

Comparison between non-responders and responders based on clinical history

	Responder	Non-responder	p-value
Age	50	56	> 0.05
Hx Sinusitis	90%	60%	> 0.05
Hx Pneumonia	10%	30%	> 0.05
Hx Bronchitis	40%	40%	> 0.05
Hx Sinus surgery	20%	5%	> 0.05
Hx IV Antibiotics	0%	20%	> 0.05
Hx Admission	0%	20%	> 0.05
IgG	1002%	783%	0.05
IgA	118%	148%	> 0.05
IgM	156%	111%	> 0.05
% Protective Pre	35%	22%	0.05
% Protective Post	80%	34%	<0.0001

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ASSESSMENT OF SERUM IL-12, IL-10, IL-8, AND IFN-γ IN PATIENTS WITH ORAL MUCOSAL LICHEN PLANUS.

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Background: Oral lichen planus is a chronic inflammatory, immune-mediated, mucocutaneous disease which rarely regresses spontaneously. The erosive form tends to progress, frequently relapses, and can become chronic leading to malignancy. This study assesses a T-helper cell cytokine IL-12, a T-regulatory cytokine IL-10, an anti-viral proliferative cytokine IFN-γ, and a pro-inflammatory cytokine with chemokine activity, IL-8, in patients with frequent relapses of erosive oral lichen planus. Methods: 97 patients age 18 to 60 years were studied including 35 with erosive oral lichen planus, 32 with non-erosive oral lichen planus and 30 healthy control subjects of similar age. The levels of serum cytokines (IL-12, IL-10, IL-8, IFN-γ) were determined by enzyme-linked immunosorbent assay ("Immunotech"; France). Results: During relapse of erosive oral lichen planus there is a marked increase in select cytokines compared with control group levels including: IL-12, 2.0 fold rise (15.3±1.1 pg/ml versus 8.6±0.6 pg/ml); IL-8, 2.8 fold rise (83.1±2.3 pg/ml versus 30.1±1.2 pg/ml); and IL-10, 1.6 fold rise (80.2±1.5 pg/ml versus 49.5±3.2 pg/ml). IFN-γ (0.5±0.2 pg/ml) however is reduced 4.6 fold versus the control group. In remission IL-12 increases 1.2 fold, IL-8 increases 2.3 fold, and IL-10 increases 1.1 fold, while IFN-γ decreases to 0.8±0.2 pg/ml, being less than in healthy controls, and 1.6 fold less than in disease relapse (p<0.05). Conclusions: Acute relapse and chronic stages of lichen planus of the oral mucosa are characterized by immunological changes detectable in peripheral blood serum including increases in concentrations of IL-12, IL-8, IL-10 and reduction in concentration of IFN-γ, characteristic of development of a recurrent inflammatory immune response.

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STIMULATORY EFFECTS OF LACTOBACILLI ON HUMAN PERIPHERAL BLOOD LEUKOCYTE IMMUNE RESPONSES.

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Introduction: Probiotics are natural microbial products which have been recently been proposed for use in patients with allergic diseases. The mechanisms of action of probiotics are not well understood. This study assesses the influence of different lactobacilli strains and their cell wall components on function of human immune cells in vitro. Methods: 14 lactobacilli strains were assessed. Lactobacilli were labeled with FITC for phagocytosis assays. Blood from healthy volunteer subjects was obtained for assessment of neutrophil, lymphocyte, monocyte and macrophage functions influenced by the lactobacilli and their cell wall components. Reactive oxygen species (ROS) production by neutrophils cultured with lactobacilli cell walls and cell lysates was studied, as well as various surface molecules. Monoclonal antibodies to CD11b, CD14, CD66b, CD69, CD80 were used to label cells studied by flow cytometry. TNF-α production was assessed. Results: Cluster analysis has shown the presence of inter-strain variations in the ability of lactobacteria to be phagocytosed by neutrophils and monocytes. There were 2 clusters with high and low numbers of cells which phagocytosed the lactobacilli. Lactobacteria cell wall components induced substantial activation of neutrophils and stimulation of generation of ROS. A weak effect of lactobacilli cell wall components on expression of CD69 by lymphocytes was seen. Lactobacilli cell walls enhanced production of TNF-α and expression of CD80 by macrophages See figures A – macrophages; B – neutrophils (exclusion gate); C – nonstimulated cells; and D-

