R. Elaine Lambert, MD, is an adjunct clinical professor of medicine at the Stanford University School of Medicine in Stanford, CA. She also practices rheumatology at Sports Orthopedic and Rehabilitation Medicine Associates in Redwood City, CA.

Dr Lambert earned her undergraduate degree in biology from Baylor University in Waco, TX, and her medical degree from the University of Texas Southwestern Medical School at Dallas. She completed her internship and residency in internal medicine, as well as her fellowship in rheumatology, at Santa Clara Valley Medical Center in San Jose, CA. Dr Lambert also completed a fellowship in clinical research at Stanford University Medical Center. She is board certified by the American Board of Internal Medicine in both internal medicine and rheumatology.

Dr Lambert has published numerous articles, abstracts, and chapters in textbooks. She has also been an invited presenter at national medical conferences. Dr Lambert is a fellow of the American College of Rheumatology and is a past chair and current board member of the Arthritis Foundation of Northern California. She enjoyed working with Stanford athletes as a team physician from 1992-2012. Dr Lambert received the highest award given to a clinician in 1994 at Stanford Medical School, the Rambar Award for Excellence in Patient Care, as well as numerous teaching awards.

This promotional program was developed in conjunction with and sponsored by GSK, based on an interview with R. Elaine Lambert, MD. Dr Lambert received a fee for participation in this program.
What are implications on risk of mortality due to organ damage associated with SLE?

Despite improved survival rates overall, SLE remains a chronic disease with higher than expected mortality rates.\(^1\) Although survival rates significantly improved in patients diagnosed between 1980 and 1992 vs patients diagnosed between 1950 and 1979, survival rates are still significantly lower for patients with SLE and the rate of SLE mortality remains high relative to the general population (Figure 1).\(^1,11\) Mortality rates are highest in younger patients and can also differ significantly based on ethnicity.\(^11,12\) An analysis of a multiethnic, multicenter cohort of patients with SLE reported 5-year survival rates were lower for Texan Hispanics (86.9%) and African Americans (89.8%) than for Caucasians (93.6%) and Puerto Rican Hispanics (97.2%) (\(P=0.021\)).\(^12\) In my own practice, I have observed more severe disease in patients of Asian descent, which is supported by reports in the literature.\(^13\)

A range of etiologies are implicated in SLE mortality. In an analysis of mortality data from 9547 patients followed for a total of 76,948 person-years between 1958 and 2001, mortality rates reported by the study were significantly higher than those seen in the general population for common causes of death. Patients with SLE were \(~8\) times more likely to die of renal causes, \(~5\) times more likely to die due to infections, and twice as likely to die due to cardiovascular disease.\(^11\) Organ damage is one of the most important correlates with these mortality data.\(^3,4\)

What organ systems are commonly associated with SLE disease activity? How can increases in SLE disease activity lead to substantial organ damage?

Organ systems commonly involved in SLE include the central nervous system, kidneys, eyes, gastrointestinal system, mucous membranes, heart, skin, hematologic system, musculoskeletal system, and lungs. SLE is a chronic, multisystem autoimmune disease, with diverse clinical manifestations that are the result of inflammation in affected organ systems. The disease is potentially life-threatening when major organs are affected.\(^3\) Specifically, the risk of cardiovascular disease in SLE is substantial (Table 1).\(^14-17\) Notably, there is a 50 times greater risk of myocardial infarction in women with SLE aged 35-44 years.\(^18\)

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**Figure 1: Estimated Rate of Death Compared to the Age-Matched General Population**\(^11\)

<table>
<thead>
<tr>
<th>General Population</th>
<th>19.2X Greater Rate</th>
<th>8.0X Greater Rate</th>
<th>3.7X Greater Rate</th>
<th>1.4X Greater Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-24</td>
<td>25-39</td>
<td>40-59</td>
<td>≥60</td>
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</tbody>
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Table 1: Risk of Cardiovascular Disease in SLE Is Substantial

