The Lowe Syndrome Trust

Newsletter

February 2020

This newsletter is a brief overview of the achievements of this small charity in the past months.

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 appeals can be found on www.lowetrust.com.

Best regards,

Andrew Thomas

Chief Executive Officer

The Lowe Syndrome Trust

E: info@lowetrust.com

T: 0207 794 8858

Lorraine Thomas

24/11/1955 – 10/06/2019

It is with great sadness we announce Lorraine Thomas, Founder, Chair and Trustee of The Lowe Syndrome Trust, has lost her long and terrible battle with cancer on 10th of June 2019. Lorraine was an amazing wife and mother, devoting her life to her only child Oscar. Her tireless endeavours to find cure for Lowe Syndrome has invaluably stimulated research into the condition, as well as providing relief and hope for many families with children affected by Lowe syndrome.

In Lorraine's memory, a beautiful service was held on 27th of June at the Hampstead Parish Church. It was attended by Lorraine's family and friends, as well as colleagues, donors, trustees, patrons and members of Scientific Advisory Board of Lowe Syndrome Trust. The reception at Freemsasons' Arms, a beloved pub of Lorraine's family and friends, also welcomed celebrity patrons of the charity, Tony Hadley and Mike Fennings.

Lorraine did not want any flowers: only donations to the Lowe Syndrome Trust. You can donate in Lorraine's memory at our website: www.lowetrust.com/donate-gift-aid/.

Andrew Thomas: continuing Lorraine's legacy as the new CEO of Lowe Syndrome Trust

After Lorraine, the founder of the Lowe Syndrome Trust, has lost her long battle to cancer, her husband Andrew Thomas has decided to continue her legacy. At the request of Charity's Trustees, he has now accepted the position of Chief Executive Officer at the Lowe Syndrome Trust.

Andrew, who was previously the Chief Financial Officer of the Trust, is determined to honour his wife's lifelong mission to find a cure for Lowe syndrome, a debilitating genetic disease affecting 1 in 500,000 people. His statement can be found on the next page.

Video from the Downing street reception can be found on YouTube:
www.youtube.com/watch?v=GwYNpBxi9gY

Lowe Syndrome
Department for Digital, Culture, Media & Sport 877 views • 3 years ago
Founder and Chair of the **Lowe Syndrome Trust**, Lorraine Thomas, gives an insight into what it is like to run a local charity. for ...

Letter from Andrew Thomas, CEO

I am extremely honoured to continue my late wife Lorraine's work and accept the Trustees' request to take the position of CEO of the Charity. Recent times have been difficult for our family, but my son Oscar who has Lowe Syndrome, is now coping well and we have been getting on, following our usual routines. We want to thank everyone for their kind messages and support.

I would like to especially thank the trustees Joseph Laycock (Chair of Trustees), Carolyn Mitchell, Penny Biziou and Jonathan Ross, and patrons Tony Hadley, Penny Lancaster, Lisa Voice, Mike Fenning and Mark Emms, and medical board, chair Professor Robert Unwin, for their unwavering support. I also like to introduce and thank Anna Bogdanova, for keeping the charity functioning, and Anastasia Lanzara, who provides amazing research support.

I hope that together we can follow on Lorraine's legacy in driving better family support, treatment and discovering a cure for Lowe syndrome.

Special thanks also go to The National Lottery Community fund team, who supported us through this difficult period. In addition to medical research, and assisted by the National Lottery grant, the charity is to help with better outreach services for UK families affected by Lowe Syndrome. We would like to provide better advice on benefits and social services, special educational needs, disability benefits and transfers from children to adult services, to help with the bureaucracy that can be overwhelming for families.

The charity continues to support several major projects which are on the cusp of breakthrough in discovering potential cures for Lowe syndrome. We will be contributing to a global Lowe Syndrome research symposium in Spring 2020, organised by our colleagues from the Lowe Syndrome Association USA and University of Montreal. This event will bring the foremost LS researchers together to advance various drug discovery projects.

Thank you everyone for your help and support.

Best regards,

Andrew Thomas

CEO, Lowe Syndrome Trust

Lowe Syndrome Trust awarded a grant from the National Lottery Fund!

