell immunity to *C. difficile* toxins. Our data show that anti-TcdB $CD4^+$ T cell responses are a more specific marker of disease than IgG titres. Tracking how toxin-specific $CD4^+$ T cell responses change following treatment and/or vaccination not only has the potential to predict relapse, but also to deliver insight into how $CD4^+$ T cell memory develops in response to this prevalent pathogen.

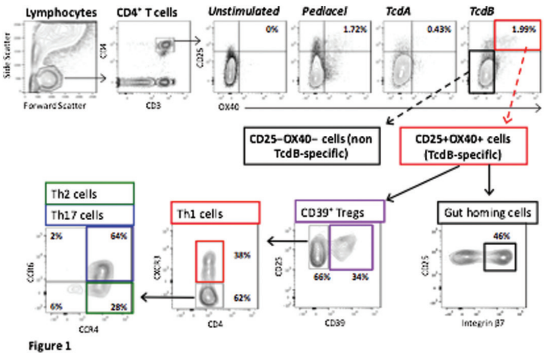
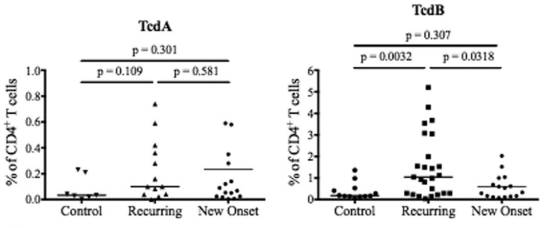


Figure 1



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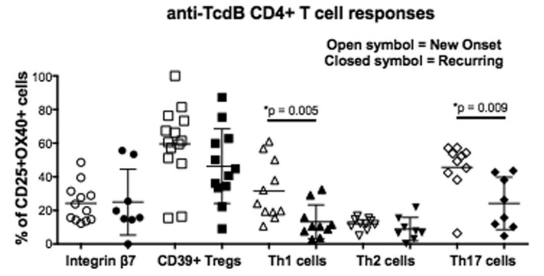

Figure 3

Disclosures. **All authors:** No reported disclosures.

1253. Discordance of SHEA/IDSA *Clostridium difficile* Disease Severity Scale in Solid Organ Transplant Patients

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Background. Solid organ transplant (SOT) patients are at high risk for *Clostridium difficile* infections (CDI) due to chronic immunosuppression and a propensity to receive antimicrobials. Management of CDI in SOT patients poses unique challenges as this population has disease-altered clinical and laboratory parameters. The objective of this study was to assess concordance between various CDI severity scales and the Society for Healthcare Epidemiology of America/Infectious Diseases Society of America (SHEA/IDSA) guidelines.

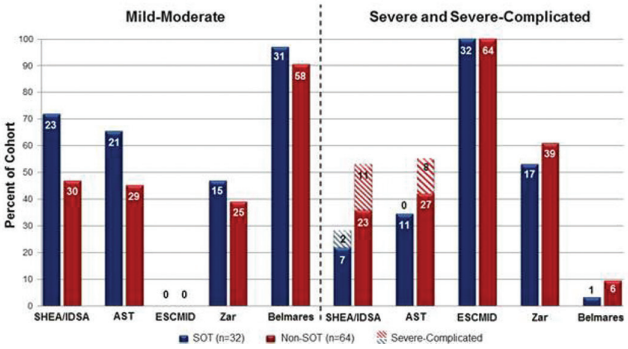
Methods. This retrospective study included all SOT recipients with a first CDI episode following transplant and time-matched (2:1) to non-SOT patients experiencing first CDI episodes between 2008 and 2016. The primary endpoint was concordance rates of CDI episodes considered mild-moderate or severe/severe-complicated in published CDI scales compared with the SHEA/IDSA guidelines. We also sought to compare the distribution of CDI severity across all scales between SOT and non-SOT patients.

Results. Overall, 32 SOT patients and 64 non-SOT patients were included. The SOT group had significantly higher leukopenia rates at CDI diagnosis; however, the magnitude of serum creatinine change did not differ between groups. According to the SHEA/IDSA scale, CDI episodes in SOT recipients were categorized as mild-moderate and severe/severe-complicated in 23 (72%) and 9 (28%) patients, respectively. Overall concordance rates among SHEA/IDSA guidelines and other scales ranged from 28% to 72%. Concordance rates were highest for mild-moderate CDI with Belmares and for severe/severe-complicated CDI with ESCMID (Table 1). No scale evenly categorized SOT and non-SOT patients across all severities (Figure 1).

