

What are Lysosomal Storage Disorders?

Lysosomal storage disorders are a group of more than 40 individual genetic disorders that affect children and adults.

Disease severity is variable. Some patients may survive into adulthood, but patients who are more severely affected die in their mid-teens or earlier.

Babies with lysosomal storage disorders usually appear normal at birth, but progressively develop symptoms in the first few years of life. Symptoms may include cardiac and respiratory difficulties, behavioural and mental regression, short stature, characteristic facial appearance, sight and hearing difficulties.

Our bodies are made up of billions of cells. Lysosomes are each cell's 'recycling centre'. Their role is to break down complex material to simple products for recycling within the cell, to build new complex material. Storage within the lysosome occurs when the recycling process fails.

A deficiency in specific proteins (enzymes) is the usual cause of this failure. Over time, the amount of storage in the lysosome increases and leads to severe physical symptoms as the material builds-up throughout the body.

'BRAINSTORMING'

ENZYME REPLACEMENT THERAPY & NEWBORN SCREENING for LYSOSOMAL STORAGE DISORDERS

Lysosomal Diseases Australia (LDA) facilitated discussion groups at the national meeting of the Mucopolysaccharide (MPS) and Related Diseases Society of Australia, held during April in Coffs Harbour. These sessions were held to provide an opportunity for patients and families to discuss issues of relevance to them concerning enzyme replacement therapy and newborn screening for MPS disorders.

Participants on the day included families affected by MPS disorders, as well as families with the lysosomal storage disorders known as fucosidosis, mannosidosis and mucopolipidosis (see Table on page 5).

The discussion groups were divided into four, and participants attended the group that represented their particular condition. The responses therefore reflect the attitudes of people with that condition.

A brief description of the clinical characteristics of each disorder and the current state of development of enzyme replacement therapy is presented. This is followed by a summary of the main points that emerged from these discussions. The responses have not been arranged in any particular order of importance.

Each Group was asked the following questions:

- Who would avail themselves of enzyme replacement therapy, if available?
- What are your major issues concerning enzyme replacement therapy?
- What is your reaction to enzyme replacement therapy if it prolonged your child's life without demonstrating much improvement in quality of life?
- Reflect on your own position. Newborn screening: what would you think of having the diagnosis completed at one-month of age?

Like the household kitchen, lysosomes can be described as 'recycling centres'. If waste material is not removed, it builds up and impairs normal functioning.

Mucopolysaccharide disorders (the 'mucopolysaccharidoses', or MPS) represent a group of 11 lysosomal storage disorders:

- MPS-I (Hurler syndrome, Scheie syndrome);
- MPS-II (Hunter syndrome);
- MPS-III A, B, C, D (Sanfilippo syndrome types A, B, C and D);
- MPS-IV A and -IV B (Morquio syndrome types A and B);
- MPS-VI (Maroteaux-Lamy syndrome);
- MPS-VII (Sly syndrome)
- MPS-IX

These disorders result from the accumulation in the lysosome of specific storage compounds known as mucopolysaccharides.

Mucopolysaccharides are long chains of sugar molecules, linked together and used by the body's cells to build connective tissue. As with many lysosomal storage disorders, the MPS group is generally characterised by a wide spectrum of clinical symptoms within each disorder, including bone and joint problems and short stature, a characteristic facial appearance, progressive brain disease, behavioural problems and early death.

Group 1:

*MPS-I (Hurler syndrome);
Mannosidosis, Fucosidosis and Mucopolipidosis*

Hurler syndrome represents the severe end of the MPS-I clinical spectrum, and is characterised by progressive brain disease, severe skeletal disease and early death.

Clinical trials to evaluate the efficacy of enzyme replacement therapy are currently in progress for MPS-I.

Whilst Mannosidosis, Fucosidosis and Mucopolipidosis are lysosomal storage disorders that exhibit physical problems they are all characterised by progressive brain disease.

Clinical trials of enzyme replacement therapy are currently not being planned for these disorders.

