LAM ACTION
Supporting women with Lymphangioleiomyomatosis

DECEMBER 2022
LAMPost

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Getting Shirty at LAMposium

From the Editor's Desk

Oh, the weather outside is frightful, but this LAMPost is so delightful... with a glass of wine on the go, let it flow, let it flow, let it flow!

As you may be able to tell, here at LAMPost Towers we are getting more than a little into the Christmas spirit, and we hope that each and every one of you are doing the same. Once again, it's fair to say this has been a challenging year for us all, so please put your feet up, relax, and we hope this edition of the newsletter can bring a bit of festive cheer to you all.

A big thank you to everybody who contributed to this edition, once again we have some fascinating articles for your perusal, and we are delighted to welcome a new contributor on board, **Kate Breen**, who answered our SOS call for new writers to help out. Kate is a copywriter by trade, so it was quite exciting to have a professional writer provide a couple of articles for us, and we hope this will inspire others to come forward with submissions for future editions.

A big shout out to **James Blackburn** and his colleagues at the **Exeter Business Hub**, who are making a donation to LAM Action instead of sending Christmas Cards this year, and they have also asked their clients to donate via a JustGiving page - a very lovely gesture of support for James's sister who is a LAM patient.

A quick reminder that the 2023 LAM Action Annual Meeting will take place in 'hybrid' form (in-person or online) on **Saturday June 10th** at the Mercure Nottingham Sherwood Hotel so please save the date and further details will be announced once we have them.

Our heartfelt congratulations go to **Dr Suzanne Miller**, Senior Research Fellow at Nottingham, for her recent award at the British Thoracic Society Conference. Well done Suzanne, very well deserved! You can read about Suzanne's award further on in this edition.

LAMPost will return in the spring, with a publication deadline of **April 5th**, please email any articles or other contributions to: lampost@office.lamaction.org.

Until then please have yourselves a merry little Christmas, wherever in the world you may be, and very best wishes for the coming new year.

The LAMPost Team

Cover Photo: Adam Davidson manning the merchandise stall at LAMposium, September 2022

Fundraising: The Cutting Crew

We're delighted to say that we have had our most successful year ever with the choose and cut your own Christmas trees. At time of writing we are nearly finished but, including wreaths, raffle and other items, look on course to have taken around £8,000 this year. Once Gift Aid on donations is taken into account that's likely to be worth a little under £10,000 for LAM Action.

We would like to thank all our lovely visitors for your generous donations and for taking part in our prize draws, we hope you love your trees and have a very happy Christmas. Congratulations to Luke and Emma who won the hampers and Louise who won 'Guess Santa's name'.

Thanks also to all those who helped us to make this happen again this year: **Helen Humphrey** for her support and tireless work making and selling wreaths, also for donating the raffle hamper and arranging the WIldjac tasting experience prize; **Mike** and **Lesley Allen** for their help with the other hamper and for assistance on the field when it's been so busy; **Wildjac Distillery, Franche Co-Op** and **Kidderminster Tesco** for contributing so kindly to our raffle prizes; **Brenda Felton** and **Ann Fairbrother** for making Santa and tree decorations to raise additional funds; Finally to our families and other friends who have lent practical support along the way, it really has made a difference. Best wishes, **Sally & Ron**












LAM Across the World

Anette Von Koch and Gill Hollis, Stockholm, August 2022

I was diagnosed with LAM in 1992, and the longer I live with LAM, the more aware I am of how special our LAM community is, both here in the UK and across the world. At LAM Action's meeting in June, we got a great response when we asked overseas LAM patient groups to send messages of support to celebrate LAM Action's 25th anniversary. And in September, UK LAM patients who attended LAMposium in Chicago came back enthusing about the welcome they received from women with LAM from many other countries.

I had my own reminder of this community when my husband Peter and I travelled to Sweden and Denmark this summer to celebrate our own 25th wedding anniversary. It was the first time we had been abroad since fleeing Valencia in March 2020 as the pandemic spread. As recipient of a single lung transplant in 2004, I'm very immunosuppressed and therefore vulnerable to Covid. Who better to find out about the position in Sweden and Denmark than from others in the LAM community? Correspondence before our trip led to catch-ups in both countries, and what a great time we had!