Conclusion. Severity scales with heavy emphasis on white blood cell counts may not adequately categorize SOT patients. Immunocompromised status may need to be considered on its own when categorizing CDI severity and prescribing therapy.

Table 1

	Number (%) of Severity Classification-Concordant CDI Episodes, in Comparison to SHEA/IDSA Guidelines		
	Overall n = 32	Mild/Moderate n = 23	Severe or Severe-Complicated n = 9
AST	23 (71.9)	18 (78.3)	5 (55.6)
ESCMID	9 (28.1)	0	9 (100)
Zar	20 (62.5)	13 (56.5)	7 (77.8)
Belmares	22 (68.8)	22 (95.7)	0



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1254. Prospective, Open-label Trial to Evaluate Efficacy of Lyophilized Fecal Microbiota Transplantation for Treatment of Recurrent *C. difficile* Infection

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Background. Fecal microbiota transplantation (FMT) has shown to be effective for recurrent *Clostridium difficile* infection (rCDI). However, significant laboratory costs for donor screening and a lack of suitable donors and laboratory facility have restricted the availability of the treatment. In order to expand access to FMT, we have investigated the efficacy of lyophilized FMT, comparing it to the published historical efficacy of frozen FMT in preventing further episodes of CDI in patients with a history of rCDI. This study was designed to be open-labeled to expedite and minimize costs associated with conducting a two-armed randomized controlled trial, given that the efficacy of frozen FMT is known to be 85%. Additionally, using lyophilized FMT offers two major advantages: 1) its prolonged shelf life reduces cost because fewer donors need to be screened; and 2) it can be transported without freezing.

Methods. This is an open-labeled, prospective study involving 50 patients with a history of 2 or more rCDI who have failed at least 1 course of tapered vancomycin therapy. Eligible patients received 2 lyophilized FMT via retention enema within 8 days of each treatment and were followed for 13 weeks post last FMT to determine efficacy and safety of FMT.

Results. The efficacy of lyophilized FMTs in preventing further episodes of CDI in patients with rCDI was 80%. The adverse events associated with lyophilized FMT were similar to frozen FMT.

Conclusion. Lyophilized FMT in treating rCDI showed similar efficacy and safety to frozen FMT. Lyophilized FMT appears to be promising in preventing further episode of CDI and increasing accessibility for patients with rCDI.

Disclosures. **All authors:** No reported disclosures.

1255. Probiotics to Reduce *Clostridium difficile* Infection: Clinical Experience in a Tertiary Care Center

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Background. There is conflicting clinical data regarding the efficacy of probiotics to prevent *Clostridium difficile* infection (CDI). The goal of this study is to compare rates of hospital acquired *Clostridium difficile* infection (HA-CDI) among patients receiving antibiotics with or without concomitant administration of probiotics.

Methods. This retrospective, cohort study compares hospitalized patients who received antibiotics alone vs. antibiotics plus a multi-strain probiotic preparation of lactobacillus over a six month time period. Probiotics were given at the discretion of the physician. The primary outcome was incidence in HA-CDI (defined as onset after hospital day three) between groups.

Results. A total of 1,576 patients met selection criteria, with 927 patients receiving antibiotics alone and 649 patients receiving antibiotics plus probiotics. HA-CDI rates were 0.9% and 1.8% ($P = 0.16$), respectively. In a subgroup analysis of patients in the antibiotic only group, patients who received similar antibiotic exposure as the probiotics group ($n = 284$) had no difference in rates of HA-CDI (1.8% vs. 1.8%; $P = 1.0$).

Conclusion. Probiotic administration did not decrease rates of HA-CDI in our institution. We recommend prioritizing resources to other CDI reduction measures such as decreasing antibiotic exposure and preventing transmission.

Disclosures. **All authors:** No reported disclosures.

1256. Efficacy of Oral Vancomycin, Oral Metronidazole, or IV Metronidazole Prophylaxis at Reducing the Risk of *Clostridium difficile* Recurrence

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Background. Secondary prophylaxis (SP) for *Clostridium difficile* infection (CDI) with oral vancomycin or oral/IV metronidazole when initiating antibiotics is common, though few studies are available to support this practice. The purpose of this study was to assess the efficacy of prophylaxis within a year of index CDI.

Methods. This retrospective chart review looks at subsequent courses of antibiotics and CDI in patients with initial positive CDI testing in 2013–16. A positive CDI test within 90 days of antibiotics was a recurrence. The use of antibiotics for SP was noted, along with other factors associated with CDI relapse. Non-parametric and exact tests were used for univariate analysis. These variables were included in a multivariate proportional hazards model.

