



AUSTRALIAN SCLERODERMA
INTEREST GROUP

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SCLERODERMA **Connections.**

SSC SCREENING CENTRE UPDATE

EDITION 6: MAY 2013



greetings,

Welcome to another edition of Scleroderma Connections, the Australian Scleroderma Interest Group (ASIG) newsletter. It has been a while since our last issue, but in the last year, recruitment of patients with systemic sclerosis (a.k.a. scleroderma) to the Australian Scleroderma Cohort Study has continued apace and there has been great

In the last year, recruitment of patients with systemic sclerosis (a.k.a. scleroderma) to the Australian Scleroderma Cohort Study has continued apace and there has been great progress in ASIG research.

The first workshop dedicated solely to ASIG research projects, old and new, was held in February and I am delighted to announce an exciting new international collaboration with scleroderma researchers from Canada, Europe and the USA (the INSYNC collaboration). We are also pleased to announce the appointment of Tien Tay as the ASIG-Scleroderma fellow for 2013.

This issue includes brief updates from conferences in the last year as well as upcoming meetings that might be of interest. ASIG has submitted abstracts again this year to EULAR and the Australian Rheumatology Association Annual Scientific Meeting in Perth. Keep an eye out for plenary presentations from Mandy Nikpour and ASIG posters. World Scleroderma Day on 29th June 2013 is another important date for the diary.

The featured screening centre in this issue is St Vincent's Hospital, Melbourne. This is the ASIG "nerve centre" where the project Officer, Candice Rabusa, is based. The ASIG database is hosted on the "St V's" hospital server and much of ASIG's research has been driven by the hardworking rheumatologists based there, Drs Wendy Stevens and Mandy Nikpour.

I am glad to feature Karen Patterson's research update on autoantibodies in the Australian scleroderma cohort in the centre version. Karen is a PhD student at Flinders University, supervised by A/Prof Jenny Walker, one of our ASIG members. Please see Dr. Walker's column in the patients' version discussing the role of autoantibodies in systemic sclerosis.

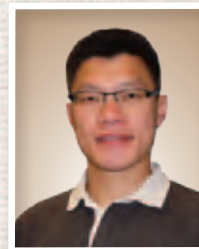
In the patients' version of this newsletter, I am pleased to announce the inclusion of a guest column from Dr Katie Ellard, a gastroenterologist from St. Leonards, Sydney who offers some helpful advice for patients with troublesome "scleroderma gut". Victoria Bartlett from St V's orthotics offers a few tips on selecting shoes and their Scleroderma/PAH consultant nurse, Barbara Gemmell, has tips for the cold winter months.

And finally, patients and doctors alike, are reminded of the importance of screening for the cardiopulmonary complications of systemic sclerosis. The contact details of your nearest screening centre are listed on the back of the newsletter.

Susanna

Susanna Proudman
ASIG Chair

new appointments.



We are delighted to announce the appointment of our new ASIG-Scleroderma Australia Research Fellow for 2013. Dr. Tien Tay

joins us from St Vincent's Hospital in Sydney where he was an Immunology and Rheumatology registrar. He has published papers on HIV medicine, Immunology and Rheumatology.

He will be working on a project describing and quantifying damage in systemic sclerosis using damage descriptors in development with Dr. Mandy Nikpour and Dr. Wendy Stevens, measuring the accrual of damage over time and assessing damage as a predictor of outcome. There is also scope to 'validate' this 'Damage Index' using the cohort established by the Canadian Scleroderma Research Group in collaboration with ASIG.



We would also like to welcome Candice Rabusa, our new Project Officer, from the Australian Institute of Health and Welfare.

Candice can be contacted on Candice.RABUSA@svhm.org.au.

profile.



From left to right: Dr. Tien Tay, Ms. Barbara Gemmell, Dr. Mandy Nikpour, Ms. Candice Rabusa, Dr. David Prior, and Dr. Wendy Stevens

St Vincent's Hospital

St Vincent's Hospital houses the largest Australian Scleroderma Screening Centre and is the aegis of the Australian Scleroderma Interest group (ASIG) administration.

