

Christmas Newsletter

*Scleroderma Unit
The Royal Free Hospital -
December 2003*

Seasons Greetings from all at The Scleroderma Research Unit



Dear Friends,

I can hardly believe that another year has gone by. I have as you can all imagine been extremely busy as the President of the Royal College of Physicians, but I have kept in daily contact with both Dr Denton and Dr Abraham. I have an intimate knowledge of what is going on in the department and whenever I can I get up to the Royal Free Hospital to talk about our research programme, attend the clinics and hear about the trials of new drugs that we are undertaking. These are very exciting times for Scleroderma. We have a much better understanding of how the disease progresses, why different organs are affected and how we can prevent progression. We have developed much more targeted therapy and have earlier diagnosis of the complications of the disease. There is a group of dedicated young doctors to take this work forward both in the Royal Free and other units around the country where there is enthusiasm, dedication and a desire to understand this very complex and difficult disease.

I wish you all a very happy Christmas and New Year, I am always pleased to hear from our patients and I do thank you for all the support you give us in our work.

With kind regards,

Professor Carol Black

Departmental News—Dr Chris Denton

Clinical Research

The past few months have been exciting and productive for clinical research projects. Some of the joint work with Dr Gerry Coghlan in pulmonary hypertension and with Professor Ron du Bios and Dr Athol Wells in lung disease has reached fruition and we are starting to understand much better the heart and lung disease that occur in scleroderma. Important clinical trials have finished notably the trial of an antibody against TGFbeta, a key growth factor in scleroderma. The results of this first study are due next year. The Royal Free treated more patients with this new potential therapy than any other centre in Europe or America. Other clinical trials are detailed elsewhere.

I have been fortunate to be able to work with a talented group of rheumatology doctors undertaking research who also join the weekly scleroderma clinic. These include Drs Lynne Shand, Voon Ong, Maresa Carulli and Magda Dziadzio. We also continue to collaborate with Dr Ed Kingdon to study kidney complications in scleroderma. Ed has moved to take up a consultant post in Brighton but continues to work closely with us in research and even send some scleroderma patients back to the Royal Free. We are also continuing our fruitful collaboration with the department of surgery to look at large blood vessel properties in scleroderma. Our previous recent work has shown that arteries as well as the skin are stiff in scleroderma patients although the significance of this observation is less clear – more research needed.

We are expanding the scleroderma outreach clinics, with new clinics in Romford (with Dr Chakravarty) and Bridgend in Wales (with Dr Tom Lawson). This year we have also increased the educational aspect of these clinics by combining visiting the hospital with lectures to the doctors there, especially on new treatments and approaches for pulmonary hypertension in scleroderma.

Additional Laboratory Research

As outlined by David Abraham, the last few months have been busy and successful for the research group. After 2 years hard work my research assistant Lowri Evans moved on to another job and her replacement is about to start. I have been fortunate to be able to recruit Dr Gisela Lindahl to the laboratory. Gisela has outstanding experience and expertise in fibroblast biology and will work on lung fibrosis and help me supervise the other research workers in my group including Voon and Maresa. Combining clinical work and laboratory work remains a challenge but it is much easier when you have such a good laboratory team.

