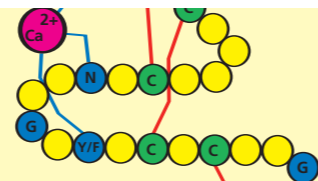


Report from Seventh International Research Symposium on Marfan Syndrome,

Ghent, Belgium, September 14 – 17, 2005



This long awaited meeting was attended by 200 scientific and medical delegates from 34 countries. The latest developments regarding laboratory research, diagnosis and management of Marfan syndrome were discussed. 53 lectures and 35 posters were presented. Key developments were as follows:

■ **The French database now contains 1,081 patients and family members with identified mutations in the Marfan gene, confirming subgroups of mutations which specifically cause newborn Marfan syndrome, or dislocated lenses, or severe heart disease. (supported by The Marfan Trust.)**

■ The Marfan mouse model is proving very useful for drug trials. Losartan is capable of normalising lung and aortic wall structure if given early enough in the newborn period. An international drug trial is being planned.

■ Professor Lynn Sakai from Oregon is trying to develop a simple diagnostic blood test for Marfan syndrome based on breakdown products of fibrillin which circulate in the bloodstream.

■ 5 new genes which can cause familial thoracic aortic aneurysms were described by several participants. These genes together explain a large proportion of families who do not appear to have Marfan syndrome, but still have dominantly inherited aneurysms.

■ **Dr Child's presentation of the results of a questionnaire survey of Marfan syndrome patients over the age of 50 in the UK (a summer project by**

Medical Student Mr Ali Hassan) indicated increased incidence of arrhythmia, cataract, partial hearing loss and familial osteoarthritis at an earlier age than the general population. These conditions can all be treated and must not be dismissed. (supported by The Marfan Trust.)

■ Beta blocker therapy in children significantly delays aortic root dilatation, gaining on average 2 years before inevitable surgery is necessary.

■ The fibrillin-1 deficient mice have failure of muscle regeneration leading to muscle weakness, probably helping to explain easy fatiguability in Marfan syndrome.

■ Dr Devereux from New York suggests trying anti-depressants (Serotonin antagonists) to help patients feel less tired.

■ Beta blocker therapy was supported as the best available medication until further drug trials are performed.

■ Timing of surgery in adults is still between 4.5 to 5 cm aortic root diameter, the standard accepted internationally.

■ Since 2000, the diagnosis of Marfan syndrome is being made at a younger age with a significant reduction in serious cardiovascular

events, in the Marfan clinic of Denver, Colorado. Preventable aortic complications have dropped from 55% in 1970 to only 10% in patients diagnosed after 2000.

■ **The use of a fibrillin-1 mutation database for screening close relatives, included prenatal diagnosis, was described by Dr Child, based on her work with Dr Paolo Comeglio in the Sonalee Laboratory. (supported by The Marfan Trust.)**

■ Hip replacement in Marfan syndrome is uncommon, however young Marfan patients with severe protrusio acetabulae are at risk of degenerative hip disease.

■ **Pre-implantation genetic diagnosis for Marfan syndrome (IVF) is now offered in France, and patients interested should contact Dr Child. This test can determine that the embryo does not have Marfan syndrome, before it is re-implanted in the mother's womb to grow to term. Interested couples do not have to leave England for this procedure as the preparation for this test can be offered here. (supported by The Marfan Trust.)**

This very interesting conference provided opportunity for exchange of information, and establishment of many new collaborations.

Anne H. Child MD, FRCP, Medical Advisor, Marfan Trust, Reader Cardiovascular Genetics, Honorary Consultant Cardiology and Genetics, St George's University of London

BUPA Great Run South



This year the Trust applied for charity places at the BUPA Great Run South which was held in Portsmouth on the 9 October. The Great Run South is now in its 14th year and is Europe's biggest 10 mile race.

This was a new venture for the Trust, as it is the first time that we have been involved in a major running event. In all 18 runners participated in the race for the Trust.

A big thank you to the runners for taking part and promoting awareness of Marfan Syndrome and the work of the Trust. At the time of going to press not all the sponsorship money has been received. The full amount raised will be advised in the next newsletter.



Sarah Burnhan who ran for The Marfan Trust

MarfanTrust News

AUTUMN/WINTER 2005

PATRONS: SIR MAGDI YACOUB FRCS, MR ANTHONY LATTER MA

www.marfantrust.org

Registered Charity No: 328070

Chairman's Report



I am pleased to report that the Charity continues to develop on all fronts. Through the efforts of the medical team at St Georges Hospital led by the Trust's Research Director Dr Anne Child, Marfan Syndrome has become widely recognised within the UK medical profession. The research undertaken at St George's has led to a better understanding of the syndrome within the wider perspective of the medical profession with consequent improvement in preventative treatment. The increased recognition and steady funding support from many organisations has enabled the Charity to fund 2 new research projects.

