

## **Rheumatoid Arthritis And Polymyalgia Rheumatica Patients Are Found To Have Low Adrenal and Sex Hormone Levels**

Cutolo, M., A. Sulli, et al. (2003). "Hypothalamic-pituitary-adrenocortical and gonadal functions in rheumatoid arthritis." Ann N Y Acad Sci **992**: 107-17.

Rheumatoid arthritis (RA) as well as most autoimmune disorders results from a combination of several predisposing factors including the relations between epitopes of the trigger agent (i.e., virus, self-antigens) and histocompatibility epitopes (i.e., HLA), the status of the stress response system including the hypothalamic-pituitary-adrenocortical axis (HPA) and the sympathetic nervous system (SNS), as well as the gonadal hormones (hypothalamic-pituitary-gonadal axis, HPG), with estrogens implicated as enhancers of the immune response and androgens and progesterone as natural suppressors. The regular observation of reduced cortisol and adrenal androgen secretion during testing in RA patients not treated with glucocorticoids should clearly be regarded as "relative adrenal insufficiency" in the setting of a sustained inflammatory process, as shown by high interleukin (IL)-6 levels. In polymyalgia rheumatica, several pathogenetic and clinical aspects of the disease might well overlap RA, at least with elderly onset RA (EORA). Therefore, reduced production of adrenal hormones (i.e., cortisol, DHEAS) at baseline in active and untreated patients with polymyalgia rheumatica was detected. The defect was mainly related to altered adrenal responsiveness to ACTH stimulation (i.e., increased 17-OHP), at least in untreated patients with polymyalgia rheumatica. Finally, normal serum estrogen and low androgen levels, but high synovial fluid estrogen and much lower androgen levels, have been found in RA patients, supporting the fundamental role of the peripheral sex hormone metabolism in the manifestations of the disease.