THE SYSTEMIC LUPUS INTERNATIONAL COLLABORATING CLINICS (SLICC) GROUP

SLICC

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SLICC INTERNATIONAL INCEPTION COHORT STUDY OF SLE

A YEARLY NEWSLETTER FROM YOUR PARTNERS IN LUPUS RESEARCH

BACKGROUND

The Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) is an international group of rheumatologists and lupologists who have been working together on lupus research since 1991. They have collaborated to develop standardized outcome measures so that physician-researchers can better measure and describe the course of lupus and its response to new therapies. These outcome measures are now widely used by lupus researchers throughout the world and allow comparisons of patient groups among centres.

REGISTRY FOR ATHEROSCLEROSIS

It is known that women with lupus develop coronary artery disease (atherosclerosis of the coronary arteries) at a higher rate and at an earlier age than the general public. In addition, women with SLE develop clinical conditions such as heart attack and angina up to five times more often than the general public.

The SLICC group has developed the Registry for Atherosclerosis (SLICC-RAS) with the goals to:

- Study the prevalence and nature of early atherosclerotic coronary artery disease (CAD) in lupus
- To identify related risk factors and to look at the contribution of disease and therapy to the presentation of these risk factors
- Develop intervention studies to change risk factors for the development of CAD including educational programs and possible drug therapies.

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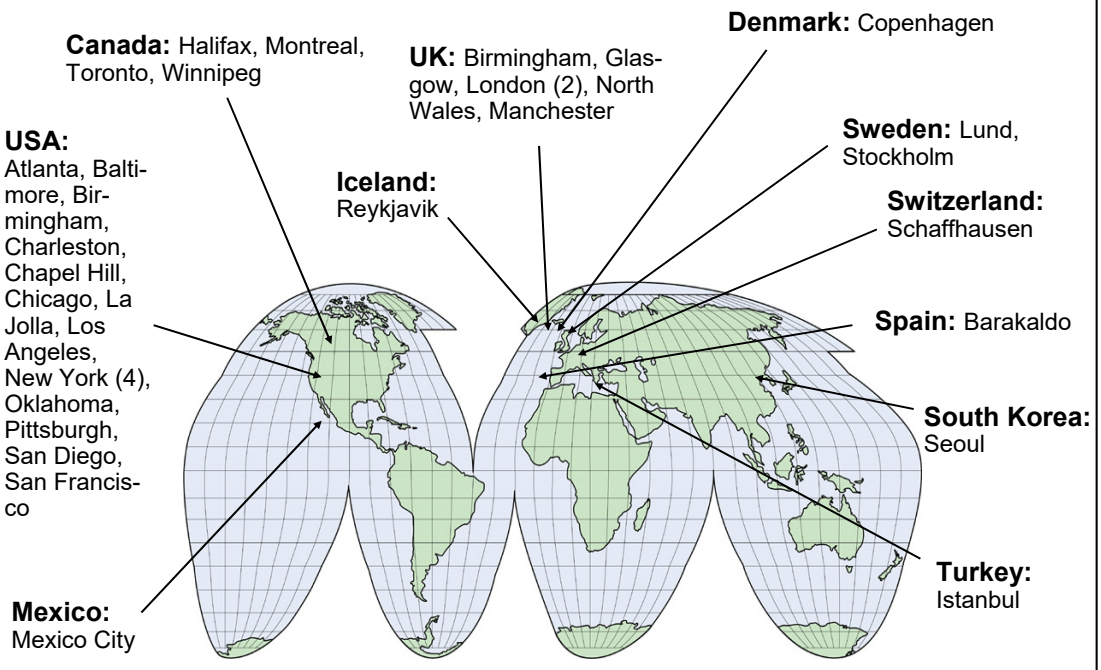
SLICC RECRUITMENT SITES FROM AROUND THE WORLD

The SLICC Registry is a multinational study with sites all over the world. As a participant in this study, you join 1663 other lupus patients from 11 countries and 33 centres around the world.

We are very thankful to you and the time you have contributed to participate in this study. We are one step closer to answering important research questions regarding lupus and CAD.



NEW CHANGES TO YOUR PARTICIPATION!

We believe the SLICC registry for Atherosclerosis in lupus is an extremely important resource to aid in the understanding of lupus and heart disease. We also recognize the registry should be maintained as a long term resource that can be accessed by SLICC clinician scientists to continue lupus research.

Our original goal for the registry was to enroll 1650 patients and follow these patients for a 10 year period. We are happy to report that many of you are just beginning to reach the 10 year follow-up mark. We have now extended our follow up from 10 years to as long as you wish to participate. We believe the data collected on patients from diagnosis onwards provides a wealth of information for lupus researcher. Extending the follow up period will allow us to study risk factors and outcomes throughout the entire course of your disease.

