The Psoriatic Arthritis Clinic now 36 years old treats over 1300 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 which has evolved from this unique facility. By extension, one could say then that our patients too are world-famous, anonymously of course, since no names are used.

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.

A scientific symposium celebrating 35 years of the Psoriatic Arthritis Research Program and honouring Dr. Gladman was held in July, 2013.

WHAT IS PSORIATIC ARTHRITIS?

Psoriasis (Ps) is a relatively common 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 is quite different from osteoarthritis.

Patients with PsA 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. Dr. Lihi Eder, our post-doctoral fellow has demonstrated that infection and heavy lifting predispose patients with psoriasis to develop PsA. She also found that while smoking predisposes people to develop psoriasis, but oddly, once patients with psoriasis smoke, they are then less likely to have 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 you already have psoriasis, our studies and those of other investigators show that there are certain genetic markers known as 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 clinic. They 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 established an extension clinic that operates within the Dermatology Department at Toronto Western Hospital. 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 PsA 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:** Over 600 patients with psoriasis *without arthritis* are also studied and are carefully followed on an annual basis. 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.

**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.

Because medical research involves complicated mathematics, the Clinic has close ties with biostatistics departments at the University of Waterloo, Canada and the MRC Biostatistics Unit.
Cambridge, England, where biostatisticians participate in analyzing the extensive amount of data generated in the Clinic. Furthermore, these biostatisticians then go on to use the data from our database to develop new statistical methods to help analyze information from other studies.

Various centers around the world have invited Dr. Gladman and Dr. Chandranto speak and share their knowledge about this disease. As a result, similar clinics are now being established in other countries.

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

In addition to clinical research (the bedside), 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 Toronto Western 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 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 the clinical features of the patients, we hope to have a better understanding of how this disease affects the different parts of the body; whether it is the hands, feet, neck, back, shoulders or nails.

There are also molecules 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. Some of these proteins were detected by a study in collaboration with Professor Diamantis at the Mount Sinai Hospital and a PhD student, Daniela Cretu.

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 is supported by The Arthritis Society.

Remy Angela Pollock, PhD student is 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. Remy has confirmed results from previous studies that have shown that psoriasis and PsA patients more often inherit their disease from their father rather than their mother. This suggests that genes passed down by the father carry special features that increase the risk of developing PsA. Remy is investigating whether these features are ‘epigenetic’ in nature. This is the first time anyone has studied the epigenetics of PsA. The project has received enthusiastic grant support from the Arthritis Research Foundation and the National Psoriasis Foundation in the United States. Preliminary results have confirmed that the approach is correct and further studies are currently underway.

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. With the gracious donations from some of our patients as well as funding 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, Post-doctoral fellow,** is studying risk factors for progression of atherosclerosis in psoriatic disease. Through a grant from Abbvie Canada, she has been able to follow patients who had ultrasound performed 3 years ago and repeat the studies to determine whether there is progression of disease and what the predictive factors might be.

The chronic inflammatory nature of psoriasis and PsA predispose patients to cardiovascular diseases such as heart attacks and stroke. Our group and others have shown that patients with PsA and psoriasis have higher chances of developing cardiovascular events compared to the general population. These events occur due to build-up of plaques within the blood vessel wall termed atherosclerosis. The atherosclerotic plaques are composed of cholesterol and inflammatory cells and are directly related to aging, high blood pressure, smoking and elevated blood levels of sugar and cholesterol. However, among patients with psoriasis and PsA, the risk of having cardiovascular diseases remains high even after controlling for these risk factors, suggesting that other factors such as inflammation or certain medications taken for arthritis may account for the excessive risk. Our group is continuing to study why this happens in our patients.

The presence and severity of atherosclerotic plaques can be assessed by ultrasound of the carotid arteries in the neck. Dr. Eder has been performing ultrasound scans of the carotid arteries in patients with psoriasis and PsA since 2009. So far more than 500 patients with psoriasis and psoriatic arthritis have been scanned. We have found that patients with PsA had more plaques compared to patients with psoriasis alone. In addition, plaques were associated with more severe psoriasis and arthritis and elevated levels of inflammatory markers in the blood. This finding suggests that more skin and/or joint inflammation lead to more plaques. In a follow-up study we will re-scan all of the patients that participated in the previous ultrasound study. We are interested
in investigating factors related to the progression of plaques over time and the effect of biologic and non-biologic medications on atherosclerosis.

The figure to the right shows the three dimensional ultrasound measurement of a plaque in the carotid artery marked in blue arrow.

Dr. Hernán Maldonado-Ficco, Clinical Research Fellow, who completed Rheumatology training at the University of Buenos Aires Argentina, joined the University of Toronto Psoriatic Arthritis Program in September 2013. During this time Dr. Maldonado-Ficco has worked on several projects.

Smoking status in psoriatic arthritis

The aim of this study was to determine the effects of cigarette smoking on clinical joint damage in patients with PsA. 1107 patients were included in this study. The results showed that current and past-smoking at baseline was associated with a lower probability of developing clinically damaged joints compared to non-smokers.

Magnetic resonance imaging in psoriatic arthritis

Magnetic resonance imaging (MRI) is an under-used tool in the evaluation of patients with psoriatic arthritis. The aim of this study was to describe when MRI scans should be used. It also served to examine the influence of MRI findings on change of treatment in clinical practice.

