Marfan Trust

Supporting Research into Inherited Aortic and Related Disorders

Newsletter Spring 2020

Welcome to the Marfan Trust Spring Newsletter of 2020. We do hope you are all safe and well in these tricky times. This Spring we all find ourselves dealing with Covid-19 and the challenges it throws up. For the Marfan Trust (the Trust), happily this means business as usual, albeit on a remote basis. In this issue:

New Gene Discovered for Spinal Curvature (Scoliosis)

The discovery of Genetic Mutation in TTLL11 Gene will allow the screening of children of a non - Marfan scoliosis parent, to identify those who have inherited this gene and are therefore at risk of developing scoliosis.

A Word from the Trustees

Chair, Michael Heath, outlines how the Trust has adapted to the recent challenges of Covid-19, moving offices, hiring new staff and completing the merger with the Marfan Association. He also details our plans for the future.

Marfan Trust Now Fully Staffed

Following nine months of significant organisational change, the Trust now has a full team of experienced permanent and volunteer staff in place to help it move forward and better meet its aims.

New FaceBook Page

Along with a new team and new offices comes a new Facebook page for the Trust. You'll find it here: **https://www.facebook.com/Marfan-Trust-102179834771903/**. Look out for lots of useful information and ideas from us. Please check it out and **"like"** us.

Marfan Trust Staff and Trustees in Zoom Meeting

MARFAN TRUST

Guy Scadding Building
Dovehouse Street
London SW3 6LY

T: +44 (0)20 7594 1605
E: info@marfantrust.org
https://www.facebook.com/Marfan-Trust-102179834771903/

…And finally,

SAVE THE DATE

for our Information Day on

3rd October 2020

See page 9 and 10 for more details

A Word from the Trustees

It was our late Chair Michael Carr (see tribute on page 12) who introduced me to the Board and gently eased me into becoming a trustee. Although illness had prevented him from being active with the Marfan Trust in recent years, in addition to his contribution for which we thank him in this publication, he did leave for me a prescient insight into the future of the Trust. This has assisted me to bring, with my fellow Trustees and our Medical Director, to where we are today. This position is what I want to explain here using a series of Thanks.

However, writing this during the rapidly unfolding COVID-19 pandemic and not knowing when you are likely to read this, I find that Dr Anne Child, Dr José Aragon-Martin together with Moira Taylor and our brand new staff members Victoria Hilton and Gurpreet Madan have successfully moved to working from home to respond to the increasing virus related enquiries we're receiving and currently remain available to you. The Trustees met virtually in early in April and The Marfan Trust will ensure that we remain in contact with you (look out for regular e-mail and social media updates), that we are effective and sustainable during the crisis, and will be ready for when things look up with a return to a normality, when the charity will again work with you all to fully deliver our Mission and Objectives. So do follow the advice, keep well and please read on.

That first of my thanks is to Trustees of the Marfan Association who have graciously worked for a smooth merger with the Trust. This support and transfer of funds brings a boost and opportunities for the Trust, now the only independent body for Marfan syndrome in the UK. A responsibility that I and our Trustees are all too mindful of.

The move to the Guy Scadding Building in South Kensington has not been without many logistical challenges. Dr Child has been brilliantly supported by Moira, volunteer Natalie Ryder and others who have given their time and experience to bring about this transfer.

Michael Heath, Chair

We all probably have an idea about the issues in moving an administrative department which has included some legal expenses, but what about a research programme as comprehensive as the Sonalee Laboratory (the Lab)? The ethical transfer of data and samples is complicated and expensive and this has taken up all Dr José Argon-Martin's capacity as the Research Director. But the Lab should soon be up and running and again making a mark in our sphere of medical research. Well done José! We look forward to funding new research projects.

My final thank you here is to you our uncomplaining supporters who must have wondered "what is going on?". With the move and merger complete and new staff in post, we will now get back to some positive engagement with you. That should be timely acknowledgements of donations or support with your fundraising activities. The pending upgrade to our website with enhanced links to our recently reengineered social media platforms will also make us more visible and assessable.

The Marfan Trust is arguably a niche Charity which will now "pack a bigger punch". We will start this with the introduction of a membership scheme later in the year; a modernised version of that of the Marfan Association. Details to follow later. As members you officially become a part of our family. For the Trust, a healthy membership becomes the foundation for its supporters and will help us to take our work forward.

In October we are planning to reconvene our Marfan Information Day, an open event to meet up and find out what is happening in our world of Marfan syndrome and related disorders, details of the day and how to become a member are in this newsletter. See page 10.

I look forward to meeting many of you or hearing that you are now members later in the year.

Please do e-mail the Trust or use our social media pages to contact us with your comments on my article and the newsletter.

Best Wishes
Michael

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Marfan Trust Now Fully Staffed


Victoria Hilton,
Trust Administrator

2019 was a year of unprecedented change for the Marfan Trust. The Trust moved locations to the Guy Scadding Building at Imperial College with the Laboratory moving to the Brompton Hospital, located behind one another in South Kensington, from St. George's University in Tooting. At the same time, we lost our permanent and acting office team members due to health and personal issues. Fortunately, we retained the help of our Strategic Marketing Consultant, Moira Taylor plus volunteers Natalie Rider and Cecilia Yee and were therefore able to keep continuity going at the Trust, albeit on a reduced basis.


Gurpreet Madan,
Fundraising Manager

Since February 2020, we're delighted to announce that Victoria Hilton and Gurpreet Madan have joined the Trust as full time staff members, Victoria as the Trust's Administrator and Gurpreet as its new Fundraising Manager. Both have significant experience: Victoria has many years of experience as a PA and administrator, having been co-ordinator for the busy IVF unit at St. Thomas' Hospital for 2 years - a post that required great empathy and tact; while Gurpreet has over 6 years of fundraising experience in Singapore and the UK, having worked at St Luke's Hospice, KIDS and Birmingham Hippodrome, among others. Please join us in welcoming them both to the Marfan Trust.