We also increased our recruitment goal from 1650 participants to 1800 participants. The SLICC group hopes to reach the new recruitment target by the end of 2011.

PATIENT REMINDERS

Please stay in touch…

The SLICC study is designed to follow participants for their entire lifetime, and a lot can change in a lifetime! Please be sure to provide your participating rheumatologist with updates if you move or change your phone number so you can be reached when it is time for your annual follow up visit. If you have moved too far away to attend your annual follow-up visit at your recruitment site, we would still appreciate being able to contact you by telephone to collect information.

ACTIVITIES TO DATE

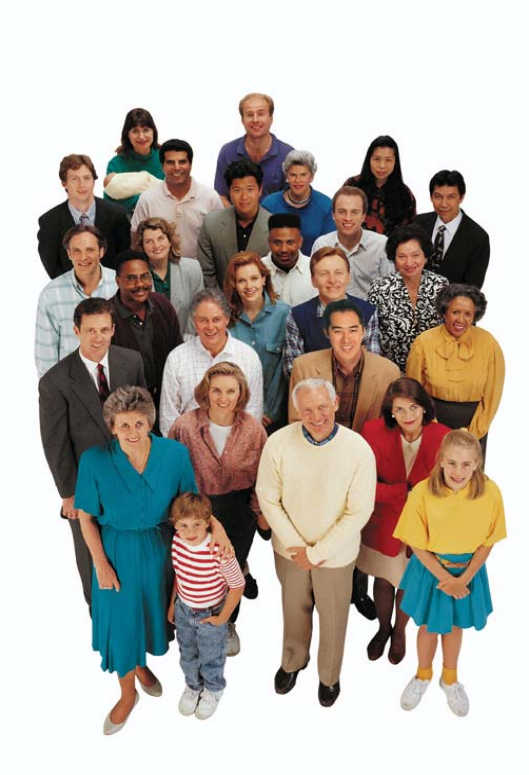
The following table provides some descriptive features of the 1663 SLICC participants enrolled:

Number of Female Participants	**1486 (89%)**
Race (%) **Caucasian / Black / Asian / Hispanic / Other**	**49 / 16 / 16 / 15 / 4**
Average Age at Lupus Diagnosis	**35**
Marital Status (married or common-law)	**756 (45%)**
Education (Post secondary)	**1024 (62%)**

What We Have Learned So Far

SLICC Members have been working hard to answer many research questions using the information collected in the first 8 years of follow-up. To date we have published 8 manuscripts in Scientific Journals. We have included a summary below of some of the new research findings that were presented at the National Scientific Meeting of the American College of Rheumatology (ACR) and International Lupus Meetings that took place in 2010.

Differences in Risk Factors by Ethnicity and Country of Residence



Although lupus can affect anyone, it is known that people from certain ethnic groups are at a higher risk to develop lupus. It is also known that the severity of lupus varies among different ethnic groups. The SLICC group wanted to look at how ethnicity and country of residence would influence the presence of lupus and heart disease risk factors.

A total of 1593 SLICC patients were studied. It was found that disease activity was higher among Asians and Hispanics and also in the countries in which they are a majority. It was also demonstrated that metabolic syndrome (a diabetic like state) was higher in Mexican and Hispanic patients. Hypertension did not show any differences according to patient country of residence, but was highest among Black patients. Permanent damage related to disease was not related to ethnicity, but was found to be higher in the United States as compared to other countries.

The differences in the presence of lupus and heart disease risk factors among different lupus patient populations may allow researchers and treating physicians to be more aware of potential risk factors for their patients.

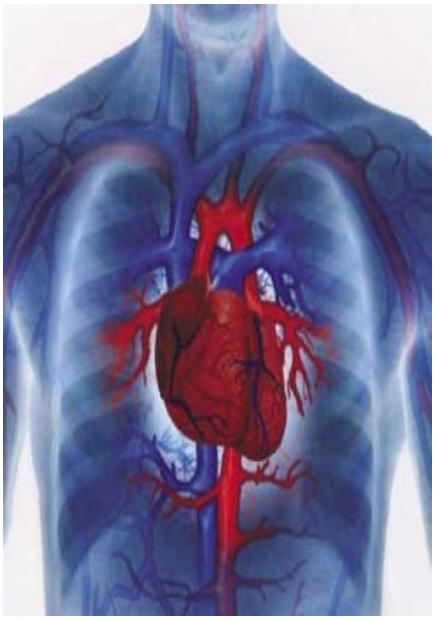
Risk Factors Associated with Survival and Mortality

Another study was presented at the ACR regarding the survival and causes of death among lupus patients. Over a 10 year period of follow up on 1593 SLICC patients, it was found that survival improved drastically. The small amount of deaths that did occur in the first 10 years of observation were caused by heart disease, lupus and sepsis (the presence of bacteria or poisons in the blood).

