Neuroendocrine regulation of autoimmune/inflammatory disease.

Interactions between the immune and nervous systems play an important role in modulating host susceptibility and resistance to inflammatory disease. Neuroendocrine regulation of inflammatory and immune responses and disease occurs at multiple levels: systemically, through the anti-inflammatory action of glucocorticoids released via hypothalamic-pituitary-adrenal axis stimulation; regionally, through production of glucocorticoids within and sympathetic innervation of immune organs such as the thymus; locally, at sites of inflammation. Estrogens also play an important role in immune modulation, and contribute to the approximately 2- to 10-fold higher incidence of autoimmune/inflammatory diseases seen in females of all mammalian species. During inflammation, cytokines from the periphery activate the central nervous system through multiple routes. This results in stimulation of the hypothalamic-pituitary-adrenal axis which, in turn through the immunosuppressive effects of the glucocorticoids, generally inhibits inflammation. Recent studies indicate that physiological levels of glucocorticoids are immunomodulatory rather than solely immunosuppressive, causing a shift in patterns of cytokine production from a TH1- to a TH2-type pattern. Interruptions of this loop at any level and through multiple mechanisms, whether genetic, or through surgical or pharmacological interventions, can render an inflammatory resistant host susceptible to inflammatory disease. Over-activation of this axis, as occurs during stress, can also affect severity of infectious disease through the immunosuppressive effects of the glucocorticoids. These interactions have been clearly demonstrated in many animal models, across species, strains and diseases, and are also relevant to human inflammatory, autoimmune and allergic illnesses, including rheumatoid arthritis, systemic lupus
erythematous, Sjogren's syndrome, allergic asthma and atopic skin disease. While many genes and environmental factors contribute to susceptibility and resistance to autoimmune/inflammatory diseases, a full understanding of the molecular effects on immune responses of combinations of neuropeptides, neurohormones and neurotransmitters at all levels has opened up this new therapeutic approach.