In Stockholm, I met Anette von Koch. We had a lovely day together, meeting in a park for fika -coffee and cinnamon buns - in warm sunshine. Like me, Anette also received a single lung transplant in 2004, but unlike me she had only been formally diagnosed with LAM the previous year, despite having suffered lung problems for over 20 years. Eager to raise awareness of the condition, in 2008 she co-founded the Swedish patient support and research group, LAM Academy, with Dr Maryam Fathi. Anette continues to be very much involved in the group; in November, she arranged for Sue Sherman of the LAM Foundation to speak at the LAM Academy's first in-person meeting since the pandemic.

The weather was far less clement when I met Hanne Danielsen, at a marina just outside Denmark's second city, Aarhus. We had lunch outside in a howling gale, much to the bemusement of the café owner, who nevertheless brought us blankets in true "hygge" style. (This is why I have no photograph of our meeting; it was too windy to keep the camera still!) Hanne also received a transplant in 2004, and it's enabled her to keep up her outdoor life; she's a keen sailor and more recently got into kayaking.

With a population of 10½ million, Sweden is the only one of the Nordic countries to have its own LAM patient group. Denmark, whose population is just under 6 million, doesn't have any formal LAM patient organisation, although women with LAM in Denmark have access to specialist doctors in Copenhagen and Aarhus, and Hanne spoke highly of hers.

I ended up spending a lot more time than I had anticipated with each of Anette and Hanne, as we discussed our shared experiences with LAM, transplantation and the pandemic, in addition to our personal and family lives. It was an absolute pleasure to meet both these wonderful women, and very uplifting.

The LAM community is welcoming and supportive, so perhaps consider seeking out other LAM ladies when you are next on your travels. We are stronger together!

For those recently diagnosed with LAM, please do not be alarmed by the references to lung transplants. Anette, Hanne and I were all diagnosed and had our transplants many years before the discovery that rapamycin (also known as sirolimus) slows the progression of LAM significantly in most women. Moreover, it's also unlikely that any of us had a mild version of LAM. Thanks to rapamycin, the outlook for women with LAM has been transformed, and has reduced considerably the number of patients requiring a lung transplant.

Gill Hollis

Just Rewards

I am a Senior Research Fellow working in Prof Simon Johnson's lab. Dr Debbie Clements, Dr Roya Babaei-Jadidi and I recently presented our work as 3 talks at the British Thoracic Society conference in London (23rd and 24th November). We received lots of interest into our research of LAM. I was entered into a competition for the Early Career Investigator of the Year award and I'm pleased to say that I won! 63 abstracts were submitted with 6 finalists giving talks.

I presented work that was funded by The LAM Foundation, while Debbie and Roya also presented work there that was funded by LAM Action and the Medical Research Council. We had a great few days in London and while it was brilliant to be awarded with Early Career Investigator of the Year award, we are all thrilled that our research into LAM was highlighted at such a large conference.

Dr. Suzanne Miller

L-R Suzanne, Roya & Debbie celebrate 40 years of the BTS

My LAM Diagnosis

In June 2017, I was diagnosed with LAM, although it took ten days for my doctors to diagnose me. I had been experiencing unusual shortness of breath for a few weeks beforehand, but I chalked it up to poor fitness. But, when I was on the way to Cork with my fiancé (at the time), two main things tipped me off that something wasn't right...

First was the increased shortness of breath walking on flat ground on the way to catch the train. The second (and most obvious) was during a swim in the hotel pool. I wouldn't call myself a strong swimmer but how quickly I ran out of breath shocked me into scrambling for the poolside. I sat there, violently coughing while my fiancé looked on concerned.

We retreated to our room, and I noticed my feet were swollen. That's when the worry really kicked in. On the way home the next day, I knew something wasn't right, so I messaged my doctor cousin about what to do.

After seeing an Out of Hours doctor, I was told to go straight to A&E. His face reflected my internal worry that this was a sign of cancer. I'm not sure where I learned that swollen feet could be a sign of cancer. Maybe it was a random documentary or the courtesy of Google.

I was somewhat used to hospitals, having to go to regular appointments growing up with Tuberous Sclerosis Complex (TSC). But being in the hospital alone as an adult, not knowing what was going was something else. I was scared.

My main comfort was that my mum lived down the road and, more importantly, my sister was an RN in the hospital. (My fiancé lived in America). I knew she'd make sure I was treated well and had the best people on the ward. She's well respected in the hospital, so I knew I had the best support possible.

