Welcome to the University of Toronto Lupus Clinic

The purpose of this newsletter is to provide our patients, their families and clinic supporters with information on the latest activities of the University of Toronto Lupus Clinic. We will include some background information about why the Lupus Clinic is special, updates on our Clinic staff and updates on some of our recent research activities.

We hope you find this publication useful.

What is Lupus?

Since there are continually new patients entering the Clinic, we will start by providing some basic information about the disease.

Most patients know that systemic lupus erythematosus (SLE) is considered an autoimmune disease. Under normal conditions, the immune system plays a key role in protecting the body from harmful agents such as viruses and bacteria; in SLE however, antibodies are directed against oneself.

In patients with SLE, the immune system produces a number of antibodies that react with cell components resulting in chronic inflammation in different parts of the body. Lupus strikes 1 in 1000 Canadians, mainly women in the child-bearing years.

About the University of Toronto Lupus Clinic

The Lupus Clinic was first established in 1970 as a patient care referral centre and was designed to promote expert care for patients with lupus, to train future rheumatologists and to facilitate research into this disease. There are now over 1600 patients registered in the Lupus Clinic, making it one of the largest centres for specialized lupus care and research internationally. Patients are referred to the Clinic from all areas of Ontario. A large proportion of patients are receiving their primary lupus care at the Clinic. Some patients are followed by their local rheumatologists, but continue to be followed in the Clinic at intervals.

Patients are evaluated by a physician, usually a rheumatology trainee, who is particularly interested in this disease. All patients are reviewed by one of the clinic directors (see page 2) either in person or by chart review. In this way, patients are evaluated in a standard way according to a specially designed format, which includes physical examination, blood and urine tests at each visit.

The Lupus Databank Research Program was established in 1987 with the fund raising assistance of volunteers, many of whom were patients at our Clinic. This databank has allowed for the long-term study of SLE to discern the natural history and response to therapy in this disease. Many important landmark studies have come from this databank.

For more information on our 40th anniversary celebrations including the Chrysalis Affair Fundraising Gala and Patient Symposium, please see page 3.
Members of the Lupus Clinic team include Clinic Directors, Drs. Paul Fortin, Dafna Gladman, and Murray Urowitz; associate staff rheumatologists and researchers Dr. Joan Wither and Dr. Carol Landolt-Marticorena; clinical research fellows and rheumatology trainees, clinic nurse, clinic phlebotomist, clinical trial nurse managers, research laboratory technicians, research associates and assistants, database programmers, data managers, biostatisticians and administrative staff.

**Dr. Murray Urowitz** is Director of the University of Toronto Lupus Clinic, Professor of Medicine, Senior Staff Physician, Toronto Western Hospital and Senior Scientist with the Toronto Western Hospital Research Institute. He is also Principal Investigator for the Systemic Lupus International Collaborating Clinics (SLICC) Registry for Atherosclerosis in SLE.

**Dr. Dafna Gladman** is Co-director of the University of Toronto Lupus Clinic, Professor of Medicine, and Senior Staff Physician, Toronto Western Hospital. Dr. Gladman is also the Director of the HLA Laboratory which is located on the 14th floor of the hospital and houses the Lupus DNA bank. Dr. Gladman is also Senior Scientist with the Toronto Western Research Institute.

**Dr. Paul Fortin** is Co-Director of the University of Toronto Lupus Clinic. He is a Professor of Medicine and Senior Staff Physician, Toronto Western Hospital. And Senior Scientist at the Toronto Western Research Institute. Dr. Fortin is Director of the Canadian Network for Improved Outcomes in SLE (CaNIOS) and Director of Clinical Research for the Arthritis Centre of Excellence.

**Dr. Joan Wither**, is a Senior Research Scientist with the Division of Genetics and Development of the Toronto Western Research Institute. Dr. Wither is a rheumatologist and basic scientist whose area of study is immune mechanisms that lead to the development of systemic autoimmune.

