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LRA by ELISA/ACT[®]

CLINICAL PEARLS UPDATE#8

Multiple Sclerosis

October 27, 2003

Dear Colleague:

Multiple sclerosis (MS) affects 2-8 million Americans according to the American Academy of Neurology and MS Society. Successful comprehensive management using LRA by ELISA/ACT[®] tests and treatment plans are illustrated in the attached abstract reports.

Functional, *ex vivo* lymphocyte response assays (LRA by ELISA/ACT) offer the most advanced tests available for determination of the individual's responses to the widest available range of substances tested by any lab in the world.

We are grateful for the opportunities to be of service to you and your patients.

Sincerely,

Russ Jaffe, MD, Ph.D., CCN, NACB
Lab Director

Yacyshyn B, Meddings J, Sadowski D, Bowen-Yacyshyn MB. Multiple sclerosis patients have peripheral blood CD45RO+ B cells and increased intestinal permeability. *Dig Dis Sci* 1996;41(12):2493-2498.

Department of Medicine, University of Alberta, Edmonton, Canada.

Increased intestinal permeability and the CD45RO isoform expression of the leukocyte common antigen on peripheral blood CD20+ B cells are found in Crohn's disease. Others have observed that multiple sclerosis (MS) patients may have an increased risk of coacquisition of Crohn's disease. The aim of this study was to identify an association between these diseases using peripheral blood CD45 isoform expression and intestinal permeability in MS. Lactulose/mannitol permeability and peripheral blood CD20+ B cell CD45RO expression were defined in healthy controls, MS patients, and patients coincidentally affected by MS and Crohn's or MS and ulcerative colitis (UC). Five of 20 MS patients had increased intestinal permeability, a finding not previously reported. High levels of CD45RO were found on circulating CD20+ B cells from patients with MS. This has not been reported previously in MS and is found in very few other conditions. Eight patients with coincident MS and Crohn's disease or MS and UC were studied. Coincident MS and UC patients expressed CD45RO on CD20+ B cells, a finding not identified in UC patients alone. A subgroup of MS patients has increased intestinal permeability. These patients express CD45RO CD20+ B cells, also found in Crohn's disease.

Sanna V, Di Giacomo A, La Cava A, Lechler RI, Fontana S, Zappacosta S, Matarese G. Leptin surge precedes onset of autoimmune encephalomyelitis and correlates with development of pathogenic T cell responses. *J Clin Invest* 2003;111(2):241-250.

Gruppo di ImmunoEndocrinologia, Istituto di Endocrinologia e Oncologia Sperimentale, Consiglio Nazionale delle Ricerche (IEOS-CNR), Dipartimento di Biologia e Patologia Cellulare e Molecolare, Universita di Napoli Federico II, Napoli, Italy.

In the work presented here, we explored the influence of leptin on the kinetics of experimental autoimmune encephalomyelitis (EAE) onset, in the EAE-associated inflammatory anorexia, and in the development of pathogenic T cell responses. We found that the expression of serum leptin increased before the clinical onset of EAE in disease-susceptible C57BL/6J (H-2(b)) and SJL/J (H-2(s)) strains of mice, which are models of chronic-progressive and relapsing-remitting EAE, respectively. This increase in serum leptin correlated with disease susceptibility, reduction in food intake, and decrease in body weight. Indeed, acute starvation, which is able to prevent the increase in serum leptin, delayed disease onset and attenuated clinical symptoms by inducing a T helper 2 cytokine switch. Furthermore, immunohistochemical analysis revealed a parallel *in situ* production of leptin in inflammatory infiltrates and in neurons only during the acute/active phase of both chronic-progressive and relapsing-remitting EAE. We also found that leptin secretion by activated T cells sustained their proliferation in an autocrine loop, since antileptin receptor antibodies were able to inhibit the proliferative response of autoreactive T cells *in vitro*. Given that leptin appears to regulate EAE susceptibility, inflammatory anorexia, and pathogenic T-cell immune function, we postulate that it may offer a potential target in the treatment of multiple sclerosis.



An additional resource is R W Soll (MD, Ph.D.)'s book, *MS: There is something you can do about it*. This is a classic based on his vast experience of the importance of delayed food / chemical allergic responses in MS. The challenge was to find the full range of items to which people reacted, as Dr. Soll was able to do through our tests.

Note: We believe the comprehensive repair program included with LRA by ELISA/ACT tests, if requested, provides the best current therapy for sustained remissions in MS and related autoimmune conditions.