I don't know if I was slow to tell the doctors of my TSC diagnosis or if they were eliminating the more obvious potential diagnoses. I was quickly cleared of cancer, thankfully. They queried if I had tuberculosis, but again, I was quickly cleared of that possibility too.

The next step was to biopsy the fluid in my right lung. While the doctors hurried to find out what the fluid was, they transferred me to another hospital that had a respiratory consultant.

During these ten days, I wasn't told anything. I understand (and understood) that the doctors were reluctant to tell me their speculations, but I do wish they could've reassured me a little. I'm thankful for the nurses who did their best, though.

But, the fear stayed with me the whole time. And now I was in a hospital without the safety net of my sister and mum. Without any answers, I resorted to Dr. Google, as did my family. After a couple of days, my eldest sister discovered a potential diagnosis of Chlyothorax-associated LAM, which lined up pretty well with my TSC condition.

Again, while the doctors analysed the original biopsied fluid and a second sample they had taken, I resorted to Google for answers. Now, with the theory of a LAM diagnosis, I fell into a rabbit hole of discovering the (outdated) material of short lifespans and probable lung transplants. My mind was overloaded with fear.

When the respiratory consultant came back to me with a confirmed LAM diagnosis, I burst into tears and messaged my fiancé through tears. I told him he didn't have to be with me anymore. But, of course, he brushed that nonsense aside and was there to comfort me.

After the doctors knew what it was, they drained the rest of the 2L of fluid from my right lung. Unfortunately, they were still unfamiliar with the best treatment to proceed with, so they discharged me, telling me to return to hospital if I felt unwell again.

For the next seven months, I was stable even with some anxiety-fuelled hospital trips. That changed in February when I had the worst health patch I've ever experienced (and hope never to experience again). In early February, shortness of breath came back, and after the chest x-ray results, they found 2L of chyle on my right lung.

Luckily, since my last visit to my country hospital, they had hired a respiratory consultant, Dr. Bolger, so I felt more looked after. He admitted from the offset that he was still learning about LAM. His honesty about his lack of knowledge was so refreshing and made me trust him even more. I knew this disease was incredibly rare, so I appreciated the transparency.

He performed a pleural tap, and I was discharged two days later. The thing I once thought was the worst thing to have to go through was becoming a standard procedure for me.

After only three weeks, I was back again. Again, shortness of breath was the indicator. This time, the respiratory team was in shock. My entire right lung was full of chyle. 6L of fluid had accumulated in those three weeks. What shocked the team most was how well my body compensated for the lung capacity loss. My o2 saturation was in the high 90s, and I had only walked down the town (in a valley) the day before.

Because of the volume of chyle, the respiratory consultant felt it best to put in a chest drain. The promise that it doesn't hurt and 'little ladies are fine with it'. Well, these ladies must be made of stronger stuff! The chest drain was one of the worst feelings of pain I've ever experienced! (The other was kidney embolisation recovery).

After two days, the drain had removed most of the fluid. During those two days, I begged nurses and my respiratory consultant to remove the drain. I didn't want to move in case I worsened the pain. My doctor finally removed the drain, and the instantaneous relief of pain I felt still stays with me to this day.

Unfortunately, the memory of the chest drain didn't have enough time to fade before I had to return to the hospital. Between the shortness of breath and the anxiety attack of probably needing another chest drain, I've never been more thankful that I lived around the corner.

This time there was only 3L of chyle on my right lung. But it was partially collapsed too. I flat-out refused the chest drain. Thankfully, my respiratory doctor listened and removed the fluid through pleural taps.

Because of the sheer trauma my body had been through over those 6-ish weeks, I found out that I would need supplemental o2 on exertion, i.e., whenever I was up and about, after completing a 6-minute walking test.

After a couple of weeks of reluctance, I accepted this eventuality. So I got my Inogen portable o2 concentrator, a big boy EverFlo version, and o2 canisters. Being 26 and wearing an o2 device understandably drew some concerned and empathetic looks.

I was self-conscious about having to wear o2, but I reminded myself that I'd rather this awkwardness than suffer the potential damage to my o2-deprived organs. Soon, I just got used to Frank (my pet name for my Inogen concentrator) and the looks.

Some concerned strangers came up to me asking why I was on o2, and other respiratory sufferers shared their experiences. I didn't mind, and I'm always happy to talk about LAM.