The St Vincent's Centre is led by Dr. Wendy Stevens, who has strong clinical specialisation in managing patients with complex systemic sclerosis. Dr Stevens' other clinical research interests include patient education and has been running biannual Scleroderma education days for patients and their families for the last 18 years.

She was joined recently by Dr. Mandy Nikpour, physician and expert epidemiologist with a research focus on systemic autoimmune disease, particularly systemic sclerosis and systemic lupus erythematosus. Dr Nikpour has been an invited speaker at several national and international meetings and has numerous research collaborations in Australia and overseas, with whom she has published papers. Her contribution to ASIG research has been fundamental in understanding the epidemiology of scleroderma in Australia. The centre was recently joined by Dr. Tien Tay, newly appointed ASIG-Scleroderma Australia research fellow who attends the weekly systemic sclerosis clinic.

One of the most important team members is Ms. Barbara Gemmell, our Scleroderma/PAH consultant nurse. Barbara is a very experienced clinical nurse with a background in community nursing. She is an important point of contact for our patients and answers questions and supports patients between clinic visits. She has extensive experience in the management of digital ulcers in systemic sclerosis. This expertise was recognised by an invitation to speak to patients at the World Scleroderma Congress in Madrid in 2012.

The centre manages about 350 patients. The rheumatologists are very well supported in the management of the many manifestations of systemic sclerosis by a team of cardiologists, respiratory physicians, gastroenterologists and colorectal surgeons. The Scleroderma Clinic is held every Thursday afternoon. The unit is currently involved in 3 clinical trials of novel therapies for digital ulcers and pulmonary hypertension in systemic sclerosis.

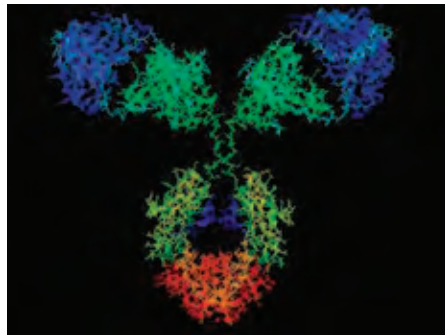
In addition to the specialist care provided by doctors, St. V's Screening Centre also takes a roundtable approach with allied health experts. Input and nomination of cases are invited from all participants who attend the monthly meeting consisting of the systemic sclerosis doctor & nurse, hand therapist, physiotherapist, dietician, occupational therapist, podiatrist and orthotist. Patients with challenging combinations of wounds, contractures, and aggressive disease states in initial work up stage are discussed to triage goals so that multiple services can be provided in the single hospital attendance. One of the major benefits of this initiative is allied health awareness of early, complex, patients whose needs will involve all disciplines, so that access to resources is well coordinated.

Autoantibodies in an Australian scleroderma cohort

By Karen Patterson, PhD candidate, Flinders University, Adelaide

A current research project by PhD student Karen Patterson, 'Autoantibodies in an Australian scleroderma cohort' under the supervision of Associate Professor Jenny Walker has yielded some interesting results.

Autoantibodies are present in up to 95% of systemic sclerosis patients and are useful in determining subsets of systemic sclerosis. Underpinning the determination of these autoantibodies by Immunoblot (Euroimmun AG, Luebeck, Germany) in 528 selected sera from the ASIG serum repository is the detailed clinical and laboratory characterisation of these patients.



Preliminary data show that there are four 'leading' autoantibodies regularly seen in systemic sclerosis patients, Topoisomerase-1, RNA Polymerase III, Centromere and RNP, however these autoantibodies can be present with concurrent autoantibodies and appear in distinct 'Clusters' under the banner of one of the leading autoantibodies. The table below demonstrates both the monospecific and multiple appearances of autoantibodies in this cohort.