There were some differences seen among the patients that survived in comparison to the patients that died. In the patients that survived it was demonstrated that they were younger at the age of diagnosis of lupus, had no history of heart disease and had used a smaller amount of steroids and immunosuppressive drugs. We hope these noted differences in survival and mortality of lupus patients will help treating physicians improve patient care by identifying preventative therapies that can be tailored to individual patients.

Description of Atherosclerotic Vascular Events Over an 8 Year Period

A large number of SLICC participants have now reached the 8 year follow up mark. This has allowed us to begin to look at long term outcomes associated with heart disease. At the most recent ACR meeting, material was presented regarding the number of vascular (arteries, veins and capillaries that carry blood to and from the heart) events that took place in the SLICC patient population within the first 8 years after diagnosis.



In the first 1593 patients 134 vascular events occurred in 96 patients. These events included: heart attack, angina, heart failure, stroke, pacemaker insertions among other events. Just under half of these events were due to atherosclerosis.

Comparisons were made between patients who had atherosclerotic events to patients that did not. We found that patients who had vascular events due to atherosclerosis were more likely to be male, older age at diagnosis, more frequently obese and often had hypertension.

These finding may help physicians develop treatment plans that can be catered to patients that might be in these higher risk groups. Further research is required to look at what treatment options may work best for these patients.

Neuropsychiatric Systemic Lupus Erythematosus (NPSLE) SLICC Study

Involvement of the nervous system by SLE is a concern for many patients with lupus. Although well recognized, there are many unanswered questions about this aspect of lupus. For example, how common are nervous system events and how many of them are due to SLE, do they become more frequent over time, how do they impact on quality of life, can they be predicted and what is the best treatment are all areas requiring further research. These and other questions are being studied within the NPSLE SLICC study which is coordinated by Dr. John Hanly and his research team at Capital Health and Dalhousie University in Halifax, Nova Scotia. Since 2002 this study has received funding from the Canadian Institutes of Health Research and has the following objectives:

- To determine the frequency of overall NP events in SLE patients and to determine which ones are due to lupus or to other causes;
- To determine the short and long-term impact of NPSLE as assessed by its' effects on patients quality of life, outcome of events, overall damage to the nervous system and patient survival;
- To determine if various antibodies produced by the immune system in lupus patients (e.g. those which react against brain tissue or cause blood clots within the brain) are associated with specific NP events.

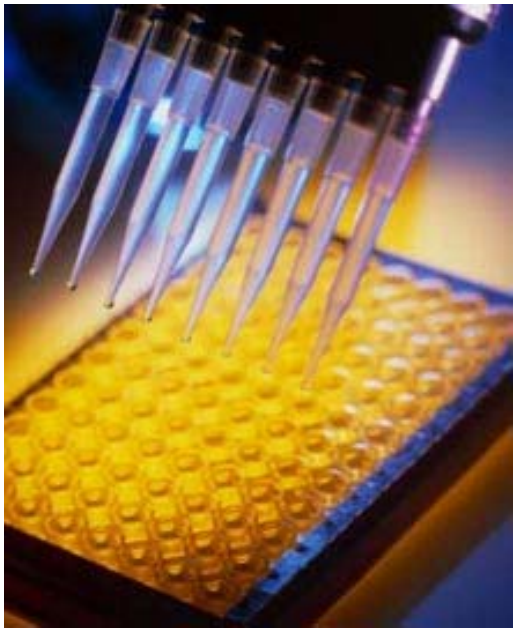
FINDINGS SO FAR FROM THE SLICC NPSLE STUDY

Enrollment into the study continues and is currently up to 1,669 patients. The results of the studies so far have provided important information related to the diagnosis and outcome of NPSLE. These results have been reported at international scientific meetings and in high quality scientific medical journals.

Measurement of Change in NP Status in SLE Patients

One of the difficulties in studying NP events in SLE patients has been the lack of a valid measurement of change, to detect improvement or worsening, over time. This is particularly problematic in NPSLE as there are a wide variety of ways in which the nervous system can be affected in lupus patients. Thus, a study was undertaken within the NPSLE SLICC cohort to see if a patient report questionnaire on health status and quality of life called the "SF-36" could be used as a measure of change in NP status. To do this, 274 patients who had at least one NP event were studied and the change in NP status over one year as assessed by a physician was compared to the change in SF-36 questionnaire scores. The results indicated that the SF-36 summary and subscale scores, in particular those related to mental health, are closely correlated with the clinical outcome of NP events. These results will provide researchers studying NPSLE with a valid outcome measure for measuring change in NP status over time and allow them to reliably assess the effects of different treatments.