In June 2018, just a year before Lorraine passed away, her dedication and hard work has been acknowledged by **The National Lottery Community Fund**, who awarded Lowe Syndrome Trust with a grant for 'Enhancing Lowe Syndrome lives' project. This is an outstanding achievement, and the Lowe Syndrome Trust aims to maintain the high standards set by Lorraine in achieving the project's goals.

The project's key aims are to reduce isolation of Lowe Syndrome families; for families to have greater knowledge of medical research and treatments, as well as have improved access to care and support by social and educational services.

"We are extremely proud to support the work of the Lowe Trust. Through its tireless fundraising and awareness raising, the organisation has been a catalyst for ground-breaking research into Lowe Syndrome.

We are pleased that Lorraine's dedication and passion for improving the lives of people with Lowe Syndrome will continue, and we wish Andrew the best of luck in his role as CEO of the Lowe Trust."

– Sacha Rose-Smith
Senior Head of Regional Funding
The National Lottery Community Fund

Facebook fundraisers

£937
in total

Over past few months, we have had some amazing people fundraising for Lowe Syndrome Trust!

Deb Harter, Oscar Thomas's cousin, hiking 84 miles along the Hadrian's Wall national trail…

Justin Sydenham, walking The Welsh Three Peaks in 24 hours in memory of Ian Sydenham…

And Kelz Whyte organised a birthday fundraiser, dedicated to her brother Cathal who has Lowe Syndrome.

THANK YOU to all our Charity supporters, no matter how big or small. Every single penny and every single thought matter a lot to us. The Lowe Syndrome community is extremely important in our work, and we would not be near potential drug therapy without your constant support and encouragement!

Events

Lowe Syndrome Trust was invited to attend **'Think Research' Rare Diseases Patient Day in March**, organised by National Institute for Health Research (NIHR) BioResource. The aim of the day is to provide insight and training in aspects of rare disease research, as well as information-gathering and networking opportunities. The event will comprise of excellent speakers including representatives from the Department of Health and Social Care, expert panel, lunchtime discussions and workshops.

Lowe Syndrome Trust is a **NIHR Non-commercial Partner**, meaning that some of the research that we fund is eligible for NIHR Clinical Research Network (CRN) support, including access to to health and social care infrastructure for research and training.

Our US colleagues **Lowe Syndrome Association** and **IRICoR** *(The Institute for Research in Immunology and Cancer – Commercialization of Research)* at **University of Montreal, Canada,** are organising an international Lowe Syndrome research symposium in **May 2020**. Specific topics include PIP2 signaling, the clinical features of Lowe Syndrome, cellular and animal models of the disorder, how compounds and drugs might affect pathways relevant to Lowe Syndrome, and share insights on how such compounds or drugs might have a beneficial impact.

Research teams

"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. Using a high content screening cell-based methodology at Telethon Institute of Genetics and Medicine (TIGEM) in Naples, we have identified 6 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."

– Prof. Antonella De Matteis, MD
Dept, of Molecular Medicine and Medical Biotechnology
University of Naples "Federico II"

"This award from the Lowe Syndrome Trust 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. The current grant will allow us to perform the screen, which will be carried out using compounds that are already approved for use in humans. 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."

– Prof. Martin Lowe, PhD
Division of Molecular & Cellular Function
Manchester University

LST team

Andrew Thomas | *Chief Executive Officer*

Andrew Thomas is an IT consultant at Dell Technologies, juggling his job with his parental duties and the CEO position at LST, overseeing grant allocation, funding management and liaison with funders, trustees and patrons. He also continues as the Chief Financial Officer of the charity, handling both internal and external financial decisions.

