Incidence of Cutaneous Lupus Erythematosus, 1965-2005

A Population-Based Study

Olayemi Durosaro, BS; Mark D. P. Davis, MD; Kurtis B. Reed, BS; Audrey L. Rohlinger, BS

Objectives: To assess trends in the cutaneous variants of lupus erythematosus (CLE) and to ascertain the incidence of CLE over the past 4 decades.

Design: Retrospective population-based study.

Setting: Community-based epidemiology project.

Patients: All Olmsted County, Minnesota, residents with any subtype of CLE between January 1965 and December 2005.

Main Outcome Measures: Incidence of CLE and disease progression to systemic LE (SLE).

Results: A total of 156 patients with newly diagnosed CLE (100 females and 56 males) were identified between 1965 and 2005. The incidence rate (age and sex adjusted to the 2000 US white population) was 4.30 (95% confidence interval [CI], 3.62-4.98) per 100,000. The age- and sex-adjusted prevalence as of January 1, 2006, was 73.24 (95% CI, 58.29-88.19) per 100,000. Nineteen patients with CLE had disease progression to SLE: cumulative incidence at 20 years, 19%; mean (SD) length to progression, 8.2 (6.3) years. Compared with a previously reported incidence of 2.78 (95% CI, 2.08-3.49) per 100,000 for SLE among Rochester, Minnesota, residents in 1965 through 1992, the incidence of CLE in Rochester was 3.08 (95% CI, 2.32-3.83) per 100,000 in 1965 through 1992.

Conclusions: The incidence of CLE is comparable to the published incidence of SLE. Our findings double the incidence of the root designation of the disease process known as LE (SLE and CLE).

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Author Affiliations: Mayo Medical School, College of Medicine (Ms Durosaro and Mr Reed), Department of Dermatology (Dr Davis), and Division of Biomedical Informatics and Biostatistics (Ms Rohlinger), Mayo Clinic, Rochester, Minnesota.

Lupus erythematosus (LE) represents a disease entity that is described by very specific clinical findings and distinct patterns of both cellular and humoral immunity.1 Clinical manifestations of LE have been shown to range from mild effects, such as disease limited to the skin in cutaneous LE (CLE), to the serious and possibly life-threatening manifestations that can be found in acute systemic LE (SLE).1 Systemic LE is defined on the basis of the 1982 criteria of the American College of Rheumatology.2 Cutaneous LE is defined as isolated cutaneous lupus lesions occurring in the absence of significant evidence of SLE. Tebble and Orfanos3 have suggested that the incidence of cutaneous variants of LE might be 2 to 3 times that of SLE. To investigate this possibility, we analyzed a community-based population of patients with cutaneous variants of LE from Olmsted County, Minnesota, over a 41-year period. To our knowledge, no population-based epidemiologic studies have reported the incidence of isolated CLE. We aimed to assess trends in the cutaneous variants of LE and to ascertain the incidence of CLE over the past 4 decades.

This study was approved by the Mayo Clinic institutional review board, Rochester, Minnesota. From the Rochester Epidemiology Project, we obtained all inpatient and outpatient medical records for residents of Olmsted County (which includes the city of Rochester) to use for our review.4,5 This computerized index system contains medical diagnoses that have been made at various health care facilities in the county, such as clinics, hospitals, and nursing homes, or made at autopsies. The system, thereby permits efficient retrieval of information for detailed review.
Diagnosis of all forms of CLE was determined by clinical, serologic, histopathologic, and immunopathologic findings. Date of diagnosis was determined as the date of fulfillment of criteria for subtype definition.