Volunteers – *Thank You!*

In the past six months we have had magnificent help from two volunteers:


Natalie Rider

Natalie Rider, an administrator in the investment world, was between jobs, and on garden leave which means her firm was paying her to the end of her contract. She volunteered to help with our Charity, because she wanted to feel she was doing some good for people with a medical condition. Because of her excellent knowledge of Microsoft software and PC's in general, she has provided vital support to all our staff. She has volunteered cheerfully to update the addresses on all our pamphlets brought from St George's University of London, or donated by the Marfan Association. We have used donations to purchase new address stickers for our present address at SW3 6LY, so as not to waste any pamphlets. A list of those available is on our website **www. marfantrust.org**.

Natalie has also helped us bank cheques, and mail out fundraising packs and items from our web shop. There is no charge for fundraising packs, although we would ask that people give us lots of time to send these out prior to the event.


Cecilia Yee (middle) and Family

Cecilia Yee, is a parent of a son with Marfan syndrome who is now at university, and doing very well. She donated a half day per week to come into the office and help with recording donations, thanking each donor, and also putting stickers on pamphlets. When she was free, her daughter Ellen Yee accompanied her and added a youthful presence and some very hard work, to our group. We are very grateful to both of them for their continued assistance.

Huge thanks to both Natalie and Cecilia who continue to support us. Anyone wishing to volunteer could either email us at **info@marfantrust.org** or call on **020 7594 1605**. We would be very glad of any offered part-time assistance.

Will you help the Marfan Trust deal with the impact of Coronavirus?

By Gurpreet Madan, Fundraising Manager

At this unprecedented time, we sincerely hope you and your loved ones are in good health. In terms of the Marfan Trust, we can assure you that we are following Government advice and have put strict measures in place to protect staff and supporters.

However as with many charities, we too have to consider the financial implications of coronavirus and the potentially damaging impact it can have on the Marfan Trust. Transparency is an important cornerstone in any relationship, so with that in mind, we would like to share with you our 2020 projected costs. We hope our honesty motivates advocates like you to lend your support. Any amount you donate, no matter how big or small, will make a massive difference to the lives of those affected by Marfan syndrome.

2020 Projected Costs Marfan Trust

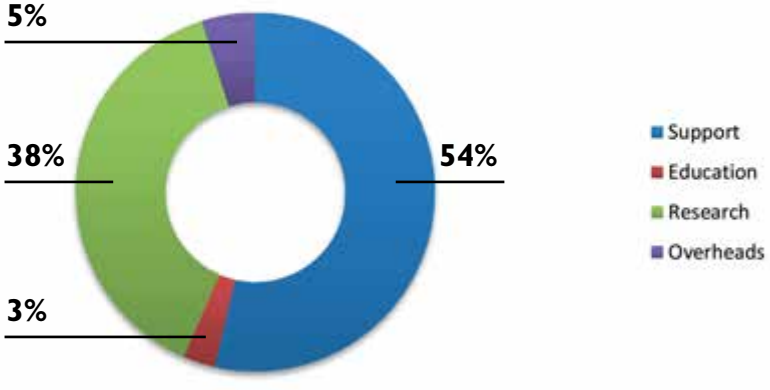
The Marfan Trust's spending is reflective of our goals – Support, Education and Research. See Chart A. Support spending during 2020 is estimated at 54% of our cost base as it includes costs of all our helpline and support services as well as running the office, including the production and distribution of our newsletters. All of this is crucial in making sure that peer-to-peer support and medical guidance are provided to those affected and their families. Our overhead cost is projected to be around 5%. This includes one off relocation, storage and insurance charges plus legal fees as a result of our move from St. Georges. All of this spending is essential in ensuring our organisation runs effectively and efficiently and is able to continue to support Marfan syndrome patients and their families.

If you can, Please Help the Marfan Trust

The Covid-19 pandemic has disrupted many supporter led fundraising events which will seriously affect our finances. We now, more than ever, need your help in ensuring the Trust continues to provide support, research, and educational literature to those affected by this debilitating disorder.

We are determined to continue to improve the treatment of patients and increase awareness of this condition. If you are in a position to support us, please consider leaving a donation on **JustGiving** or **Virgin Money Giving** or by making a **direct bank transfer to us (BACs)**. Please visit **http://www.marfantrust.org/get-involved/donate/** for more information on the various ways you can donate to us. **NB:** please be aware that due to the current situation, it is difficult for us to process cheques at this time.

Chart A **Charitable Spending £181,350 per year**



New Gene Discovered for Spinal Curvature (Scoliosis)

By Dr Anne Child MD FRCP, Medical Director

At this unprecedented time, we sincerely hope you and your loved ones are in good health. In terms of the Marfan Trust, we can assure you the discovery of Genetic Mutation in TTLL11 Gene (which leads to ciliary defects and is associated with idiopathic scoliosis in a five-generation UK Family) will allow us to screen children of a non - Marfan scoliosis parent, to identify those who have inherited this gene and are therefore at risk of developing scoliosis.

Background

Genetic mutation in TTLL11 Gene leads to ciliary defects and is associated with idiopathic scoliosis in a five-generation UK family. See Chart B.

Adolescent Idiopathic Scoliosis (AIS) is a three-dimensional spinal curvature which affects about 3% of the general population. There is a strong genetic component. The Marfan Trust funded Louise Ocaka in her laboratory research supervised by Dr Aragon-Martin and Dr. Anne Child, to study a large UK family with dominantly inherited scoliosis. Louise found the location of the gene on chromosome 9 and successfully submitted this as her PhD thesis. Several years later, the project was taken up again by another PhD student, Miss Hélène Mathieu who is working between our research unit and the University of Montreal, supervised there by Professor Florina Moldovan. She has successfully pursued this gene and discovered that a mutation in TTLL11 contributes to the scoliosis in affected members of this family.