Anna Bogdanova | *Charity Manager / Project Coordinator*

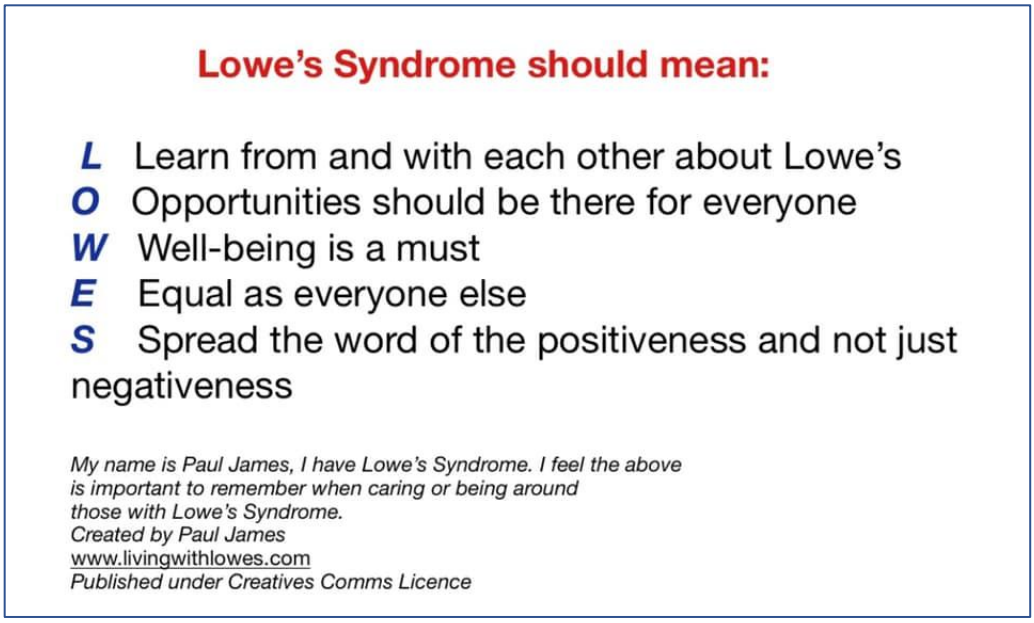
Anna holds a bachelor's degree in Neuroscience and is now pursuing master's degree in Health Psychology. She is responsible for day-to-day charity operations, as well as assisting in global operations. Her duties include strategic planning for the Charity development, as well as financial planning and project guidance. Other duties include family outreach, social media coverage and grant applications management.

Anastasia Lanzara | *Clinical Research Consultant*

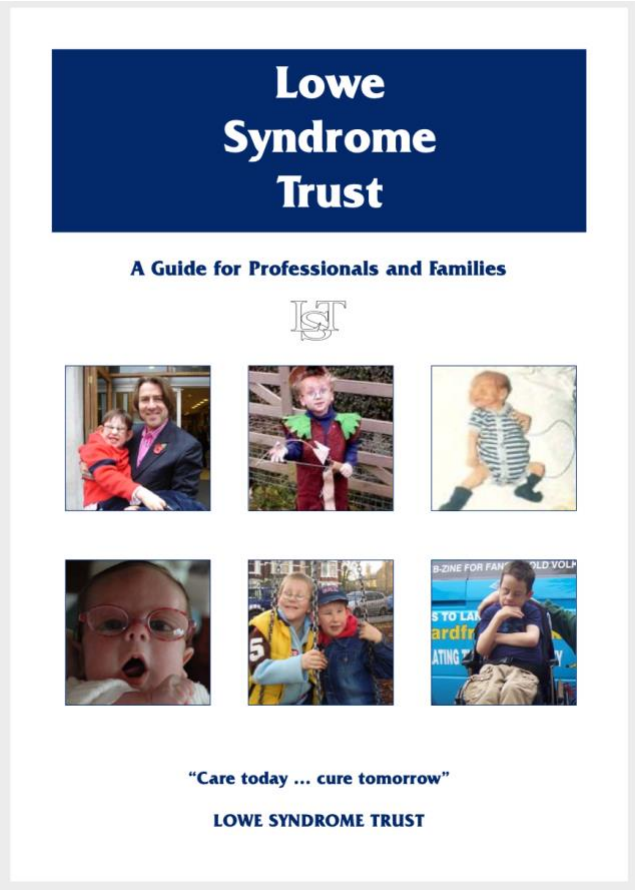
Anastasia holds Psychology degree from University of Bath, spending one year working as a research assistant in Boston College. Further, she achieved Master of Research qualification in Clinical Research at Imperial College London. She has extensive knowledge of clinical aspects of research, which is particularly important in light of the breakthrough developments in curing Lowe Syndrome. Her role is to advise the team on clinical advances and research-oriented decisions made within the Charity.

