Further information about ASIG can be found at:
http://rheumatology.org.au/rheumatologists/asig-public.asp

ASIG
AUSTRALIAN SCLERODERMA INTEREST GROUP

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ASIG
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SCLERODERMA connections.

EDITION 7: MAY 2014

SSC SCREENING CENTRE UPDATE

greetings,

Every year, we lament the speed with which the last 12 months have passed but this year seems to have rolled on more quickly than any other! Maybe it is a reflection of ASIG's increasing activities? Nearly 1500 patients have given their consent to be enrolled in the Australian Scleroderma Cohort Study (ASCS). More research projects are underway and the number of publications continues to grow. The research concerning ASIG's new pulmonary hypertension screening algorithm under the stewardship of Mandy Nikpour and Wendy Stevens has been particularly fruitful with well-received presentations at the American College of Rheumatology Annual Scientific Meeting in November, the Systemic Sclerosis World Congress in February and new publications. Mandy and the recent ASIG-Scleroderma Australia research fellows have been developing a new Damage Index with input from experts around the world and our "INSYNC" inception cohort collaboration with North American and European groups progresses apace.

We would like to thank our patients who have participated in the ASIG study and generously contributed their data. We are much indebted to the hardworking nurses and doctors who devote their time and energy to caring for and finding better ways to treat SSc!

We are delighted that the inaugural ASIG Research Fellow, Dr Vivek Thakkar, has completed his Doctor of Medical Science thesis entitled *'Novel biomarkers in the early detection of pulmonary arterial hypertension in systemic sclerosis.'* He is now leading a new Australian Scleroderma Screening Program (ASSP) site in his practice at Liverpool Hospital, NSW.

I would like to thank A/Prof Eli Gabbay from the University of Notre Dame in WA who has some good news about breathlessness for our patients: that breathlessness is not simply an expected symptom of systemic sclerosis (SSc) and that with vigilance and early diagnosis of what is really going on, the outlook can be bright. His article appears in the patient version of the newsletter.

Finally, another major achievement, again driven by Mandy, has been the successful application for NHMRC funding for a multicentre randomised controlled trial of anticoagulation with apixaban in SSc-related pulmonary arterial hypertension. The first patient should be enrolled later this year.

Susanna

Susanna Proudman
ASIG Chair

8 years and counting – what's new?

The ASIG database was built in 2007 as part of the wider aim of the ASSP to create a system to link data collected from the screening centres. Its primary function is to investigate whether there are predisposing factors associated with the progression of SSc. Ongoing funding from Actelion was received to build and maintain the database which is now on its 8th year. The ASIG database has grown bigger and stronger in 2014 with a total of 1,457 patients enrolled in the ASCS starting from 350 patients enrolled in 2007.

Mean Age at recruitment	57 years old (± 13 years)
Male : Female ratio	1:7
Disease type	25% diffuse, 67% limited
Race	1% Aboriginal and Torres Strait Islander, 86% Caucasian, 4% Asian, <1 % Hispanic, <1% Other
Mean disease duration from first non-Raynauds to recruitment	11 years (±10 years)
Mean length of follow-up	2.3 years (± 2 years)

A recent upgrade was made to accommodate the data harmonisation needed for the International Systemic Sclerosis Inception Cohort (INSYNC) study, to include newly available treatments to support the required data for newly proposed research. For a specific list of upgrades please see the remote access page including new documents such as the ASIG DB codebook, and ASIG request form. Efforts are now being directed to updating patient records through follow-ups and consistent data entry.

Furthermore, we are also adopting a more advanced software called caTissue to manage our biobank, which will be linked to the existing ASIG database. This will improve ease of management of the DNA and sera records as well as saving the TQEH Rheumatology Research Laboratory time in tracking our precious samples. We hope to implement caTissue by 2015.

Liverpool Hospital

It's a great pleasure and privilege to lead the Liverpool Hospital as the latest addition to the Australian Scleroderma Interest Group (ASIG). Liverpool Hospital is the major health service for South-Western Sydney, and a principal referral and teaching hospital of the University of NSW and the University of Western Sydney. An experienced team of rheumatologists, immunologists, nursing staff and allied health work together to manage a range of complex connective tissue diseases (CTD) including scleroderma, lupus, sjogren's, myositis and vasculitis amongst many others.

Our CTD clinic is one of the busiest public hospital clinics in the state making it ideally placed for excellent clinical care and research opportunities. We are also continuing to grow our relationships with the patient support groups of Scleroderma Australia and Scleroderma New South Wales respectively, for it is the patients that inspire us to continue to excel in our clinical and research endeavors.