<table>
<thead>
<tr>
<th>Cardiovascular Outcome</th>
<th>Elevated Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonfatal myocardial infarction</td>
<td>• 10.1 times greater risk compared with expected rates(^a)</td>
</tr>
<tr>
<td>Coronary heart disease (CHD)</td>
<td>• 7.5 times greater risk of CHD compared with expected rates(^a)</td>
</tr>
<tr>
<td></td>
<td>• 17.0 times greater risk of death due to CHD compared with expected rates(^a)</td>
</tr>
<tr>
<td></td>
<td>• SLE patients presenting for cardiac catheterization are &gt;20 years younger than controls</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>• 2.7 times greater risk of hospitalization compared with women without SLE (age 18-44 only)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>• Prevalence higher in SLE than in controls (33% vs 20%)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>• 7.9 times greater risk of stroke compared with expected rates(^a)</td>
</tr>
<tr>
<td></td>
<td>• 2.1 times greater risk of hospitalization for cerebrovascular event compared with women without SLE (age 18-44 only)</td>
</tr>
</tbody>
</table>

\(^a\)Expected rates based on the Framingham models.

Additionally, nephritis impacts the majority of patients as SLE progresses.\(^{19}\) Renal damage is one of the most important predictors of mortality for patients with SLE.\(^{20}\) The prevalence of renal damage is higher in African American and Hispanic patients than in whites; it is also higher in men than in women.\(^{19,21}\)

**How does early organ damage associated with SLE impact mortality risk? Can organ damage occur even with low/moderate SLE disease activity?**

Early organ damage is associated with a reduced 10-year survival rate. In a prospective cohort study, 25% of patients with early damage (defined as initial SDI ≥1 at the time of initial assessment)* died within 10 years, compared to 7.3% of patients with no early damage (defined as SDI=0) (P=0.0002).\(^{22}\) Overall, one-third to one-half of patients with SLE accrue permanent organ damage within 5 years of diagnosis.\(^4,5\) In my opinion, these data reinforce the idea that, although clinicians may think patients with low or moderate disease activity suffer less organ damage, the potential exists for damage to accrue quickly, and therefore, we should reconsider the cumulative damage that may occur in a short period of time. In fact, data from a prospective analysis of Systemic Lupus International Collaborating Clinics International Research Network cohort patients reported that patients still accrued organ damage even with low/moderate disease activity. Despite early control of disease activity, organ damage increases over time (Figure 2).\(^5\)

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**Figure 2: Disease Activity and Organ Damage\(^5\)**

<table>
<thead>
<tr>
<th>Disease Activity Over 5 Years of Follow-Up (N=298)</th>
<th>Percentage of Patients With Organ Damage Over 5 Years of Follow-Up (N=298)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image_url" alt="Graph" /></td>
<td><img src="image_url" alt="Graph" /></td>
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</table>

SLEDAI-2K=SLE Disease Activity Index 2000.

\(*\text{SDI=The Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.}\)
What factors can contribute to increased SLE disease activity and subsequent organ damage?

Multiple factors result in the systemic immune dysregulation that leads to SLE. The etiology of the disease is unknown, but environmental triggers such as ultraviolet light, multiple genetic polymorphisms, and sex hormone interactions with female predominance are thought to have major roles in initiating the immune dysregulation that in turn leads to SLE. Immune dysregulation can result in tissue injury and damage in SLE (Figure 3). In SLE, defective clearance mechanisms fail to remove cellular material exposed through normal apoptosis. The failure of normal immune checkpoints leads to loss of self-tolerance.

Abnormal immune cells treat the body’s own cellular components like foreign pathogens and produce autoantibodies. SLE is characterized by the pathologic production of antibodies directed against self-antigens. Antinuclear antibodies are a hallmark of the disease, as is abnormal activation of B cells and T cells. Autoantibodies form immune complexes with self-antigens that get deposited in tissue, and defective clearance mechanisms allow these complexes to persist. The deposition of autoreactive B cells and immune complexes in tissues results in inflammation and can lead to organ damage. Uncleared cellular debris from damaged tissue stimulates additional immune response and inflammation, creating a vicious cycle of immune overactivity.

![Figure 3: Immune Dysregulation in SLE](image-url)

- DNA, Apoptotic Cells
- Defective Clearance Mechanisms
- Low Complement
- Antigen-Presenting Cells
- Cytokines
- Innate Immunity
- Adaptive Immunity
- T Cells
- B Cells
- Autoantibodies
- Immune Complexes
- Complement Activation
- Tissue Injury and Damage

mDC=myeloid dendritic cells; pDC=plasmacytoid dendritic cells; MØ=macrophages.
Given the significance of SLE disease consequences, early and accurate diagnosis is particularly important. What clinical factors, including variable disease course and disease manifestations, make diagnosis of SLE challenging?