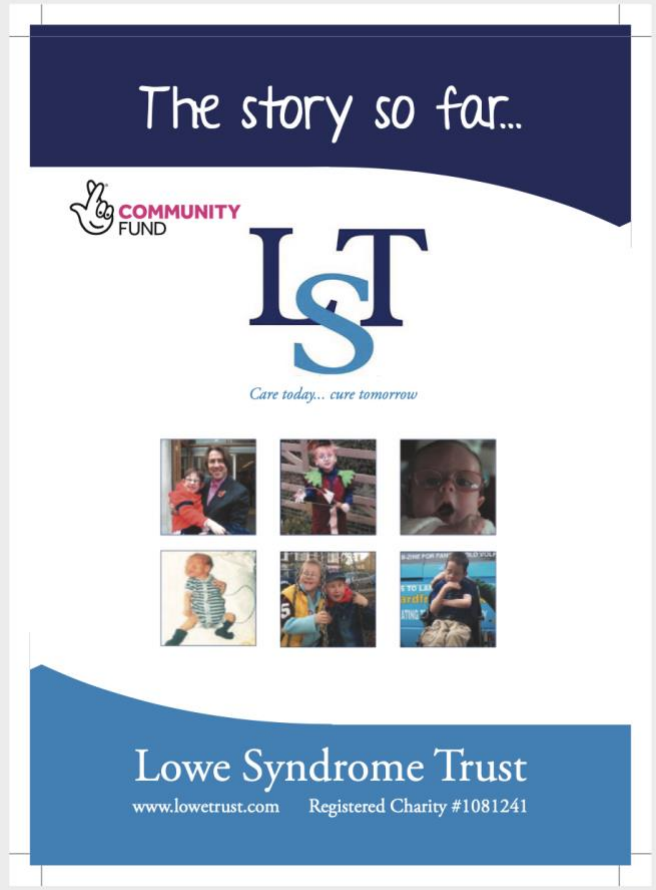
We would like to draw your attention to the website livingwithlowes.com, which was created by Paul James, who himself has Lowe syndrome. Being a very active member of the community, Paul not only raised money for Lowe Syndrome Trust, but also worked with bodies such as the NHS and Commission for Social Care Inspection to consult on leaflet designs, advise on the needs of people with learning disabilities, help with events organisation, carry out learning disability trainings and many other achievents that carry invaluable contribution to the LS community.

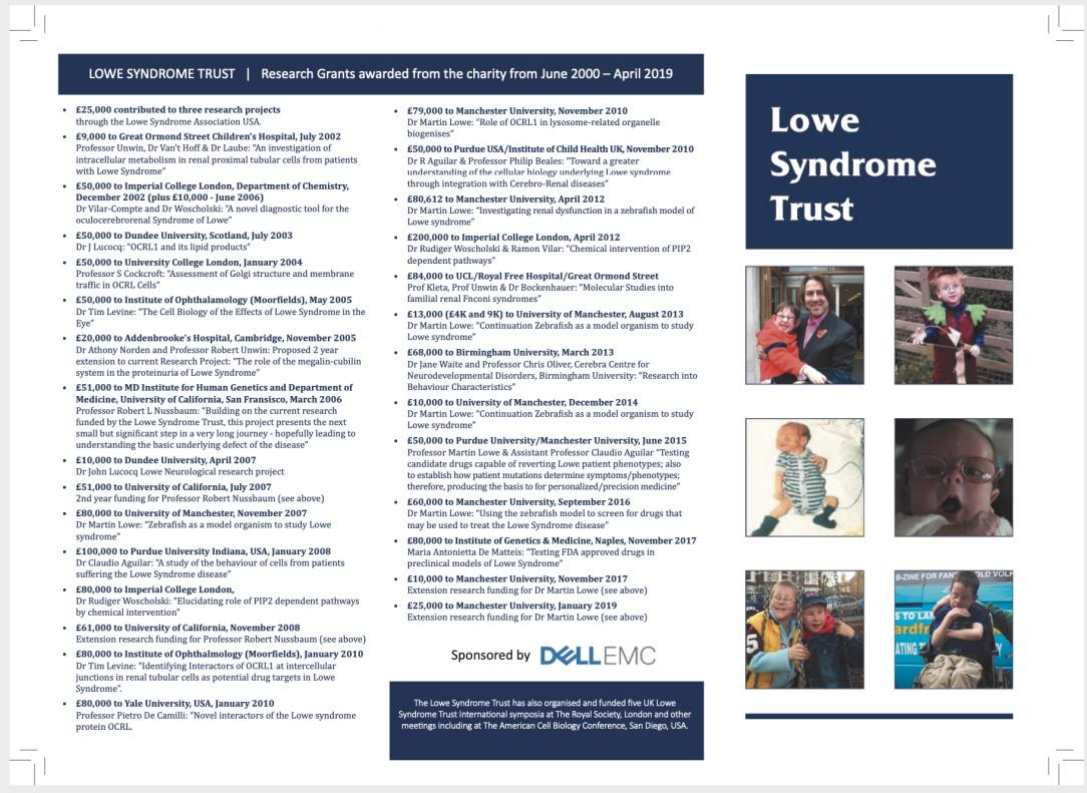
Paul James also produced two graphics for the Lowe community such as healthcare proffesionals and carers, to encourage inclusion and understanding of those affected by Lowe syndrome.



