



The Lowe Syndrome Trust

December 2016/2017 Newsletter

This newsletter is a brief overview of the achievements of this small charity during the past year.

The Lowe Syndrome Trust was founded as a small voluntary charity in June 2000 with an aim to raise funds to support research into Lowe Syndrome and support families and medical professionals.

All research projects, events, a full story about the charity including TV and Radio can be found on www.lowetrust.com

Best wishes

Lorraine Thomas

Founder, Chair & Trustee
The Lowe Syndrome Trust

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Research

The Lowe Syndrome Trust awarded funding to support two new research grants. Manchester University & University of Napoli.



Antonella De Matteis, MD, Professor of Biology Dpt. Molecular Medicine and Medical Biotechnology University of Napoli Federico II - Medical School £80,000

"We are delighted and honoured to receive this award from the UK Lowe Syndrome Trust. This grant will allow us to continue our studies aimed at the identification of drugs, currently on the market for other purposes, which can counteract Lowe syndrome signs and thus can be "repositioned" and used as therapy for Lowe syndrome. In fact our group, which supported the foundation of AISLO (Associazione Italiana Sindrome di Lowe) 15 years ago and which has contributed important insights into the cellular mechanisms underlying Lowe syndrome during this time, decided few years ago to develop a "repositioning" pharmacological approach for the cure of Lowe syndrome. We have already started this approach at the Telethon Institute of Genetics and Medicine (TIGEM) in Naples, using a high content screening cell-based methodology and we have identified six marketed drugs that are able to correct some of the alterations observed in kidney cells derived from Lowe patients or in cells where OCRL, the gene mutated in Lowe syndrome, has been silenced. With the present project that will be run in collaboration with Prof. Olivier Devuyst (University of Zurich) we will test these drugs on the mouse model of Lowe syndrome developed by Prof. Robert Nussbaum. We believe that the identification of drugs that are able to correct the proteinuria in this model will represent a key step towards the development of a pharmacological treatment of Lowe syndrome". Antonella de Matteis



Professor Martin Lowe, Manchester University £10,000

"I am delighted to receive this award from the Lowe Syndrome Trust. It will allow us to continue our research using the zebrafish model for Lowe Syndrome that we developed using previous funding from the Trust. We have shown that the zebrafish model recapitulates many of the symptoms seen in Lowe Syndrome patients including neurological and renal impairment, allowing us to investigate the underlying mechanisms that lead to these symptoms. Our current work is aimed at using zebrafish to perform a screen to identify drugs that may be used to treat Lowe syndrome. We are making genetically modified strains of zebrafish that allow us to easily and rapidly assess kidney function, which will be used to perform drug screening in a high throughput manner. The current grant provides continuation funding that will allow us to perform the screen itself, which will be carried out using compounds that are already approved for use in humans, meaning that any 'hits' from the screen can be rapidly translated for use in the clinic. We are extremely grateful to the Lowe Syndrome Trust for their ongoing support of our research, which we hope will lead to improved treatments for Lowe patients in the future."

The Lowe Syndrome Trust meets with Director of Research and Evidence Department of Health



Lorraine Thomas, Chair of the Lowe Syndrome Trust and Lowe funded researchers Martin Lowe and Rudiger Woscholski, met with Dr Louise Wood to discuss the charity and how Dr Wood might be able to advise how the charity could seek substantial funding for drug screening using Zebra fish. The meeting was convened in the hope Dr Wood would be able to advise on possible links to help the charity. Pictures Louise Wood, Martin Lowe, Rudiger Woscholski