A total of 168 MRI scans were performed on 125 patients (135 axial and 33 peripheral MRI performed). Of the axial MRI scans, the predominant reasons were for suspected inflammatory (51.1%) or degenerative (24.4%) disease. But MRI results revealed inflammatory and/or structural change in 34.1% vs 54.8% with degenerative axial changes. Of the MRI scans of the extremities-arms/hands or legs/feet, 60.6% of scans were on hands alone and 21.2% on feet alone. The main reasons were for sub-clinical(doctor being unsure of) inflammation (78.8%) while inflammatory arthritis was the MRI diagnosis in 72.7%. Out of 32 patients with a treatment change within 6 months of their MRI, the findings did influence treatment change in 56.3%, but were insufficient to effect treatment change without clinical findings (100%). In conclusion MRI is very useful in evaluating patients with active PsA; however, despite influencing treatment decisions, it has not replaced clinical examination as the primary tool in determining if medication change is required.
Indirect comparison between different anti-TNF medications in psoriatic arthritis.

TNF-α blockers created a major change in the treatment of PsA patients. These biologic agents have been found to be effective in controlling different aspects of the disease such as peripheral joint arthritis, enthesitis, dactylitis and psoriasis. The objective of this study was to determine if differences in treatment response were evident between four TNF-α blockers. 349 patients received anti-TNF therapy. No differences were identified in the comparative efficacy between four different anti-TNF medications. Monoclonal antibodies were used most frequently along with methotrexate.

Dennis Wong (Summer Student)

As a second year medical student at the University of Toronto, he is currently working on a clinical research project under the supervision of Dr. Gladman and Dr. Chandran. His project focuses on the most severe form of PsA, termed Psoriatic Arthritis Mutilans (PsAM). Patients with PsAM have severe damage to the joints in their hands and feet, resulting in shortening and destruction of the fingers and toes. Although physicians have long recognized this form of PsA, there is still a lack of consensus on the exact definition of the disease. Only recently had a survey been conducted in the medical community to identify features that are broadly agreed to be associated with PsAM. He is now investigating whether physicians can reliably assess these features in X-rays in order to achieve consistent identification of PsAM patients. Having reliable assessment will drive future research in PsAM so that patients at risk can be identified early and proper therapeutic intervention can be applied to preserve quality of life.

Taryn Gitter (Medical Student)

Taryn Gitter is a medical student from the University of British Columbia who had the opportunity of doing a research project with Dr. Gladman and Dr. Chandran this summer. Her project focused on the economic impact of psoriasis and involved in distributing questionnaires to patients with psoriasis who are part of the IPART research program. Some of these patients completed the questionnaire in person when they came in for their visit while other questionnaires were completed over the phone. These patients were asked questions regarding the direct and indirect costs associated with their health over the past year. Direct costs included the cost of medications, therapies, health care services and physician visits and indirect costs included cost of missed work and early retirement. Overall, 200 patients were recruited. The results of this study will be
compared to a study done by a previous summer student that looked at the economic impact of psoriatic arthritis (PsA). Approximately 30% of patients with psoriasis will develop PsA. While psoriasis causes some disability and reduced quality of life, PsA can also lead to significant joint damage, disability and comorbidity. With the advent of biologic therapies the course of psoriasis and PsA may change and there may be a reduction in the incidence of PsA. High cost and stringent prerequisites for drug approval however have prevented many patients from accessing biological therapies or have resulted in them receiving the drugs too late. This study will be used to determine if the use of biologic agents earlier in the course of disease is cost effective.

**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. Many centers have started using our definitions and methods to study their own patients. 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 collaborative transdisciplinary national research program focusing on “Genetic and Pathogenesis Studies and Outcome Measures for Patients with Spondyloarthritis (SpA)” extending from genetics to clinical epidemiology that includes a group of diseases affecting the spine and peripheral joints, which likewise include PsA. The first five years (2006-2010) of SPARCC’s existence have been secured by a 5-year National Research Initiative (NRI) grant through The Arthritis Society (TAS).

In 2007, Dr. Gladman established the International Psoriasis and Arthritis Research Team (IPART), a highly successful international consortium, is the convergence of experienced and accomplished
dermatology and rheumatology researchers who are working together to investigate the biology of cutaneous 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, Amgen 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 have an idea about 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. We believe that by studying the disease in detail we will be able to find the cause and then the cure for psoriatic arthritis.**

**PATIENT ADVISORY COMMITTEE**

**Ina Campbell**, Patient Advisory Committee Member for the Psoriatic Arthritis Research Program. It may seem strange that there is a Patient Advisory Committee (PAC) for the Psoriatic Arthritis Program but there is a small but significant role for patients in a number of areas. The Committee helps the medical staff in reviewing the patient newsletter and in writing lay summaries for grant applications, in planning of the topics for the annual Patient Information Session, in occasionally participating in research or in conference work where patient representation is needed and generally in being a sounding board for areas where patient interests are involved. We really do
learn from each other and the Committee has in turn come to appreciate how knowledgeable and hard-working our internationally respected medical staffs are and how very fortunate we are to be attending this clinic.

**BOOK**

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

![Book images]

**VIDEO**

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

[http://www.uhnres.utoronto.ca/studies/cpsrd/](http://www.uhnres.utoronto.ca/studies/cpsrd/)

**WHAT ARE OUR FUTURE PLANS?**

- To continue with our efforts in identifying prognostic (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, particularly with respect to anti-TNF agents and methotrexate.
- 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

Menkes Family Plaque unveiling May 28, 2014

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.

The Psoriatic Arthritis Research Team

PSA TEAM PHOTO
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