How Hormones Affect Lupus Treatment

**Introduction**

Systemic lupus erythematosus (SLE) is a syndrome characterized by dysregulation of the immune system and widespread inﬂammation that can involve multiple organs and body systems. Skin and joints are most frequently affected. SLE afﬂicts women up to nine times more frequently than men and usually manifests during the childbearing years. SLE is identiﬁed serologically by autoantibodies to DNA, RNA, other nuclear antigens, and cytoplasmic/cell surface molecules. Numerous studies (human and animal models) provide evidence for bi-directional communication between the immune and endocrine systems and disruptions in communication that contribute to susceptibility and severity of disease. This article will discuss the impact of hormones and hormone-related factors in SLE from the perspectives of researchers in basic science, clinical science, and clinical practice.

**Clinical Practitioner Perspective**

By Ida Dzifa Dey, M.B. Ch.B., M.W.A.C.P. and David A. Isenberg, M.D., F.R.C.P., F.A.M.S.

Dey is a clinical research fellow and Isenberg is a professor at the Centre for Rheumatology, Department of Medicine, University College London Hospitals, London.

Systemic lupus erythematosus (SLE) is a highly variable multisystem autoimmune rheumatic disease (ARD). It is clearly not a homogenous disease entity but a variable syndrome with some patients manifesting mild clinical signs (e.g., skin rash), whereas others present with potentially fatal disease (e.g., nephritis, cerebral involvement).

Classification and Diagnosis

In 1971, the American College of Rheumatology published preliminary criteria for the classiﬁcation of SLE for clinical trials and studies and revised these criteria in 1982 and 1997. These classiﬁcation criteria are often used as the basis for diagnosis, although strictly speaking, they have not been formally validated for that purpose. They consist of four cutaneous, four systemic, and three laboratory components.1 These criteria show about 90 percent sensitivity and speciﬁcity but have weaknesses (e.g., patients with cutaneous lupus can be diagnosed as having SLE without any systemic features). The Systemic Lupus International Collaborating Clinics (SLICC) group has recently re-examined the criteria—incorporating new knowledge of autoantibodies, neuropsychiatric lupus, and advances in imaging—recognizing the importance of low complement and the need for biopsy-proven lupus nephritis to be a “stand alone” criterion. At least four of these criteria need to have been present at some time, not necessarily simultaneously, for lupus to be diagnosed.2 The diagnosis should be based on clinical signs and symptoms in general, and supported by laboratory evidence.

Epidemiology

Lupus is the third most common ARD. Its incidence rates vary with a worldwide annual incidence from 1.8 to 7.6 cases per 100,000. Current studies suggest the incidence may be increasing.

Differences in prevalence rates occur among people of the same race in different geographical locations. African Americans/African Caribbean women have a higher rate of SLE, followed by Asians, then Caucasians.3 One in 10,000 white males, one in 1,000 white females, and one in 250 African American females have SLE in the United States. Previous studies reported low rates of SLE in Africa,4 but paradoxically high rates among black women in the Americas, the Caribbean, and Europe, suggesting the importance of environmental inﬂuences. However that may not necessarily be the case and the apparent lower rate in Africa may be due to under-reporting.

Ninety percent of persons with SLE are female. The disease frequently starts in women of childbearing age. The use of exogenous hormones has been associated with lupus onset and ﬂares, suggesting a role for hormonal factors in the pathogenesis of the disease.5 The female-to-male ratio varies from 4.3 to 13.6:1 during the childbearing years, but the pre-puberty and post-menopause sex ratios are almost identical between females and males (2.3:1 and 2.2:1), implicating a correlation of maximal female sex hormone production with the onset of SLE.6 Of interest, SLE seems to be common in men with Klinefelter syndrome (genotype XXY) [see story, page 24], also suggesting a strong hormonal inﬂuence.

Clinical Features – How Lupus Affects the Body

There is a wide spectrum of clinical features and patients are highly variable in their disease manifestations. Almost every organ in the body can be affected, from the skin to the central nervous system. It is important to recognize differences between active ongoing disease activity and organ damage. Approximately one-third of patients develop other autoimmune diseases, notably autoimmune thyroid disease, Sjögren’s syndrome [see story, page 24], and antiphospholipid syndrome.

Management Systemic Lupus Erthematosus (SLE)

The social and psychological effects of both the chronic disease and its therapy, combined with its effects on fertility and pregnancy, must be recognized and dealt with by physicians and patients. Some general advice needs to be given to patients, such as appropriate rest and avoiding excess stress. Avoidance of ultraviolet light exposure is recommended, because this may cause disease ﬂares and a photosensitive rash. A diet low in saturated fats and high in ﬁsh oils and avoidance of both smoking and estrogen-containing contraceptive pills are advised. Because fatigue is common, a careful exploration of causes of fatigue (including anemia, hypothyroidism, and ﬁbromyalgia) by the physician is important. Vitamin D supplementation may have beneﬁts in the treatment of patients who are deﬁcient.

Pharmacological therapy is directed at organand non– organ-threatening disease, organ-speciﬁc measures, and adjuvant therapies (e.g., bone and renal protection). Patients with SLE are treated with four main groups of drugs, often in combination: non-steroidal anti-inﬂammatory drugs (NSAIDs), antimalarials, corticosteroids, and cytotoxic drugs.

Complications of therapy include osteoporosis, hypertension, and metabolic syndrome.

Biological therapies directed at immune processes implicated in the pathogenesis of the disease are being developed and show promise for the future.

Resource

Endocrine News, How Hormones Affect Lupus Treatment (05, February 2020). Retrieved from: https://endocrinenews.endocrine.org/managing-lupus/