**Dr. Carol Landolt-Marticorena** is a staff rheumatologist and Assistant Professor of Medicine who in addition to seeing patients is a basic science researcher with specific interest in biomarkers for renal disease in SLE.

Drs. Wither’s and Landolt’s laboratories are located on the 14th Floor, Toronto Western Hospital where they carry out molecular studies in mice and humans working closely with the Lupus Clinic.
It is exciting to share with our patients an opportunity to be a part of a major milestone in the fight against lupus. On April 2, 2011, colleagues, patients, family and friends will gather at the Four Seasons Hotel in Toronto for the Chrysalis Affair to celebrate 40 years of the Lupus Clinic and Databank Research Program at the Toronto Western Hospital and recognize the contributions and accomplishments of Dr. Murray Urowitz.

The Lupus Clinic and Databank research program, established by Dr. Urowitz, is one of the largest such databanks in the world with more than 1,500 patients and over 38,000 clinic visits. The Clinic has allowed for numerous findings that have changed the way lupus is diagnosed and managed and has produced some of the world’s best lupus researchers and clinicians.

Dr. Urowitz’s teaching excellence is exemplified by his having won the outstanding clinical teacher award a remarkable 8 times. The research and commitment from Dr. Urowitz and the team at the Lupus Clinic has lead to improved tests and techniques for lupus diagnosis, better methods for living with the disease through the use of effective pharmacologic therapies and exceptional patient care. Dr. Urowitz’s life long contribution to lupus care and research was recognized by the Lupus Foundation of America last year with the Evelyn Hess Award.

This fundraising gala will help establish the Murray B. Urowitz Fellowships in Lupus Research at the Toronto Western Hospital. Please consider supporting this tribute and honouring Dr. Murray Urowitz by attending this event. Individual tickets are $750. If you are unable to attend, please consider making a donation or pledge that will help to provide the next generation of lupus researchers the opportunity to learn from the very best.

For more information on tickets and tables sales or to make a donation please contact the event manager, Amber Bernard, at 416.340.4800 ext 6279 or visit www.chrysalisaffair.ca.

Lupus Ontario Presents – SLE Update
Toronto Lupus Clinic - Lupus Research from Around the World
Sunday April 3, 2011
MaRS Centre Auditorium, 101 College Street, Toronto
12:30 Registration, Presentations 1:00 – 3:00 p.m.

Lupus Ontario is hosting a patient symposium on Sunday, April 3rd that will feature presentations from past Toronto Lupus Clinic trainees who will speak on their current research in lupus.

For more information on this event and to register please contact Lupus Ontario at: 1-877-240-1099 or (905) 415-1099 or online at www.lupusontario.org.
Education and Training for Future Care & Research

The Lupus Clinic is part of the University of Toronto Rheumatology Training Program and hosts several trainees from Canada and abroad who have completed their specialty training in rheumatology and who come to our Clinic to gain further training and expertise in the management of patients with SLE and in clinical research. The trainees are known as clinical research fellows and many of them are also pursuing advanced degrees in clinical or genetic epidemiology through the University of Toronto Institute of Medical Sciences. We will outline some of the clinical research fellows’ research projects in the next section of the newsletter.

In addition to the clinical research fellows, senior residents from the Rheumatology Training Program of the University of Toronto work in the Clinic for a period of six months as part of their rheumatology training. These fellows often go on to practice rheumatology in the community or pursue further research or academic postings.

Our Clinic encourages the participation in research of medical students at all levels of their training by participating in summer student programs and supervising research electives for general medical residents.

The Clinic has also been involved in the training of allied health professionals such as epidemiologists, biostatisticians, and psychology students. We also participate in the University of Waterloo co-operative education program for Health Science students and have close ties with the biostatistics programs at the University of Toronto and University of Waterloo.

Research Update

In this section of the newsletter we will provide a brief summary of results of a selection of our current research studies.