Newer diagnostic assays mean that many additional systemic sclerosis associated autoantibodies can now be obtained in clinical practice. However, the clinical relevance of these rarer and less specific autoantibodies remains uncertain but may help to explain some of the heterogeneity observed among autoantibody subsets and perhaps why disease trajectory remains stable in some patients and progresses in others. Further analysis with the most up-to-date data extraction is underway to determine additional clinical associations, including any associations with malignancies.

Table 1: Frequency of Monospecific and Multiple appearance of Autoantibodies in an Australian Scleroderma Cohort

| Autoantibody | Ro52 | Ku | PM-Scl | Th/To | NOR90 | Fibrillarin | RNAPol III | CENP | Topo 1 | PDGFR |
|--------------|------|----|--------|-------|-------|-------------|------------|------|--------|-------|
| Ro52 | | 6 | 40 | 8 | 7 | 3 | 25 | 102 | 27 | 1 |
| Ku | | | 1 | 0 | 0 | 3 | 3 | 5 | 1 | 0 |
| PM-Scl | | | | 4 | 4 | 2 | 14 | 51 | 20 | 0 |
| Th/To | | | | | 1 | 0 | 1 | 4 | 0 | 0 |
| NOR90 | | | | | | 0 | 5 | 11 | 1 | 0 |
| Fibrillarin | | | | | | | 2 | 1 | 2 | 0 |
| RNAP III | | | | | | | | 13 | 3 | 0 |
| CENP | | | | | | | | | 16 | 1 |
| Topo 1 | | | | | | | | | | 1 |
| PDGFR | | | | | | | | | | |
| Monospecific | 23 | 3 | 12 | 3 | 1 | 1 | 33 | 83 | 68 | 0 |
| Multi – Abs | 164 | 12 | 83 | 12 | 17 | 6 | 48 | 146 | 47 | 2 |
| Total | 187 | 15 | 95 | 15 | 18 | 7 | 81 | 229 | 115 | 2 |

ASIG Research Publications

Gene-Siew Ngian, Wendy Stevens, David Prior, *et al.* Survival and Predictors of Mortality in Australian Patients with Connective Tissue Disease-Associated Pulmonary Arterial Hypertension. *Arthritis Research & Therapy* 2012 14:R213.

V. Thakkar, W. Stevens, D. Prior, *et al.* N-Terminal Pro-Brain Natriuretic Peptide in a Novel Screening Algorithm for Pulmonary Arterial Hypertension in Systemic Sclerosis. *Arthritis Research & Therapy*, 2012, 14:R143.

Moore O, Goh N, Corte T, *et al.* Extent of Disease on High-Resolution CT Lung is a Predictor of Decline and Mortality in Systemic Sclerosis-Related Interstitial Lung Disease. *Rheumatology (Oxford)* 2013;52:155-60.

Nikpour M, Stevens W, Proudman S, *et al.* Should patients with scleroderma-related pulmonary arterial hypertension be anticoagulated? *Internal Medicine Journal*, accepted March 3, 2013.

Thakkar V, Moore OA, Stevens W, *et al.* Performance of Screening Algorithms in Systemic Sclerosis-Related Pulmonary Arterial Hypertension: A Systematic Review. *Internal Medicine Journal*, accepted March 11, 2013.

Vivek Thakkar, Wendy Stevens, David Prior, *et al.* The inclusion of N-Terminal pro-Brain Natriuretic Peptide in a Highly Sensitive Screening Strategy for Systemic Sclerosis-Related Pulmonary Arterial Hypertension. Submitted

Abstracts submitted to ARA:

Podium presentations:

Nikpour *et al.*, Early Mortality in Systemic Sclerosis: Rationale for Forming a Multinational Inception Cohort of Patients with Scleroderma (the INSYNC study). ARA-ASM, Perth May 2013.

Poster presentations:

Nikpour *et al.*, Early Accrual of Organ Damage in Systemic Sclerosis: Rationale for Forming a Multinational Inception Cohort of Patients with Scleroderma (the INSYNC study). ARA-ASM, Perth May 2013.

