

THE GLOBAL IMPACT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Systemic lupus erythematosus (SLE) is an inflammatory illness characterized by protean clinical features, a predilection for afflicting young females, and an unpredictable course. Manifestations range from fatigue and arthritis to life threatening carditis, cerebritis, and nephritis. Although the etiology of this disease remains elusive, its hallmark is aberrant auto-antibody production. These antibodies are either directly toxic to tissues, or form immune complexes that induce inflammation when deposited in capillary beds.¹ Due to therapeutic advances over the last 50 years, the 5-year survival rate has increased from less than 50% to over 90%;² this statistic, however, is misleading, as the long-term survival rate (68%) continues to be poor.² The causes of mortality suffered within the first 5 years of developing SLE are often related to the disease itself (26%), or to infection (37%), in contrast to late mortality, where infection (30%) and vascular disease (30%) are major causes of death.²

The improved 5-year survival rate of SLE patients has necessitated taking a more comprehensive view of lupus patients in order to evaluate the spectrum of disease over time. Although lupus patients survive longer, they are vulnerable to cardiac disease. Women with SLE aged 35–44 years were found to have a rate of myocardial infarction 52 times that of women of the same age range without SLE.³ Protracted courses of glucocorticoids, along with the more traditional risk factors of obesity, hypercholesterolemia, hypertension, renal disease, and a sedentary lifestyle, all contribute to this excess cardiovascular disease. Factors specific to SLE, such as the presence of antiphospholipid antibodies, may contribute to increased cardiovascular morbidity. The onset of cardiac disease in lupus patients occurs 10–20 years earlier than in the general population, potentially incapacitating men and women in the prime of their lives.

Although renal disease is no longer a major cause of mortality,² significant morbidity persists. Roughly half of all patients diagnosed with SLE developing renal disease at some

point during their illness.⁴ Despite receiving the recommended treatment of cyclophosphamide and prednisone, lupus patients with diffuse proliferative glomerulo-nephritis (the more severe form of renal disease that develops with in SLE) have only a 71% renal survival rate at 5 years.⁵ Eventually, a significant proportion of patients with SLE require renal replacement therapy.

The widespread use of glucocorticoids for the treatment of SLE also contributes to a high rate of osteoporosis and osteoporotic fractures.^{6,7} Early ovarian failure (due to cytotoxic treatment), renal disease, lack of activity, and lack of vitamin D exposure, are all potential contributors to osteoporosis. The use of bisphosphonates, an effective therapy for osteoporosis, is relatively contraindicated for renal failure and in women of child-bearing potential, 2 major limitations to their use in SLE patients. Avascular necrosis of bone is a fairly common development in lupus patients, another result of glucocorticoids.⁸ Avascular necrosis often affects the hip or shoulder joints, causing debilitating arthritis, and often requiring arthroplasty.

The discoid lesions of lupus commonly involve the face and scalp, and may result in irreversible scarring and patchy alopecia. Glucocorticoids produce obesity, a cushingoid appearance with centripetal fat distribution, moon facies, and a buffalo hump between the shoulders. These physical changes may contribute to patients' feelings of low self-esteem, isolation, and depression, and may affect their attitudes toward their disease. Longitudinal studies have demonstrated that attitudes toward disease have a significant impact on self-perceived function.⁹ SLE affects many young women at an age when careers are chosen and decisions about families are made. Not surprisingly, receiving a diagnosis of a chronic, unpredictable illness at such a pivotal time has adverse effects on both the emotional state and overall psyche of these patients.

Systemic lupus erythematosus (SLE) is a multisystem disease, and its management requires the use of specialists and invasive procedures such as hip replacements and hemodialysis, all of which places a significant burden on the healthcare system. The direct cost per patient has been estimated to be approximately \$5,000 (1997 Canadian dollars) per year in Canada and the United States, and slightly less in the United Kingdom.¹⁰ This figure, however, does not account for the indirect cost due to lost productivity. After taking into account the patient's lost wages, the lost wages of family members who take

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care of the patient, and the value of lost household work performed by the patient, the indirect cost to society per patient is estimated to be approximately \$15,000 (1997 Canadian dollars) per year in Canada and the United States, and slightly less in the United Kingdom.¹¹ Because SLE affects predominantly women, whose contribution to the workforce is undervalued compared to that of men, and who perform most of the household work, the economic value of which is also underestimated, this indirect cost is probably also underestimated. In addition, SLE occurs at an age before an individual achieves full earning potential, a factor not considered by most indirect cost models.

Systemic lupus erythematosus (SLE) is not an equal opportunity disease, disproportionately affecting minority populations. Some of the highest rates of SLE have been observed [recorded?] in African Americans, with prevalence rates as high as 375 per 100,000, 4 times the rate for Caucasians.^{12,13} In the United Kingdom, rates 5 times that of Caucasians have been observed in the Afro-Caribbean population.^{14,15} Reports of SLE in West Africans are rare, and SLE is believed to be uncommon; however, no population-based studies are available to confirm or contradict this conjecture, and a study of the immigrant population in South London found SLE to be 3 times more common in West Africans than Caucasians.¹⁶ The prevalence rates of SLE in Hispanics and Asians, while greater than those for most European populations, are generally less than rates for populations of West African ancestry. In Hawaii, SLE is 4 times more common among native Hawaiians and Asians, compared to Caucasians.¹⁷

Does SLE have different manifestations in different ethnic groups? Does race contribute to the severity of SLE? Compared to Caucasians, African Americans with SLE have a less favorable prognosis.^{18,19} What remains controversial is whether this variance is due to ethnicity or to socioeconomic factors, though studies controlling for socioeconomic status have suggested that socioeconomic factors play the greater role.²⁰ In the United States, a study of subjects with recent-onset SLE found the disease to be more active in its early stages in African Americans compared to Caucasians,²¹ although the disease activity appeared to become similar between ethnic groups over time. This cohort included Hispanics, who also had more disease activity compared to Caucasians.²¹

The manifestations of SLE also vary among ethnic groups. Compared to Caucasians, African Americans have more renal and central nervous system involvement, while Hispanics have more renal and cardiac disease.²² African-American and Hispanic patients develop renal disease after the diagnosis of SLE more frequently than do Caucasians (50.5%, 43.1%, and 14.3%, respectively).⁴ Additionally, lupus nephritis in African Americans does not respond as favorably to treatment as in Caucasians.⁵ Ethnic differences in disease manifestations of SLE are reported among different Asian ethnic groups.²³

This ethnic variability in both the manifestations of SLE,

and their degree of severity, makes comparisons between treatment groups in clinical trials difficult. Systemic lupus erythematosus (SLE) affects primarily minority populations, not only in the developed world, but also those of the developing countries of the Caribbean, Latin America, and Africa.^{24–26} Access to specialized resources is more limited in developing nations, which means SLE has the potential to have a greater negative impact on mortality and morbidity than in the developed world. The challenges that remain in the battle against SLE are not only to develop better, less toxic therapies, but to improve access and acceptability of health care to minority populations, as therapy may not be uniformly effective in all groups. Data on SLE from many parts of the world remain sparse; obtaining such information could help researchers capture the true complexity of the disease, and, perhaps, offer more hope to those most likely to suffer the worst complications.

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