Improved Outcome Measures for use in Clinical Trials – Dr. Zahi Touma

Zahi Touma joined our program in 2007 after completing medical school in Kursk State University and Rheumatology training at the American University of Beirut. Zahi is in the process of completing a PhD in Clinical Epidemiology with the University of Toronto. His area of research is in the development of improved outcome measures in lupus. In recent years there have been several new drugs that have been tested for the treatment of SLE, but only one drug has shown a moderate benefit in clinical trials. Many investigators believe that one reason for the failure of new drugs is the lack of appropriate outcome measure. After extensive background research Zahi went on to develop a new instrument that would measure partial, but significant improvement in SLE which differed from the instruments currently in use. The instrument he developed is called the SLEDAI-2K-50 (SRI-50) and it is a data retrieval form completed by the physician. Zahi went on to carry out studies testing the reliability of this instrument in the Clinic setting and has presented his findings at several scientific meetings. The first paper has now been accepted for publication. Zahi has also developed a web-based training module for physicians to learn how to use the SRI-50.

Patient reported quality of life measures are also an important tool in testing the effectiveness of new drugs. With the assistance of all of our patients who complete these questionnaires at their clinic visits, Zahi has been testing a newer lupus-specific quality of life measure against the standard measure used across all diseases known as the SF-36. Analysis has shown that there is no strong benefit to using this new questionnaire over the SF-36, but this work is ongoing.
Serologically Active Clinically Quiescent SLE – Dr. Amanda Steiman

Dr. Amanda Steiman is currently a second year rheumatology trainee who began doing research in the Lupus Clinic in her second year of internal medicine residency. Amanda’s research looks at a sub-group of patients who have achieved clinical remission of their disease for at least two years, but continue to show elevated levels of auto-antibodies in their blood during that time. This subset of patients is referred to as Serologically Active, Clinical Quiescent (SACQ). Amanda used the extensive data collected over time in our database to see if patients who had extended periods of clinical inactivity and went on to experience a flare showed any difference in the autoantibody profiles prior to the flare. In other words was there a way to predict flare based on changes in autoantibody profiles. Her work would indicate that a change in autoantibody profiles was not predictive of flare. Throughout her residency and rheumatology training Amanda has continued to carry out research looking at associated clinical and laboratory features of SACQ patients. She presented her work as an oral presentation at the American College of Rheumatology National Scientific meeting in 2009 and was the recipient of the Ian Watson award for best lupus research paper presented at the Canadian Rheumatology Association meeting in February 2010 for her work.

We are very pleased that Amanda has chosen to spend further years of clinical research fellow with our Clinic and obtain a graduate degree from the Institute of Medical Science. She has developed a proposal for a further study which will test other blood tests (or biomarkers) that may better predict when a patient is going to flare which she will carry out during this extended period of training.

Measurement of Early Coronary Artery Disease – Lihi Eder

Dr. Lihi Eder completed her rheumatology training in Israel and came to Toronto to work with Dr. Gladman in the Psoriatic Arthritis Program and complete a PhD in Clinical Epidemiology. Lihi also sees patients in the Lupus Clinic and has carried out a study looking at different methods of assessing early atherosclerosis (thickening of the lining of the arteries) using ultrasound. It is known that patients with lupus are at increased risk for developing coronary artery disease at an earlier age than the general population. An early indicator of atherosclerotic disease is the deposit of plaque in the lining of the arteries which can be detected by ultrasound examination of the coronary arteries of the neck. Previously researchers have used measurement of the thickness of the artery as a measurement of the degree of atherosclerosis. Lihi set out to test if a newer technique of measuring the area of the artery that is affected by plaque would be a better indictor of early atherosclerotic disease than the standard measure of carotid artery thickness.

