

QUESTIONS & ANSWERS ABOUT LOWE SYNDROME

1. What is Lowe Syndrome?

Lowe Syndrome (LS) is a rare genetic condition that causes physical and mental handicaps and medical problems. Also called oculo-cerebro-renal (OCRL) Syndrome, it was first described in 1951 by Dr. Charles Lowe and colleagues. In some cases Lowe Syndrome is the result of an original mutation and the mother is not the carrier.

2. What causes Lowe Syndrome?

Lowe Syndrome is caused by a defective gene that results in the deficiency of an enzyme called phosphatidylinositol 4,5-bisphosphate. This enzyme is essential to normal metabolic processes that take place in a certain part of the cell called Golgi apparatus. Because of the enzyme deficiency, cell functions that are regulated by the Golgi are abnormal, leading to various developmental defects including cataracts, kidney and brain problems. How the enzyme deficiency leads to these defects is not yet completely understood.

3. What are the common features of Lowe Syndrome?

- Cataracts in both eyes, found at birth or shortly after
- Glaucoma (*in about half of cases*)
- Poor muscle tone and delayed motor development
- Mental retardation, ranging from borderline to severe
- Seizures (*in about half of cases*)
- Severe behavioural problems (*in some cases*)
- Kidney involvement (*"leaky" kidneys or renal tubular acidosis*)
- Short stature
- Tendency to develop Rickets, bone fractures, scoliosis and joint problems
- Short life span due to progressive renal failure, seizures and other causes: life expectancy may increase in the near future as knowledge increases
- Arthritis (swelling of the joints)
- Respiratory illness
- Cysts
- Undescended testicles
- Constipation
- Tooth decay

4. What are boys with Lowe Syndrome like?

Generally, they are affectionate and sociable, love music and have great senses of humour.

5. How is Lowe Syndrome treated?

There is no cure, but many of the symptoms can be treated effectively through medication, surgery, physical and occupational therapies and special education.

6. What about Research?

In 1992 the gene that causes LS was found. In 1995 researchers discovered that the missing gene defect causes an enzyme deficiency. Researchers are continuing to investigate the function of the gene and the complicated biochemistry and cellular mechanisms of LS. Other areas that researchers have investigated in recent years include behaviour problems and clinical care. The Lowe Syndrome Trust was founded in June 2000 with an aim to fund Lowe medical research which will hopefully lead to better treatments and eventually a cure for the disease.

7. Can Lowe Syndrome be prevented?

In families in which a case of LS has occurred, a special eye examination can help determine carrier status of at-risk females. Research currently underway may lead to a more definitive genetic test for carrier status. Various family planning options are available, including parental testing. Families should consult with a geneticist to learn more about their options.

8. Where are diagnostic tests done?

To diagnose Lowe Syndrome within the UK, a DNA test can be requested via a consultant from Dr Andrew Wallace at St Mary's Hospital Regional Genetics Services, Manchester. A skin sample can also be taken and sent to the Biochemical Genetic Laboratory at Baylor College of Medicine in Houston, Texas. Prenatal diagnosis is also provided at this laboratory. Physicians and families should contact the Lowe Syndrome Trust to find out further information on these tests.

9. How can I learn more?

Contact the Lowe Syndrome Trust for a copy of the Living with Lowe Syndrome: A guide for Families, Friends and Professionals. Single copies are free. More information can be found on the LST website www.lowetrust.com

ABOUT THE LST

Lowe Syndrome is a devastating genetic disease that affects thousands of little boys born with cataracts (*either blind or partially sighted*), stunted growth, poor muscle tone, rickets, scoliosis, arthritis (*some never walk*), kidney problems and mental impairment. In spite of these handicaps the little boys have extremely happy and cheeky personalities. Sadly, few survive to become adults. Yet today, it may be within our grasp to help cure this disease. The Lowe Syndrome Trust is a registered charity, founded in June 2000 as the only UK charity to raise money for medical research to cure this disease. With your help, we can be one step near to a cure.

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CARE TODAY ... CURE TOMORROW!

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LOWE SYNDROME TRUST
Research Grants awarded from the charity
since it was founded in June 2000 (as at Feb 2008)

- **£25,000 contributed to three research projects** through the Lowe Syndrome Association USA.
 - **£9,000 to Great Ormond Street Childrens Hospital**
 Professor Unwin, Dr Van't Hoff & Dr Laube:
 "An investigation of intracellular metabolism in renal proximal tubular cells from patients with Lowe Syndrome"
 - awarded July 2002.
 - **£50,000 over 3 years to Imperial College London, Department of Chemistry (plus £10,000 - June 2006)**
 Dr Vilar-Compte and Dr Woscholski:
 "A novel diagnostic tool for the oculocerebrorenal Syndrome of Lowe"
 - awarded 5th December 2002.
 - **£50,000 over 3 years to Dundee University, Scotland**
 Dr J Lucocq:
 "OCRL1 and its lipid products"
 - awarded 18th July 2003.
 - **£50,000 over 3 years to University College London,**
 Professor S Cockcroft:
 "Assessment of Golgi structure and membrane traffic in OCRL Cells"
 - awarded 4th January 2004.
 - **£50,000 over 3 years to Institute of Ophthalmology (Moorfields)**
 Dr Tim Levine:
 "The Cell Biology of the Effects of Lowe Syndrome in the Eye"
 - awarded 12th May 2005.
 - **£20,000 over 2 years to Addenbrooke's Hospital Cambridge**
 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"
 - awarded 5th November 2005.
 - **£51,000 one year project to MD Institute for Human Genetics and Department of Medicine, University of California, San Francisco**
 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"
 - awarded 20th March 2006.
 - **£10,000 to Dundee University April 2007**
 Dr John Lucocq Lowe Neurological research project
 - **£51,000 to University of California July 2007**
 This is the second year funding for Professor Robert Nussbaum (listed above)
 - **£80,000 to University of Manchester November 2007**
 Dr Martin Lowe
 "Zebrafish as a model organism to study Lowe syndrome"
 - **£80,000 to Purdue University Indiana, USA January 08**
 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 the role of PIP2 dependent pathways by chemical intervention"
 - **£61,000 to University of California November 2008**
 Extension research funding for Professor Robert Nussbaum (listed above)
 - **£80,000 to Institute of Ophthalmology (Moorfields) London – 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
 "Investigating the Role of OCRL1 in lysosome-related organelle biogenesis"
 - **£50,000 to Purdue USA/Institute of Child Health UK – November 2010**
 Dr R Aguilar and Professor Philip Beales
 "Toward a greater understanding of the cellular biology underlying Lowe syndrome through integration with Cerebro-Renal diseases"
- The Lowe Syndrome Trust has also funded three Lowe Syndrome Trust International symposiums at The Royal Society, London and The American Cell Biology Conference, San Diego, USA.

Lowe Syndrome Trust