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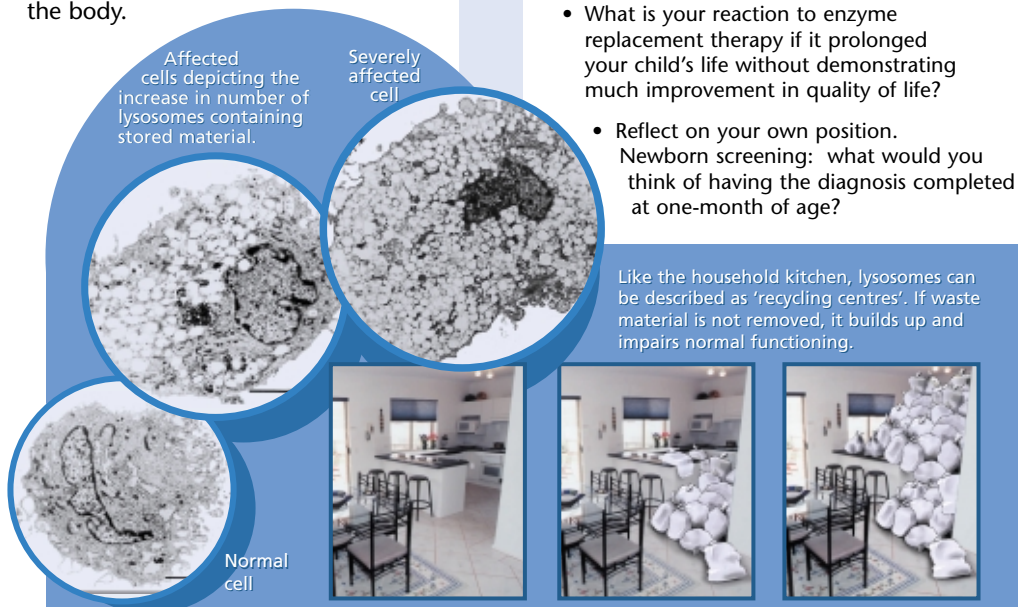
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'BRAINSTORMING' ENZYME REPLACEMENT THERAPY & NEW for LYSOSOMAL STORAGE DISORDERS

Group 2:

MPS-II (Hunter syndrome)

As with MPS-I, there is a wide spectrum of clinical severity in MPS-II, from physical symptoms to progressive brain disease.

Clinical trials of enzyme replacement therapy for MPS-II are being planned.

Group 3:

MPS-III (Sanfilippo syndromes)

MPS-III comprises a sub-group of four disorders, commonly known as types A, B, C and D. Whilst all four disorders exhibit physical problems, this group is primarily characterised by progressive brain disease.

Clinical trials of enzyme replacement therapy are currently not being planned for these disorders.

Group 4:

*MPS-I (Scheie syndrome);
MPS-II (Hunter syndrome);
MPS-IV (Morquio syndrome);
MPS-VI (Maroteaux-Lamy syndrome)*

Some MPS disorders exhibit primarily physical symptoms, such as bone and joint problems, without progressive brain disease. Because of this, these disorders are commonly referred to as 'mild'. This is a largely artificial division, however, which does not accurately reflect the progressive severity of clinical problems experienced by this group of patients. This group includes some patients affected by MPS-I. Both forms of MPS-IV are characterised by significant bone and skeletal changes and short stature, as is MPS-VI.

Clinical trials of enzyme replacement therapy have commenced for MPS-I and MPS-VI, and are being planned for MPS-II.

Q:

Who would avail themselves of enzyme replacement therapy, if available?

Participant comments: The majority of participants stated that they would take-up the opportunity of enzyme replacement therapy, if available. The potential for an improved quality of life was seen as its primary benefit, particularly increased independence, decreased pain and halting or reversing disease progression. It is generally seen as a step towards a permanent cure, not a cure in itself, but one that would prolong the life of a child and reduce their disease burden until such time as a permanent cure is available.

Those who indicated they would decline enzyme replacement therapy were concerned that it may adversely affect the rate of deterioration. Further concerns related to the financial, social and emotional costs that may be associated with treatment.

There were general concerns associated with enzyme replacement therapy. In particular, this centred around the uncertainty that still exists with this therapy, its benefits and risks, and the lack of available data on its efficacy. Many felt that enzyme replacement therapy did not yet offer a 'cut and dried' solution.

Q:

What are your major issues concerning enzyme replacement therapy?

Participant comments: Enzyme replacement therapy was generally considered by participants to pose less medical risk than bone marrow transplantation. There were concerns about its implications, however, such as the absence of data on its side-effects and long-term effects, the safety of the treatment, and mortality and treatment complication rates.

Other issues of concern that were highlighted include:

- the perception that many children seem to be beyond the age where therapy could be of benefit; this was also expressed in terms of eligibility for receiving treatment if the child is beyond a certain age;
- access to therapy may ultimately be a financial one for families;
- medical ethics and accountability of those proposing the treatment;
- pressure to start therapy and remain on it, irrespective of personal beliefs and decisions;
- the frequency of enzyme infusion and the effects of mutations upon its effectiveness and use;
- the need to have an idea of disease severity and progression;
- problems related to extending life expectancy;
- being at the 'cutting-edge' and the reliance of patients and parents on medical 'pioneers' in this field

Group 1 participants drew attention to the political aspects of therapy, such as issues concerned with financial support to enable access to therapy; 'fast-tracking' drug availability; the use of the media in promoting lysosomal storage disorders, and drawing experience from other groups (e.g. HIV/AIDS activists).