I won't lie, I found some devilish comfort in seeing a few smokers lock eyes with me before guiltily stubbing out their cigarettes, thinking I was a young cancer warrior. I've had many family members die of smoking-fuelled cancers, so even a moment's pause of reflection for those smokers was rewarding.

After a few months of using o2, my respiratory consultant recommended starting on Sirolimus (Rapamune) at 1 mg a day. And during August 2018 and dosage experimentation, we settled on a two mg-a-day dosage.

And so, I continued on sirolimus and supplemental o2 until the following May, when I had another check-up and a 6-minute walking test under the care of Dr. Cormac McCarthy. Chest x-ray and PFTs came back stable. My 6-minute test o2 saturation didn't dip below 90.

I didn't need my concentrator anymore! I was one of the lucky Lammies. I had hoped that I would become healthy enough to come off o2, but I was also accepting the fact that I may never.

The new-found care-free confidence I discovered while on o2 was an amazing silver lining. I didn't care about the looks I got anymore. My health was in a good spot, and that's all that mattered to me. My priorities shifted.

I left the rare disease clinic with my sister and Frank (turned off), elated and in disbelief that I didn't need supplemental o2 anymore.

Since May 2018, my LAM has remained stable, and I haven't needed to go to the hospital with respiratory issues.

I'm incredibly grateful to the LAM Foundation and LAM Action for providing the crucial treatment information to my doctors and me to make sure I was getting the best care possible.

Kate Breen

L-R Kate, her eldest sister Rachel, and middle sister Kelly

London Marathon & Great Scottish Run 10K

Sunday October 3rd saw both the London Marathon and the Great Scottish Run 10K taking place.

All of our 6 runners in the London Marathon did us proud, coming home safely with some very impressive times. A very big thank you to **Alex Hanna, Andy Judge, Nicki Curwood, Rosie Duncan, Oli Wingrave** and **Jason Springate** for all your hard work and great fundraising efforts on behalf of LAM Action.

Nicki Curwood: I loved it... the crowds, the atmosphere and overwhelming support and good wishes. I felt quite emotional at the start, having taken a few years and a few setbacks to get there, but just felt pure happiness and joy running through the streets of London! Thank you for the opportunity and for your support.... I might even try and do it again!

Nicki Curwood with her medal

Oli Wingrave: I enjoyed it, I was impressed by the crowds and the other runners. Lots of memory sights and sounds and great to raise money for LAM Action. I was in the zone that last few miles, what I hadn't realised is that along the route a lot of people shout out your name in encouragement, which really helps.

Oli Wingrave stopped off at Mile 11 for a chat and a selfie with the LAMPost Editor

Allison Hamilton had taken part in the Great Scottish Run 10K a few times previously, but this was her first time competing as a visually impaired runner. Together with her running guide, Liz Deans, she posted a quite phenomenal time - well done Allison and Liz, we are very proud of you!

Allison: It was great to see big events back after the COVID lockdown, the weather stayed dry and there was a great atmosphere as usual. We finished in 1 hour and 8 minutes, not too bad considering both myself and Liz were carrying injuries.

Adventure to Chicago – September 2022

The UK Representatives at LAMposium: L-R Amy Dicker, Hollie Gorensweigh (LAM Centre Nurse), Prof. Simon Johnson, Andrea Jones, Jade Larkin, Harriet Saunders

Before being diagnosed with LAM in 2019, I loved travelling and I never had any worries about air travel. But following chest surgery and two years of shielding, my confidence dropped hugely and my anxiety levels went through the roof. At the end of 2021, I decided that I wanted to attempt a challenge each year to really tackle the world full on like I once had.

One evening as I was contemplating this and I was feeling very confident, I spontaneously booked myself and my partner Adam a place in a summer super sprint triathlon (400m sea swim, 12km bike, 2.5km run). I was never a very good swimmer, but with four months until the event, I trained twice a week in the pool, learned how to do the front crawl (even if it wasn't up to a high standard – as long as it would see me through the 400m sea swim!) and attended regular gym classes to ensure I had the fitness to complete the triathlon. I was really nervous for the big day, but with Adam by my side, a shiny new bike and some well-trained lungs I was able to complete the event, without too many tears, at a relatively decent pace. This is one achievement I am mega proud of, as before my diagnosis I would have never even considered taking part in a triathlon, let alone actually finishing one!

