

The Researcher

The CSRG Newsletter

FALL—WINTER 2011

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The Fifth Annual Meeting of the CSRG

The Fifth Annual Scientific Meeting of the CSRG took place from October 27th to 30th at the Hilton Hotel in Quebec City. This meeting was held within the Canadian Arthritis Network’s Annual Scientific Conference. Once again, we held our meeting in conjunction with Scleroderma Society of Canada’s, and were joined by Sclérodémie Québec as well. This provided a great opportunity for investigators, researchers, trainees, and consumers to meet and discuss ongoing research projects, as well as future research endeavors.

On Friday night, the CSRG, CaNIOS, SSC and SQ came together for a dessert reception, where patients and researchers had a chance to meet and converse while savouring delicious sweets. The turnout was great, and overall the night was a success. A special thank you to Actelion for partially sponsoring this event!

On Saturday, CSRG investigators were given the opportunity to present talks to SSC and SQ. Topics included clinical manifestations and treatments in scleroderma (Dr. Ariel Masetto), gastro-oesophageal complications (Dr. Janet Pope), heart and pulmonary involvement (Dr. Peter Docherty, Dr. Tamara Grodzicky), sleep disturbances (Dr. Murray Baron), and psychological health and well-being (Marielle Bas-

sel). Overall, these presentations were very informative and covered the various complications that often arise for scleroderma patients.

During a combined lunch, trainees and researchers were assigned to sit at specific tables with consumers, which allowed for further discussion about ongoing research projects and latest findings. This was complemented by a poster session, where students were able to present the projects they had been working on for the past year.

All in all, this was yet again another very successful meeting where students and researchers were able to showcase their work and meet with the consumers who inspire it.



Marielle Bassel and Bob Buzzza

We would like to thank the Canadian Arthritis Network, the Scleroderma Society of Canada and Sclérodémie Québec and their sponsors for their help in organizing this conference as well as all our rheumatologists, researchers, and trainees whose participation made this event possible. ■

The 6th Annual Scientific Meeting of the CSRG will take place September 28th and 29th in Vancouver, BC. For more information, please contact Maria Scolack (mcolack@jgh.mcgill.ca) or Sabrina Gravel (sgravel@jgh.mcgill.ca).

A potential clue in skin fibrosis

Fibrosis represents a common pathway leading to tight skin and organ failure in scleroderma and has no effective therapy. Deffective repair and excessive tissue scarring lead to pathological fibrosis. It is known that the protein phosphatase and tensin homolog (PTEN) activate certain proteins that promote tissue repair and thus could be a key mediator in fibrogenesis.

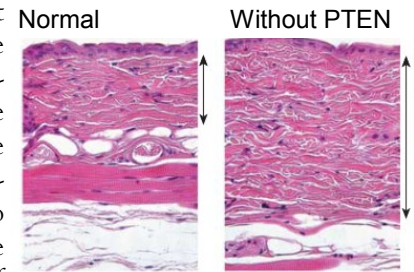
CSRG scientists found that PTEN is reduced in the skin cells of scleroderma patients. They used skin cells (fibroblasts) of mice that could not produce PTEN to examine how such cells would react.

Mice skin cells that didn't have PTEN would produce three times more fibrosis than normal ones,

due to excess collagen.

PTEN appears to be a potential regulator of fibrogenesis; therefore molecules that could increase PTEN production may represent anti-fibrotic treatments. However, PTEN doesn't

seem to be the only player in fibrogenesis. More studies need to be done on scleroderma skin cells to understand the complete course of



Note the thickness of the dermis (arrow, right-hand side of the pictures) this condition. ■

The Scleroderma Patient-centred Intervention Network (SPIN)

The Scleroderma Patient-centered Intervention Network (SPIN) is an international collaboration of scleroderma patients and patient organizations, clinicians, and researchers, with the goal to develop an infrastructure that can be used on an ongoing basis to test accessible, low-cost interventions to reduce disability and improve quality of life for people with scleroderma.