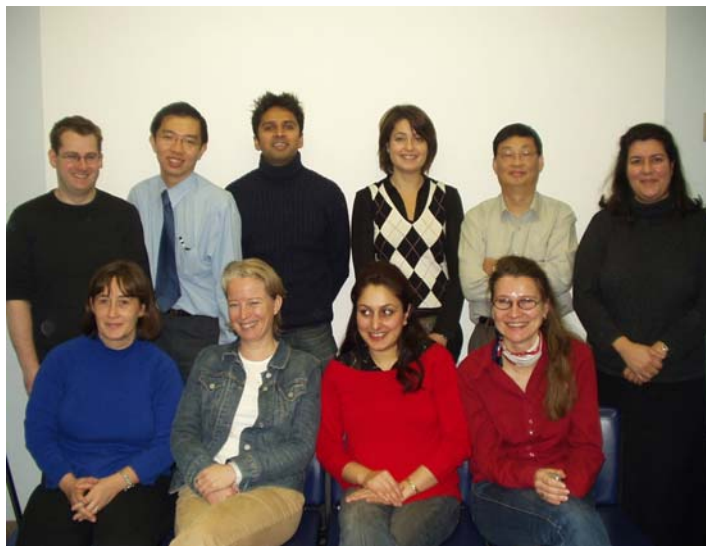
Travel

This has been a busy year with travel to Montpellier to lecture on a scleroderma course, to Madrid and Leipzig to speak on childhood scleroderma as well as to the USA for the annual scientific meeting of the American College of Rheumatology. In April I was fortunate to spend 2 days as a “visiting professor” with Professor Alan Tyndall’s unit in Basel. Professor Tyndall has great expertise in stem cell transplantation in scleroderma and it was a pleasure to meet with his clinical and research group. Closer to home have been a series of lectures to rheumatologists in Wales (Bangor), London, Stevenage and Derby hospitals.

Clinical Trials

We are excited to have a number of new trials for scleroderma. These include three studies of bosentan treatment. This new drug has been proven to help pulmonary hypertension but may also benefit other aspects of scleroderma. It is being tested as a way of treating finger ulcers from Raynaud’s (in scleroderma – the RAPIDS study), as a treatment for lung fibrosis (the BUILD-2 study) and as a long term treatment to improve function in pulmonary hypertension (TRUST study). We are also just about to start a trial of anti-TNF treatment in scleroderma with infliximab, a drug already proven as a powerful treatment for arthritis.

Chris Denton



Some of the department staff (L-.R)

Back row: Alan Holmes, Voon Ong, Vineeth Rajkumar, Maresa Carulli, Yun-Liang Chen, Markella Ponticos,

Front row- Carmen Fonseca, Gisela Lindahl, Mojghan Sabetkar, Magdalena Dziadzio

Research & Laboratory News—Dr D Abraham

Research and Laboratory News

As we move towards the end of 2003, it is a good time to reflect on the progress that has been made in Raynaud's and Scleroderma research over the past year. Research has gone well over the last six months and there have been some major achievements. We now have examined in more detail the different genes that are expressed in scleroderma and how some of the genes control the changes in the immune system, the blood vessels and how this is likely to lead to the development and progression of scarring and fibrosis. We have also been working in the laboratory on Bosentan and Iloprost, two treatments that are widely used. These research studies are aimed at understanding exactly how these treatments are influencing the disease process and which types of cells are most affected. Finally studies carried out by **Vineeth Rajkumar**, one of our research assistants. He has investigated the early changes that take place within blood vessels and has identified some important differences between normal and scleroderma blood vessels. We are very excited by these studies, because it may be possible to prevent these early changes and help to protect the blood vessels from more damage. Much of this work will be published in scientific journals and has advanced our overall understanding of the pathogenesis of Raynaud's and Scleroderma. This information will be invaluable to us as we direct our research efforts into the development of more effective therapies.

Another very important item of news is that **Dr Jill Norman** has moved her entire research group from UCL to the Royal Free Hospital. Dr Norman is an expert in kidney diseases and fibrosis, and with whom we have collaborated with in the past. This development means that we now have a much larger group of scientist within the Royal Free Hospital with common objectives - to find to root cause fibrosis in scleroderma and to define the best way to treat. This can only help in obtaining more support for clinical and research studies into the disease process and increase the profile of Scleroderma within the scientific community, and to provoke more widespread interest.

Research and Equipment Grants

Since May 2003 we have been awarded the following grants:

The Arthritis Research Campaign - We have been awarded two ARC BSc grants for training of medical students to work in the laboratory. These are ongoing research projects related to Raynaud's and Scleroderma, specifically on the role of free radicals and oxidative stress and the mechanisms of fibrosis in model systems.

The Engineering and Physical Sciences Research Council - has awarded us a joint grant with Dr Mark Eastwood to study the role of Stem cells in changes to the blood vessel under different bio-mechanical stimuli.