Thakkar *et al.*, Asymmetric dimethylarginine levels in the early detection of Systemic Sclerosis related Pulmonary Arterial Hypertension. ARA-ASM, Perth May 2013.

Additional research:

Collaboration with Prof Matt Brown in Brisbane and a study quantifying the burden of disease of systemic sclerosis are underway. Watch this space.

research.

International Systemic sclerosis iNception Cohort (INSYNC)

In November 2012, a few ASIG executive members visited Montreal in Canada to embark on a collaboration with the aim of establishing an international inception cohort of patients presenting for the first time with systemic sclerosis. This was instigated by Murray Baron of the Canadian Scleroderma Research Group with ASIG and several other investigators, Patricia Carreira from Spain, Nicolas Hunzelmann, from Germany and Tracy Frech from the USA.

Two main themes emerged from that meeting. Firstly, a study of the mortality of inception and prevalent patients according to duration of disease using data from existing databases would be a good way to commence the collaboration and provide insights into the similarities or otherwise, between the two largest existing cohorts with comprehensive data. This could be expanded into a study of damage accrual and development of a damage index. This is a challenging measure to develop as it can be difficult to distinguish between irreversible organ and tissue damage in systemic sclerosis and other concepts such as disease activity and severity. Plans are underway to develop a delphi exercise to canvas expert opinion regarding the most appropriate measures for a damage index. This will build on preliminary work done by the Canadian Scleroderma Research Group and will lead to the development of the first globally accepted damage index for assessing the outcomes of this disease.

The second and main goal of the collaboration is to establish an international inception cohort (INSYNC) in which to study damage, mortality and more detailed research questions prospectively.

This collaboration brings ASIG to the forefront of international research on systemic sclerosis, particularly as ASIG will lead the mortality study. Data harmonisation of the ASIG database is needed as well as a special focus on patient follow-up by ASIG centres. Data harmonisation is a computer based process that enables data collected in existing databases to be merged without repeating data entry. Some minor changes to the ASIG database are planned with the next upgrade to ensure we have enough similar data fields to the Canadian Scleroderma Research Group to allow comprehensive data harmonisation. This will allow direct comparisons between the groups to be made and for data to be pooled.

ASIG Research Fellow for 2014

Expressions of interest are sought from MBBS graduates with an interest in research in systemic sclerosis (SSc).

ASIG has established a national database to collect prospective clinical and investigative data from SSc patients. This forms the basis of the Australian Scleroderma Cohort Study and is a valuable resource for a range of research projects. These include quantifying burden of disease and linking databases while maintaining a clinical focus including some clinical work.

The group invites expressions of interest from physicians and advance trainees who are interested in one of the following options. Training in rheumatology is NOT a pre-requisite.

- A 12 month research fellowship with a view to submitting publications from the project

OR

- A fulltime student enrolled in a Masters of Philosophy, PhD, or Professional Doctorate.

The successful candidate would commence in February 2014 and receive supervision and support from experienced clinicians and researchers.

Option 1: The fellow would be employed fulltime for a period of 12 months. This position would suit any physician with an interest in developing research skills. A salary package of \$50,000 will be offered.

Option 2: The student would be an Australian resident enrolled or planning to enrol in a fulltime graduate research degree. Funding would be according to NHMRC guidelines and may be tax exempt depending on the individual's circumstances. Initial funding is for the first year, to a value of \$50,000 total package.

Queries should be addressed to:

Dr Mandy Nikpour,
mnikpour@medstv.unimelb.edu.au

Or Chair of ASIG, Susanna Proudman,
sproudman@internode.on.net

Or Secretary of ASIG, Wendy Stevens,
wendy@svhrheum.com

Submissions should be emailed to:

Asig.PROJECT@svhm.org.au

conferences.