Groups 2 and 3 had particular concerns about the practicalities of administering enzyme to a child where behavioural problems are a prominent issue, and the continued impact upon family resources this would entail, for example one parent having to remain at home for this purpose.

Q:

What is your reaction to enzyme replacement therapy if it prolonged your child's life without demonstrating much improvement in quality of life?

Participant comments: A variety of responses were received to this question. A parallel was drawn between the option of enzyme replacement therapy and a time when parents were in the dilemma of considering bone marrow transplantation for their child.

The central issue of concern is the potential for enzyme replacement therapy to prolong life and improve the disease burden in body tissues, but not necessarily halt progressive brain disease.

Group 2 noted that studies to date do not provide an answer as to the likelihood of this particular outcome.

In Group 3, 80% of participants stated they would not use enzyme replacement therapy

in this situation. Some felt that since enzyme replacement therapy for MPS disorders with progressive brain disease seemed to be a "long way off", research into other, more practical options may be more beneficial. These options included developing more effective calming techniques and behavioural management.

Participants in Group 3 considered that their current "path" is somewhat clearer than for families with MPS-I for example, where therapy is being trialed and may offer benefit to some patients, but possibly not those with neurological dysfunction. This was seen as a cause of significant "distress" to parents. It also raised a potential point of conflict between the 'haves' and 'have nots', and the difficulties this could raise in families with more than one affected child.

Some participants felt that the option of taking up enzyme replacement therapy in this situation may depend upon the stage of the disorder, and the hope that it offered to prolong life with the expectation of the development of more effective treatments.

On-going access to professional assistance is seen as important, particularly in relation to expectations of disease progress and assisting families in decision-making. The need for professional honesty is an important issue. It is recognised that decisions about whether to commence or prolong therapy under these circumstances are personal and should be respected, irrespective of the outcome, but it was noted that pressure may arise to adopt the course towards therapy because "others are doing it". Group 2, in particular, noted that if it becomes clear that enzyme replacement is not having a beneficial effect upon brain disease, families would like the right to withdraw from treatment.

Concerns were raised in Group 2 about the on-going community cost of using therapy that is unlikely to result in an improved quality of life, and philosophical questions about the value of human life. This reflected a general concern amongst the groups that decision-makers may rely on the financial aspects of treatment rather than on medical/social/emotional grounds when making a decision about whether to commence or continue treatment, without considering the potential impact upon the patient and family.

A particular concern of families where progressive brain disease is a significant problem relates to the increased life expectancy offered by enzyme replacement therapy, and the on-going difficulties parents would face without continued support and respite services. There is recognition that the burden of care may not decrease as both the child and parents age.

Q:

Reflect on your own position. Newborn screening: what would you think of having the diagnosis completed at one-month of age?

Participant comments: Most participants would wish to have the option of newborn screening if therapy was available for a particular disorder, or if the promise of therapy was on the horizon. There was recognition that early diagnosis would require accurate knowledge of the disorder and its likely progression. The impact on families of individuals missed on newborn

NEWBORN SCREENING

screening (false-negatives) is an important issue.

The actual timing of a diagnosis is generally not seen to be as important as the manner in which the diagnosis is communicated to the family. Access to comprehensive counselling by appropriately qualified and trained professionals at the time of diagnosis is important, as is community and professional education. Parents requested that the counselling process be transparent and that the counsellor be self-aware and honest about the process of newborn screening.

Some participants considered that early diagnosis allows decisions to be made about early intervention and exploring various treatment options (e.g. diet, physiotherapy, bone marrow transplantation, enzyme replacement), as well as offering reproductive choice for future pregnancies and the relief of avoiding unnecessary and prolonged medical investigations. The majority of participants valued the "power" and choice that knowledge would give them.

The issue of parental bonding time with a newborn child is an important one. Some parents expressed gratitude that they had the opportunity of enjoying the time with their affected child before diagnosis, and also the opportunity of having more children before a diagnosis has been made. It was recognised that having a diagnosis in the absence of symptoms makes decisions about reproduction difficult.

Group 3 participants made the point of asking why newborn screening for these disorders should be introduced at a time when research and enzyme production timelines are so very long.