Some CTD patients will develop heart and lung complications as a natural part of their disease, and we are able to offer expertise in assessing and managing these conditions. In some cases, we arrange for patients to be seen in our multidisciplinary pulmonary hypertension clinic where we work closely with our respiratory and cardiology colleagues to provide accurate and timely care.

Overall, it's an exciting time for our service, and we look forward to serving the wider scleroderma and CTD community as an Australian Scleroderma Screening Centre. In order to be seen, a valid referral from your local doctor or specialist needs to be provided to the Rheumatology Department at the Liverpool Hospital.

It is our great pleasure to announce the appointment of our new ASIG-Scleroderma Australia Research Fellow, 2014. Dr. Nava Ferdowsi, who joins us from St Vincent's Hospital in Melbourne has just completed her advanced rheumatology traineeship with extensive experience in managing SSc patients. She will continue to develop the disease Damage Index with Dr Mandy Nikpour and Dr Wendy Stevens. The Damage Index is currently progressing well with the international working group further clarifying the concept of damage in SSc and developing the items to potentially include in the index. Once this is done the SCTC will perform a Delphi exercise to determine which items are most important to include in the index. The Damage Index could have multiple applications including measuring damage accrual in clinical trials, enrichment of cohorts and prediction of outcome in SSc patients. Generous contributions to fund the research fellow were received.

ASIG also welcomes Dr Jenny Hao, visiting fellow from Beijing, China. Dr Hao is a rheumatologist with expertise in lupus, SSc and other connective tissue diseases. Her research interest is in SSc-associated PAH. She has recently completed a study comparing the accuracy of three screening algorithms (DETECT v. ESC/ERS v. ASIG) for pulmonary arterial hypertension in SSc, which was also presented at the third Systemic Sclerosis World Congress and the 2014 ARA-ASM. She is now analysing data on the early mortality in SSc in collaboration with the INSYNC group.

Antiphospholipid antibodies in an Australian scleroderma cohort

By Dr Kathleen Morrisroe, Rheumatology Registrar, St Vincent's Hospital Melbourne

Antiphospholipid antibodies (APLA) are traditionally associated with deep vein thrombosis and recurrent miscarriage in primary antiphospholipid syndrome and in systemic lupus erythematosus. In SSc, the prevalence and associations of these antibodies is less well defined. Recently, we sought to determine the prevalence and clinical significance of antiphospholipid antibodies in SSc. Our study comprised data on 940 patients with SSc (diagnosed according to ACR and Leroy/Medsger criteria). The prevalence of APLA in our cohort was 24%, with anti-cardiolipin antibody (ACA) being the most prevalent. The majority of APLA were of low titre. Our analyses showed a significant association between APLA and pulmonary arterial hypertension (PAH), interstitial lung disease (ILD), coexistent pulmonary hypertension and ILD (ILD-PH), Raynaud's phenomenon and digital ulcers. These identified associations are further strengthened by the demonstration of a dose-response effect, where higher titre antibodies were associated with a higher risk of developing PAH and ILD.

The common association of Raynaud's, digital ulcers and PAH with APLA suggest that these vascular manifestations may have similar pathogenic mechanisms. The association between APLA and PAH supports the role of micro-thrombosis in the pathophysiology of PAH and may be an explanation for the survival advantage seen with anticoagulation in some observational studies. Possible applications of our findings include the use of APLA to identify patients at high risk of developing PAH and a means for gaining better insight into disease pathogenesis so that targeted therapies may be developed.

Table 1: Correlates of APLA determined using univariate logistic regression

Disease manifestation	ACA type	Odds ratio	95% CI	p value
PAH	ACA-IgG	1.70	1.01-2.93	0.047
	ACA-IgG >40	4.60	1.02-20.8	0.047
ILD	ACA-IgM	2.04	1.40-3.00	<0.0001
	ACA-IgG	1.84	1.20-2.80	0.005
	ACA-IgM >20	2.36	1.17-4.76	0.016
	ACA-IgG	1.84	1.20-2.83	0.005
	ACA-IgG >20	2.15	1.03-4.50	0.041
ILD-PH	ACA-IgG	2.10	1.05-4.20	0.036
Digital ulcers	ACA-IgG	1.76	1.16-2.67	0.008
Raynaud's	ACA-IgM	2.39	1.08-5.27	0.031

There was no significant association of anti-phospholipid antibodies with renal crisis, myocardial disease, gut involvement, highest quartile peak MRSS, disease subtype, other autoantibodies, deep vein thrombosis, pulmonary emboli and death.

announcements.