2012 ACR Meeting

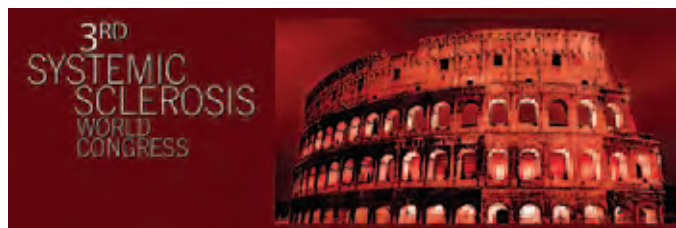
The 2012 American College of Rheumatology meeting was held in Washington DC in November 2012. All the scleroderma research groups presented work, often derived from large patient cohorts like ASIG. Some abstracts focussed on developing tools for predicting pulmonary arterial hypertension which aren't reliant on annual echocardiogram in every patient which tied in nicely with Vivek Thakkar's work on screening algorithms. Similarly, there is considerable interest in identifying tools for predicting outcomes in patients with interstitial lung disease related to systemic sclerosis. This included pulmonary function tests and imaging as published by Owen Moore for ASIG, as well as biomarkers, even the simple C-reactive protein.

5th World symposium on Pulmonary Hypertension

The 5th World symposium on Pulmonary Hypertension was held in Nice on the 27-28 of February to the 1st of March 2013. The symposium is held every 5 years and has grown from just 50 delegates at the initial meeting in 1973 to over 1000 attendees at the meeting in Nice. This growth reflects the increasing interest and research that is occurring in this field. The format for the meeting is 12 taskforces, who have been working together on different aspects of the condition, present summaries of their reviews to the full group for discussion. The discussion was lively and stimulating and the major advances in the last 5 years, in both our understanding of the condition and its management, were presented.

Upcoming conferences

The 13th International Workshop on Scleroderma Research is being held in Boston 3rd-7th August 2013. This is a stimulating cross-disciplinary meeting with a focus on basic science. www.bumc.bu.edu/sclerodermaworkshop



The 3rd World Scleroderma Congress to be held in Rome, 6-8th February 2014, is a very clinical meeting with both academic and patient programs. www.sscworldcongress.org

education.

Want to learn more about the cardiopulmonary complications of systemic sclerosis?

Recent Australian initiatives for fostering education and training in the field of pulmonary hypertension (PH) also provide opportunities for learning more about systemic sclerosis.

The Actelion Clinical Excellence Program (ACEP), independently developed by Australian experts, is a comprehensive on-line program for health professionals who want to become proficient in all aspects of the diagnosis and management of PH. If you would like to learn more about ACEP, contact Derren Rushton, Medical Manager, Actelion Pharmaceuticals: derren.rushton@actelion.com.

The Pulmonary Hypertension Society of Australia and New Zealand is a "not-for-profit" organisation that focuses on ongoing education in PH and collaborative research. Regular updates of published work in the area of PH and an annual multi-disciplinary conference are two of the services offered. Membership is free. See www.phsanz.com.au.

screening.

Access to screening for cardiopulmonary complications of systemic sclerosis

Current international guidelines recommend that all patients with systemic sclerosis (SSc), irrespective of disease subtype or duration, should be screened annually for pulmonary arterial hypertension (PAH).

This complication occurs in nearly 12% of Australian patients with SSc. The ASIG algorithm uses annual echocardiogram and pulmonary function tests as well as comprehensive clinical assessments to ascertain risk of PAH and to identify progressive interstitial lung disease.

Access to screening for cardiopulmonary complications of SSc is freely available at all ASIG centres around Australia (listed on the back of this newsletter) and is intended to complement usual rheumatology care.

If you would like to learn more about referring your patients with SSc for screening, please contact: Asig.PROJECT@svhm.org.au.

Further information about ASIG can be found at:

<http://rheumatology.org.au/rheumatologists/asig-public.asp>

contact.

RESEARCH QUERIES

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QUEEN ELIZABETH

Catherine Hill
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Queensland

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*Australian
Rheumatology
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