Serum monomeric prolactin levels predict SLE disease severity

Elevated serum prolactin levels are common in patients with systemic lupus erythematosus (SLE). In mouse models, elevated prolactin is associated with high disease activity, but clinical reports have been inconclusive. Serum prolactin normally circulates predominantly as monomeric prolactin (23 kDa), with lesser amounts of 'big' prolactin (dimeric/trimeric, 45–50 kDa) and macroprolactin (>100 kDa). Researchers in Mexico investigated the relationship between SLE activity and serum levels of the different prolactin isoforms.

Total serum prolactin levels were not associated with disease activity. Patients with active SLE had higher levels of monomeric prolactin than those with inactive disease, and there was a negative correlation between disease activity and serum levels of 'big' prolactin and macroprolactin.

The results indicate that hyperprolactinemia per se does not predict greater SLE disease activity, but that greater severity of disease correlates with higher serum levels of monomeric prolactin. Macroprolactin has been shown to have biological activity *in vitro*, but the authors suggest that the high molecular weight of the protein impedes its ability to cross capillary walls *in vivo* and, therefore, limits its effect on disease activity. Patients with prolactin-modulated SLE could benefit from drugs that reduce prolactin levels; bromocriptine, which inhibits prolactin secretion from the anterior pituitary gland, has been shown to have beneficial effects on SLE disease activity in clinical trials.

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Original article Leños-Miranda A and Cárdenas-Mondragón G (2006) Serum free prolactin concentrations in patients with systemic lupus erythematosus are associated with lupus activity. *Rheumatology* 45: 97–101

A new model for rheumatoid arthritis etiology in a subgroup of patients

Following a series of epidemiologic and experimental studies, Swedish researchers have suggested that smoking, in a subset of patients with RA who have HLA-DR alleles encoding the shared epitope (SE), could trigger

rheumatoid arthritis (RA)-specific immune reactions to citrullinated proteins.

Several studies were performed, including a population-based case-control study that evaluated the SE genotype, anticitrulline antibody status and smoking history of 913 newly diagnosed patients with RA and 631 controls; a case-control study that analyzed "pre-RA" plasma samples from a blood bank in Northern Sweden; and a bronchoalveolar lavage study that reported anticitrulline antibody levels in samples from eight healthy individuals (four smokers, four non-smokers) and four patients with pulmonary inflammatory conditions.

The studies demonstrated that HLA-DR SE genotype and smoking status were risk factors for developing RA only in anticitrulline-antibody-positive individuals. When both risk factors were present, such individuals had a 21-fold increased relative risk, compared with individuals in whom both risk factors were absent. The studies also found that smoking was associated with high levels of citrulline-modified proteins in the lungs.

The authors hypothesize that long-term exposure to cigarette smoke might accelerate the citrullination of autoantigens present in the lungs. An autoimmune response to the citrullinated proteins might then be induced in individuals with particular HLA-DR SE genotypes, which could occur years before clinical onset of RA. The authors also note that additional genes, environmental stimuli and immune reactions might be involved in the pathogenesis of RA in other patient subgroups.

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Original article Klareskog L *et al.* (2006) A new model for an etiology of rheumatoid arthritis. *Arthritis Rheum* 54: 38–46

Etanercept plus DMARDs is better than DMARDs alone for patients with rheumatoid arthritis

Etanercept can bind to and neutralize extracellular tumor necrosis factor, and has proven clinical efficacy in reducing the disease symptoms of patients with rheumatoid arthritis (RA) who cannot tolerate or do not respond to conventional disease-modifying antirheumatic drugs (DMARDs). A new, Taiwanese study has confirmed these results, and shown that serum levels of rheumatoid factor (RF) and