Lowe syndrome is a genetic disorder that typically leads to kidney failure, which is the major cause of morbidity in Lowe patients. There is currently no effective treatment or cure for this devastating condition. Using funding from the Lowe Syndrome Trust (LST) my laboratory has developed a zebrafish model that faithfully recapitulates the clinical manifestations of Lowe syndrome. Using this model we have identified the underlying mechanisms that lead to the renal impairment seen in Lowe syndrome. The next goal is to exploit the unique power of the zebrafish model to screen for drugs that rescue the renal phenotype, which could then be used in the clinic to treat Lowe syndrome patients. As a first step towards achieving this objective we have generated a zebrafish strain that allows us to monitor kidney function in living animals, which can be exploited to screen for compounds that rescue the renal deficiency of the Lowe model. We would now like to perform a drug screen using the zebrafish renal reporter. The screen will exploit existing libraries of FDA-approved compounds, meaning that any 'hits' identified in the screen will be approved for use in humans, and thus can be repurposed for the treatment of Lowe syndrome and taken directly into the clinic. The renal symptoms of Lowe syndrome are similar to those of several other renal disorders, sharing common pathogenic mechanisms, and moreover, the process defective in the renal tubule of Lowe syndrome is the same as that affected by many nephrotoxic agents including commonly used therapeutics. Hence, the reporter strain we have generated, and any 'hit' compounds we identify in the screen, are likely to have utility beyond Lowe syndrome. They could therefore be exploited to screen for renal function in other diseases and chemically induced kidney damage, as well as treatment of these conditions. It is also worth pointing out that in a separate project, LST funded research has resulted in the development of new rationally designed chemical lead compounds that have the potential to treat Lowe syndrome. These compounds and their derivatives would also be part of the screen. We also have access to human patient cell lines, obtained through LST funding, that could be used to validate 'hits' prior to going into the clinic. We believe the work is at an exciting stage, but unfortunately, due to the intrinsic uncertainty associated with any type of drug screen, it has proven difficult to obtain funding for this project through the Research Councils.

Professor Martin Lowe, University of Manchester Dr Rudiger Woscholski, Imperial College London

Fundraising Charitable bookings

Visit a Charitable nominated restaurant and the charity will receive £1 for every diner. Follow the link below to find your restaurant/Lowe Syndrome



I am proud to be Trustee of the Lowe Syndrome Trust, a very small UK charity, supporting Lowe families and raising funds to support vital research to find better treatment and cure of this devastating disease. Lowe Syndrome affects

Donate to the Lowe Syndrome Trust when you book a table at this restaurant.

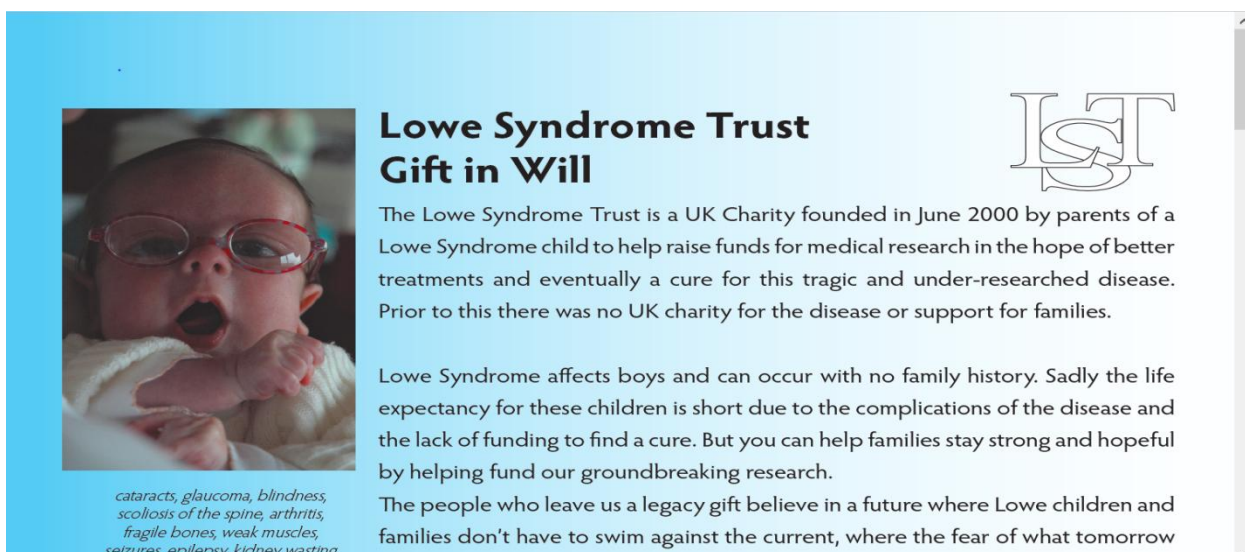
The charity is registered with CHARITABLE BOOKINGS !!
(just select Lowe syndrome Trust as favourite)
<https://itunes.apple.com/gb/app/charitable-bookings-giving/id1058902592?mt=8>

"I am proud to be a Trustee of the Lowe Syndrome Trust"

Gift to Will

The charity has produced a "Gift to Will" for those wishing to leave a legacy in their Will for Lowe Syndrome research.

This form is on www.lowetrust.com or email lowetrust@gmail.com



**Lowe Syndrome Trust
Gift in Will**

The Lowe Syndrome Trust is a UK Charity founded in June 2000 by parents of a Lowe Syndrome child to help raise funds for medical research in the hope of better treatments and eventually a cure for this tragic and under-researched disease. Prior to this there was no UK charity for the disease or support for families.