We are very pleased to announce that Dr Mandy Nikpour's application for the 2013 NHMRC grant round has been successful. The clinical trial will investigate anticoagulation in SSc-related PAH. Dr Nikpour also received an Early Career Fellowship for a project on *'Optimising Accuracy and Cost-Effectiveness of Screening for Pulmonary Arterial Hypertension in Scleroderma.'*

Another milestone of note is the completion of the inaugural ASIG Research Fellow's research studies, Dr Vivek Thakkar has completed his Doctor of Medical Science thesis entitled *'Novel biomarkers in the early detection of pulmonary arterial hypertension in systemic sclerosis.'* An ASSP site has now been established in his practice at Liverpool Hospital, NSW.

ASIG Research Publications

Publications that kept our scientific team busy in 2013

Recent Publications

Thakkar V, Stevens W, Prior D, Youssef P, Liew D, Gabbay E, Roddy J, Walker JG, Zochling J, Sahhar J, Nash P, Lester S, Rischmueller M, Proudman SM, Nikpour M. **The inclusion of N-Terminal pro-brain natriuretic peptide in a sensitive screening strategy for systemic sclerosis-related pulmonary arterial hypertension: a cohort study.** Arthritis Research & Therapy 2013 Nov 19;15(6):R193.

Thakkar V, Moore OA, Stevens W, Nikpour M. **Performance of Screening Algorithms in Systemic Sclerosis-Related Pulmonary Arterial Hypertension: A Systematic Review.** Internal Medicine Journal, 2013 Jul;43(7):751-60. doi: 10.1111/imj.12167.

Nikpour M, Stevens W, Proudman S, Buchbinder R, Prior D, Zochling J, Williams T, Gabbay E, Nandurkar H. **Should patients with scleroderma-related pulmonary arterial hypertension be anticoagulated?** Internal Medicine Journal, 2013 May;43(5):599-603. doi: 10.1111/imj.12111.

Morrisroe KB, Stevens W, Nandurkar H, Prior D, Thakkar V, Roddy J, Zochling J, Sahhar J, Tymms K, Sturgess A, Major G, Kermeen F, Hill C, Walker J, Nash P, Gabbay E, Youssef P, Proudman SM, Nikpour M. **The association of antiphospholipid antibodies with cardiopulmonary manifestations of systemic sclerosis.** Clinical Experimental Rheumatology, 2014 Feb [Epub ahead of print]

Accepted at ARA

Podium presentations:

A Quinlivan, V Thakkar, W Stevens, D Prior, C Rabusa, P Youssef, E Gabbay, J Roddy, J Walker, J Zochling, J Sahhar, P Nash, S Lester, C Hill, M Rischmueller, S Proudman, M Nikpour. **Cost savings with a biomarker-based screening algorithm for pulmonary arterial hypertension in systemic sclerosis.**

Lester S, Patterson K, Walker J, Charlesworth J, Stankovich J, Stevens W, Sahhar J, Nash P, Roddy J, Hill C, Nikpour M, Rischmueller M, Proudman S, Brown M, Zochling J. **Associations between HLA DRB1 Alleles and autoantibodies in systemic sclerosis.**

Poster presentation:

Y Hao, V Thakkar, W Stevens, D Prior, C Rabusa, P Youssef, E Gabbay, J Roddy, J Walker, J Zochling, J Sahhar, P Nash, S Lester, C Hill, M Rischmueller, S Proudman, M Nikpour. **A comparison of the predictive accuracy of three screening algorithms (DETECT v. ESC/ERS v. ASIG) for pulmonary arterial hypertension in systemic sclerosis.**

Systemic sclerosis Damage Index (SSc-DI), Quantifying organ damage in systemic sclerosis

By Dr Tien Tay, PhD candidate, University of Melbourne,
2013 ASIG-Scleroderma Australia Research fellow

Systemic sclerosis (or scleroderma; SSc) is a multi-organ autoimmune disease with significant morbidity and mortality. Unlike other rheumatological conditions, SSc typically has a slow and progressive course which makes it difficult for rheumatologists to measure disease activity. There are various indices to measure health status in SSc with their limitations. However, none of the indices measure organ damage per se.

We have formed a Working Group for Damage Index under the auspices of Scleroderma Clinical Trials Consortium (SCTC) to develop and validate the SSc Damage Index (SSc-DI). This is an international multi-disciplinary collaboration led by Dr Mandy Nikpour. The SSc-DI is intended to be a weighted composite multi-organ score and will focus mainly on objective measures. We envisage that the SSc-DI would have potential applications in research and in clinical studies.

I presented preliminary data from the Australian Scleroderma Cohort Study and the concept of organ damage at the 3rd Systemic Sclerosis World Congress in Rome earlier this year. Our data showed significant accrual of damage in those with early disease, particularly for skin/musculoskeletal, respiratory and gastrointestinal systems (Table 1). Organ damage in SSc occurs early and accumulates rapidly in the first four years since disease onset. Based on the initial survey among the SCTC Working Group members, most experts agreed that organ damage in SSc is permanent and irreversible which involves the loss of anatomical structure or physiological function or functional reserve. Furthermore, disease damage should be differentiated from disease activity and severity, and it should prognosticate morbidity and/or mortality.