The University of Montreal research unit managed to introduce this gene into a zebrafish model and produced scoliosis in the zebrafish. This confirms that this gene can cause scoliosis.

How Does it Work

In the embryonic period, cilia which are small hair-like attachments on specialised cells, have a role in wafting fluid flow which provides nourishment to developing bones especially growth plates in the spine. They also have a role in patterning left-right development, which is impaired in scoliosis patients. Moreover, another ciliary gene POC5 can cause scoliosis in humans.

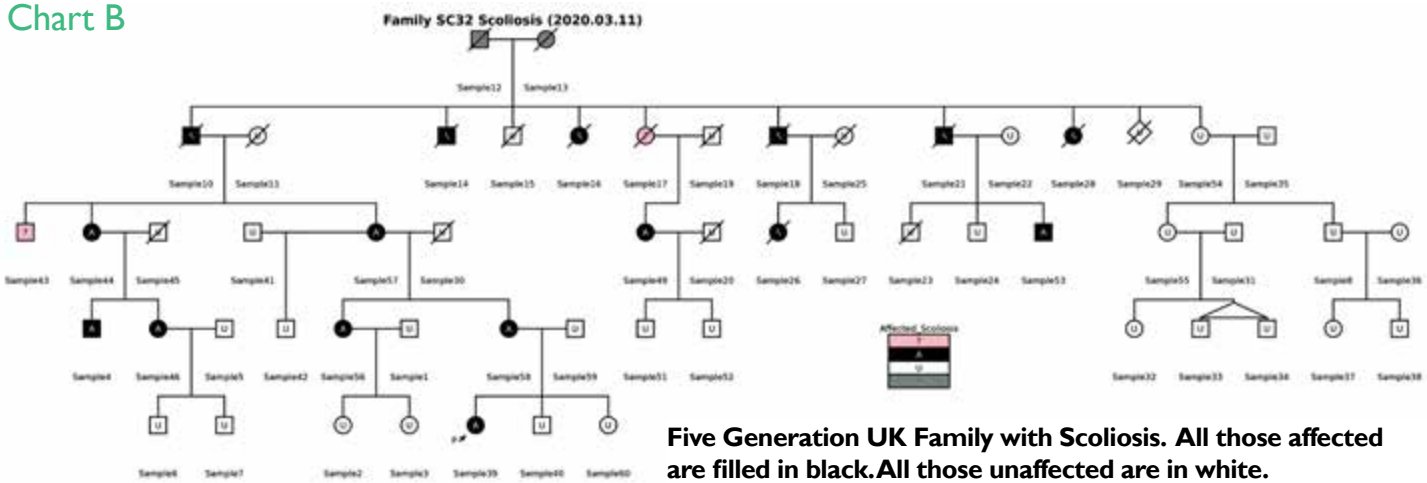
The mutation in TTLL11 in this family leads to abnormal ciliary development which results in shorter cilia, which are ineffective. Moreover, spinal deformity was observed in zebrafish model, once a mutation in the zebrafish TTLL11 was introduced.

Conclusion

The impact of this finding will allow us to screen children of a scoliosis parent who carries the gene mutation, to identify those who have inherited this gene and therefore are at risk of developing scoliosis. They should be observed at frequent intervals especially during the rapid adolescent growth phase when the curve usually develops. Thus, treatment with bracing or spinal surgery when necessary can be offered at the optimal time.

In future, further work may lead us to discover medication or gene therapy which can halt this abnormal development of the spine.

Chart B



Five Generation UK Family with Scoliosis. All those affected are filled in black. All those unaffected are in white.

Aortic Irbesartan Marfan Study (AIMS) Results Press Release

By the AIMS Trial Consortium

Results from the recent study found that the drug Irbesartan reduces aortic dilatation in children and young adults with Marfan syndrome.

Summary of Research Project and Findings

The Aortic Irbesartan Marfan Study (AIMS) was a UK research study carried out in 22 centres, that tested the effects of Irbesartan, a commonly used medicine to treat high blood pressure, on aortic size compared to placebo, in patients with Marfan syndrome. Marfan syndrome is a condition that often runs in families and is associated with stretching of the aorta which is the main artery that comes out of the heart. Stretching of the aorta is linked to serious complications such as tearing of the inside of the aorta (dissection) which can reach the outside of the aorta (rupture) which can lead to death. Slowing stretching of the aorta in Marfan Syndrome is a common goal of management and most patients with Marfan syndrome have the width of the aorta measured on an annual basis.

In the AIMS trial about 200 patients aged 6-40 years old received either Irbesartan or placebo (inactive treatment that looks like Irbesartan) for about 4 years and had their aortic diameters measured using careful echocardiography (ultrasound) measurements each year. On average Irbesartan was associated with smaller aortic diameters compared to placebo over the 4 year follow up period (about 1mm less over the study period) and was well tolerated by participants that took part in the study. These results indicate that Irbesartan could be used as a strategy to reduce aortic diameter in patients with Marfan Syndrome especially those at higher risk of aortic complications. AIMS was funded by the British Heart Foundation, Marfan Trust and Marfan Association.

Scientific Summary

Background

Marfan syndrome is a common dominantly inherited genetic disorder caused by mutations in the gene that encodes for the elastic components of fibrillin-1 which is a key constituent of arterial walls. Cardiovascular complications of Marfan syndrome including dissection and rupture of the aorta, the main blood vessel coming out of the heart, are important causes of premature death and disability. Slowing progression of aortic dilatation is a key target of treatment to improve outcomes in patients with Marfan syndrome.