The presentation and symptoms of SLE may vary and evolve over time (Figure 4).27

![Figure 4: SLE Symptoms Present Before Diagnosis or Ever (N=130)](chart)

- **Total Positive Before Diagnosis**
- **Total Positive Ever**

Diagnosis can be challenging due to similarity and overlap between SLE manifestations and multiple other conditions, and accurate diagnosis may take several years.3,7,8 Additionally, SLE may co-present with other autoimmune diseases.28 Unfortunately, no single test is sufficient to establish a diagnosis.3,7,8

The challenge of diagnosis is evident in data from a study of 263 patients with presumptive SLE who were referred to an autoimmune disease center: 48% of these patients were ultimately diagnosed with a different disorder.29

In addition to the clinical impact of SLE, what are other implications of SLE on healthcare services utilization and on patient-related issues such as work loss and impaired functionality?

SLE is associated with high rates of healthcare utilization.9 However, reductions in disease activity are associated with reductions in healthcare resource utilization and costs.30 Employed patients with SLE have greater work absenteeism, lost wages, and work disability than the general population.31,32 In a 2013 study, hourly employees with SLE reported losing an average of $346/week due to their condition.31 Work loss is a common consequence of SLE.10 In a cross-sectional study of 143 ambulatory patients with SLE, 42.7% of patients reported a formal work disability over an average of 9.2 years’ disease duration.32 In a longitudinal cohort study conducted between 2002 and 2009, 33% (160/484) of patients stopped working during the 4-year study period.10

In addition to increased healthcare resource utilization and decreased ability to work, patients with SLE have impaired function affecting multiple aspects of their daily lives (Figure 5). In a prospective study of 829 patients with SLE, 91% had ≥1 valued life activity affected by SLE, and 49% were unable to perform ≥1 valued life activity.33 In my opinion, it is important for practitioners to understand this devastating impact on patients’ daily lives.

**CNS**=central nervous system.

*Length of follow-up ranged from 9.4 years prior to diagnosis to 6 years post diagnosis.27
What were the key findings of a survey conducted with SLE patients, their supporters who provide patient care, and rheumatologists, that provided insights regarding patient experiences with this condition? What opportunities exist to enhance communication between SLE patients, supporters, and healthcare providers?

A GfK Roper North America survey* of 957 members of the lupus community, including patients, family members and/or friends, and rheumatologists, revealed a serious gap between what patients experience and what they are willing to share with others, including their rheumatologists. Data from the survey indicated communication gaps about symptoms between doctors and patients: 52% of patients with lupus reported they minimized their symptoms when speaking to their physicians, and 53% of doctors believed that patients were open and honest with them about their symptoms. However, 72% of physicians who participated in the survey disagreed that patients tend to underreport their symptoms. In my clinical experience, I agree that the communication challenges are 2-sided: patients may underestimate their symptoms, and clinicians may overestimate how well patients’ symptoms are being managed.

I feel that effective communication always poses a clinical challenge, particularly in a disease like lupus where clinicians cannot rely on test results alone and instead need to continually evaluate their patients’ level of function.3 I find that asking questions to create a dialog is important, and questionnaire tools such as the Lupus Checklist from GSK are available for this purpose. Clinicians should also ensure that their patients with SLE understand that they may experience different symptoms at different times.28 Because symptoms and disease activity can wax and wane, patients must be made aware that they may not experience linear improvement during the course of their disease.3 In my practice, I try to leave communication pathways as open as possible in the available time during office visits. I recommend that family members participate in appointments, because they may provide information the patient does not. Patients should also be encouraged to contact the clinician’s office between appointments if concerns arise. Additionally, I make patients aware of local and online support groups, seminars and educational opportunities. I find it can be helpful to use a multidisciplinary approach in the management of patients with SLE, which includes recommending counseling for patients dealing with interpersonal and family issues due to the unpredictability of their disease or who are concerned about passing on the potential for SLE to their children. I also give patients direction on exercise and nutrition.

*Data from the 2011 National Burden of Lupus survey funded and developed by GSK. This survey included 957 people in the lupus community—502 people who reported being diagnosed with SLE, 204 supporters (family members or friends) of people with lupus and 251 rheumatologists.34
References
34. Data on file. GSK group of companies. Research Triangle Park, NC.

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