Table 1: Frequency of organ damage at 2 & 4 yrs

Disease damage indicator	2 years n (%)	4 years n (%)
Skin / Musculoskeletal	**21 (11%)**	**42 (23.1%)**
Digital gangrene or amputation	3 (1.6%)	5 (2.7%)
Joint contractures	12 (6.6%)	31 (17.0%)
Muscle weakness	11 (6.0%)	19 (10.4%)
Gastro-intestinal	**7 (3.8%)**	**13 (7.1%)**
Oesophageal stricture	2 (1.1%)	3 (1.6%)
Bowel dysmotility / pseudo-obstruction	1 (0.5%)	2 (1.1%)
Anal incontinence	4 (2.2%)	8 (4.4%)
Cardiovascular	**8 (4.4%)**	**12 (6.6%)**
Myocardial disease + either conduction defect or LV dysfunction	4 (2.2%)	5 (2.7%)
Respiratory	**9 (4.9%)**	**22 (12.1%)**
Pulmonary fibrosis + either FVC<70% or DLCO <50%	5 (2.7%)	15 (8.2%)
Pulmonary hypertension + RV dysfunction or dilatation	2 (1.1%)	6 (3.3%)
Renal		
Renal crisis ever + eGFR <60 ml/sec	1 (0.5%)	1 (0.5%)
Genitourinary		
Erectile dysfunction (men)	6 (17.1%)	11 (31.4%)

ASIG Research Fellow for 2015

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 (ASCS) 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 advanced 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 2015 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

American College of Rheumatology meeting 2013

ASIG participated at the ACR by presenting the Asymmetric Dimethylarginine (ADMA) levels in the early detection of SSc-PAH. The talk was delivered by Dr Vivek Thakkar and received positive feedback. A poster on quantifying change in pulmonary function as a prognostic marker in SSc-ILD was presented on behalf of Dr Owen Moore. The Trination's group (Canada, Australia and the USA) also presented their study showing the association between anti-fibrillarin antibodies with more severe gastrointestinal involvement and poorer survival in SSc.

An important outcome of the meeting was the release of the 2013 ACR/EULAR classification criteria for SSc, led by Dr Frank van den Hoogen. The new criteria are said to have better sensitivity and specificity than the criteria devised in 1980. They are also easier to apply and would allow for more patients to be classified correctly, however, validation from other populations is encouraged by the group. The paper is available here:

http://www.ncbi.nlm.nih.gov/pubmed/24092682
http://www.acrannualmeeting.org/

Third Systemic Sclerosis World Congress 2014

The third Systemic Sclerosis World Congress recently held in Rome in February 2014 was a big success with ASIG contributing two oral presentations and two posters. The congress was attended by Australian delegates Drs Wendy Stevens, Susanna Proudman, Mandy Nikpour, Tien Tay, Nava Ferdowsi, Vivek Thakkar and Ms Barbara Gemmell.

Tien Tay, previous ASIG-Scleroderma Australia fellow talked about his research on early accrual of organ damage in SSc as part of the *'Management and Assessment of Newly Diagnosed SSc'* session. The talk was very well-received and the quality of the questions reflected the importance of the study.

As part of the session entitled *'Pulmonary Arterial Hypertension'*, a comparison of the predictive accuracy of the DETECT v. ESC/ERS v. ASIG screening algorithms was presented by Mandy Nikpour on behalf of Dr Jenny Hao. The study found that the DETECT and ASIG algorithms out-perform the ESC/ERS guidelines but the choice of SSc-PAH screening algorithm ultimately depend on cost and ease of application. The results of the comparison were very well accepted.

The poster presentation was on *'Cost Savings with a Biomarker-Based Screening Algorithm for Pulmonary Arterial Hypertension in Systemic Sclerosis'*. The study compared the costs of SSc-PAH screening using the ASIG-developed algorithm against the conventional TTE-based algorithm. The ASIG algorithm was more accurate than the existing algorithm, reduces the number of ECHOs and RHCs performed, the overall costs of screening, and the cost of diagnosing each case of PAH.

Another poster presentation was the *'Early mortality in Australian and Canadian scleroderma patients'*, which was co-authored with the Canadian Scleroderma Research Group (CSRG). The results suggest that prevalent cohorts underestimate mortality in SSc by failing to capture early deaths, particularly in diffuse disease. The results provide a compelling rationale for establishing a large multi-national inception cohort of patients with SSc to more accurately quantify early mortality in this disease. In the future, the Canadian, German, Spanish and Australia collaboration intends to combine their data to form the INSYNC inception cohort in order to better understand early mortality in SSc. The poster won one of the 5 awards out of the 356 entries in the conference.