The Golden Charitable Trust - have continued their long-term support of our basic research in Scleroderma with an emphasis on moving rapidly into clinical trials and patient treatment.

The Nightingale Charitable Trust - have provided

continued support of our research studies into the root cause of scleroderma and potential avenues for treatment.

The Raynaud's and Scleroderma Association - have funded a 1 year fellowship for Dr Lynne Shand to examine the natural history of skin fibrosis in scleroderma and a 2 year award to Dr Voon Ong to examine a protein called MCP-3 in scleroderma.

The Scleroderma Research and Development Action Committee for support to examine the role of blood vessel changes in Raynaud's and Scleroderma

The Scleroderma Society - has provided support to assist setting up a proteomic laboratory at the Royal Free, which will enable us to examine many of the proteins produced in Scleroderma and to study their function.

The Laboratory and New Staff

There are two new members of the research team. **Ms Rim Abdi** joined us in July to study aspects of the genetics of Scleroderma with **Dr Carmen Fonseca**. This is part of our ongoing collaboration with Professor Ron duBois and Ken Welsh at the Brompton Hospital. **Dr Gisela Lindahl** joined the laboratory in September. Dr Lindahl is a very experienced scientist who has work on pulmonary fibrosis for a number of years and will work with Dr Chris Denton on a project aimed at understanding to control of collagen in pulmonary fibrosis. **Mojhgan Sabetkar** who has been with us for the last 18 months working on an Arthritis Research Campaign grant has just been awarded her PhD doctorate degree and is going to stay with us for another year to continue her laboratory studies examining the protein profiles in scleroderma. Mojhgan's long-term aim is however to enter Medical School and study for her Medical Qualification in the Rheumatological specialty.

National and International Meetings

Many of the research staff, including Dr Maresa Carulli, Dr Richard Stratton, Dr Chris Denton attended the American College of Rheumatology meeting in the US in October. Much of the ongoing laboratory studies were presented at this meeting both as oral presentation and as posters. Drs Andrew Leask and Xu Shiwen are about the leave for a meeting in Japan. This is one of the most important meetings in the year, and it is here that Andrew and Xu have been invited to give lectures on their research work. The Department of Rheumatology also co-organises The London matrix group which hosts a monthly lecture series bringing together most of the prominent research and clinical scientist in London who are working scleroderma, fibrosis, tissue repair and allied rheumatological diseases. This series of lectures has attracted a lot of interest within the London research community and has been able to entice some excellent speakers from the UK and abroad.

Dr David Abraham



News From Our Nurse Specialists

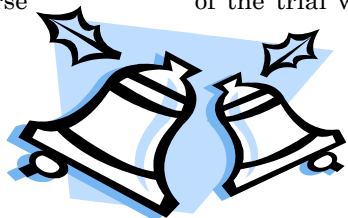
The specialist nursing team has expanded dramatically over the last year and we are pleased to be developing the services we can offer to patients.

Doesn't time fly? Since last Christmas we have welcomed two new nurses to our team: Leo Gonzalez is our clinical trials nurse, and Joanna Smee is working with Clare as pulmonary hypertension nurse. Along with Helen (clinical nurse specialist), Clare (pulmonary hypertension specialist nurse) and Rachel (education nurse) the team now comprises five members, not forgetting Sharon, our clerical assistant who is worth her weight in gold.

The team have all been very busy over the past twelve months doing our best to ensure that we can offer a seamless service to patients. As usual we have been honoured to be asked to speak at various patient groups and meetings around the country. Helen and Rachel gave a talk about clinical trials at the Raynaud's and Scleroderma Association annual conference in Chester, Rachel spoke at the Scleroderma Society autumn meeting at the Royal Free and Clare was heavily involved in the Pulmonary Hypertension Association UK annual conference in Cambridge in October teaching at the patient study day and leading seminars. We feel it is important that all patients are fully educated about their disease and are grateful to be given the chance to inform patients about their choices.