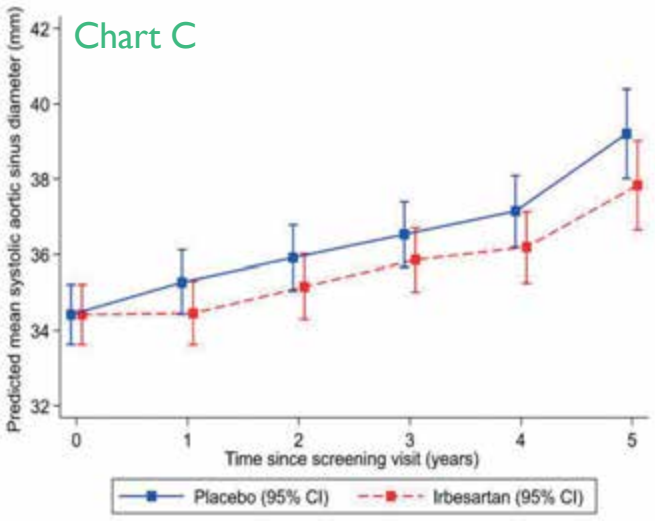
Experimental models of Marfan syndrome suggest that angiotensin-II receptor blockers could favourably alter biological pathways that contribute to the progression of aortic dilatation. Previous randomised trials have tested the effects of the angiotensin receptor blocker losartan on aortic dilatation in patients with Marfan syndrome without showing consistent results.

Methods

AIMS was a University/NHS led randomised placebo-controlled trial testing the effect of the angiotensin receptor blocker irbesartan on aortic dilatation in children and young adults with Marfan syndrome. Performed in 22 UK centres, 192 patients age 6-40 years old were randomised to Irbesartan 150-300mg (depending on weight) or matching placebo. Participants had a median age of 18 years with 25% aged between 6 and 11. Aortic sinus diameter was assessed by transthoracic echocardiography and analysed by an independent core laboratory at baseline and at yearly intervals for up to 5 years. AIMS was unique in that it studied both children and adults and is the only trial to have studied the effect of Irbesartan, a selective angiotensin-1 receptor inhibitor.

Results

Irbesartan treatment reduced the rate of aortic dilatation (the primary endpoint) by 0.22 mm/year (95% confidence interval 0.02 to 0.41 mm/year, p=0.030) from 0.74mm/year in the placebo group to 0.53mm/year in patients treated with irbesartan (Figure). See Chart C.



Aortic enlargement in patients on Irbesartan (red) significantly reduced in comparison to those patients on placebo treatment (blue) over 5 year period.

There was also evidence of a difference in the rate of change in aortic Z-score which is a measurement correcting for growth. Systolic blood pressure was also reduced in the Irbesartan group. Irbesartan was well tolerated with no observed differences in adverse events between groups. There was no difference in the proportion of patients that underwent cardiac surgery.

Conclusions

The AIMS trial has shown that Irbesartan can reduce aortic dilatation in children and young adults with Marfan syndrome. Further work is needed to understand the clinical impact of this observation to reduce the risk of serious aortic complications like dissection and rupture and potentially improve the quality of life in Marfan syndrome.

Organisation of the AIMS Trial

AIMS was an investigator led study sponsored by the Royal Brompton and Harefield NHS Trust, London UK. The study was led by Dr Michael Mullen, consultant cardiologist at the Bart's Heart Centre and Queen Mary University, London. Funding was through a special project grant from the British Heart Foundation with additional financial support from the UK Marfan Trust and Marfan Association. Irbesartan and matching placebo were supplied under contract by Sanofi Research. The drug was packaged and distributed by Brecon Pharmaceuticals Ltd. The study was managed by the Clinical Trials and Evaluation Unit at Royal Brompton Hospital from 2010 until 2014 and then by the Clinical Trials Unit at the London School of Hygiene and Tropical Medicine from 2014 who also undertook the statistical analysis. The echocardiography core lab was based at John Radcliffe Hospital in Oxford.

Marfan Trust – Research Update

By Dr José Antonio Aragon-Martin, Director, Sonalee Laboratory

Dr. José Aragon-Martin

We hope everybody is doing well, keeping healthy and fit under the current circumstances. We wanted to give you an update on what's happening to our research into Marfan syndrome at the Sonalee Laboratory. Fortunately, when we saw that the early stages of the Covid-19 outbreak were taking us to a similar scenario as Italy and Spain, we decided to prepare well in advance to work remotely.

So, at this important time in our lives, the Sonalee Lab wants to reassure everyone that we have not stopped working and that we are still on target to continue with our research programme.

Research Projects Underway (Dry lab)

As a result, the Sonalee Lab is currently concentrating on the following research projects which are all essential to our further understanding of Marfan syndrome and its treatment:

1. Writing ethical approval forms for several projects on Marfan syndrome and related fibrillinopathies, including: Marfan syndrome, Thoracic Aortic Aneurysm and Dissection (TAAD), Ehlers-Danlos syndrome (EDS), Scoliosis, Ectopia Lentis;
2. Working with the legal and logistics of transferring samples from our previous location to Imperial College, and communicating with all interested parties;
3. Educating ourselves on Next Generation Sequencing (NGS) analysis of large genetic datasets through learning different computer programmes (bwa, samtools, gatk, ANNOVAR, SnpSift, SnpEff and others);
4. Analysing large datasets processed on NGS platforms from Marfan syndrome and related fibrillinopathies projects; and
5. Working on several papers to be published in 2020 on novel genes: one is related to Scoliosis and the other to TAAD. These two clinical features are related to Marfan syndrome and the hope is that they will help us to better understand this syndrome.

A heartfelt thank you to all for your continuing kind donations to the Marfan Trust, the primary funding body of the Sonalee Laboratory, and for all those fundraising so hard on our behalf.

Sonalee Laboratory Progress Report & Wish List

By Dr José Antonio Aragon-Martin, Director, Sonalee Laboratory

Projects:

1. Genotype-Phenotype correlations in Marfan syndrome. The AIMS trial on Marfan syndrome patients is allowing us to study the effect of the drug on each particular mutation. We are working on the creation of an AIMS-UK group to study the genotype (mutation found) versus the phenotype (clinical features) in each patient to observe any differences between the placebo and the drug. This will refine the significance of the AIMS trial findings, and possibly the creation of an international consortium where we will be able to study samples around the world on other trials on the Losartan drug, and compare mutations between drugs and placebo to better understand the effect of the drug on the patient.