Lihi performed coronary artery ultrasound in two groups of lupus patients, those with a previous history of coronary artery disease (those who had events such as heart attack, angina or stroke) and those with no history coronary artery disease. Lihi reported the preliminary results of this work at the American College of Rheumatology National Scientific Committee meeting in October of 2010. The early analysis suggests that measurement of plaque area was better associated with patients with known coronary artery disease. This would indicate that this technique may be a better measure for early identification of those patients who may go on to have coronary artery disease in future. The objective of this area of research is to find ways to identify patients early who may at increased risk for coronary artery disease in order to take preventative steps. Lihi’s work is ongoing.
The Lupus Nephritis New Emerging Team (LuNNET) – An Update

LuNNET is now in its fifth year of operation with a total of 248 patients. Patients continue to be followed, data are being analyzed and manuscripts will be written. This study is divided into 4 cohorts. **Cohort 1:** Kidney biopsies from a retrospective cohort of 244 patients with Lupus (archived at UHN) have been re-scored by 2 independent pathologists using the new ISN/RPS classification of lupus nephritis. A manuscript is in preparation assessing the agreement between the two pathologists in classification of these biopsies. Another manuscript is in preparation investigating associations between the biopsy scores and other clinical features. **Cohort 2:** This is an intensively followed group of patients with and without Lupus Nephritis who were newly diagnosed or had active disease at the time of enrollment. We have over 100 patients in this group that are followed quarterly for the first 2 years and annually for an additional 3 years. Clinical data are collected and blood (plasma, serum) and urine samples are stored for analysis of several biomarkers and genetic studies. **Cohort 3:** This is a less intensively followed cohort in which clinical data is collected annually for 5 years from patients with or without lupus nephritis who had active/or inactive disease at the time of enrollment. Blood and urine samples have been collected and stored at baseline and year one for analysis of several biomarkers and genetic studies. **Cohort 4:** Blood, urine and tissue biopsies have been collected from 40 patients with Lupus Nephritis that required a renal biopsy procedure. Clinical data are also available on these patients. Longitudinal follow-up (up to 6 months) is available on 25 of these patients. Clinical data collected includes medications and disease activity measures. Environmental exposures, data on quality of life and health care resource utilization have also been collected from patients in Cohorts 2 and 3. The paper on analyzing the health cost of patients living with lupus has been accepted and is in press in the Journal of Rheumatology.

The Role of Fatty Acid Composition in Disease Activity and Cardiovascular Disease in Systemic Lupus Erythematosus

Dr. Fortin and his colleagues received a 3-year grant from The Arthritis Society to study the impact of nutritional factors and in particular the composition of fatty acids in the blood on lupus disease activity, disease damage, the health of blood vessels and the risk for heart disease. This study requires 200 patients with and without previous history of heart disease. Patients who agree to participate in this study will be asked to provide fasting blood samples and complete questionnaires to assess their diet and physical activity. An ultrasound procedure will be performed on the blood vessels to assess the presence of plaques, rigidity and thickness of the arterial walls. This study has had a very good progress to date as currently more than 80 patients are participating in this project.

B-Cell Tolerance

B-cells are immune cells that produce antibodies. When we get infections, antibodies bind to the infecting organism to help clear it from the body. Our bodies have many mechanisms that prevent us from producing antibodies that bind to our tissues and ensure that antibodies are only produced when foreign organisms such as bacteria invades. These mechanisms are defective in SLE where antibodies are made that bind to normal tissues causing damage (called autoantibodies). Studies in mice that develop an illness similar to lupus have shown that certain types of B cell abnormalities lead to production of lupus autoantibodies. In this study Dr. Wither’s team is studying the blood of patients with lupus to see if similar B cell abnormalities are present.
The Systemic Lupus International Collaborating Clinics (SLICC) is an international group of rheumatologists and lupologists from centres in 11 countries who have been working together on lupus research since 1987. The SLICC group has been working on the important area of heart disease in SLE through the development of the Registry for Atherosclerosis. The University of Toronto Lupus Clinic is the coordinating centre for the SLICC Registry.