This event helped my confidence hugely, and I felt like I was really starting to get my spark back. Around this time, I was made aware that travel grants were available for LAM patients who wanted to attend the world-renowned LAM Foundation LAMposium in Chicago in September 2022. At the time, although my confidence was growing, I was still very anxious about flying, particularly because of the uncertainty about how my body would respond to flying, particularly long distance.

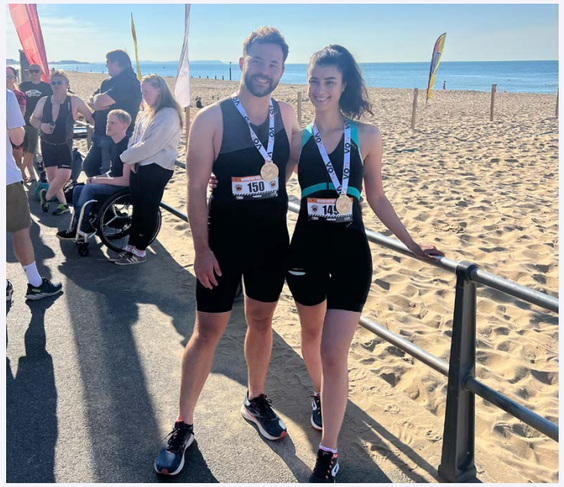
After some serious consideration, and the support of my friends, family and LAM Action, I decided that this would be a fantastic and life-changing opportunity which I would regret turning down. Thanks to the extremely generous grant from Shellie Owens with the Shellie Owens First-Time Attendee (SOFTA) travel grant, I was able to book the trip to go with Adam. I was fuelled to go and experience the jam-packed weekend attended by a mixture of patients from all over the world alongside world class professionals for a hybrid patient-researcher conference, where there would be many talks available for patients, families as well as academic and clinical professionals. The thought of this really settled my anxiety, and the flight was no trouble at all. It was a very exciting moment when I stepped off that plane, after flying for the first time in over four years, and I was ready to get to the conference and get stuck into the conference. Adam also was able to volunteer on the merchandise stand alongside other partners of LAM patients which was a great experience for him. The experience was absolutely wonderful, although it was overwhelming at times with the sheer amount of information available and the number of different opportunities. It was also invaluable to meet so many inspirational women who also had LAM.

Over the course of three busy days, I attended many interesting talks which included 'LAM Clinical Trials: What Have We Learned?, 'LAM Science Forum' (in which our very own Professor Johnson was on the panel!) and various other presentations by world renowned LAM experts. It was reassuring to hear about the amount of work that has and will continue to go into researching LAM.

I met so many inspirational women who shared similar experiences to me, and I felt honoured to have been invited to share my story for the 'Living with LAM: Together We RISE' session. This was a panel discussion alongside two other LAM patients and a carer on stage to a crowd of around 200 people, which was quite a nerve-wracking experience. It was truly a pleasure sharing my story with so many wonderful and caring people. The weekend was concluded with a spectacular gala ball, where everybody could glam up for an evening of drinks, amazing food and raising money for the LAM Foundation – the generosity of people is incredible. There was also a heart-warming part in which every LAM patient in attendance was presented with a red rose as part of the Annual Rose Ceremony. We ended the week with a few days exploring the beautiful city of Chicago after the conference had finished.

This experience was truly life changing. And although I found it challenging at times, as it was overwhelming to be reminded of the reality of the disease, it was something I never would have been able to experience if I didn't have LAM. I felt really supported and reassured by meeting so many other women, and I felt a real sense of connection with many of them. I am so extremely grateful to for the SOFTA award as well as the support I received from the LAM Foundation. I would encourage anyone else who has considered attend the LAMposium to do so, and really make the most of it. Take everything in, talk to women and their families. It was very reassuring and insightful for Adam to meet other partners of LAM patients, and he took home a lot from this experience. I hope that we can go again in the future, and I am really looking forward to the LAM Action in-person meeting in June 2023.

Harriet Saunders



Taking part in the Summer Super Sprint Triathlon

As the song says, 'The Windy City is mighty pretty'

Speaking at the 'Living with LAM: Together We RISE' session

History of LAM Action: The Contribution from Clinical Studies

Easter Island, where Rapamycin was discovered

Anne Tattersfield continues her look back at how far we have come and how much progress has been made during the first 25 years of LAM Action. In part 2, Anne focuses on the clinical studies that have helped develop effective treatment for the condition.