Lowe Syndrome affects boys and can occur with no family history. Sadly the life expectancy for these children is short due to the complications of the disease and the lack of funding to find a cure. But you can help families stay strong and hopeful by helping fund our groundbreaking research.

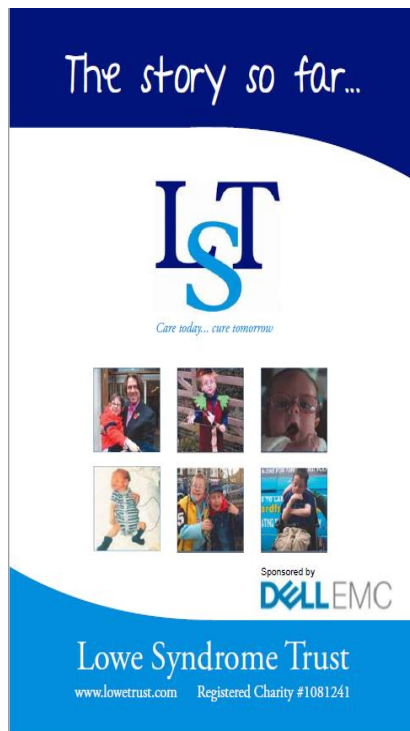
The people who leave us a legacy gift believe in a future where Lowe children and families don't have to swim against the current, where the fear of what tomorrow

cataracts, glaucoma, blindness, scoliosis of the spine, arthritis, fragile bones, weak muscles, seizures, epilepsy, kidney wasting

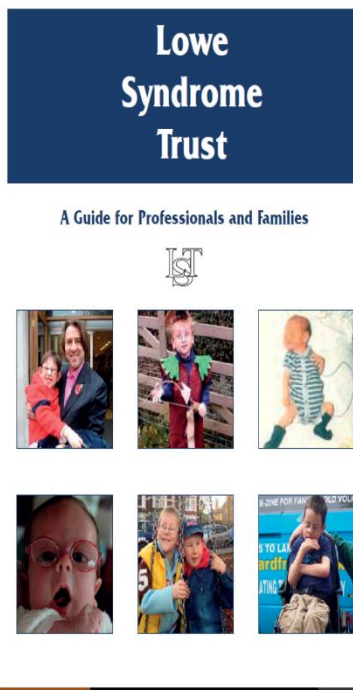
IST

Lowe Syndrome Trust information brochures

These are all on the website or can be mailed to you.



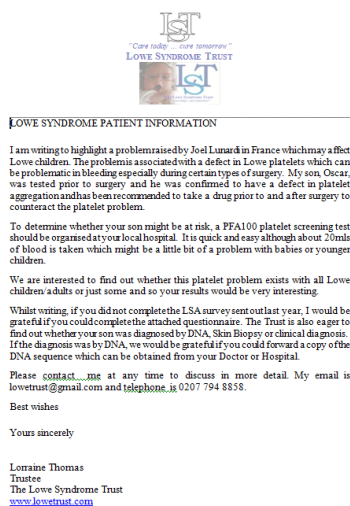
Lowe Story of the Charity



Lowe Syndrome Medical book



Lowe brief leaflet including Dents



Lowe letter about Lowe blood platelet disorder

Lowe Syndrome – A&E Information Sheet

Parents – please complete this and take along with a copy of the **LOWE SYNDROME TRUST** regarding your child.

Patient name: _____ DOB: _____

Specialist name: _____ Institution: _____

Telephone: _____ Email: _____

Clinicians – this sheet provides background information for Lowe Syndrome, also known as Oculocerebrorenal syndrome of Lowe (OCRL). For further information, please use the details above to contact the specialist responsible for this patient, who is happy to advise on details of the medical management.

Lowe Syndrome – Rare, X-linked recessive disorder, affecting males

- Causes physical and mental handicaps
- Affects the eyes, brain, kidneys, muscles and bones
- There is currently no cure, and treatment is supportive

Eyes – Born with cataracts, usually removed early in life

- 50% of cases suffer raised intra-ocular pressure leading to glaucoma

Kidneys – Kidney disorders can cause features of renal Fanconi syndrome, including:

- o polyuria and/or polydipsia; this can lead to dehydration
- o low-molecular weight proteinuria
- o elevated urinary calcium, which can cause kidney stones
- o metabolic acidosis
- o phosphate wasting, which can cause rickets

Abdomen – Pain can be due to constipation resulting from dehydration

- Acute pain can also be caused by kidney stones, so an U/S should be considered

Surgery/ blood – If surgery is required that risks major blood loss, it is important to note that many Lowe's patients have an impaired platelet function, evident from prolonged closure times in the PFA-100 system. The bleeding risk can be ameliorated with ε-aminocaproic acid.