2. Mapping the Marfan gene. We have a large Marfan syndrome database which contains mutations from samples that have variability in their clinical features. We are studying families with the same mutation (or similar mutation) to clarify the consequence of each mutation, and therefore in the future, we will be able to predict the different clinical features and arrange a better and healthier management of the condition.

We are still collaborating with a research group led by Dr. Sinha in Cambridge, UK, where we are studying multiple drugs within cultured cells from Marfan syndrome patients. This study is very important since it is a great opportunity for the Marfan syndrome community to test different drugs at a time when it could be very expensive to arrange a clinical project of such proportions.

3. Novel genes for dislocated lens phenotype – Ectopia Lentis (EL). We are creating an international consortium of ophthalmologists specialising in dislocated lens. This group is organised under the auspices of the Marfan Trust. One of the leading specialists is Mr Aman Chandra, a very good friend of the Sonalee lab, and continuous collaborator in the study of EL. We are pursuing a better understanding of this phenotype found in Marfan syndrome, but the Sonalee Laboratory has been creating an EL database of patients in whom the genetic involvement is unknown. Understanding the genetic involvement of different proteins in EL can help differentiate overlapping conditions from Marfan syndrome.

4. Novel genes for hypermobility Ehlers-Danlos syndrome (hEDS). There are 4 common types of Ehlers-Danlos syndrome that we know, and type 4 (vEDS which involves the cardiovascular system – aneurysms and dissections of the aorta) is the most fatal one. We are working with families with a type of EDS involving hypermobile joints (hEDS) for which a gene has not been found yet. We intend to find the gene/genes from hEDS families and to better understand this type of connective tissue disorder as well as the involvement of these genes in the rest of the connective tissue disorders' family.

5. Novel genes for familial thoracic aortic aneurysm and dissection phenotype (FTAAD). The main phenotype found in Marfan syndrome is TAAD. When it is inherited it is called familial TAAD (FTAAD). We know from networking at international meetings that the group of genes involved in TAAD has been enlarging rapidly in recent years. The structure, composition and maintenance of the aorta is obviously very complicated. There must be many more genes involved in the aneurysm phenotype since we have a cohort of patients (70%) with no gene identified as yet.

Sonalee Laboratory Wish List

This project list above reflects the studies we're working on, but not the amount of work behind it. In order to keep up with the work that Marfan Trust is investing in the Sonalee Lab, we need to finance some full time expert help. In the meantime medical students can be taken on staff to learn about Marfan Syndrome during a summer project.

Summer Student Projects

Some of the jobs that need doing in the Lab to further our projects include:

- Family pedigree drawing and storage in a format that can be easy to update and keep electronically.
- Adding phenotype (clinical features) of each patient in a database.
- PCR, variant analysis and interpretation on the different projects.
- Bioinformatics.

Laboratory Technician
Ideally we would have a technician for each job, but just to have one technician is now a HUGE necessity. This is because it is vital that the Sonalee Lab gets fully up to speed on the recent scientific advancements of the last few years. e.g. Next Generation Sequencing (NGS) is fairly new and we have a lot to learn about the manipulation of the data created, however, to further our research it is crucial that we also keep on top of rapidly evolving scientific developments.

To help us with these projects, we badly need donations to cover the following:

1. Three named summer studentships at £1000 each for 6 weeks project. The donor has an opportunity to add their name or a family member's name to the studentship.

2. A laboratory technician educated at least to BSc level in a related subject. Salary Scale Grade Level-1a £21,570 for the first year). Funding for subsequent years will be sought from other sources.

Please, please help us get the Sonalee Lab up and running with the help in needs ASAP. Huge thanks.

To donate visit http://www.marfantrust.org/get-involved/donate/

Marfan Trust – Wish List

Our recent office move to the National Heart and Lung Institute has inevitably meant many expenses have been incurred. If you wish to sponsor an item on this list, please donate indicating the chosen item.

- New Address labels for leaflets - £216
- Removals van - £368
- 2 x 3 drawer under desk filing cabinets - £100
- Dragon voice recognition software (voice recognition typing programme) - £350
- Weigh Scale for postage - £36
- Reprinting Basic Info Leaflets - £98
- 5 x freezer sample storage racks - £150 (£30 each)

Many Thanks

SAVE THE DATE – Information Day

SATURDAY, 3 OCTOBER 2020, 09.30 – 16.30

Guy Scadding Building,
Dovehouse Street, SW3 6LY
Nearest Tube: South Kensington

Following our move to the Guy Scadding Building, which has a lovely large lecture theatre, we can announce a planned one-day conference for families with Marfan syndrome as well as interested physicians, Covid-19 allowing of course. If the event cannot be physically held, we will try and offer a virtual event instead.

If you are interested, please see programme below, and register your interest by emailing **info@marfantrust.org.** If you don't have access to email, then please call **+44 (0)20 7594 1605** to register. Until the Covid-19 situation is clearer, we cannot yet unfortunately confirm places and will not ask for payment until we are sure the conference can go ahead. We are very much hoping at this time that it will, and will confirm either way as soon as we can. Please check our website **http://www.marfantrust.org/** for updates.

Regrettably, children under sixteen are not allowed due to a lack of creche facilities. There is no parking, but there is easy access from South Kensington underground station by foot (10 minutes) or by taxi. Catering is available for lunch at an additional cost, or you can bring your own. We hope to see as many of you as possible at this meeting, however there is an upper limit of 100 participants due to the lecture hall size. So please do register early.