Special mention should be made of Barbara Gemmell, SSc/PAH nurse from St Vincent's Hospital in Melbourne). She gave a very accessible and informative presentation on *'Taking care of your ulcers'* in a session on *'Ulcers and the hands'* in the exceptionally well-attended Patient Programme. Barbara also presented posters on *'Scleroderma model of care – team meeting, a unique collaborative approach'*, *'Interaction between health care workers for people with scleroderma'* and *'Effect on physical and functional outcomes in scleroderma with a structured long term physiotherapy program in a single study case design'*.

ASIG is increasingly gaining recognition in the international research arena, with other groups now approaching ASIG for collaboration. This is a result of all the hard work and passion that its dedicated members put into the study.

Mark your calendar

Members are reminded of the following scientific meetings:

The next **EULAR Annual European Congress of Rheumatology** will take place from 11th – 14th of June 2014 in Paris, France. http://www.eular.org/index.cfm?framePage=/congress_2014.cfm

The **2014 American College of Rheumatology Annual Meeting** will be held on the 14th – 19th Nov Boston.

The **14th International workshop on Scleroderma Research** will be held in Cambridge, UK on the 1st -5th of August 2014. This is a stimulating cross-disciplinary meeting with a focus on basic science. http://www.bumc.bu.edu/sclerodermaworkshop/

watch this space.

The following studies are currently in the pipeline and definitely something to watch out for in the coming year:

Incidence and prevalence of muscle disease in SSc
Proudman S, Limaye V, Maundrell A

Validation of 2013 ACR/EULAR classification criteria for SSc in the Australian population
Proudman S, Murthy S, Limaye V, Maundrell A

The clinical significance of low C3 and C4 levels in SSc
Nikpour M, Esposito J

Vitamin D deficiency and SSc- prevalence and clinical associations
Sahhar J, Proudman S and Foreman C

The efficacy of Mycophenolate and Azathioprine in SSc Interstitial Lung Disease
Sahhar J, Owen C

Associations between HLA DRB1 Alleles and Autoantibodies in SSc
Lester S, Patterson K, Walker J, Charlesworth J, Stankovich J, Stevens W, Sahhar J, Nash P, Roddy J, Hill C, Nikpour M, Rischmueller M, Proudman S, Brown M, Zochling J

Genetics of SSc
Brown M and Cremin K

Troponin levels in SSc
Sahhar J, Ngian-Siew G

Measuring CXCL4 as a biomarker in the Australian SSc cohort
Youssef P, Adelstein S, Nguyen M

A Multi-Centre Double-Blind Randomised Placebo-Controlled Trial of Oral Anticoagulation in SSc-Related Pulmonary Arterial Hypertension
Nikpour M, Stevens W

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PATIENT NEWS

EDITION 7: MAY 2014

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Susanna

Susanna Proudman
ASIG Chair

donations.

ASIG Research Program

Thank you to Mr Bill Pexton and to the family and friends of the late Mr David Willis and Ms Joan White for their generous donation to the research fund. Donations assist a number of our projects such as biomarker research, maintenance of the national database and funding of a PhD student.

There are two ways to make a donation to the fund:

Cheques can be made out to "ARA-ASIG" and mailed to:

ASIG Executive Officer
PO Box 296
Carlton South, VIC, 3053.

Electronic Funds Transfer (EFT) to:

Account Name:	ARA-ASIG
Bank:	CBA
BSB:	063-449
Account No:	1019 7446
Description:	ASIG research

Please send an email to ASIG.project@svhm.org.au to confirm your EFT.

Please note: Donations to ASIG cannot be claimed as tax deductions.

Liverpool Hospital

It's a great pleasure and privilege to lead the Liverpool Hospital as the latest addition to the Australian Scleroderma Interest Group (ASIG). Liverpool Hospital is the major health service for South-Western Sydney, and a principal referral and teaching hospital of the University of NSW and the University of Western Sydney. An experienced team of rheumatologists, immunologists, nursing staff and allied health work together to manage a range of complex connective tissue diseases (CTD) including scleroderma, lupus, sjogren's, myositis and vasculitis amongst many others.

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Overall, it's an exciting time for our service, and we look forward to serving the wider scleroderma and CTD community as an Australian Scleroderma Screening Centre. In order to be seen, a valid referral from your local doctor or specialist needs to be provided to the Rheumatology Department at the Liverpool Hospital.