In May this year The Trust held a Marfan Medical Day at the Royal College of Physicians in London. The aim was to give all levels of staff within the medical profession a brief insight into the various aspects of Marfan Syndrome. A number of presentations were given by Dr Child and her guest speakers, highlighting the Trust's 5 year Research Project. This Project has resulted in a better understanding of gene mutations and therefore how the condition may be treated both in the short and long term. In addition, various speakers presented on the current speciality treatment of major affected organs of the body.

The feedback was very positive from those who attended and the Trust plans to hold further events in 2 – 3 years.

Dr Child also attended the Seventh International Research Symposium held in Ghent in September, where various leading

international medical delegates discussed the latest developments, in research, diagnostics and management of the syndrome. This was an invaluable exercise in an exchange of views, ideas and research technology in which the Trust is proud to have been able to play a part.

The 2 new research projects which the Trust has initially agreed to support include examining the heart and the largest artery from the aorta which passes through the neck, using Tissue Doppler Echocardiography. This will form part of the UK's contribution to the planned National and International Drug trial to show that a new drug is better than the best old drug Atenolol. The other project is studying the importance of Arrhythmia (palpitations) in patients. These projects are in addition to the on-going gene/mutation project which is helping to correlate the clinical problems shown in sufferers and the type of mutation and its location in the gene.

These projects create a major financial burden for the Trust and funding is increasingly difficult. The Charity has been very active in trying to identify sources of funding and has been successful in securing support from a range of organisations through letters of appeal. As ever, we have a number of tireless supporters who raise money through their personal efforts and charity events such as those held in the Sun Public House in Carshalton. The Trust also had 18 runners representing the Charity in the BUPA Great South Run at Portsmouth. To these and many others we are eternally grateful.

We have again applied to the UK Lottery Fund for a significant donation and hope to hear a positive result in April 2006.

It is vital that we raise at least £150,000 in the next twelve months, if the Trust is to continue to maintain and support the level of research currently underway and planned for the next period. I would urge everyone to help us, no matter how small the donation or gesture. We are, once again, sponsoring Christmas Cards and what better way to send festive greetings to your loved ones and help the Trust to secure the funding it so badly needs? An order form is enclosed with the Newsletter.

Finally, I would like to express my sincere thanks to my fellow Trustees and the members of the research team at St George's. Without their support, energy, advice and commitment we would not have come this far. We have achieved so much and yet there is so much more to be done. **Thank you.**



Marfan Trust 2005 Christmas cards are now on sale.

Please support the work of the Trust by buying our Christmas cards. Not only will you be supporting research into the cause and possible prevention of Marfan Syndrome, you will also raise the profile for the majority of people who have never heard of it. If you would like to order any cards, please complete the enclosed order form and return it to the Charity Administrator in the pre-paid envelope.



Marfan Medical Day

On Friday 27 May 2005, a Marfan Medical Day was held at the Royal College of Physicians in London.

The conference was organised and sponsored by the Trust and was aimed at cardiologists, doctors and nurses to discuss all features of Marfan Syndrome and major aspects of modern management. The British Heart Foundation had given the Trust an educational grant towards the

cost of the conference.

Specialist speakers in each field had been invited to speak at the conference. Each speaker was given a time slot of 25 minutes for their presentation. The Cardiologist and Marfan Syndrome, Dental Aspects of Marfan Syndrome, Rheumatological Aspects of Marfan Syndrome are just some of the subjects that were discussed.

The conference proved to be

very valuable and we received positive feedback from the delegates who attended. Ideas for several new collaborative research projects sprang up during discussions between the speakers, who were pleased to meet other specialists interested in Marfan Syndrome.

It is hoped that another conference will be held for interested parties in the future.

Cambridge Summer Music Festival

On the 20 July 2005 at the Cambridge Summer Music Festival there was a special evening with Sir John Tavener, soprano Patricia Rozario and representatives of the heart surgeon Professor Sir Magdi Yacoub. Admission to the concert was free but the audience was asked to give a donation which was split between the Marfan Trust and the Chain of Hope charities.

Sadler's Wells Theatre

On the 15 – 17 September, Random Dance, resident company at Sadler's Wells, performed Amu (of the heart) – a large scale contemporary dance and music event featuring 50 musicians, 7 singers and 9 dancers. Choreographer, Wayne McGregor, in collaboration with heart imaging specialists Dr Philip Kilner and Dr Sonya Babu-Narayan, interpreted both the physical functions and symbolic resonances of the human heart. Sir John Tavener created the score for the dance, which was played live by Southbank Sinfonia. A collection was made at each of the performances, which was split between the Marfan Trust and the Chain of Hope charities.