As you know the department is very committed to research into these sometimes devastating conditions and as such recruitment to clinical trials continues with fervour. This year has seen us begin some very exciting trials to add to our ongoing trials and as usual we are keen to hear from anybody who would like to take part in any of them. It is only by having people willing to take part in clinical trials that advances in treatment can be made.

INFLIXIMAB – This is an exciting new treatment for the treatment of early (less than 12 months) diffuse scleroderma. It has already been used with much success in the related conditions of rheumatoid arthritis and Crohn's disease and it is hoped it may lead to a possible new treatment for scleroderma. There is no placebo (dummy drug) involved, and patients receive five infusions over the course of the trial which lasts 48 weeks in total.



RAPIDS 2 – This trial is looking at the use of a drug called bosentan in the cure and prevention of finger ulcers. Some of you may have taken part in the first study RAPIDS a couple of years ago. That trial showed that bosentan did seem to cure and prevent ulcers occurring and so the company concerned have asked us to take part in the follow up trial. To take part you may have either limited or diffuse scleroderma but you must currently have an ulcer on your finger. There is a placebo arm to this trial so a percentage of people on the trial will receive a dummy treatment to allow comparison with the active treatment to be made. The trial lasts approximately 6 months and involves monthly visits to the hospital.

SSTEP – This ongoing trial is looking at the use of oral iloprost in patients with limited or diffuse scleroderma and is looking at it's effect on the large blood vessels and the prevention of major organ involvement in patients with scleroderma. Patients would only need to visit the hospital once every six months, however you do need to be aware that the trial lasts five years and also has a placebo arm.

BUILD 2 – This is another of our new trials which is also using the drug bosentan. It is investigating whether bosentan can treat, or prevent progression of, lung fibrosis. You can have either limited or diffuse scleroderma although you must have diagnosed lung fibrosis. The trial lasts for 1 year and involves monthly visits to the hospital. Again, there is a placebo arm to this trial.

ORAL ILOPROST IN PULMONARY HYPERTENSION – It is well documented that iloprost when inhaled or given intravenously can successfully slow the progression of pulmonary hypertension and this ongoing trial is investigating whether giving iloprost as a tablet has the same effect. This trial lasts only four months although regular visits to the hospital and tests are involved.

TRUST – This new trial is investigating whether the use of bosentan improves quality of life in patients with pulmonary hypertension. It lasts for 1 year and you would need to visit the hospital monthly. However there is no placebo arm on this trial and everyone who takes part will receive bosentan.

If you would like more information on any of these trials then please do call us on 020 7830 2326.

Our Nurse Specialists Continued

It is of vital importance that the profile of these rare diseases is raised and all the nurses have been active attending national and international meetings with other healthcare professionals, trying to achieve this aim amongst other nurses.

With this in mind Helen and Rachel have written a short book entitled "The Role of the Nurse in Raynaud's and Scleroderma". This is currently available free to any nurses who would like it so if you have a district nurse or a GP nurse who would like to see a copy please ask them to call us on 020 7830 2326 or the Raynaud's and Scleroderma Association on 01270 872776.

After the Christmas break we will be straight back to work and are full of plans for how the nursing service should develop over the coming months. We are hoping to be able to set up a national network of nurses and other health professionals interested in scleroderma in order to ensure that ideas and resources can be shared and the support offered to patients standardised. This is something already in the development stages in the pulmonary hypertension service. We are also hoping to be able to organise a conference for nurses about scleroderma and related conditions. We hope that this will attract nurses with an interest in these areas from across the country and by raising awareness among nurses thereby improve the care available to patients. During 2004 it is also anticipated that Clare will be able to start a nurse-led clinic for some patients with pulmonary hypertension. Next year will also see the advent of new clinical trials, in particular a trial of the drug beta interferon, which, it is hoped, may potentially lead to a new treatment for scleroderma.

These are but a few of the plans we have for next year and beyond and we hope you'll be able to be part of them. But until then from all of us to all of you, "Merry Christmas and a Happy New Year".

*Helen, Clare, Rachel, Leo,
and Joanna*



Vascular Studies — Kevin Howell

News from the Blood Flow Studies lab

There is plenty to tell you all about since the Spring Update...