Contacts & Materials







LOWE SYNDROME TRUST | Research Grants awarded from the charity from June 2000 – April 2019

- **£25,000 contributed to three research projects** through the Lowe Syndrome Association USA.
- **£9,000 to Great Ormond Street Children's Hospital, July 2002** Professor Unwin, Dr Van't Hoff & Dr Laube: "An investigation of intracellular metabolism in renal proximal tubular cells from patients with Lowe Syndrome"
- **£50,000 to Imperial College London, Department of Chemistry, December 2002 (plus £10,000 - June 2006)** Dr Vilar-Compte and Dr Woscholski: "A novel diagnostic tool for the oculocerebrorenal Syndrome of Lowe"
- **£50,000 to Dundee University, Scotland, July 2003** Dr J Lucocq: "OCRL1 and its lipid products"
- **£50,000 to University College London, January 2004** Professor S Cockcroft: "Assessment of Golgi structure and membrane traffic in OCRL Cells"
- **£50,000 to Institute of Ophthalamology (Moorfields), May 2005** Dr Tim Levine: "The Cell Biology of the Effects of Lowe Syndrome in the Eye"
- **£20,000 to Addenbrooke's Hospital, Cambridge, November 2005** Dr Athony Norden and Professor Robert Unwin: Proposed 2 year extension to current Research Project: "The role of the megalin-cubilin system in the proteinuria of Lowe Syndrome"
- **£51,000 to MD Institute for Human Genetics and Department of Medicine, University of California, San Fransisco, March 2006** Professor Robert L. Nussbaum: "Building on the current research funded by the Lowe Syndrome Trust, this project presents the next small but significant step in a very long journey - hopefully leading to understanding the basic underlying defect of the disease"
- **£10,000 to Dundee University, April 2007** Dr John Lucocq Lowe Neurological research project
- **£51,000 to University of California, July 2007** 2nd year funding for Professor Robert Nussbaum (see above)
- **£80,000 to University of Manchester, November 2007** Dr Martin Lowe: "Zebrafish as a model organism to study Lowe syndrome"
- **£100,000 to Purdue University Indiana, USA, January 2008** Dr Claudio Aguilar: "A study of the behaviour of cells from patients suffering the Lowe Syndrome disease"
- **£80,000 to Imperial College London,** Dr Rudiger Woscholski: "Elucidating role of PIP2 dependent pathways by chemical intervention"
- **£61,000 to University of California, November 2008** Extension research funding for Professor Robert Nussbaum (see above)
- **£80,000 to Institute of Ophthalmology (Moorfields), January 2010** Dr Tim Levine: "Identifying Interactors of OCRL1 at intercellular junctions in renal tubular cells as potential drug targets in Lowe Syndrome".
- **£80,000 to Yale University, USA, January 2010** Professor Pietro De Camilli: "Novel interactors of the Lowe syndrome protein OCRL.
- **£79,000 to Manchester University, November 2010** Dr Martin Lowe: "Role of OCRL1 in lysosome-related organelle biogenises"
- **£50,000 to Purdue USA/Institute of Child Health UK, November 2010** Dr R Aguilar & Professor Philip Beales: "Toward a greater understanding of the cellular biology underlying Lowe syndrome through integration with Cerebro-Renal diseases"
- **£80,612 to Manchester University, April 2012** Dr Martin Lowe: "Investigating renal dysfunction in a zebrafish model of Lowe syndrome"
- **£200,000 to Imperial College London, April 2012** Dr Rudiger Woscholski & Ramon Vilar: "Chemical intervention of PIP2 dependent pathways"
- **£84,000 to UCL/Royal Free Hospital/Great Ormond Street** Prof Kleta, Prof Unwin & Dr Bockenhauer: "Molecular Studies into familial renal Fnconi syndromes"
- **£13,000 (£4K and 9K) to University of Manchester, August 2013** Dr Martin Lowe: "Continuation Zebrafish as a model organism to study Lowe syndrome"
- **£68,000 to Birmingham University, March 2013** Dr Jane Waite and Professor Chris Oliver, Cerebra Centre for Neurodevelopmental Disorders, Birmingham University: "Research into Behaviour Characteristics"
- **£10,000 to University of Manchester, December 2014** Dr Martin Lowe: "Continuation Zebrafish as a model organism to study Lowe syndrome"
- **£50,000 to Purdue University/Manchester University, June 2015** Professor Martin Lowe & Assistant Professor Claudio Aguilar "Testing candidate drugs capable of reverting Lowe patient phenotypes; also to establish how patient mutations determine symptoms/phenotypes; therefore, producing the basis to for personalized/precision medicine"
- **£60,000 to Manchester University, September 2016** Dr Martin Lowe: "Using the zebrafish model to screen for drugs that may be used to treat the Lowe Syndrome disease"
- **£80,000 to Institute of Genetics & Medicine, Naples, November 2017** Maria Antonietta De Matteis: "Testing FDA approved drugs in preclinical models of Lowe Syndrome"
- **£10,000 to Manchester University, November 2017** Extension research funding for Dr Martin Lowe (see above)
- **£25,000 to Manchester University, January 2019** Extension research funding for Dr Martin Lowe (see above)

