The Psoriatic Arthritis Clinic now 38 years old and has treated over 1400 patients who are being closely followed and thus constitutes the largest and the most comprehensively studied group of psoriatic arthritis patients in the world. Both the clinic and the doctors associated with it are recognized internationally for the expertise in research and management of psoriatic disease.

The purpose of this Newsletter is to update our patients on advances in both scientific and clinical research and treatment. We also provide some basic information about psoriatic arthritis for new patients entering the Clinic.

**WHAT IS PSORIATIC ARTHRITIS?**

Relatively common, psoriasis (Ps) is a skin disease affecting 3% of the population. One-third of these patients may then develop psoriatic arthritis (PsA) which is a systemic inflammatory arthritis associated with psoriasis. Psoriatic arthritis may lead to damaged joints if not treated promptly and is quite different from osteoarthritis.

Patients with PsA often first arrive at the clinic with a lot of pain, swelling and stiffness of the affected wrists, hands and/or knees and feet joints. They may also suffer neck or other back pain.
Frequently patients have swelling of whole digits (fingers or toes), so called “sausage digits” or dactylitis, and/or inflammation at the sites where tendons insert into bones called enthesitis (plantar fasciitis being an example). PsA was poorly understood and was not treated very aggressively by physicians prior to 1978. Fortunately, this clinic has played a large role in understanding the disease and its severity and how it affects the lives of patients. Treatment options have greatly improved for patients through the research carried out by this clinic. However, the actual cause of the disease and the reason for its persistence still remain somewhat of a mystery but it is actively being investigated.

**What Causes Psoriatic Arthritis?**

Evidence shows us that whether someone develops psoriatic arthritis depends both on their own body's genetic make-up, i.e. their immune system's ability to handle things, and the environmental stresses placed on their body. Sometimes injury (an insult to skin or joints or the immune system) may trigger psoriasis or arthritis. Our studies as well as others have demonstrated that infection and heavy lifting predispose patients with psoriasis to develop PsA. Smoking predisposes people to develop psoriasis, and likely also to PsA. Current investigations continue to focus on the relationship between genetic and environmental factors.

**Are hereditary factors important in Psoriatic Arthritis?**

About 40% of patients with PsA have relatives with either psoriasis or PsA, suggesting a rather significant hereditary contribution. Close blood relatives of patients with psoriatic arthritis have about 30 times the risk of developing psoriatic arthritis compared to the general population. If one already has psoriasis, our studies and those of other investigators show that there are certain genetic markers including human lymphocyte antigens (HLA) that may identify those patients with psoriasis who are more likely to develop PsA.

We are currently looking at the role of other genes as well, in collaboration with centres in Newfoundland, Vancouver, Rochester and Ann Arbor through the International Psoriasis and
Arthritis Research Team (IPART). We hope the patients and their families will continue to support our efforts.

**HOW DOES THE PSORIATIC ARTHRITIS CLINIC AND RESEARCH PROGRAM OPERATE?**

Lack of knowledge regarding PsA prompted Dr. Dafna Gladman to establish the Psoriatic Arthritis Clinic at the University of Toronto in 1978. Then, in October of 2010, Dr. Vinod Chandran who had trained with Dr. Gladman for a number of years joined the Clinic as staff physician. Every Monday morning between 9:00 a.m. and 12:30 p.m. and every Wednesday afternoon, between 1:00 p.m. and 5:00 p.m. patients attend the PsA clinic. Patients are initially evaluated by either a rheumatology resident (in their second year of rheumatology training) or a rheumatology fellow (doctors who have completed their rheumatology training and are doing further training and research specializing in psoriatic arthritis). All patients are then reviewed by either Dr. Gladman or Dr. Chandran, in order to provide expert advice regarding treatment and most importantly, continuity of care.

In 2011, Dr. Chandran and Dr. Rosen, dermatologist, established an extension clinic that initially operated within the Dermatology Department at Toronto Western Hospital, but most recently moved to the Rheumatology section on the first floor. Dr. Chandran recognized the need to screen all psoriasis patients in order to diagnose PsA earlier. This allows for an earlier start of treatment and it thereby improves outcomes for patients. In this clinic all patients who are referred to the Dermatology Clinic for a diagnosis of psoriasis are evaluated by a rheumatologist for the presence of PsA.