Preliminary Conference Programme

09.10 to 09.50	Registration and Tea/coffee
09.50 to 10.00	Welcome/Amalgamation of Marfan Trust and Marfan Association/Support, Research and Education – Michael Heath, Chair, Marfan Trust
10.00 to 11.00	Update on Aortic surgery - Session Chairman, Professor John Pepper, Royal Brompton Hospital
11.00 to 11.30	AIMS Trial results (Irbesartan in Marfan Syndrome): Is it better, and how do we obtain it? - Dr Graham Stuart, Children's Hospital Bristol
11.30 to 12.00	Dislocated lenses: What causes it and why? - Mr Aman Chandra, Consultant Ophthalmologist and Dr José Aragon-Martin
12.00 to 12.30	Q & A
12.30 to 14.00	**Lunch (bring your own or purchase in cafeteria) – a chance to meet others with Marfan syndrome and young people with Marfan syndrome**
14.00 to 14.30	How we handle the transition from Paediatric to Adult Marfan Clinic – Drs Nitha Naqvi and Christoph Nienaber, Consultant Cardiologists Royal Brompton Hospital
14.30 to 15.00	Pectus chest deformities: New treatment - Mr Ian Hunt, St Georges Hospital, London
15.00 to 15.30	Student Research Prize presentation: Pain Management in Marfan syndrome - Dr Natasha Anieh-Benno
15.30 to 15.45	Presentation of Daniel Finkletaub Student Prize by Mrs Carole Finkletaub
15.45 to 16.30	Psychosocial Aspects of Marfan syndrome (speaker TBA)
16.30 to 17.00	Tea and farewell

Helpline Case Reports

Irbesartan Availability Enquiry

On pages 6-7 you will see a press release indicating that the AIMS Trial co-funded by British Heart Foundation and the Marfan Trust/ Marfan Association, in which many of you participated, was successful. Irbesartan has been shown to be effective in delaying aortic root widening, and thus prolonging life in Marfan syndrome. However, many people are asking how to access this medication for themselves and their children.

A father with Marfan syndrome, Nicolas Beer, on Irbesartan as a result of the drug trial, rang to ask how his three-year-old son Ronnie, who is also affected could be put on Irbesartan. The child's paediatric cardiologist is still using beta-blocker (Atenolol) as the drug of first choice, however this is known to cause side effects in children, such as fatigue and depression. Irbesartan, on the other hand, is very well tolerated by most children, and has very few side effects. However, there have been no drug trials in children under the age of six using Irbesartan, hence the doctor's reluctance to prescribe it.

There have however been reports in literature of successful use of Losartan, a cousin of Irbesartan, with almost the same action, in seriously affected new-borns with Marfan syndrome. Since there are no drug trials of Irbesartan in children under six planned, we feel that the cardiologist could successfully trial Irbesartan in children under six, because of the severity of the condition if not treated. The earlier the child is treated, the better the long-term outcome, since the growing aorta responds well to this medication.


Ronnie and Nicholas Beer

The paediatric cardiologist was contacted by a member of our Advisory Board and an explanation was offered, together with a suggestion as to the amount of medication. The children in our AIMS trial were started on 75mg daily, and this was tolerated. It is a low starting dose, and the blood pressure and side effects if any should be monitored frequently until its use is established in the child concerned. It is more effective than beta-blocker, because it has 24-hour action with one dose in the morning. However, beta-blocker treatment also treats a tendency to palpitations. If the child shows any irregularity of heartbeat, it is probably better to start on Atenolol, and add Irbesartan as the child grows larger and can tolerate double medication.

If patients are having difficulty persuading their cardiologist to try Irbesartan, they should take our press release found on pages 6-7 to their cardiologist and discuss this with them.

Coronavirus Enquiries

We have had many requests from patients of all different ages for advice specific to Marfan syndrome. See below and also the online advice from the Marfan Foundation USA which is very comprehensive, and can be found at **https://www.marfan.org/covid19**

Q1: A worried parent wondered if their adult son should self-isolate. The son is awaiting aortic root replacement surgery, now delayed owing to the coronavirus crisis. He works with the general public and the nature of his job makes it hard to maintain a two-metre distance from customers. He is taking care to stay safe, but the added complications of his asthma and epilepsy are preying on the parent's mind.

A1: The son is at risk because he has heart involvement and asthma. Therefore if he caught the virus, he would have a greater risk of developing pneumonia. Also he has an underlying condition of epilepsy and the fever may increase his likelihood of having an attack. Since he cannot remain at a six-foot distance from his customers, I would recommend that he self-isolate until the government gives us direction to return to work. He should speak to his employer about pay during this time.

Q2: Two anxious parents felt their respective jobs may place their 12-year-old Marfan-afflicted child at heightened risk. One parent works in a busy supermarket while the other spends alternate weeks in an office among a small group of people. How should they protect the child in these circumstances, while retaining a degree of normality? Meanwhile the child is on a regime of Atenolol because of the widening of the aortic valve.

A2: If the child has no lung disease, they are not at highest risk of pneumonia, however, the aortic involvement means that they are at higher risk than the general population. Because the schools are closed, they will be self-isolating to a degree. If they become bored perhaps they could develop a new interest like art, gardening or playing a guitar.

The risk from the office-based parent is minimal, provided they stay six feet from colleagues at work, and change out of work clothes and wash hands upon returning home. Working in a supermarket is more problematical, however, particularly because the parent cannot keep six feet from their customers. They should wear gloves and wash hands frequently. They should try not to touch their face. They should also change out of clothes upon arriving home and wash before greeting family.

Q3: An adult male suffers from Marfan syndrome and an attendant weak wall of the heart and ectopic heartbeat. Is he at higher risk from COVID-19?

A3: Yes, he is at a somewhat increased risk because he has a "cardiac dysfunction". He is not at high risk if he has no history of lung disease. I suggest he works from home if possible, and isolates until the government gives the green light to return to work.

Q4: A teacher with Marfan syndrome and a self-healed tear of the abdominal aortic valve asked if she can continue going to school to help look after her key worker children.