LDA thanks the MPS Society and its members for agreeing to participate in these sessions. Our particular thanks go to:

The Society President,
Mrs. Teresa Llewellyn-Evans, for her support and input into the preparation of this document, and to the session Facilitators -

Dr. Jenny Ault,
Ms. Bronwyn Butler,
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Dr. John Rogers,
Ms. Margaret Sahhar,
Dr. Ravi Savarirayn,
Professor David Silence, and
Dr. Ed Wraith

Discussion groups will also be held with support groups for other lysosomal storage disorders over the coming months. It is intended that the issues identified in these sessions will form the basis of Focus Groups for more in-depth discussion of particular issues raised. Position Papers will be formulated from these discussions and presented for endorsement by the Human Genetics Society of Australasia (HGSA).

The information gathered through this process will complement the data collected from the Health Related Quality of Life

research study that is also being conducted by LDA.



HEALTH-RELATED QUALITY OF LIFE STUDY

Assessment of lysosomal storage disorders has traditionally relied on clinical examination by doctors and the results of laboratory tests. However, these approaches provide only limited information about the impact of the disorders on the broader day-to-day lives of affected individuals and their families, and little is known about their quality of life.

As a first step to address this issue, Lysosomal Diseases Australia is funding a new study on the quality of life of parents caring for children with lysosomal storage disorders. For statistical significance, the study will include parents from Australia and the United Kingdom and will be conducted by the Research and Evaluation Unit at the Women's and Children's Hospital in Adelaide.

Before undertaking the main study, it is first necessary to develop a reliable questionnaire, which can be used to obtain information about the impact of lysosomal storage disorders on parents. Appropriately qualified research staff from the Women's and Children's Hospital will be contacting parents of children with lysosomal storage disorders over the coming months to discuss the content of the questionnaire.

The parental study is intended to be the first in a series of studies that assess quality of life issues for people with lysosomal storage disorders and their families. The breadth of information that will be examined makes it necessary to focus on particular groups at different times. However, this should not restrict anyone from participating in this or a later study if they so wish. This focus is designed to ensure that we obtain this important information in the best manner possible, and to enable us to produce high quality research that will benefit both affected individuals and their families.

For more information about the study, please contact the study coordinator, Ms. Fiona Arney (Tel: (08) 8204 7790).

FABRY

Fabry disease is a lysosomal storage disorder that affects at least 1 in every 117,000 Australians. It is due to a deficiency of the lysosomal enzyme, alpha-galactosidase (α -galactosidase), and has been described in people from most parts of the world. Fabry disease is inherited in an X-linked recessive pattern, which means that females carry the gene and males are affected (see X-linked recessive inheritance below)

The disorder was first described independently in 1898 by Dr. Fabry from Germany and Dr. Anderson from England. Both were dermatologists. It was not until 1965 that the inheritance pattern was recognised by an American geneticist, Dr. Opitz. The deficient enzyme was first recognised by Dr Roscoe Brady (who pioneered enzyme replacement therapy in Gaucher disease, another lysosomal storage disorder) in 1967, and in 1970 it was specified as α -galactosidase by Kint and co-workers. The gene was discovered in 1986 by Bishop and co-workers.

The enzyme, α -galactosidase, is responsible for the breakdown of glycosphingolipids (complex compounds composed largely of sugars and fats). When the enzyme is deficient, there is an accumulation of these glycosphingolipids in blood vessels, body fluids and the cells of many tissues, particularly the nerves, kidney, heart and eyes.

During childhood and adolescence the main features in males are pain and paraesthesia (burning and tingling) of the hands and feet; hypohydrosis (reduced sweating); and the development of angiokeratoma which are the characteristic changes in the blood vessels of the skin and mucous membranes.

Angiokeratoma appear as clusters of tiny dark red to black dots around the umbilicus (navel), buttocks, thighs, genitalia, and back (see accompanying photograph). They can also occur on the inside of the mouth. The pain is very severe and can either be constant or occur in episodes (Fabry crises) which can last a few days. Clouding of the front of the eye (cornea) and the lens develop at a young age. With advancing age the kidneys become affected and protein leaks out in the urine (proteinuria), the blood pressure increases

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DISEASE

(hypertension) and gradually kidney failure develops. The involvement of the blood vessels of the heart and brain may lead to heart disease (myocardial infarcts [heart attacks], heart failure and disorders of the function of the heart valves) and brain disorders (strokes, seizures, brain haemorrhage, and personality changes). Other features include arthralgia (painful joints), diarrhoea, weight loss and disturbed temperature sensation. Intelligence is normal.

