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# HIGH PREVALENCE OF SUBCLASS-SPECIFIC BINDING AND NEUTRALISING ANTIBODIES AGAINST CLOSTRIDIUM DIFFICILE TOXINS IN ADULT CYSTIC FIBROSIS SERA: POSSIBLE MODE OF PROTECTION AGAINST SYMPTOMATIC CLOSTRIDIUM DIFFICILE INFECTION

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**Introduction** Despite multiple risk factors and a high rate of colonisation for Clostridium difficile (CD), the occurrence of C. difficile infection (CDI) in patients with cystic fibrosis (CF) is rare. The aim of this study was to compare the prevalence of CD toxin-specific IgA, IgG and anti-toxin neutralising antibodies (NAb) in the sera of adults with CF, symptomatic CDI (without CF) and healthy controls (HC).

**Method** Subclass-specific IgA and IgG responses to highly purified whole CD toxins A and B (toxinotype 0, strain VPI 10463, ribotype 087; toxin A 200 mg/mL, toxin B 100 mg/mL), toxin B from a CD toxin-B only expressing strain (CCUG 20309, 90 mg/mL) and precursor form of B fragment of binary toxin, pCDTb (200 mg/mL), were determined by a validated protein microarray assay. NAb to CD toxins A and B were evaluated using a Caco-2 cell neutralisation assay. Clinical and demographic information was collected from medical records. All statistical analyses were performed on natural log-transformed data using GraphPad Prism version 6. For grouped multiple comparisons, the Kruskall-Wallis test and the Dunn's post hoc test was applied; p£0.05 was statistically significant.

**Results** Serum IgA anti-toxin A and B levels and NAb against toxin A were significantly higher in adult CF patients (n=16; median age, 28 years (range 19–49 years)] compared with HC [n=17; 32 years (range 22–89 years)] and patients with symptomatic CDI (n=16; 36.5 years (range 19–49 years)]; p£0.05. The same pattern of response prevailed for IgG, except that there was no difference in anti-toxin A IgG levels between the groups. Systemic IgG anti-toxin B antibody responses predominated and high titre sera did not correlate with high neutralising potential. Compared with HC (toxins A and B) and CDI patients (toxin A), CF sera exhibited significantly stronger protective anti-toxin NAb responses.

**Conclusion** A superior ability to generate robust humoral immunity to CD toxins in the CF population is likely to confer protection against symptomatic CDI. This protection may be lost in the post-transplantation setting, where symptomatic CDI is a significant complication. Sera-monitoring of anti-CD toxin antibody titres may be of clinical value to identify transplant recipients displaying low levels of specific antitoxin antibodies who may be at risk of developing severe CDI. These individuals could be offered prophylactic passive or (when available) active immunotherapies.

**Disclosure of Interest** T. Monaghan: None Declared, O Negm: None Declared, B MacKenzie: None Declared, M Hamed: None Declared, C Shone: None Declared, D

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