Autoantibodies May Predict Subsequent NP Events in SLE Patients



As an initial attempt to find ways of identifying which patients are more likely to develop nervous system events related to lupus, 1,047 patients enrolled in the SLICC cohort were examined upon enrollment into the study cohort for the presence of up to five lupus auto-antibodies. Patients were then assessed over several years for the occurrence of NP events. The results indicated that the presence of two lupus auto-antibodies (lupus anticoagulant and anti-ribosomal P antibodies) identified around the time of diagnosis of SLE is associated with an increased risk for certain types of NP events (stroke and psychosis respectively) over the ensuing years. The numbers of patients with these antibodies and NP events was quite small, so these results will acquire confirmation as the study progresses.

FUTURE PLANS

Metabolic Syndrome Study

The Canadian Institutes of Health Research awarded funding for a study examining Metabolic Syndrome in patients with SLE which will use data from the SLICC Registry. Premature heart disease is a significant problem in patients with lupus. We have found that a pre-diabetic state (the metabolic syndrome) is more common in SLE but the causes are unclear. This pre-diabetic state is itself an important risk factor for the development of future heart disease. We suspect that both steroid therapy and inflammation related to the condition together cause this problem to develop. This study will examine what factors in SLE over time increase the risk of developing the metabolic syndrome. In particular, we wish to study whether certain SLE patients inherit a greater sensitivity to steroids that increase their risk of developing this pre-diabetic state. This study will allow us to better understand the risks associated with steroid therapy in SLE and to help us better target steroid doses on an individual basis. It will also help us suggest ways to reduce the risk of future heart disease in SLE. As noted previously this study requires that we get fasting samples from patients. For this reason your doctor may ask you to fast for 12 hours before coming for your clinic visit.

NP-Manifestation Studies

Due to the large number of patients enrolled in the cohort, and the increasing duration of follow-up, we are now able to examine individual NP manifestations such as seizures, mood disorders and other events. These studies will allow us to determine the outcome of specific types of nervous system disease and subsequently improve the ways in which these are monitored and treated. The results of the studies to date have already provided valuable insight into this important manifestation of lupus. Additional work over the next few years will improve our understanding and treatment of this condition which will be to the benefit of all patients with and without NPSLE.

Lupus Nephritis Study

Lupus nephritis is a kidney disorder that is a complication of SLE. SLE may damage different parts of the kidney, leading to kidney damage and in some cases kidney failure. Lupus nephritis has been reported in 28-73% of the lupus population and is more frequent and severe in certain ethnic groups. Despite improvements in the range and efficacy of immunosuppressive therapy over the past 20 years, nephritis remains a serious complication of SLE that is associated with morbidity and cost to patients and health care systems worldwide.

The SLICC group aims to look at data related to kidney function on patients participating in the SLICC registry. We hope to gain knowledge regarding lupus nephritis in order to predict the long-term clinical outcomes and health care utilization in patients with lupus nephritis.

PARTICIPATNG SLICC RECRUITMENT CENTRES

Do you have a question or do you want to reach the research staff at your SLICC Recruitment site to stay in touch? See below for the names of participating rheumatologists and their contact numbers.

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Dr. Sang-Cheol Bae, Hanyang University College of Medicine**, Seoul, Korea (2) 290-9203**

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Dr. Ann Clarke & Dr. Sasha Bernatsky, Montreal General Hospital**, Montreal, Canada** (514) 934-1934 x 44251

Dr. Mary Ann Dooley, University of North Carolina, **Chapel Hill, USA** (919) 966-4191

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Dr. Ronald van Vollenhoven, Karolinska Hospital, **Stockholm, Sweden** (468) 5177-6077

Dr. Daniel Wallace, Cedars-Sinai Medical Center, **West Hollywood, USA** (310) 360-9197

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FUNDING OF THE SLICC REGISTRY FOR ATHEROSCLEROSIS: A TRULY COLLABORATIVE EFFORT

The SLICC Registry have been partially funded by a grant from the Canadian Institutes of Health Research. However, the registry could not continue it's operation without the generous support of the following patient groups:

Lupus Foundation of Ontario
New Jersey Chapter of the Lupus Foundation of America
Lupus UK
The Tolfo Family—Dance for the Cure Fundraiser
Western New York Chapter of the Lupus Foundation of America
Nashville Chapter of the Lupus Foundation of America
Long Island-Queens Chapter, Lupus Foundation of America
Lupus Ontario
The SLICC Registry has also been supported by donations from the Conn Smyth Foundation and the Lupus Flare Foundation

THE SLICC MEMBERS WOULD LIKE TO THANK THESE PATIENT GROUPS FOR THEIR EXTENSIVE SUPPORT.

The SLICC group continues to apply for funding from granting agencies for specific research projects, but our core operating costs for data and specimen collection are not normally funded through these grants. SLICC will continue to rely on the generous donations from our patient partners in support of this important work.