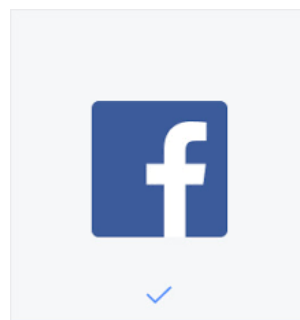
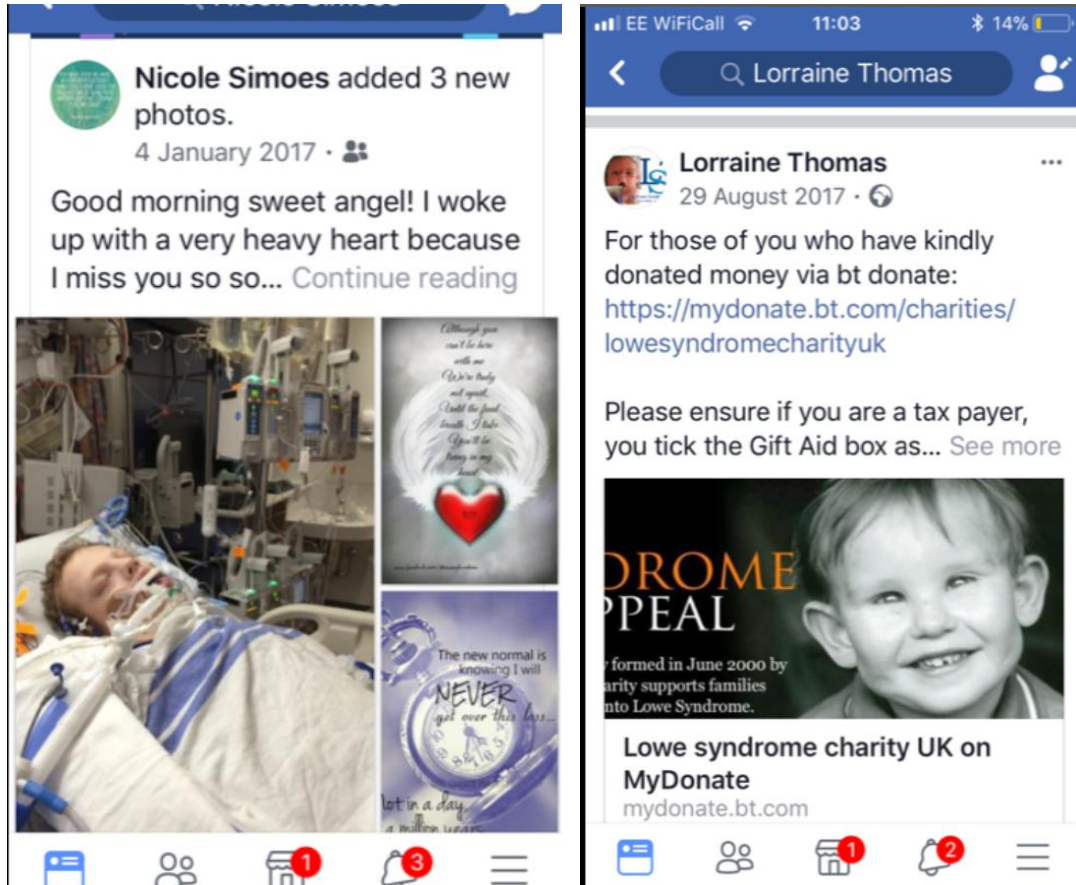
LST This information sheet has been prepared by the Lowe Syndrome Trust (Registered Charity 1081241)
Web: www.lowetrust.com Phone: (448) (0) 207 794 8858 E-mail: lowetrust@gmail.com

Lowe Accident & Emergency sheet for all patients

Facebook

The Lowe Syndrome Trust has a FB page with updates and video/magazine articles.

Search under lowe trust



Thank you to all those of you that have supported the charity by donations or organising events to fund Lowe Syndrome Research. I would also like too thank the Lowe Syndrome Trustees, Scientific Advisory Board and Patrons.