A4: Because she has Marfan syndrome she is at somewhat higher risk. If she does not have any history of lung disease, she is not at highest risk. I think she will be fine, but she should work only with the older children and should avoid lifting other small children. She should also wash her hands often. This virus can survive on desks and counters for 72 hours. When she arrives home, she should change and wash. She should additionally not wear work clothes after hours while cooking or contacting other family members.

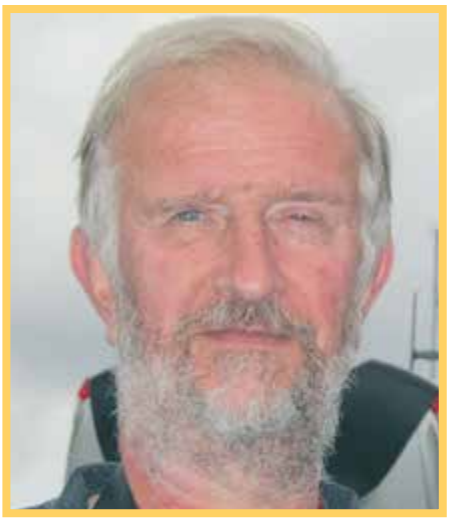
In Memory

Dr. Michael Carr
Kieran Doggett • Helen Jacobs

Tribute to Dr. Michael Carr, Former Marfan Trust Chair, who Passed Away on 14th February 2020

By Anne Child MD FRCP, Medical Director of Marfan Trust, Honorary Consultant RBHT, on behalf of the Chair, Trustees, Medical and Scientific Staff of the Marfan Trust

We sadly have to report the recent death of Dr. Michael Carr, former Chair of the Marfan Trust. Dr Carr was a much admired and appreciated long serving Chair of the Marfan Trust Charity, at a critical time in its development. His specialist training in academic inspection (Ofsted) equipped him for this leadership role as the Trust expanded into a new research programme, hiring staff for laboratory Molecular Genetics which characterised the normal fibrillin protein structure, and its mutations in over 500 UK patients. All results were published and contributed to the international gene map held in Paris.



Dr. Michael Carr

During his tenure, six PhD students and 15 Bsc/MSc Students graduated successfully, after making Marfan syndrome and related conditions their thesis subjects. He encouraged publication, and was especially proud to hear in the week before his death, of the successful completion and publication of the AIMS trial (a national drug trial of Irbesartan), which was proven to be a new effective treatment, delaying aortic expansion, and extending the life span of the 1 in 3000 population worldwide affected by Marfan syndrome. This six-year study was co-funded by British Heart Foundation, Marfan Trust and Marfan Association.

Michael's own diagnosis came late in life, and he was very forthcoming in presenting how it affected him and his family, lecturing to patient and medical audiences. He contributed his talk at the Royal Society of Medicine to our website.

Always cheerful, inspiring and optimistic, he encouraged all aspects of Marfan Trust activity: Research, Education and patient support, and has left the Trust truly established as the voice of 3000 UK families. He gave his support wholeheartedly to Trustee Michael Heath who has succeeded him as Chair.

All Trustees and staff will miss him greatly, but his legacy will live on as we amalgamate with our sister organisation, the Marfan Association, and spearhead continued growth of research and support.

Help Raise Funds in Michael's Honour

In honour of Michael's life, Michael's stepson, Guy Padmakumara Potter, will be doing the London to Brighton Cycle Ride on 13th September 2020 to raise funds for the Marfan Trust. He would also like to encourage others to join him. He aims to raise £1,000 for the Trust. Please support him in his efforts by visiting his Go Fund Me page **https://www.gofundme.com/f/guy-padmakumara-campaign-for-marfan-trust** and contact him through the Marfan Trust at **info@marfantrust.org** if you're interested in participating.

"Mike came into my life when I was 10.... He had a profound impact upon me, and my siblings.....Mike became a larger than life character in what was a somewhat madcap household. Indeed, he was often at the centre of the chaos!.....Fortunately, as Mike aged, understanding of Marfan's improved, and new treatments emerged that extended the expected lifespan. Mike's first major surgery was at 50 and from this time the medication he had to take increased dramatically. All this he bore with no complaint.....It must have been an intense struggle just to keep going but Mike never waned in his desire to be with us.

Guy Padmakumara Potter

In his later years Mike became a Trustee of the Marfan Trust and eventually its Chair. He cared deeply for those who also suffered from the Syndrome, and wanted to help by supporting both research and all those directly affected by the condition, believed to be about 10,000 people in the UK. I don't want Mike's death to be an end to that, and so I'm cycling from London to Brighton on 13th September in aid of the Marfan Trust. All you need to do is donate toward my campaign. I think we can raise £1,000, but I hope it can be more. You can make that happen. Please give now, and tomorrow we'll see better treatments, and perhaps, an end to Marfan syndrome. Thank you."

Guy Padmakumara Potter

Helen Louise Jacobs - 2nd February 1971 to 6th April 2020

By Len and Angela Jacobs and Dr Anne Child

We were deeply saddened to hear of the death of Helen Jacobs. Helen was the eldest of Len and Angela Jacob's four children, a much-loved daughter, sister, and a very special aunt. She was diagnosed with Marfan syndrome when she was three years old and during her life had four heart operations, several procedures and a lensectomy. She also developed a spinal curvature which recently affected her mobility.

In spite of her health problems Helen achieved a BA with honours in English at Exeter University. She had a great love of the English language and insisted on its correct usage acquiring a reputation for correcting \errors in grammar and spelling. She also volunteered to help medical students at exam time by demonstrating aspects of the Marfan syndrome to test their knowledge and understanding.

Helen Jacobs

She enjoyed swimming. She was particularly talented in the field of music and played the piano. She will be remembered especially as Musical Director of Nota Bene, a Bristol based ensemble - a role which she carried out for twenty-four years, spending much of her time composing and working on musical arrangements. She will be fondly remembered and sadly missed by family and friends.