Directed by CSRG investigator Dr. Brett Thombs, SPIN's members include key centres in Canada, the US and Europe, as well as patient representatives from Canadian patient organizations, the US Scleroderma Foundation, and the Federation of European Scleroderma Associations (FESCA). In July 2011, a CIHR-funded meeting was held to refine the SPIN organizational structure, as well as investigative and knowledge

transfer frameworks to develop, test, and disseminate accessible interventions. This meeting also permitted detailed outlining of intervention areas and aided in the preparation and submission of a full emerging team grant application for 5-year funding from CIHR, for which the early-phase letter-of-intent was reviewed very favourably. ■

Lisa Jewett

Highlighted Member: Dr. Paul Fortin

Dr. Fortin obtained his medical degree from Université de Laval in Quebec City and graduated from McGill University in Rheumatology. He then obtained a Master's degree in Public Health from Harvard University School of Public Health. He followed three years of special training in clinical epidemiology as a Harvard post-doctoral research fellow under the direction of Dr. Matthew H. Liang at the Robert Breck Brigham Multi-Purpose Arthritis Center of the Brigham and Women's Hospital.

In 1995, he created the Canadian Network for Improved Outcomes in SLE (CaNIOS) with the specific goal of running a multi-centre, randomized, and controlled Study of Methotrexate in Lupus Erythematosus (SMILE). CaNIOS brought together many lupus experts who, despite their limited indi-

vidual cohorts, were able to pool information for the completion of SMILE.

Dr. Fortin's new role in Quebec City will be to develop clinical services and research for those with systemic autoimmune rheumatic diseases. In addition to his lupus work, he has chosen to contribute next to clinical and research work in systemic sclerosis and to become and active member and a recruiting centre for the CSRG. He has also already started a dialogue with Drs Baron, Hudson and Thombs on common research interests that span all SARDs and lupus and scleroderma in particular. ■



Scleroderma renal crisis

Several forms of renal disease are recognized in Systemic Sclerosis (SSc). The most dramatic of these is scleroderma renal crisis (SRC), which usually manifests as malignant hypertension and progressive renal failure. SRC is uncommon but its impact on people's health is devastating. CSRG researchers undertook a study to determine the prevalence of renal disease and the course of renal function over time in SSc patients.

This study included 561 patients who were in the CSRG registry. Their renal function was compiled for the study visits they completed between 2004 and

2009. Among the study subjects, 20% had abnormal renal function with no history of SRC and 5% had a history of SRC at their first study visit.

The analyses showed that patients with abnormal initial renal function experienced the same annual decline as patients with normal initial renal function, which is similar to that observed in the general population.

Renal dysfunction is common in SSc, even among those without a history of SRC. However, it is generally mild and renal function declines at a rate similar to the general population. These data are of considerable prognostic value for clinicians caring for SSc patients. ■

Statins against digital ulcers

Some drugs may have more than one effect. For example, aspirin reduces pain, reduces inflammation but also reduces blood clotting. We think that similarly the drugs commonly used to lower cholesterol called statins have another possible benefit in that they may promote the growth of new blood vessels. If this were proven to be true, this would have enormous implications. For example, in coronary artery disease, the damage to the heart is caused by blocked arteries. If statins could enhance new blood vessel growth in the heart, this may improve blood flow to the heart muscle and protect against heart attacks. Also in diseases where there is poor blood flow to a limb, for example in diabetes, new vessel growth may protect from gangrene.

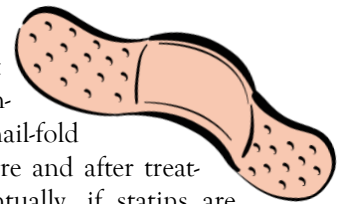
To date, although it has been hypothesized that statins may have this effect, it has never really been proven in humans. One reason is that it is not easy to prove that new vessels have grown. The rheumatologists of the CSRG will attempt to do just that.

They will study statins in scleroderma. One of the clinical features of scleroderma is the presence of abnormal blood vessels, which can cause ulcers on the fingertips. In fact, it is possible to see with a simple microscope the blood vessels in the skin near the fingernail. In scleroderma, there is an obvious drop out of these vessels so it will be easy to assess new blood vessels.

The CSRG investigators hypothesize that if statins do have the ability to cause new vessel growth, they will be

able to detect that by examining the nail-fold vessels before and after treatment. Eventually, if statins are proven to help vessel growth, this will also facilitate the healing of digital ulcers.