At the start of the 1990s virtually nothing was known about LAM (Lymphangioleiomyomatosis). It was as if we were faced with a blank piece of paper. So the early clinical studies were designed to start to fill in the gaps, mainly by collecting information or measurements from patients with LAM, or by documenting such events over time. The knowledge gained from these early studies provided patients with more information and allowed us to plan intervention and treatment studies, such as the Rapamycin study.

This article is concerned only with clinical studies carried out in the UK leading up to and including the Rapamycin (sirolimus) and doxycycline studies. Laboratory studies looking into possible underlying mechanisms were being carried out in parallel in Simon Johnson's laboratory but are not discussed here.

UK clinical studies which have helped our understanding of LAM

Some of the early clinical studies provided useful negative findings helping to identify lines of research that were not worth pursuing. Our very first study, for example, found no evidence to suggest that use of the oral contraceptive pill was related to the development of LAM. A later case control study (a study in which women with LAM are compared with women of the same age but without LAM) found no difference in family history, peri-natal or early life events between the two groups suggesting these were not relevant to why some women develop LAM.

Our first large study involved Simon Johnson travelling around the country to review the hospital notes of the 47 women with LAM we were aware of in the mid-1990s, and who gave their permission. Documenting lung function over time showed a very wide variation in the rate of decline in lung function between different women (see Figure 1). The rate of decline tended to be less in post-menopausal women and in those taking progesterone, but the numbers were too small to give definitive answers. Collecting data on rate of change in lung function, (FEV1 and gas transfer factor), provided us with a useful tool for assessing patients in the clinic and for designing drug intervention studies. Studying hospital notes provided valuable information on the age at which symptoms of LAM were first noted, how many women had received hormone treatment for LAM, and the frequency of complications such as pneumothorax, kidney angiomyolipomas and chylous pleural effusions.

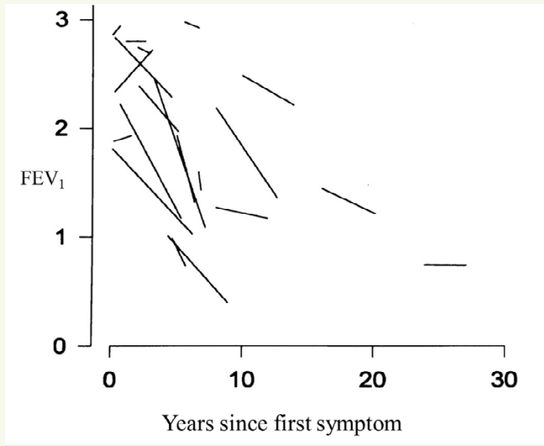


Fig1: Graph showing the change in FEV1 over time in individual women with LAM from our early study, published in 1999. There is a large variation between different women, with some showing a much faster rate of decline than others.

In a further questionnaire study, we asked patients how long after their first symptom of LAM they noted certain critical events, including how long it was before they found they were breathless walking on the flat, or required oxygen or a lung transplant. This study confirmed our hunch that for most patients the progress of LAM was slower than was suggested in the text books, and that life expectancy was considerably better. We found that 91% of patients were alive after 10 years, whereas the text books at that time suggested a figure of 50%. This study was before the drug Rapamycin was available for treatment, and the outlook for women now is of course much better still.

The Rapamycin Story

The Rapamycin story starts on Easter Island, also known as Rapa Nui, where scientists discovered a small organism in the soil which inhibited the growth of certain fungi. The active material was extracted and called Rapamycin, after Rapa Nui, and heralded in 1975 as a new anti-fungal agent. Further research showed that Rapamycin had other, and potentially more important, properties in that it reduced the proliferation of cells growing in the laboratory and the activity of some of the immune cells responsible for rejecting transplanted organs. Scientists then showed that the mechanism underlying the actions of Rapamycin was due to inhibition of the mTOR pathway, a pathway that modulates cell growth.

LAM can occur either on its own (sporadic LAM) or as part of Tuberous Sclerosis Complex (TSC). Unlike sporadic LAM, TSC is inherited and the two genes responsible, TSC1 and TSC2, were identified in the 1990s. So research workers, including Simon Johnson, looked at LAM tissue from patients with sporadic LAM and Lisa Henske in the USA found definitive evidence of a link between mutations in these genes to LAM. In normal tissue TSC1 and TSC2 produce proteins which inhibit mTOR, and thereby prevent excessive cell growth. But since protein concentrations are reduced in LAM tissue, cells grow more avidly to produce the pathological changes characteristic of LAM.