The long-term goals of this registry are to allow researchers to determine the frequency and nature of early atherosclerotic coronary artery disease in SLE, and to identify associated risk factors and develop preventative interventions.

The Registry includes patients who are newly diagnosed with SLE and involves the collection of clinical and laboratory data as well as family history and lifestyle information related to heart disease on an annual basis for a minimum of five years. In addition laboratory samples are being collected for centralized testing of inflammatory measures and banking of DNA.

Over 1650 patients are now enrolled in the Registry. These individuals represent an ethnically, culturally and geographically diverse group of newly diagnosed SLE patients. A secondary study of neuropsychiatric manifestations is coordinated in Halifax and data and laboratory samples are shared between both studies.

Partial funding has been obtained for the Registry through a grant from the Canadian Institute of Health Research, and thankfully several lupus patient groups have provided generous financial support for this important project including The Lupus Foundation of Ontario and the Ontario Lupus Association.

SLICC Registry for Atherosclerosis in SLE

These are just a few of the current studies being carried out at the Lupus Clinic. 

We would like to thank our patients and their families for their ongoing support and participation in these studies.
Lupus Clinic Nurse

The Lupus Clinic has been very fortunate to have Anne Cymet, RN come on board as the Lupus Clinic nurse. In this article Anne will outline her function as an essential part of the patient care team.

As the nurse in the clinic I wear many hats. I may be an educator, advisor and a friend all on the same day. The opportunity to use my varied nursing skills on any given day makes the role of the ambulatory nurse unique and exciting.

One of my hats is to promote healthy living, determine risk of developing associated complications such as heart disease and osteoporosis and advise you in the prevention of these complications. When you are seen in clinic we will review together any risk factors you have for developing heart disease and osteoporosis and work on modifying the risks you have control over.

I also ensure that cholesterol tests, bone mineral destiny tests and eye exams are up to date. I will also assist you in managing your medications and provide education for you and your family on lupus.

I work closely with the clinic doctors and you may receive phone calls or e-mails from me with instructions or questions about your care. I may call you to discuss abnormal results or ask you about how you are doing when the doctors start you on new medications.

In conjunction with Lupus Ontario I facilitate monthly patient support group meetings held in the Lupus Clinic. You may get more information or sign up for e-mail notices concerning these support group meetings at http://www.lupusontario.org

You may call or e-mail me if you have any concerns regarding your health. I look forward to seeing you in the clinic.

Clinical Trials in SLE

Over the last 3-4 years the Lupus Clinic has participated in a number of clinical trials of new drugs in systemic lupus. One trial has resulted in a new drug called Belimumab or Blyss™ being considered for approval for use in lupus by the FDA in the United States and application is being submitted for approval with Health Canada.

Drs. Fortin, Gladman and Urowitz are actively involved as consultants in the development and execution of these trials. It is anticipated that several new drugs will be ready for testing within the next one to two years.

Currently we are seeking patients who have either active arthritis or kidney disease for two clinical trials. Joan Blair is the nurse manager of our Clinical Trials program. If you are interested in participating in a clinical trial of new therapies in SLE or would like more information please contact Joan at 416-603-5800 ext. 3259.
Acknowledgements

Once again we would like to extend our thanks to the many supporters of the University of Toronto Lupus Databank Research Program. This includes Lupus Ontario who provide support through the Geoff Carr Lupus Fellowship Lupus Foundation of Ontario who continue to provide support for the summer students as well as many private donors.

Dance for the Cure

The 15th Annual "Dance for the Cure" took place on January 26\textsuperscript{th}, 2011. The event organized by Tiziana Tolfo, her family and friends, raises funds for lupus research and awareness. For the past six years, part of the proceeds from this event has been donated to the SLICC Registry for Atherosclerosis. We would like to gratefully acknowledge the hard work that Tiziana her family and friends put into this wonderful event and their continued support. Further information can be found at www.danceforthecure.ca

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