For research purposes, all PsA patients are examined in a standard way, according to a specially designed format, which includes a complete history, a physical examination, blood and urine tests and x-rays at regular intervals. This information is entered into a computer database. In this way, patients can be compared and knowledge about the disease process acquired.
Early diagnosis of psoriatic arthritis: Patients with psoriasis without arthritis are also studied and are carefully followed on an annual basis. So far close to 650 patients have been recruited. Following a large group of patients with psoriasis alone allows us to investigate clinical and genetic predictors for the development of PsA. This will make earlier diagnosis possible and help us start the best treatment early in the disease process. Based on this clinic we were able to determine that the frequency of PsA among patients with psoriasis is higher than previously expected, and that the high risk for developing PsA continues throughout the course of psoriasis.

Family based studies: Affected family members of patients with psoriasis and PsA are also followed as part of our research program. This allows us to look at genetic associations of the disease features and course.

Analyzing or Studying the information: Because medical research involves numbers and complicated mathematics, the Clinic has close ties with biostatistics departments at the University of Waterloo, Canada, the MRC Biostatistics Unit, Cambridge, England, and the Lunenfeld Research Institute at the Mount Sinai Hospital, where biostatisticians participate in analyzing the extensive amount of data generated in the Clinic. Furthermore, these biostatisticians are able to use the data from our database to develop new statistical methods to help analyze information from other studies.

How does research move from bedside to laboratory bench and back again?

In addition to clinical research (at the examining table), our program also includes a molecular genetics laboratory. This “wet lab” is located on the 5th floor of the new Krembil Discovery Tower of The Krembil Research Institute. Through grants from the Canadian Institute of Health Research (CIHR), The Arthritis Society and a generous donation, the laboratory is well equipped to process and biobank samples as well as perform a multitude of genetic and other biomarker studies supporting our local research, as well as participating in projects with other national and international centers.

Translational research is the detailed study of clinical disease combined with cellular or...
molecular information leading to the development of specific patient-centered therapies which brings us back to the ‘bedside’ for treatment. Thus, the strength of our clinic lies in the linkage of the extensive clinical information collected at the “bedside” with genetic and molecular data generated in the “wet-bench lab” allowing for “translational research”.

What are some of the projects the PsA wet-lab is currently working on?

The PsA research laboratory is looking at the genes involved in PsA and what role these genes play in different aspects of the disease. Currently the laboratory is looking at gene activity (also known as gene ‘expression’) in PsA. Genes for a certain feature of the disease may be present in the DNA of a person, but these genes may only be active at particular times in the course of the disease. By looking at the active genes and at the same time the clinical features of the same patients, we hope to have a better understanding of how these genes affect the different parts of the body; whether it is the hands, feet, neck, back, shoulders or nails.

There are also molecules such as protein particles circulating in our blood that may help us understand why certain patients have more severe symptoms than others. Our lab is trying to see if there is a special pattern of these molecules, called ‘biomarkers’ that is unique to PsA. Through a very generous donation, the lab was fortunate to acquire a Luminex 200, a high-tech piece of equipment that is used to investigate both genes and biomarkers. Using this machine we have been able to identify soluble biomarkers for psoriatic disease, as well as biomarkers that distinguish patients with PsA from patients with psoriasis without arthritis and more recently from patients with osteoarthritis. Some of these proteins were detected by a study in collaboration with Professor Diamandis, Director of Laboratories at University Health Network and Mount Sinai Hospital.

We are also working on cellular biomarkers for PsA in collaboration with Professor Christopher Ritchlin at the University of Rochester, Rochester, New York. This work has been supported by The Arthritis Society.
Remy Angela Pollock, received her PhD degree after investigating how PsA is passed down in families and what role ‘epigenetic’ factors play in PsA. Epigenetic means that they are not encoded in the cell’s genetic DNA sequence, but they are passed down alongside the DNA and may modify the DNA. Remy has found that there are epigenetic marks that are associated with paternal transmission. She has also found that there are epigenetic marks that distinguish patients with PsA from those with psoriasis alone. Current investigation is focused on the types of cells that might be relevant.

**Clinical trials program**

We have participated and continue to participate in drug trials that are sponsored by the companies that produce the new medications. We are fortunate that there have been a few drugs under investigation including oral medications such as apremilast and tofacitinib, and a number of new biologic agents that are directed specifically against IL-17. We continue to participate in trials because we believe it is important for new drugs to be available to our patients.