The fact that Rapamycin acts on the same pathway as the proteins that are deficient in LAM led to the idea that Rapamycin might substitute for these proteins and help to inhibit mTor, thus providing a possible treatment for patients with LAM and TSC. Rodent studies reinforced this possibility so by 2003 the scene was set for the next stage of research, to test the hypothesis in patients.

In the UK the Nottingham team decided to study the effects of Rapamycin in patients with sporadic LAM or TSC in collaboration with scientists in Cardiff who had long been involved in TSC research. We chose patients with kidney angiomyolipomas (AMLs) because measuring the size of AMLs would be more sensitive to any change due to Rapamycin than measuring lung function. The study took many months to get off the ground due to excessive bureaucracy (one form was 300 pages long), and because there were few suitable patients and not everyone wanted to or could take part. Eventually in 2005 the first UK patient started Rapamycin, and consequently we were able to report the results of measurements made over the first year of treatment in 13 patients. The main finding was a 26% shrinkage in the size of their AMLs (see Figure 2), confirming the findings in an early study in the USA. Our study was too small to detect any significant change in lung function.

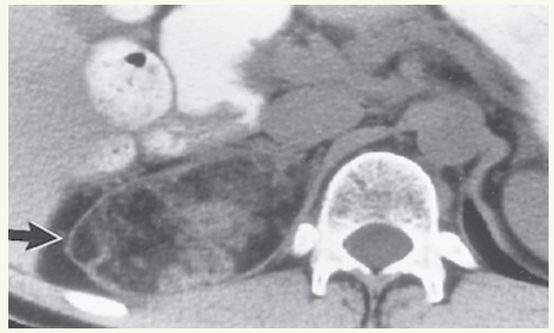


Fig2: A CT scan showing a cross section of the abdomen with an arrow pointing to an angiomyolipoma (AML). When these were measured in patients before and after taking Rapamycin there was a 26% reduction in size after a year.

The important question for patients with sporadic LAM of course was whether Rapamycin would reduce the decline in lung function over time. Because the number of patients with LAM in the USA is much larger Frank McCormack and colleagues were able to study this. They enrolled 89 patients with LAM into the Multicentre International Lymphangioleiomyomatosis Efficacy and Safety Trial (MILES trial) which was sufficiently large to be able to compare the effects of Rapamycin and placebo on lung function. The findings of the MILES study published in 2011 showed not only that lung function was largely maintained whilst women were taking Rapamycin but also that it deteriorated once Rapamycin was stopped. Rapamycin was associated with some adverse effects in both studies, as expected, but the benefits were such that Rapamycin was confirmed as a treatment for LAM.

The next intervention trial in the UK was based on Simon Johnson's laboratory work which showed that doxycycline, a cheap and widely available antibiotic, inhibited enzymes thought to be active in LAM. When compared to placebo in a 2 year study however, doxycycline showed no benefit and nothing to suggest it might be useful for women with LAM. Although disappointing, finding out what doesn't work is part of the process of developing new treatments.

How did these clinical studies help LAM patients?

It may be difficult for women diagnosed with LAM today to appreciate how lost and isolated patients felt 30 years ago when given a diagnosis of LAM. Few facts were known, the internet was not widely available, there was no social media and they were very unlikely to meet other women with LAM. The information from the early clinical studies from the UK and elsewhere helped women to feel that they weren't alone and placed them in a much better position to plan their future. The findings on pneumothorax, AMLs and pregnancy enabled doctors to give patients better advice, improve management and clarify what seemed to be 'best practice' for managing these conditions.

This then led to the production of guidelines for diagnosing and managing LAM. In Europe this happened through Eurolam a small group of European doctors with an interest in LAM and some representative patients with LAM from different European countries. At the second meeting in Nottingham it was decided to appoint a task force to produce formal guidelines under the aegis of the European Respiratory Society, with Simon Johnson and Jean Francois Cordier as joint chairs. Using strict criteria to assess the strength and quality of each recommendation the committee was able to publish the ERS Guidelines for the Diagnosis and Management of Lymphangioleiomyomatosis in 2011. These and subsequent guidelines from the US and Japan were particularly helpful in countries where there was limited expertise in managing LAM.

A further valuable outcome from our clinical studies relates to the data we collected on decline in lung function in individuals with LAM over time. This is useful in the clinic when patients want to plan for the future; for example when considering whether to embark on pregnancy or take Rapamycin. It was also essential background for planning intervention studies.