Results. We found 597 antibiotic episodes in 230 patients. 130 episodes (21.8%) received SP. The difference of recurrence rates with and without antibiotics, 9.2 % vs 10.7%, was not statistically significant. No difference was seen when metronidazole was used, but vancomycin SP reduced the rate to 7.5% (6/80, $P = 0.45$). Probiotics were associated with a higher rate of recurrence (16.7 vs. 8.9%, $P = 0.025$). Proton pump inhibitors were also associated with a slightly higher rate of CDI recurrence (13.0% vs. 8.4%). The rate of relapse fell significantly with increasing time since the index case of CDI by logistic regression (P = 0.011). In multivariate regression, relapse was associated with shorter time from index CDI, shorter durations of antibiotics, and the use of probiotics.

Conclusion. This retrospective study does not support the routine use of metronidazole in subsequent antibiotic courses following CDI. The use of probiotics paradoxically increased the rate of CDI relapse in this study. The limitations of this retrospective study do not eliminate the possibility of utility of vancomycin as prophylaxis, but this requires further evaluation.

Disclosures. **All authors:** No reported disclosures.

1257. Tetracyclines are Associated with a Reduced Risk of *Clostridium difficile* Infection: A Systematic Review and Meta-analysis

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Background. Efforts towards antibiotic stewardship help reduce risk of *Clostridium difficile* infection (CDI) but there is a need to delineate antibiotic choices to reduce CDI risk. Tetracyclines may be associated with a low risk for CDI but the evidence is conflicting. We conducted a systematic review and meta-analysis to determine the relationship between tetracyclines use and CDI.

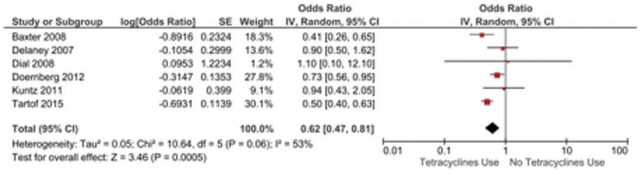
Methods. A systematic search of Medline, Embase, and Web of Science was performed from January 1978 up to December 2016 including studies assessing the association between tetracyclines and CDI; compared with other antibiotics; to assess the risk of CDI after exposure to tetracyclines vs. other antibiotics. Study quality was assessed using the Newcastle-Ottawa scale. Weighted summary estimates were calculated using generalized inverse variance with random-effects model using Review Manager version 5.3 (Cochran Inc).

Results. Six studies; 4 case control and 2 cohort studies reported the association of CDI with tetracyclines or other antibiotics prior to CDI including patients from 1993 to 2012. Meta-analysis of all studies using the random-effects model demonstrated that tetracyclines were associated with decreased risk of CDI compared with other antibiotics (OR, 0.62; 95% CI, 0.47–0.81; $P = .0005$). There was significant heterogeneity among the studies, with an I^2 of 53% (Figure 1). No publication bias was seen.

Subgroup analysis of studies evaluating the risk of CDI with doxycycline only also demonstrated a decreased risk of CDI with doxycycline compared with other antibiotics (OR, 0.55; 95% CI, 0.40–0.75; P = 0.0002). A subgroup analysis based on CDI diagnosis definitions revealed a decreased risk of CDI with tetracyclines (OR, 0.59; 95% CI, 0.44–0.80; P = 0. 0006) in studies that used clinical definitions (presence of diarrhea with a positive stool test), but not among the studies that used ICD-9 codes for CDI diagnosis (OR, 0.95; 95% CI, 0.45–2.01; P = 0.90).

Conclusion. Tetracyclines are associated with a lower risk of developing CDI compared with other antibiotics. It is reasonable to use these over other antibiotics when appropriate (community acquired pneumonia, bronchitis, chlamydia, rickettsial or spirochetal infections) to reduce the risk of CDI.

Forest plot demonstrating decreased odds of CDI with tetracyclines use by a random-effects model



Disclosures. **All authors:** No reported disclosures.

1258. Durability and Long-Term Clinical Outcomes of Fecal Microbiota Transplant (FMT) Treatment in Patients with Recurrent *C. difficile* Infection

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Background. Fecal microbiota transplant (FMT) has been shown to be safe and effective for treatment of recurrent *C. difficile* infection (RCDI). The aim of this study is to determine factors impacting the durability of FMT and assess patient long-term clinical outcomes and satisfaction with the procedure.

Methods. Eligible patients who had received FMT for RCDI at Emory Hospital between July 1, 2012 and December 31, 2016 were contacted via telephone for a follow up survey. Of 232 patients who received FMT, 27 were deceased and 15 were unable