At the moment, rheumatologists are still working on the preliminary aspect of this project: determining the best way to assess ulcers, approaching colleagues from around the world who would like to collaborate, writing funding requests to various agencies. This project is very promising and innovative, and we are hoping to get the proper funding to start the experiment! ■



Hopes in early detection of lung problems

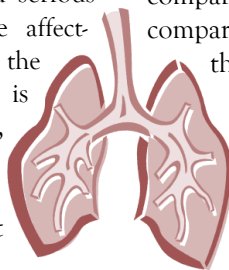
Interstitial lung disease (ILD) is a common and serious complication of scleroderma (SSc). It is a disease affecting the tissue and space around the air sacs of the lungs (interstitium). The spectrum of SSc-ILD is broad. Some patients have mild, stable abnormalities, others slowly progressive disease and others, yet, rapidly progressive disease. Researchers would like to determine if there are molecules in the blood that could predict eventual lung problems.

Two molecules, KL-6 and SP-D are suspected to be indicators of potential lung problems. In a recent study, these molecules were measured in the serum of 33 scleroderma patients, and

compared to that of 25 healthy subjects. The results were compared to the lung capacity of the patients, to determine if there was a correlation.

Researchers of the CSRG found that the more SP-D is present in the blood, the more rapidly lung function declines.

These findings mean that there are molecules in the blood that can help determine early lung function decline, and therefore help early treatment options. However, we will need to make a bigger experiment with more samples to be able to generalize. ■



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2012 Meetings

- The sixth Annual Scientific Meeting of the CSRG will take place from September 28th to 29th in Vancouver, BC. Once again, this meeting will take place in conjunction with the Scleroderma Society of Canada's annual meeting. You can contact your local Scleroderma Society for more information, or visit www.scleroderma.ca for more details.
- The 2012 EULAR meeting will take place in Berlin, Germany, from June 6-9. Visit <http://www.eular.org/> for more details.

• Following the successful experience of the 1st World Congress in Florence, the second congress will take place in Madrid, Spain, and will focus on clinical and translational aspects of systemic sclerosis with the aim of updating clinicians involved in the field. Based on the feedback from the participants in the 1st congress, more time will be devoted to areas such as clinical problem solving, young investigator activities and networking between health professionals and patients. Please visit:

www.sscworldcongress.org/

Thank you!

2011 was another successful year for the Cure Scleroderma Foundation. Pierina and her team of volunteers worked very hard again this year to organize many events to help raise much needed funds for the CSRG. *The Beatles* show is a good example of such an event. It not only helped raise money for our Group but it also helped to raise awareness and to educate people about Scleroderma. Thank you CSF!

Also, a special thank you to Ann, her husband and his choir, for a very nice Christmas concert! It was not only a nice way to raise funds for Scleroderma research, but also a nice prelude to the Holidays!



The Canadian Scleroderma Research Group (CSRG), under the direction of Murray Baron, MD, is a group of Canadian rheumatologists and researchers working towards the same goal: better understand Systemic Sclerosis (or scleroderma) in order to better treat the people living with this disease.

In order to achieve their objectives, the CSRG has created a registry of adult patients suffering from scleroderma in Canada. They received grants from the Canadian Institutes of Health and Research (CIHR) to create this database, and as of today there are more than 1300 patients in the registry. The CSRG also have received support from private donations, the Cure Scleroderma Foundation, Scleroderma Society of Canada, Scleroderma Ontario, as well as several Canadian pharmaceuticals companies. This has allowed researchers from across Canada and from various disciplines to study the specificities and manifestations of the disease, looking for commonalities in the data. Since the CSRG started in 2004, more than 85 scientific papers on Scleroderma have been published.

The Cure Scleroderma Foundation

Pierina Nero, a patient who was diagnosed with Scleroderma in 2000, established the Cure Scleroderma Foundation (CSF) in 2005 in order to raise much needed funds which will enable the CSRG to continue with their research into Scleroderma and to promote awareness about this rare and uncommon disease.



FONDATION CURE SCLÉRODERMIE
CURE SCLERODERMA FOUNDATION

To make very much needed donations, please contact the Cure Scleroderma Foundation via our own website:

csrg-grcs.ca