The large MILES study in the US, complemented by the smaller studies like ours, has had major and very positive consequences for many women with LAM. Using Rapamycin has reduced the rate of deterioration in lung function, preserved a good quality of life for much longer, reduced the need for lung transplantation and increased life expectancy. Rapamycin isn't a cure of course but it has had life changing benefits for many patients. It is very unusual for such rapid progress to be made for diseases as rare as LAM is.

The momentum in research, management and treatment also contributed to the establishment of the UK National Centre for LAM in Nottingham in April 2011. This was another important milestone for women with LAM, providing specialist clinical care and best management of all aspects of LAM. The National Centre spearheaded the prescribing of Rapamycin for women felt likely to benefit. In conjunction with Nottingham University the LAM Centre is also a hub for clinical trials, the evaluation of biomarkers and laboratory research into the molecular basis of LAM.

Finally it's important to remember that the clinical trials discussed in this article were only possible because of the support of LAM Action, all the women with LAM across the UK who agreed to fill in questionnaires over the years, all who committed to take part in the Rapamycin and doxycycline studies, when the effects of the drugs on LAM were unknown, and everyone who raised funds to support the studies. It's been a real team effort and we are immensely grateful to everyone.

I want to thank Simon Johnson for checking the final proof and Gill Hollis for her invaluable contribution to an early proof (and her eagle eyed editing).

Anne Tattersfield

Making the Most of Your Christmas Shopping

Nothing beats the excited faces of your loved ones opening their presents during the festive period. It makes all of the stress and panic of shopping worth it. Whether you're all sorted for Christmas or living up to your last-minute shopping reputation, you can support charities like LAM Action with just a few clicks during your online shopping.

Two fantastic ways you can give back to the LAM community from the comfort of your home are by opting in for **Amazon Smile** and **Give as You Live** while shopping online. Setting these up means every eligible purchase will donate a percentage to LAM Action. It's effortless to do, and you will keep donating until you switch it off.

smile.amazon.co.uk

Amazon Smile lets you shop on Amazon as usual while automatically donating 0.5% of every eligible net purchase (excluding shipping fees, VAT, and returns) to your chosen charity.

Also, it's worth keeping an eye out for Amazon events like Prime Day throughout the year. Amazon Smile donated 1% of eligible net purchases during their 48-hour event this year.

Whenever you see 'Eligible for smile.amazon.co.uk donation' under a product, you'll know you're donating to a worthy cause.

Setting Up on Desktop

1. Go to **https://smile.amazon.co.uk/** in your web browser (Make sure to bookmark it, as shopping through Amazon.co.uk won't trigger donations).
2. Click Get Started, sign in, and follow the simple set-up process.
3. You can choose a charity category or type LAM Action in the search bar.
4. Once your charity is selected, just shop like you usually would.

Setting Up on Mobile

1. Download the Amazon app from the Apple Store or Play Store.
2. Once signed in, go to Settings (found by tapping the three horizontal lines).
3. Scroll down until you see Amazon Smile.
4. Simply turn it on and set up LAM Action as your chosen charity.
5. Then return Home and continue shopping as normal.

Give as you Live® Online

Give as You Live works in a very similar way to Amazon Smile. But, it includes 6,000 high-street retailers and online giants like Marks & Spencers and eBay.

Depending on what you buy and which retailer you choose, you can donate around 7% towards LAM Action.

You can donate using Give as You Live by shopping through their website and their app.

Shopping on Website

1. Go to **https://www.giveasyoulive.com/** and sign up.
2. You'll be prompted to choose a charity, so simply type in LAM Action or search using the category section.
3. Once you've chosen your charity, you'll be encouraged to add a Donation Reminder extension. (This extension will remind you when you land on a donation-eligible website).
4. Then, just type in your favourite shops or use the drop-down menu to find the perfect shops for you.

Shopping on App

1. Download the Give as You Live app from the Apple Store or Play Store.
2. Once you open the app, follow the introduction steps.
3. Shopping through the app is similar to desktop browsing.
4. Search for the shop you want, and the app will redirect you to the shop's website to shop as normal.
5. **Many retailers will redirect you to their app. To keep Give as You Live tracking donations, it's important to stay on the desktop version of their website.**

So, make the most of the January sales and set your accounts up now!

Kate Breen