Alexandra Rose Day – Annual Flag Day 2006

Wednesday 14th June in London, Saturday 10th or 17th in most other places.

The Trust can raise worthwhile funds by taking part in the "Alexandra Rose Day", national Flag Day, to be held in June 2006.

By linking the Marfan Trust with Alexandra Rose Day's national identity, and by selling their familiar rose emblem to members of the public, we can be part of a national event and raise instant cash for ourselves!

We need as many volunteers as possible. So if you have a couple of hours to spare please help us. You can collect near home, at work, or at a site chosen by yourself. Further information can be obtained from the Charity Administrator on 020 8725 1189 or e-mail, hdydyk@sgul.ac.uk.

A surprise visit from Emeritus Professor Peter Beighton, Department of Human Genetics, University of Capetown, South Africa (middle) who came to discuss results of a collaborative research project, which were explained by Dr Paolo Comeglio (left) and Dr Anne Child.

Sonalee Laboratory Research Project – Marfan syndrome fibrillin-1 mutations in Cape Town population.

In 1991, the gene for Marfan syndrome (fibrillin-1) was discovered and an international database now holds over 600 mutations causing Marfan syndrome in different populations and with different phenotypes. Professor Beighton wondered if the Cape Town population, which is very racially mixed , derived from original Hottentot genes and added Asian, black and Caucasian genes, would produce mutations similar to those already described in Caucasian populations.

A pilot study of 9 individuals with Marfan syndrome or marfanoid habitus carefully selected from his population of cases studied over many years, included five females, and four males. One was of Indian ancestry, four of European Caucasian ancestry, and four Cape mixed

ancestry with genetic input from Bushmen, Hottentots, Javanese, Indian, Indigenous African (Angola and Madagascar) and European stock.

The results were to be of direct value to the families concerned, to support diagnosis and to provide genetic screening for other at risk family members as well as correct genetic counselling for future generations.

Results

Using the Sonalee Laboratory dHPLC gene analyser, the fibrillin-1 genes of each patient were analysed by Dr Paolo Comeglio and Mr Gavin Arno.

Four new mutations were found, confirming the diagnosis of Marfan syndrome, and providing the basis for medical therapy, and diagnostic screening for offspring who bear a 50:50 risk of inheriting the mutation. One of these mutations was a severe one in the newborn region (exons 24-32) in a child requiring heart

Photo (L-R): Paolo Comeglio, Professor Beighton and Dr Child.



valve repair by the age of three.

The negative tests provided limited reassurance to 6 patients and their families that they probably do not have Marfan syndrome, although they have a Marfan-like body build.

Lastly, mutations in this population are not different from those found elsewhere worldwide since various races are genetically more similar than they are different.

This study was performed by Dr Paolo Comeglio and Mr Gavin Arno, with funding from the Marfan Trust. Results are to be published in a Cape Town medical journal by Professor Beighton to raise awareness of the importance of this test in making a diagnosis.

Fundraising

A special **thank you to Tina Young** for arranging 4 Quiz nights at her local pub The Sun in Carshalton. £500 was raised as a result of the quiz nights. Thank you to all those who participated.

The Marfan Trust relies entirely on donations and the generous help of our supporters. There are many ways to donate to the Marfan Trust. Your donation will help us continue our vital research into finding preventive treatment.

Donate in memory

Make a donation in memory of a loved one Remember someone close to you by making a donation in their memory. This is a valuable and positive way to celebrate the life of a loved one, whilst helping the Marfan Trust make a difference for the future.

Gift in your Will

Leave a legacy to the Marfan Trust. A gift in your will to the Marfan Trust will help us save lives, by planning vital research far into the future. Together we can bring better treatments and more effective methods of prevention to all those suffering from Marfan Syndrome. Request an information pack for more information.

By Post

To make a gift by post, please make your cheque or Postal Order payable to 'Marfan Trust' for the amount you wish to contribute.

**Marfan Trust, Charity Administrator
Cardiac & Vascular Sciences
St George's University of London
Cranmer Terrace, London, SW17 0RE**

Gift Aid

Under the Government's Gift Aid scheme, the Marfan Trust can reclaim the tax made on donations. This means that we can get 28 per cent more money, at no extra cost to you. So if you are a UK taxpayer, please contact the Charity Administrator for a Gift Aid Form.

For further information about the work of the Trust please contact:

Helga Dydik, Charity Administrator, Cardiac and Vascular Sciences
St George's University of London, Cranmer Terrace, London SW17 0RE
Tel No: **020 8725 1189** Fax No: **020 8725 3416** e-mail: **hdydyk@sgul.ac.uk**