It is our great pleasure to announce the appointment of our new ASIG-Scleroderma Australia Research Fellow, 2014. Dr. Nava Ferdowsi, who joins us from St Vincent's Hospital in Melbourne has just completed her advanced rheumatology traineeship with extensive experience in managing SSc patients. She will continue to develop the disease Damage Index with Dr Mandy Nikpour and Dr Wendy Stevens. The Damage Index is currently progressing well with the international working group further clarifying the concept of damage in SSc and developing the items to potentially include in the index. Once this is done the SCTC will perform a Delphi exercise to determine which items are most important to include in the index. The Damage Index could have multiple applications including measuring damage accrual in clinical trials, enrichment of cohorts and prediction of outcome in SSc patients. Generous contributions to fund the research fellow were received.

ASIG also welcomes Dr Jenny Hao, visiting fellow from Beijing, China. Dr Hao is a rheumatologist with expertise in lupus, SSc and other connective tissue diseases. Her research interest is in SSc-associated PAH. She has recently completed a study comparing the accuracy of three screening algorithms (DETECT v. ESC/ERS v. ASIG) for pulmonary arterial hypertension in SSc, which was also presented at the third Systemic Sclerosis World Congress and the 2014 ARA-ASM. She is now analysing data on the early mortality in SSc in collaboration with the INSYNC group.

Breathlessness and Scleroderma: the news is actually GOOD

By Professor Eli Gabbay, Notre Dame University (WA). Professor Gabbay also developed the first screening program in Australia and currently runs a private practice in Perth.

Although not a Rheumatologist (I am a respiratory physician who specialises in heart and lung conditions that can cause problems in people with connective tissue disease), I meet patients with Systemic Sclerosis (SSc; or Scleroderma) every day and I am impressed by how well read you are about the condition and how it might affect you now and into the future. Whilst knowledge is important, sometimes I find that patients can be overwhelmed by all the information available and I find some of it is frankly contradictory and confusing (and I have a medical degree!!).

On that background, I thought it useful to allay some of the fears and myths about heart and lung problems that can develop in scleroderma. Firstly, the sobering news: Scleroderma, like virtually any chronic condition, can increase the risk of heart and lung (cardiorespiratory) problems. The most common cardiorespiratory problems in scleroderma are the same as the most common cardiorespiratory issues in people who don't have scleroderma; they are hypertension (high blood pressure) and ischaemic heart disease such as angina. The prevention of these relatively common conditions in society remain what I am sure you already know about; good nutrition, avoidance of smoking, regular exercise and regular check-ups by your GP to monitor Blood Pressure and some simple blood and perhaps urine tests.

Now for the good news: Whilst it is true that patients with Scleroderma are at an increased risk of some uncommon conditions such as pulmonary hypertension (High blood pressure in the lung circulation) and interstitial lung disease (ILD; scarring in the lung), the overwhelming majority of people with scleroderma will not develop these uncommon problems. Further, if these conditions develop, there are numerous highly effective treatments available.

And the news gets better!! In most patients, the scarring of the lungs that can occur is mild and more often does not progress so that for the majority, some simple and healthy lifestyle adjustments are all that is required. If treatment with medications is required, in my experience they are almost always very effective and needed for a defined period of time ie NOT lifelong.

Pulmonary hypertension (high blood pressure in the lung circulation) is a potentially very serious condition but again the news is mainly good. There are different types of Pulmonary Hypertension and not all are going to get worse or cause you progressive symptoms. Even for the most serious form of Pulmonary Hypertension known as PAH, treatments are very effective especially if started earlier than later and most patients who develop PAH will live meaningful and long lives albeit on therapy.

The trick, in my view, for patients with scleroderma, is to remain vigilant. I think a previous Prime Minister said: be Alert NOT Alarmed! I recommend to my patients the following mantra:

Maintain a regular exercise program; it is important for your usual health and also you will notice any reduction in your exercise capacity earlier. Report to your GP any change in what you can do.

Understand that breathlessness needs a diagnosis. If for example your GP suggests that your breathlessness is due to being unfit then prove him or her right (or wrong). Increase your exercise program, which is safe to do unless you get chest pain or light headedness. If the problem is only your fitness then you will get better quickly. If you don't, then the answer is SOMETHING ELSE. As a general rule, an established diagnosis (ie knowing what is wrong with you) is more easily dealt with than the unknown.

Finally I would also recommend to patients that you are regularly screened for some of the rarer conditions that can occasionally complicate scleroderma and your rheumatologist will be able to advise you on this. The screening tests are non-invasive (which is Doctor Speak for they don't hurt!!) and Australia leads the way with a national screening program under the auspices of ASIG. We are constantly refining the best way to screen patients and getting better at it. And the treatments we have keeping getter better.