Age- and sex-specific incidence rates were estimated assuming that the entire population of Olmsted County from 1965 through 2005 was at risk. The numerator was the number of incident cases during the period. The decennial census data from 1965 through 2005 were used to determine the denominator. To determine the prevalence, the number of prevalent cases as of January 1, 2006, was divided by the Olmsted County population on that date. The population structure of US whites in 2000 was used for age and sex adjustment. Study data on CLE were compared with previously published data for SLE (strictly defined) from a study of Rochester residents (as opposed to all Olmsted County residents).8 Ninety-five percent confidence intervals (CIs) for the incidence rates were calculated assuming a Poisson error distribution. Progression to SLE was estimated using the Kaplan-Meier method.

### RESULTS

**PATIENT CHARACTERISTICS**

Search of the Rochester Epidemiology Project database identified 683 medical records for review. Among these, 527 patients were excluded because (1) they did not meet the criteria set for the subtypes of CLE or the diagnosis was made before 1965 or after 2005 (n=169); (2) they were diagnosed as having possible SLE (n=344); or (3) they had drug-induced LE (n=14). Therefore, the cohort included 156 patients with CLE (100 females and 56 males) with first diagnosis between 1965 and 2005. The final diagnosis of CLE in all cases was made by a dermatologist.

The mean (SD) age at diagnosis was 48.5 (16.2) years (median [range], 47.4 [14.5-89.2] years). The mean (SD) time from diagnosis of CLE to last follow-up pertinent to dermatology was 3.7 (5.2) years.

### INCIDENCE, PREVALENCE, AND PROGRESSION

The incidence rate of CLE, age and sex adjusted to the 2000 US white population per 100 000, was 4.01 in 1966 through 1975, 3.03 in 1976 through 1985, 5.54 in 1986 through 1995, and 3.97 in 1996 through 2005 (Table 1). The incidence of CLE in Olmsted County during the entire period, 1965 through 2005, was 4.30. The overall female to male ratio of CLE from 1965 through 2005 was 1.79:1. However, on comparison between sexes by decade, the incidence of CLE from 1966 through 1975 was approximately the same in males and females, whereas the other 3 decades showed an apparent female predominance (Table 1 and Figure 1).

Of the 156 patients with CLE, 129 had CDLE, 23 had SCLE, 3 had lupus panniculitis, and 1 had bullous LE. The age- and sex-adjusted incidence rates were 3.56 per...
100,000 for CDLE and 0.63 per 100,000 for SCLE (Table 2). Among the patients with CDLE, the incidence rate was 2.52 for the localized form and 1.04 for the generalized form (Table 2). Among the patients with SCLE, the incidence was 0.17 for the annular type and 0.46 for the psoriasiform type (Table 2). For the rare subtypes lupus panniculitis and bullous LE, the incidence rates were 0.07 and 0.03, respectively (Table 2). We found an incidence rate of 0.38 in patients with drug-induced LE (Table 2). The age- and sex-adjusted prevalence of CLE on January 1, 2006, was 73.24 per 100,000.

To directly compare our incidence data for CLE with the corresponding data for SLE, we used data obtained from a previous study by Uramoto et al. The incidence of SLE in Rochester from 1965 through 1992 was 2.78 per 100,000 (95% CI, 2.08-3.49). In comparison, from our data we calculated the incidence of CLE in Rochester during the same period (1965-1992) to be 3.08 per 100,000 (95% CI, 2.32-3.83) (Figure 2).

Nineteen of the 156 patients (12.2%) had disease progression to SLE; the mean (SD) time from CLE diagnosis to SLE progression was 8.2 (6.3) years. Of these 19 patients, 9 had the localized discoid subtype of CLE, 4 had the generalized discoid subtype of CLE, 2 had the lupus panniculitis subtype of CLE, and 4 had the psoriasiform subtype of CLE. By Kaplan-Meier analysis, the cumulative incidence of SLE among patients who had a diagnosis of CLE was 5% at 5 years, 10% at 10 years, 15% at 15 years, 19% at 20 years, and 23% at 25 years (Figure 3).