Fabulous Fundraisers ♥

Huge, huge thanks to all our fundraisers. We would not be able to continue without you. Thank you all so much and please, please….Keep Giving! Here are just a few examples of the great work that you're all doing on our behalf.

Kris O'Neill Cracks the Cannonbawz Run

Kris raised a whopping £2,500 from the Cannonbawz run, an annual challenge he set up 6 years ago to support Marfan charities in honour of his brother Liam, who has Marfan syndrome, as well as the Scottish Air Ambulance Service. The Cannonbawz Run is a driving challenge set in scenic Scotland. Last year 60 cars set off from Elgin High Street on a two day event around the NC500. The overnight stop included live entertainment and a charity auction. The weather for the two days was fabulous and drivers and passengers very much enjoyed the stunning sights and the lovely food en route. Well done Kris! It sounds like a really great way to fundraise.

Frances McGoldrick Wows at Whisky a Go Go

Frances raised £365 by holding an old "skool" disco to raise money for, and awareness of, Marfan syndrome. On the night she held a raffle and a "closest £1 to be rolled to the bottle of whiskey" challenge. She's hoping to make this an annual event. Funds were raised in honour of Ciarán (10) who was diagnosed with Marfan's almost two years ago. Way to go Frances!

Karen Jacobs Veganuary Va Va Voom

Karen raised £360 by successfully completing Veganuary and going plant based in January on behalf of the Marfan Trust. We wonder if she can share some of her recipes with us as well as her secrets of staying on the straight and narrow? Huge thanks Karen.

Adam Furneaux Glorious Golf Fundraiser

Adam Furneaux raised £300 as part of his golf Captain's drive in. In January 2020 Adam became the Junior Captain at Churston Golf Club for the year. As part of this, he was able to nominate a charity for the Club to support. Very happily for us, he nominated the Marfan Trust. The first fundraiser he did was a drive in where he tee'd off on the 1st tee and people had to guess where the ball was going to land, while at the same time donating to his nominated charity, the Marfan Trust. He also held a cake stall on the day to raise extra funds. He plans to raise more funds as the year progresses. Thanks so much Adam.

Adam had a lensectomy in both eyes when he was 7 years old and a detached retina at 13 years old. Now 16, he has been playing golf since he was 6 in spite of these health issues with further surgery scheduled. We wish him lots of luck for this and indeed every success in his golf going forward. We would also very much like to thank Adam's Mum, Nicola, for her unwavering support over the years, which has included providing us with Beverley Holidays **(https://www.beverley-holidays.co.uk/)** prizes to auction off at our various drives.

Amy Millburn Tackles the #TwoPointSix

In tribute to her late son Kieran Doggett, Kieran's Mum, Amy, has been heavily involved in a variety of fundraising events on behalf of the Marfan Trust, from holding a School Pizza Day (Kieran's favourite cuisine) to taking part in the 2.6 challenge where she will have walked a marathon 2.6 times by the end of May 2020. That's a very impressive 68.1 miles or 109.6km. She is doing this to raise money and increase awareness of Marfan syndrome. Kieran was diagnosed with Marfans only after his passing in August 2019 at the age of just 14. Sincere sympathies and huge thanks to Amy.

Turn Old Postage Stamps into Donations

Used postage stamps can be sold to stamp dealers for cash to raise money for charity. For many years Pauline and Raymond Moses have collected used stamps cut from envelopes for the benefit of the Marfan Association. They very kindly continue to do this for the benefit of the Marfan Trust. So if you are able to cut out and collect used stamps, please send them to:

Mr and Mrs R. Moses, The Waves, Coast Drive, St. Mary's Bay, Romney Marsh, Kent TN29 0HN.

Donations

If you would like to make a donation, please do so by BACs A/C No: 00017677; SORT CODE: 40-52-40 or by the other online methods detailed in **http://www.marfantrust.org/get-involved/donate/**. Don't forget to download, print and sign our Gift Aid form **http://www.marfantrust.org/get-involved/donate/gift-aid** and email it to us at **info@marfantrust.org**. If you donate via Just Giving or Virgin Money, Gift Aid can be dealt with directly online when making your donation.

Cheque Donations During Lockdown

We always love receiving donations, however, lockdown has given us some logistical issues when it comes to processing cheques. Also we cannot access the office to reach them! If possible, please therefore make you donation via BACs or the other online methods detailed in **http://www.marfantrust.org/get-involved/donate/.**

If this is impossible, then please send your cheques, made out to the Marfan Trust, along with your completed Gift Aid form **http://www.marfantrust.org/get-involved/donate/gift-aid** c/o Dr Anne Child, 24 Oakfield Lane, Keston, Kent BR2 6BY until the situation has normalised. Huge thanks!

Amazon Smile

Don't forget to make all your Amazon purchases with Amazon Smile as Amazon will donate 0.5% of your purchase price (excluding VAT, returns and shipping fees) to the Marfan Trust if you select us as your chosen charity. For more info and sign up, visit **https://smile.amazon.co.uk/about.**

Marfan Trust Shop & Help With Fundraising During Lockdown

All our web shop and fundraising items are stored in our offices which we cannot currently access due to lockdown. So we're really sorry to say that we're not able offer any physical items at this time. Please therefore do not try and buy anything in our web shop.

We can, however, forward images of our logo to you to help with your fundraising efforts and make your efforts known via our social media and other communications. Our Fundraising Manager, Gurpreet Madan, would also be very happy to help you with all your fundraising ideas. Please email **info@marfantrust.org** if you would like to receive logo images and/or if you would like us to help you with your fundraising efforts. We would be more than happy to do so.

Marfan Trust Information Leaflets

Most of these can be found online at **http://www.marfantrust.org/marfan-syndrome/faqs-and-resources**. Please scroll down to the end of the page to find them, then simply click on the title of interest to access a PDF version to download.

Marfan Trust Communications

If you would prefer to not receive any of our communications in future, please email **info@marfantrust.org** and let us know which ones you would like not to receive: all communications/ paper newsletters/e-mails.