In May I attended the European Congress of Medical Thermography in Krakow, Poland, and I spoke about how we use thermal imaging at the Royal Free Hospital to help us diagnose Raynaud's phenomenon. Local patients with Raynaud's often attend my lab prior to being referred to our Nurse Specialist Helen Wilson for advice. This means the thermography results are available before the appointment with Helen, and she can use the results to ensure only patients with Raynaud's phenomenon are placed on her clinic. If the patient requires different advice we are able to book them onto a more appropriate clinic. This use of thermography to ensure patients are seen by the most appropriate doctor or nurse seems to be unique in the UK, and there was a lot of interest at the meeting in our results.

In September I was in Bath for the second UK Symposium on Medical Infrared Thermography, which some of you may recall was staged at the Royal Free Hospital last year. I spoke about using thermography to study morphoea, and my colleague Liz Joyce from Royal Free Medical Electronics spoke about her recent MSc. project on imaging connective tissue with terahertz frequencies.

In recent weeks we have been able to start a study with Great Ormond Street Hospital which we hope will bring us a better understanding of the skin and blood flow changes in morphoea. Thermography is being used along with laser and ultrasound imaging techniques, and this is likely to keep us occupied well into 2004. Maria-Teresa Visentin from Great Ormond Street, and Antonia Lavorato from Royal Free Medical Physics are important members of our team that make this study run smoothly.

I remain on the committee of the UK Thermography Association as the representative of medical members. Since thermography is used for lots of industrial applications too, some of the committee meetings are in distinctly non-medical venues. Last month I was inside Didcot power station, which was very interesting, and next month's meeting is to be at AWE Aldermaston, where nuclear weapons are designed. I am not quite sure what to expect on that day!

Merry Christmas and a Happy New Year to everyone.

Kevin



Talking About the Disease—Kim Fligelstone

Hello again,

As many of you will know I am a patient who has had Systemic Sclerosis for many years, I was diagnosed in 1988 with diffuse disease. I have been working as a part time volunteer at the Royal Free since 1992. I have several duties at work but by far the most pleasant is visiting patients on the ward [see below]. I also Chair the Scleroderma Society, a self help group founded in 1982 to help patients and their families with scleroderma. This role takes me all over the country meeting people, and my latest jaunt took me to Appleby Grammar School in Cumbria where I spent 10 minutes talking to over 500 pupils in school assembly first thing on Monday morning. I don't know about you but mornings are not my best time of day! But it was worth it just to know that 565 people now know a little bit more about scleroderma!

I have been visiting a patient who has very severe small bowel involvement if anyone reading this would like to contact me with a view of offering support/tips for me to pass on I would be very grateful.

If anyone would like to talk to me on the telephone or would like a visit on the ward my contact number is:

020 7794 0500 ext: 5131 or 020 8961 4912

Kim

CTGF blister fluid study—Dr M Dziadzio & Dr R Stratton

We would very much like to thank all patients, their friends and relatives for participation at our CTGF blister fluid study. We are now collecting and analysing the findings and will keep you informed about the results once they are completed.

Family Day — Saturday 15 May 2004

A date for your diary in 2004. We receive a lot of positive feedback about Family Day so I hope you will be able to join us. We have enclosed a book of raffle tickets — for the Family Day Draw. The raffle has, over the past few years, raised valuable funds and we are very grateful to all those who buy tickets. If you would like more raffle tickets please contact Pamela Yeomans on 01273 672686.

We also receive many donations from patients and their friends, for which we are extremely grateful. We would especially like to thank Mrs Ferrell's company Graphite —who sent us £4000; and a donation of £5,000, by a donor who wishes to remain anonymous.

Communicating With Us

Direct

Ade *020 7830 2284*
Helen/Rachel *020 7830 2326*
Clare *020 7472 6354*
Kevin Howell *020 7472 6550*
Scleroderma Appts *020 7830 2151*

Via the switchboard on 020 7794 0500

Kim Fligelstone Ext 5131
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