Lupus erythematosus was originally recognized as having different forms by O’Leary in 1954. Subsequently, Gilliam and Sontheimer proposed a general classification of the distinct subtypes of CLE in 1981. Our study showed the incidence of CLE—including SCLE, CDLE, bullous LE, and lupus panniculitis—to be 4.30 per 100,000 from January 1965 through December 2005, with a female predominance and an average age at onset of 48.5 years. Also, the incidence rate of CLE was found to be highest overall in 1986 through 1995.

To our knowledge, no previous studies in the literature have investigated the incidence of all forms of CLE. Previous studies have reported SLE incidence rates of between 1.5 and 7.6 per 100,000. Although we are not able to make a direct comparison to SLE incidence rates,
a study by Uramoto et al showed the incidence of SLE from 1950 to 1992 in Rochester to be 3.06 per 100,000. To compare the results of the Uramoto and colleagues’ study on SLE incidence with those of our CLE study, we calculated the incidence of CLE and SLE in Rochester from 1965 through 1992. Our calculations showed the incidence of CLE to be slightly higher than that of SLE in the same period.

In the decadal analysis, our data showed the incidence of CLE to be somewhat stable over the past 40 years. In contrast, the incidence of SLE in the same period obtained from the study by Uramoto et al was noted to be increasing. This increase could be attributed to early diagnosis of SLE, aided by the well-recognized criteria for SLE definition as compared with the criteria set for CLE.

The prevalence of CLE as of January 2006 was 73.2 per 100,000. A previously reported prevalence of SLE in the continental United States by Hochberg ranged between 14.6 and 50.8 per 100,000 persons, whereas Tebbe and Orfanos reported an incidence between 17 and 48 per 100,000. Our results indicate a higher incidence and prevalence of CLE than those reported for SLE during the same period in these previous studies, which emphasizes the importance of recognizing these cutaneous forms of LE in the clinical setting to achieve better patient outcomes.

A study by Popovic et al showed the incidence of SCLE in Sweden to be 0.7 cases per 100,000. Although our results (0.63 per 100,000) are similar to the incidence of SCLE in Sweden, they cannot be directly compared because the Swedish study included only 1996 through 2002 and had a larger population than that of Olmsted County. The incidence of SCLE in Popovic and colleagues’ study may be slightly higher because serologic tools such as tests for the Ro and La antibodies have only been available in the past couple of decades. Also, the definition of SCLE by Sontheimer et al was made in 1979, which suggests that some cases in our study from earlier decades may have been misdiagnosed. The incidence of annular SCLE in our study (0.17 per 100,000) was lower than that of psoriasiform SCLE (0.46 per 100,000).

The incidence of CDLE in our study was 3.56 per 100,000 persons: 1.04 per 100,000 for the generalized form and 2.52 per 100,000 for the localized form. To our knowledge, no results have been published with which to compare our results. However, the incidence of the discoid subtype was similar to the SLE incidence reported by Uramoto et al. Our results do not directly support a statement by Tebbe and Orfanos that suggested that the incidence of CDLE is 2 to 3 times the incidence of SLE. The incidence rate of CDLE obtained in our study is probably an underestimation: LE is disproportionately diagnosed in Asian and African American patients, and the population of Olmsted County is predominantly white and not ethnically diverse.

Lupus panniculitis is a rare form of CLE. As would be expected, the estimated incidence was only 0.07 per 100,000 in our study. Another rare subtype is bullous LE, the incidence of which was 0.03 per 100,000 in our study. Both of these subtypes are referred to as nonspecific LE because their histopathologic characteristics are not distinct for LE and may be seen as features of other disease processes.

Cutaneous LE had a female predominance during the last 3 decades of our study, a finding that might suggest that SCLE, which was first described in 1979 by Sontheimer et al, is a predominantly female form of LE-specific skin disease. However, before 1979, many patients with SCLE were classified under the O’Leary designation of “disseminated discoid lupus,” and others were not classified as having a form of CLE at all. Therefore, it is possible that during the later phases of our study, more cases of SCLE were being diagnosed, producing an enrichment of female sex in the overall population of patients with CLE.