**How we train Clinicians and Researchers of the Future**

The University of Toronto Psoriatic Arthritis Program hosts trainees from many levels of medicine and related fields. In particular, Clinical Research Fellows (qualified physicians who have completed their training in rheumatology) come to our Centre to gain expertise in the management of PsA patients and learn clinical research methodology. Many of them also pursue graduate degrees in epidemiology (the “where and when” of diseases) or genetics through the Institute of Medical Science, University of Toronto, as part of this training. These trainees come from across Canada and around the world and go on to set up local institutional clinics modeled on the Psoriatic Arthritis Program here. They continue to work with us in research through our multi-centre research programs. Through our Legacy Campaign as well as granting agencies, we have been able to hire research fellows specifically to train in our Clinic and assist us in carrying out this valuable research. The clinic also hosts medical students and undergraduate students through summer
research scholarships. These students work in the clinic and laboratory and have carried out many important projects.

**Examples of current research being carried out by trainees:**

**Cardiovascular disease in psoriasis and psoriatic arthritis**

**Dr. Lihi Eder,** who was Post-doctoral fellow in our program has now been appointed on staff at the University of Toronto and Women’s College Hospital, but is also cross-appointed to the UHN so that she can continue to carry out research within our program. She has been studying risk factors for progression of atherosclerosis in psoriatic disease. A study funded by a grant from Abbvie Canada, in which patients with psoriasis and PsA had carotid ultrasound studies 3 years apart to determine progression of atherosclerosis has been completed and is currently undergoing analysis. Dr. Eder recently received grants from the National Psoriasis Foundation in the US and from The Arthritis Society to further study the metabolome in patients with psoriatic disease in relation to ultrasound-detected atherosclerosis. Dr. Eder recently demonstrated that certain HLA alleles are associated with atherosclerosis.

**Dr. Kristy Yap** who recently completed training with us performed a study on back disease in PsA. She specifically investigated whether published criteria for inflammatory back pain performed well among patients with PsA. She found that while there was moderate agreement between physician assessment and inflammatory back pain criteria, none of the criteria performed well in accurately identifying patients with axial PsA. Thus the recommendation was that all patients with PsA should be imaged regardless of whether they complain of back pain.

**Priya Patel** - A medical student from the University of Toronto who spent her summer working with Dr. Dafna Gladman and Dr. Cheryl Rosen in the departments of rheumatology/dermatology investigated if patients with psoriasis and PsA are being appropriately managed for comorbidities
associated with their condition, and which physicians are managing these patients. Patients were asked to complete a comorbidity questionnaire at clinic visits or over-the-phone that asked if they had their blood pressure, weight, blood sugar and cholesterol levels checked by their family physician, rheumatologist, dermatologist and/or any other specialist. In addition, patients were asked if they are taking any medications to manage their comorbidities and if they had a bone mineral density test to check for signs of osteoporosis. Lastly, the responses from PsA patients to the comorbidity questionnaire were compared with information recorded in clinic visits by physicians to look for any discrepancies that might indicate a gap in patient-physician communication. Overall, there were more than 255 patients enrolled into the study over the summer and the results will help determine if the management of patients can be improved to lead to better health outcomes.

**Anastasiya Muntyanu** a first year medical student at the University of Ottawa continued with work she started last summer in the laboratory and concentrated on identifying the cell types responsible for the expression of cytokines and chemokines in the blood of patients with psoriatic disease compared to healthy controls.

None of this research would have been possible without the patients. We need to give a huge thank you to the patients for their willingness to participate in ongoing research which helps us better understand the mechanisms of the disease which could be used to provide better patient care in the future.
WHAT IS THE SCOPE OF OUR NATIONAL AND INTERNATIONAL PRESENCE?

We are now part of a number of Canadian and International multi-centre collaborative groups for psoriasis and PsA. Research in this area is now going on all over the world thanks in large part to the training our international research fellows have received under Dr. Gladman and the international recognition that her work has received. Various centers around the world have invited Dr. Gladman and Dr. Chandran to speak and share their knowledge about this disease. As a result, similar clinics are now being established in other countries.

In 2003, Dr. Gladman established the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA). This is an informal, international group of rheumatologists, dermatologists, radiologists, methodologists and other interested participants who have gathered to study psoriasis and PsA and are involved in both research and education. Both Drs. Gladman and Chandran are actively involved in GRAPPA.