Sponsored by DELL EMC

The Lowe Syndrome Trust has also organised and funded five UK Lowe Syndrome Trust International symposia at The Royal Society, London and other meetings including at The American Cell Biology Conference, San Diego, USA.

Contacts & Materials

info@lowetrust.com

www.lowetrust.com

PLEASE SUBSCRIBE TO **THE NEWSLETTER** AT OUR WEBSITE!

The Lowe Syndrome Trust
www.facebook.com/TheLoweSyndromeTrust

Over time, Lowe Syndrome Trust produced various brochures, booklets and leaflets to support and enhance general understanding of Lowe syndrome, to address specific medical problems related to LS, to advertise grants and sponsorships, as well as to celebrate Charity's achievements and news.

On LST website, you can find…

Inspiring story of LST	**90-page medical book**	**Latest newsletter**	**Leaflet**
Blood platelet disorder: letter to GP	**A&E sheet for patients with LS**	**87-page general booklet**	**Faimily registration consent form**

(If you would like a paper copy of any of these documents, please contact us via email or Facebook with your postal address)

Lowe syndrome community of parents have also created a Facebook group, where they share advice and suppsort with each other. You can join it by searching 'Lowe Syndrome Parents' or via the link:

www.facebook.com/groups/1418717108395463

Lowe Syndrome – A&E Information Sheet

Parents – please complete this and take along with a copy of the most recent clinical report 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:
  - polyuria and/or polydipsia; this can lead to dehydration
  - low-molecular weight proteinuria
  - elevated urinary calcium, which can cause kidney stones
  - metabolic acidosis
  - phosphate wasting, which can cause rickets

Abdomen
- Pain can be due to constipation resulting from dehydration
- Acute pain can also be caused by kidneys 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.