cells cultured with lactobacilli cell walls, to view the effects of lactobacilli on various leukocytes. A significant immunomodulatory effect was induced by the studied lactobacilli strains as well as isolated lactobacilli cell walls. Conclusion: Lactobacilli cell wall components stimulate reactive oxygen species formation by neutrophils; enhance the expression of CD80 molecules; and increase production of TNF-α. There are inter-strain variations in the immune modulation induced by lactobacilli. These characteristics suggest that select lactobacilli strains could be employed to influence human immune responses.

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CENTRAL NERVOUS SYSTEM VASCULITIS IN COMMON VARIABLE IMMUNODEFICIENCY.

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Introduction: Common variable immunodeficiency (CVID) is a heterogeneous disorder characterized by impaired B cell differentiation with defective immunoglobulin production. B cell maturation and toll-like receptor 7 and 9 function are impaired. CVID is associated with infectious, inflammatory, autoimmune and malignant conditions. Neurologic manifestations of CVID are reported in the literature, but clinical descriptions of Central Nervous System (CNS) vasculitis are limited. Case Report: A 24-year old female with history of immunodeficiency, type 1 diabetes mellitus, and autoimmune disorder referred to clinic for evaluation. Around age 10 years refractory Immune Thrombocytopenic Purpura with platelet count of 3000 manifested as easy bruising, non-responsive to Intra Venous Immunoglobulin (IVIG) prompted splenectomy. Over the next few years she developed recurrent sinopulmonary and genital Herpes Simplex Virus (HSV) infections, chronic lymphadenopathy, hypogammaglobulinemia, anergy to vaccines and was diagnosed with CVID. A year after diagnosis she had acute left sided headache with narrowed vision and photophobia. Brain MRI revealed a left frontal mass of unknown etiology. Neurosurgical evaluation considered brain biopsy; but on reimaging, the lesion resolved, which ruled out suspected cancer. Migraine prophylaxis and abortive treatment, was associated with radiographic resolution of the lesion. 9 months later she developed seizures. EEG was normal but a new hyperintense flair enhancing signal was identified in the right cerebellar hemisphere. Differential diagnosis included hemangioblastoma versus glioma. Her seizures were well controlled with seizure and anti-inflammatory medications. No behavioral changes, weakness or alterations of gait, balance or coordination were reported except headache. After extensive evaluation (MRI with and without gadolinium) enterovirus infection, HIV, neurosarcoid and malignancy, spinal cord lesions were ruled out. Repeat MRI two weeks later revealed resolution of the right cerebellar lesion, consistent with resolution of an inflammatory process. Conclusion: Clinical features and MRI findings suggest a CNS inflammatory process secondary to autoimmunity which is not uncommon in CVID. Clinical descriptions of CNS vasculitis in CVID are limited. Clinicians should consider vasculitis in the differential diagnosis when evaluating neurologic symptoms in CVID.

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EFFICACY AND SAFETY OF RECOMBINANT HUMAN C1 ESTERASE INHIBITOR FOR ACUTE ATTACKS OF HEREDITARY ANGIOEDEMA: AN OPEN-LABEL STUDY.

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Rationale: Hereditary angioedema (HAE) due to C1 esterase inhibitor deficiency is an autosomal dominant disorder characterized by recurrent attacks of subcutaneous/submucosal edema. Recombinant human C1 esterase inhibitor (rhC1INH) has been shown to be effective for treatment of acute HAE attacks, including repeated treatments for multiple attacks. The current study evaluated safety and efficacy of rhC1INH for repeated treatment of acute HAE attacks in an open-label extension of a randomized controlled study. Methods: Patients experiencing eligible angioedema attacks at any anatomical location were treated with rhC1INH (50 IU/kg up to 4200 IU). The time to onset of symptom relief at the primary attack location was assessed as time from start of study drug infusion to onset of sustained beneficial effect, using a Treatment Effect Questionnaire. Time to minimal symptoms for all attack locations was assessed for