Dr. Gladman is also an executive board member and co-founder of the Spondyloarthritis Research Consortium of Canada (SPARCC), a national research program focusing on “Genetic and Pathogenesis Studies and Outcome Measures for Patients with Spondyloarthritis (SpA)” that includes a group of diseases affecting the spine and peripheral joints, which likewise include PsA.

In 2007, Dr. Gladman established the International Psoriasis and Arthritis Research Team (IPART), a highly successful international group of dermatology and rheumatology researchers who are working together to investigate the biology of cutaneous (skin) psoriasis (PsC) and PsA and examine risk factors for arthritis in psoriasis patients. Its operations for the first five years (2007-2012) were funded by the Canadian Institutes of Health Research (CIHR) New Emerging Team (NET) grant which provided the core funding, as well as the National Institutes of Health (NIH) in the United States, and subsequently by The Arthritis Society (TAS) and various industry support from Abbvie, Janssen, Celgene, Amgen, UCB and Novartis. IPART has made significant progress in its research program, particularly in the areas of clinical, genetic, and biomarker studies, and has
proven to be an extremely effective platform for the discovery of genes and biomarkers that distinguish PsC from PsA patients.

In order to ensure that patient appropriate outcome measures are included in clinical trials, our clinic also participates in an organization known as Outcome Measures in Rheumatology Clinical Trials [OMERACT] which organizes international conferences every two years to discuss and vote on what should be done in the research work in the various rheumatic diseases. Psoriatic arthritis patients are involved in the discussions with the rheumatologists.

_In summary_, we have learned a great deal about the disease process in psoriatic arthritis. We now know that the disease may be more serious than previously suspected, at least in certain patients. We appreciate the need to diagnose and treat patients early in order to prevent damage, deformity and mortality. We now know the type of patient who needs to be treated more aggressively. We are currently developing an approach based on the recently identified markers for disease progression in psoriatic arthritis. Finally, we sincerely believe that by studying the disease in detail we will be able to find the cause and then the cure for psoriatic arthritis.

**WHAT ARE OUR FUTURE PLANS?**

- To continue with our efforts in identifying predictive factors for disease progression, joint damage, poor quality of life, and mortality in psoriatic arthritis.
- To identify genetic factors associated with drug response and sensitivity.
- To identify biomarkers for disease progression and response to therapy.
- To continue our ‘family study’ by increasing our multi-case family collection, as well as sibling trios and sibling pairs, so that we have enough data on these families to be able to identify gene(s) responsible for susceptibility to psoriatic arthritis.

**A Special Thank You to Our Supporters**

This Clinic owes a huge debt to all who have been treated and voluntarily agreed to participate in our research studies here. Without you our discoveries about this disease and the treatments now
available would not necessarily have been possible. Also we are immensely grateful to our financial donors, big or small, who support our work as well. Without you, we could not be doing this work.

Thank you to our Patient Advisory Committee Members for your feedback and support.

Patient Advisory Committee Members from left to right back row: Raffick Hasmath, Ina Campbell, Jennifer Boyle, Dan Dunsky, Roland MacDonald. Front row left to right: Andy Winton, Dr. Vinod Chandran, Dr. Dafna Gladman and Vaune Davis.

Award presentation - 2015 Mentor of the Year for Region 3: Dr. Gladman

Dr. Gladman was awarded the Royal College Mentor of the Year (Region 3) which took place this year in May 2016. This award “recognizes Fellows of the Royal College who have had a significant impact on the career development of students, residents or Fellows. Nominees must have shown themselves to be an excellent role model in demonstrating the qualities or competencies of Manager, Scholar and Professional as described in the CanMEDS Framework.”
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Canadian Rheumatology Association
National Psoriasis Foundation
Arthritis Research Foundation

BOOKS AVAILABLE: Drs. Chandran and Gladman co-authored two books one directed to patients and one to physicians providing general information about psoriatic arthritis.

VIDEO A video about the Psoriatic Arthritis Clinic can be found on the following link:

http://www.uhnres.utoronto.ca/studies/cpsrd/

FIND US ON FACEBOOK

http://www.facebook.com/IPART.INFO

http://www.uhnres.utoronto.ca/studies/cpsrd/

OTHER USEFUL LINKS

http://www.canadianpsoriasisfoundation.org/
http://www. arthritis.ca
https://www.psoriasis.org

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Video:

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