As I say the news is actually GOOD!!

Systemic sclerosis Damage Index (SSc-DI), Quantifying organ damage in systemic sclerosis

By Dr Tien Tay, PhD candidate, University of Melbourne,
2013 ASIG-Scleroderma Australia Research fellow

Systemic sclerosis (or scleroderma) is a multi-organ autoimmune disease with significant morbidity and mortality. Unlike other rheumatological conditions, scleroderma typically has a slow and progressive course which makes it difficult for rheumatologists to measure disease activity. There are various indices to measure health status in scleroderma with their limitations. However, none of the indices measure organ damage per se.

We have formed a Working Group for Damage Index under the auspices of Scleroderma Clinical Trials Consortium (SCTC) to develop and validate the SSc-DI. This is an international multi-disciplinary collaboration which is led by Dr Mandy Nikpour. The damage index is intended to be a weighted composite multi-organ score and will focus mainly on objective measures.

I presented preliminary data from the Australian Scleroderma Cohort Study (ASCS) and the concept of organ damage at the 3rd Systemic Sclerosis World Congress in Rome earlier this year. Our data showed significant accrual of damage in those with early disease, particularly for skin/musculoskeletal, respiratory and gastrointestinal. We envisage that the damage index would have potential applications in research and in clinical studies than an activity index which is harder to define.

Interested in being part of the ASCS?

ASIG offers a screening service for pulmonary hypertension and interstitial lung disease for patients with SSc and mixed connective tissue disease. This involves annual visits for screening tests and clinical assessments and is intended to complement, not replace, the care provided by rheumatologists.

If you are an eligible patient diagnosed with scleroderma you are invited to enrol in the Australian Scleroderma Cohort Study (ASCS), although this is not compulsory. This means consenting to your de-identified data being collated with that of other patients. You will be asked if you are willing to provide blood taken at baseline for genetic studies and annually for biomarkers. You will also answer questionnaires relating to your medical history and health and general wellness. The data and blood will then be analysed to better understand the complications of scleroderma in the hope to find better ways to treat this disease.

ASIG Research Publications

Publications that kept our scientific team busy in 2013

Recent Publications

Thakkar V, Stevens W, Prior D, Youssef P, Liew D, Gabbay E, Roddy J, Walker JG, Zochling J, Sahhar J, Nash P, Lester S, Rischmueller M, Proudman SM, Nikpour M. **The inclusion of N-Terminal pro-brain natriuretic peptide in a sensitive screening strategy for systemic sclerosis-related pulmonary arterial hypertension: a cohort study.** Arthritis Research & Therapy 2013 Nov 19;15(6):R193.

Thakkar V, Moore OA, Stevens W, Nikpour M. **Performance of Screening Algorithms in Systemic Sclerosis-Related Pulmonary Arterial Hypertension: A Systematic Review.** Internal Medicine Journal, 2013 Jul;43(7):751-60. doi: 10.1111/imj.12167.

Nikpour M, Stevens W, Proudman S, Buchbinder R, Prior D, Zochling J, Williams T, Gabbay E, Nandurkar H. **Should patients with scleroderma-related pulmonary arterial hypertension be anticoagulated?** Internal Medicine Journal, 2013 May;43(5):599-603. doi: 10.1111/imj.12111.

Morrisroe KB, Stevens W, Nandurkar H, Prior D, Thakkar V, Roddy J, Zochling J, Sahhar J, Tymms K, Sturgess A, Major G, Kermeen F, Hill C, Walker J, Nash P, Gabbay E, Youssef P, Proudman SM, Nikpour M. **The association of antiphospholipid antibodies with cardiopulmonary manifestations of systemic sclerosis.** Clinical Experimental Rheumatology, 2014 Feb [Epub ahead of print]

Accepted at ARA

Podium presentations:
A Quinlivan, V Thakkar, W Stevens, D Prior, C Rabusa, P Youssef, E Gabbay, J Roddy, J Walker, J Zochling, J Sahhar, P Nash, S Lester, C Hill, M Rischmueller, S Proudman, M Nikpour. **Cost savings with a biomarker-based screening algorithm for pulmonary arterial hypertension in systemic sclerosis.**

Lester S, Patterson K, Walker J, Charlesworth J, Stankovich J, Stevens W, Sahhar J, Nash P, Roddy J, Hill C, Nikpour M, Rischmueller M, Proudman S, Brown M, Zochling J. **Associations between HLA DRB1 Alleles and autoantibodies in systemic sclerosis.**

Poster presentation:
Y Hao, V Thakkar, W Stevens, D Prior, C Rabusa, P Youssef, E Gabbay, J Roddy, J Walker, J Zochling, J Sahhar, P Nash, S Lester, C Hill, M Rischmueller, S Proudman, M Nikpour. **A comparison of the predictive accuracy of three screening algorithms (DETECT v. ESC/ERS v. ASIG) for pulmonary arterial hypertension in systemic sclerosis.**

Update on the Third Systemic Sclerosis World Congress

The third Systemic Sclerosis World Congress recently held in Rome in February 2014 was a big success with ASIG contributing two oral presentations and two posters. The congress was attended by Australian delegates Drs Wendy Stevens, Susanna Proudman, Mandy Nikpour, Tien Tay, Nava Ferdowsi, Vivek Thakkar and Ms Barbara Gemmell.