Overall, CLE is regarded as a variant of SLE with a less severe course and a better prognosis. However, CDLE and SCLE last for many years and may lead, like SLE, to severe work-related disability and limited life quality. Also, in a small proportion of patients with CLE, SLE develops during the course of their disease, which implies a considerable amount of medical management and costs for the community. Early recognition of patients with CLE who are at risk for SLE development and preventive measures against disease-triggering factors are important tasks for physicians of patients with CLE. Signs of nephropathy, elevated antinuclear antigen titers, and arthralgias may serve as predictors for transition into SLE. In our study, disease in 12% of the patients with CLE progressed to SLE, with the average time to progression being 8.2 years. A 1959 case series by Scott and Rees studying the relationship between SLE and DLE reported that most cases of DLE progressed to SLE within 2 years. The discrepancy between our epidemiologic study and their report could be a result of earlier diagnosis of DLE in more recent years. Furthermore, early diagnosis often leads to early management, which might also stall the progression of cutaneous forms of LE to SLE, thereby explaining the difference in results between the 2 studies. Our findings have important implications for physicians and illustrate the importance of follow-up in this population of patients. For future studies, it will be helpful to investigate the characteristics of the patients whose disease progresses to SLE. Our study did not address the incidence of CLE in the context of patients diagnosed as having SLE. It would be beneficial for future studies to address this interesting question.

Our study had several limitations. The Rochester Epidemiology Project database is limited in that diseases are entered only after they are recognized by the physician and are subsequently recorded before they are retrieved for research purposes. As a result, if, for any given patient, a disease entity has not been brought to medical attention or no documentation of the disease exists, that case of the disease would not be identified. Also, it is important to recognize that the racial profile of Rochester is not representative of the United States—certain racial and ethnic groups are underrepresented in the city’s population. According to the 2005 US census, the population of Olmsted County was 89.9% white, 5.2% Asian, 2.8% Hispanic, 3.6% African American, and 0.3% American Indian and native Alaskan or other ethnic group. Furthermore, making the diagnosis of CLE...
involves the clinical judgment of the physician; therefore, there is room for error because of the subjective nature of clinical diagnosis.

It is important also to consider the possible effect of latitude on the incidence of CLE in our study, despite inadequate data to support this idea. The skin lesions in CLE are photosensitive; therefore, disease prevalence might be higher in areas of the country with more ambient sun exposure. In the same vein, disease susceptibility may also be different among whites. As a result, it is important to note that Olmsted County has a high prevalence of whites of Scandinavian descent, which could also affect the data. Finally, the study had some limitations because of its retrospective nature and the low population of Olmsted County, which cannot be compared with the average city in the United States.

In conclusion, the results of our study revealed that the incidence of cutaneous forms of LE is comparable to the published incidence of SLE. The high incidence of CLE emphasizes the importance of following up these patients and recognizing the clinical presentation of disease. Although the cutaneous form of LE has a more indolent course, monitoring the patient's disease is still essential because the disease in some cases progresses to the systemic form, which has a more dire prognosis. Early recognition of CLE by the physician translates to early management and, hopefully, to preventing transition of the disease to the systemic form.

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Correspondence: Mark D. P. Davis, MD, Department of Dermatology, Mayo Clinic, 200 First St SW, Rochester, MN 55905 (davis.mark2@mayo.edu).

Author Contributions: Ms Durosaro, Dr Davis, and Mr Reed had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Davis and Reed. Acquisition of data: Durosaro and Davis. Analysis and interpretation of data: Durosaro, Davis, and Rohlinger. Drafting of the manuscript: Durosaro, Davis, and Reed. Critical revision of the manuscript for important intellectual content: Durosaro, Davis, and Rohlinger. Statistical analysis: Rohlinger. Obtained funding: Davis. Administrative, technical, or material support: Davis. Study supervision: Davis.

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REFERENCES