**TITLE:** Anti-vinculin Antibodies: Multicenter Validation of a Diagnostic Blood Test for Irritable Bowel Syndrome  
**CONTACT (NAME ONLY):** Mark Pimentel  
**ABSTRACT STATUS:** Sessioned  
**AUTHORS/INSTITUTIONS:** M. Pimentel, C. Chang, W. Morales, K. Chua, S. Weitsman, E. Marsh, Z. Marsh, GI Motility, Cedars Sinai Medical Center, Los Angeles, California, UNITED STATES|A. Lembo, Beth Israel Deaconess Medical GAS, Boston, Massachusetts, UNITED STATES|  

**ABSTRACT BODY:**

**Purpose:** Data have accumulated that a significant portion of irritable bowel syndrome (IBS) cases begin after acute gastroenteritis. Human and animal work suggests that exposure to acute gastroenteritis leads to small intestinal bacterial overgrowth (SIBO) through neuropathic events. Cytolethal distending toxin B (CdtB) from bacteria known to cause gastroenteritis is important in this process through molecular mimicry and auto-antibodies to vinculin (cell migration and adherence protein found predominantly on nerves and epithelium). In this multicenter study, we assess anti-vinculin antibodies as a predictor of IBS compared to healthy subjects and inflammatory bowel disease (IBD).

**Methods:** Subjects (18-65 years) with Rome-positive IBS were recruited from Cedars-Sinai Medical Center and Beth Israel Deaconess Medical Center. Subjects were assessed for symptoms and demographics followed by collection of sera. Subjects were excluded if they had concomitant GI disease, previous GI surgery, adhesions, unstable thyroid disease, diabetes, or HIV. Healthy controls were recruited based on the completion of a GI symptom questionnaire. On this questionnaire, subjects had to have marked <10 for bloating, diarrhea, abdominal pain, and constipation, inclusive on a 0-100 VAS. Subjects with IBD were recruited from an expert tertiary care medical center. Subjects with Crohn’s disease or ulcerative colitis were excluded if there was a history of biologic therapy and current prednisone use. Serum from all three groups was used to perform and ELISA to determine antibodies to human recombinant vinculin.

**Results:** In total 165 IBS, 30 IBD, and 26 healthy control subjects were evaluated. Demographics were similar between groups. Overall, IBS had a significantly greater optical density in the ELISA for anti-vinculin antibodies compared to IBD and healthy subjects. Comparing the two major centers for IBS recruitment, results from both centers were similarly abnormal (P=NS). Interestingly, subjects with a history of acute gastroenteritis, even higher levels of antibodies were seen (p<0.05).

**Conclusion:** Anti-vinculin antibodies are elevated in IBS compared to non-IBS. This is the first diagnostic test for IBS based on serum and a pathophysiologic mechanism of IBS through acute gastroenteritis precipitated molecular mimicry and autoimmunity.

(no table selected)
Financial Relationships: Not Applicable
Initiated Research: Investigator
Investigator Contribution: Yes
Performed Analysis: Investigator
Secondary Analyses: Not Applicable
Study Results: Yes
Submit:
Supported by Industry Grant: No
Purpose: IBS is a heterogeneous condition defined and sub-grouped according to predominant symptoms. Subtle irregularities in circulating cytokines have been observed in IBS. However it is unclear whether the changes observed are associated with gastrointestinal inflammation, reflect associated co-morbidities or are a consequence of symptoms or associated stress. Our aim was to determine whether circulating cytokine levels are associated with distinct IBS subgroups.

Methods: Patients aged between 18 and 65 years with a clinical diagnosis of a functional gastrointestinal disorder were recruited from a specialty clinic in Cork University Hospital. IBS, IBS subtype, and the presence of other functional disorders were diagnosed as per Rome III criteria. The presence of comorbid psychological and somatic disorders was defined by validated questionnaires. Plasma levels of IL-1β, IL-6, IL-8, IL-10, IL-12p70, IL-13, TNF-α, and IFN-γ were determined by electrochemical luminescence. IBS subgroups showing significantly higher levels of IL-6 were incorporated into a multiple regression analysis.

Results: Fifty eight patients attended a baseline visit. Thirty returned for a second visit after a mean interval of 69 days. Twenty two returned for a third visit after a mean interval of 120 days (range 76-166 days) after the baseline visit. Nineteen patients completed all three visits and met Rome III criteria for IBS on at least one visit. Twenty one healthy controls completed a single visit. IFN-γ was significantly lower [HC 3.04 (2.35-4.77) pg/mL; IBS visit one: 1.76 (1.49-2.45) pg/mL; IBS visit two: 2.32 (1.78-2.93) pg/mL; IBS visit three: 1.92 (1.56-2.41); p<0.05] and IL-6 significantly higher [HC 5.77 (4.39-7.68) pg/mL; IBS visit one: 8.24 (6.07-11.19) pg/mL; IBS visit two: 7.72 (5.84-13.20) pg/mL; IBS visit three: 8.95 (5.49-14.55) pg/mL; p<0.05] in those with IBS compared to healthy controls. IBS-D, IBS-M, comorbid depression, severe abdominal pain, and a comorbid functional oesophageal disorder were all associated with higher levels of IL-6. Multiple regression showed that both depression and anxiety were independently associated with higher levels of IL-6 in patients with IBS.

Conclusion: Higher levels of plasma IL-6 are associated with the presence of psychological comorbidity in those with IBS. This suggests that disturbances in circulating cytokine levels in IBS may be centrally mediated rather than reflecting inflammation at the mucosal level.