Tien Tay, previous ASIG-Scleroderma Australia fellow talked about his research on early accrual of organ damage in scleroderma as part of the *'Management and Assessment of Newly Diagnosed SSc'* session. The study provides the rationale for derivation and valuation of a disease damage index in SSc. The talk was very well-received and the quality of the questions reflected the importance of the study.

As part of the session entitled *'Pulmonary Arterial Hypertension'*, a comparison of the predictive accuracy of the DETECT v. ESC/ERS v. ASIG screening algorithms was presented. Mandy Nikpour delivered the presentation on behalf of Dr Jenny Hao. The study found that the DETECT and ASIG algorithms out-perform the ESC/ERS guidelines but the choice of SSc-PAH screening algorithm ultimately depend on cost and ease of application. The results of the comparison were very well accepted.

The poster presentation was on *'Cost Savings with a Biomarker-Based Screening Algorithm for Pulmonary Arterial Hypertension in Systemic Sclerosis'*. The study compared the costs of SSc-PAH screening using the ASIG-developed algorithm against the conventional TTE-based algorithm. It was found that the ASIG algorithm has better accuracy than the existing algorithm, reduces the number of TTE and RHC performed, reduces the overall costs of screening, and reduces the cost of diagnosing each case of PAH.

Another poster presentation was the *'Early mortality in Australian and Canadian scleroderma patients'*, which was co-authored with the Canadian Scleroderma Research Group (CSRG). The results suggest that prevalent cohorts underestimate mortality in SSc by failing to capture early deaths, particularly in diffuse disease. The results provide a compelling rationale for establishing a large multi-national inception cohort of patients with SSc to more accurately quantify early mortality in this disease. In the future, the Canadian, German, Spanish and Australia collaboration intends to combine their data to form the INSYNC inception cohort in order to better understand early mortality in SSc. The poster won one of the 5 awards out of the 356 entries in the conference.

Special mention should be made of Barbara Gemmell, Scleroderma/PAH nurse from St Vincent's Hospital in Melbourne). She gave a very accessible and informative presentation on *'Taking care of your ulcers'* in a session on *'Ulcers and the hands'* in the exceptionally well-attended Patient Programme. Barbara also presented posters on *'Scleroderma model of care – team meeting, a unique collaborative approach'*, *'Interaction between health care workers for people with scleroderma'* and *'Effect on physical and functional outcomes in scleroderma with a structured long term physiotherapy program in a single study case design'*.

ASIG is increasingly gaining recognition in the international research arena, with other groups now approaching ASIG for collaboration. This is a result of all the hard work and passion that its dedicated members put into the study.

Scleroderma Australia

Scleroderma Australia and Arthritis South Australia are hosting another patient seminar on the 29th of May 2014 (Thursday), 9.30am – 3.30pm. The seminar will be held at 118 Richmond Rd, Marleston, South Australia 5033.

Guest Speakers:

Associate Professor Susanna Proudman
MB, BS FRACP

Consulting Rheumatologist at the Royal Adelaide Hospital.

Robyn Sims
President of Scleroderma Australia

Karen Patterson
BMS BSci (Hons)

PhD Candidate Immunology Department, Flinders University and CSIRO Nutrigenomics and DNA Damage Diagnostics Laboratory.

Seba Med
Product information and display.

announcements.

We are very pleased to announce that Dr Mandy Nikpour's application for the 2013 NHMRC grant round has been successful. The clinical trial will investigate anticoagulation in SSc-related PAH. Dr Nikpour also received an Early Career Fellowship for a project on *'Optimising Accuracy and Cost-Effectiveness of Screening for Pulmonary Arterial Hypertension in Scleroderma.'*

Another milestone of note is the completion of the inaugural ASIG Research Fellow's research studies, Dr Vivek Thakkar has completed his Doctor of Medical Science thesis entitled *'Novel biomarkers in the early detection of pulmonary arterial hypertension in systemic sclerosis.'* An ASSP site has now been established in his practice at Liverpool Hospital, NSW.