The advancing kidney disease is the main cause of death. If untreated, the average age of death in males is 41 years. Both the quality and duration of life have been improved by advances in dialysis and transplantation to treat the kidney disease; improved pain management using drugs such as phenytoin and carbamazepine; and general improvements in the management of cardiac and nervous system disease.

Females who carry the gene usually have either no symptoms or much milder symptoms than the males. The most common finding in females is a whorl-like pattern in the lens of the eye. A special instrument called a slit-lamp is required to detect it.

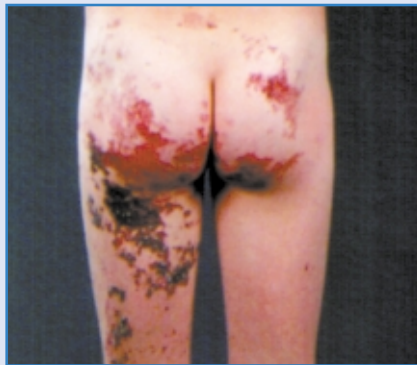
In males the diagnosis is made by the measurement of the enzyme, α -galactosidase, in blood cells or cultured skin cells. In females the enzyme activity may be reduced but this test is not reliable. A more reliable test in females is direct testing of the change in the gene if it has been identified in affected males in the family. If gene testing is not available for the family then it may be necessary to measure the enzyme activity in hair roots. In carrier females some of the hair roots have very low α -galactosidase activity and some normal. (See Diagnosis of affected males and carrier females).

X-linked Recessive Inheritance

All of our characteristics are controlled by genes, which are packaged on structures called chromosomes and exist in every cell of the body. Humans usually have 46 chromosomes, and two of these, the X and the Y, determine our sex. Females have an XX pattern and males an XY pattern. The gene for Fabry disease is located on the X chromosome. Males have only one X chromosome, and if there is a mistake in any gene on the X chromosome, disease results. If a female has the gene for Fabry disease on one of her two X chromosomes this usually causes her no major problems as the back-up copy of the gene on the other X chromosome usually compensates. Such a female is said to be a carrier for the Fabry gene.

When a carrier female (Diagram 1) has children, she can pass on either the X chromosome with the Fabry gene (shown as X^F) or the partner X chromosome. Her children therefore have a 1 in 2 or 50/50 chance of inheriting the gene from her. If the child is a girl she will have a 1 in 2 chance of being a carrier. If the child is a boy, he will have a 1 in 2 chance of being affected. Overall, there is a 1 in 4 (or 25%)

chance for an affected boy with each pregnancy, regardless of the outcome of previous pregnancies.



Typical skin rash seen in patients affected by Fabry disease. Fabry disease is an 'X-linked disorder', which means that females 'carry' the genes, but males are affected. However, symptomatic female carriers are not uncommon.

Photos reproduced courtesy of Dr. Eric Haan, Director, South Australian Clinical Genetics Service, Women's and Children's Hospital.

When a male with Fabry disease has children (Diagram 2), he will pass on his X^F chromosome containing the Fabry gene to all of his daughters who will all therefore be carriers. He will pass on his Y chromosome to his sons who will therefore be unaffected.

Diagnosis of affected males and carrier females

In males, the diagnosis of Fabry disease is made by measuring the level of α -galactosidase activity in blood or cultured skin cells. Affected males have very low enzyme activity and the test is diagnostic of the condition.

However, this test is not reliable for the identification of carrier females.

The gene for Fabry disease was discovered in 1986. If a particular change ('mutation') in the Fabry gene has been identified in an affected male, his female relatives can be tested for their carrier status by specific gene analysis to determine the presence or otherwise of the mutation. This method offers a definitive result for the individual.

Before the Fabry gene was isolated and mutations responsible for the disorder were found, it was often necessary to measure the enzyme activity in up to 100 individual hair roots to determine carrier status for females. This is a time-consuming and resource-intensive process, as enzyme activity in each hair root required measurement individually. With the identification of the gene, the method of choice for identifying carriers for Fabry disease is analysis of the mutation(s) identified in a Fabry-affected male within the family.

Treatment

Clinical trials to determine the effectiveness of enzyme replacement therapy as a treatment for Fabry disease are currently underway in Australia and elsewhere. This form of therapy, where commercially manufactured α -galactosidase is infused into patients every two weeks, is being

developed separately by two US companies, Transkaryotic Therapies Inc. and Genzyme Corporation. Results of clinical trials held to date were made public at the recent American Society for Human Genetics meeting held in Philadelphia, and suggest that these therapies have positive effects in patients.

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X-linked Recessive Inheritance

Diagram 1

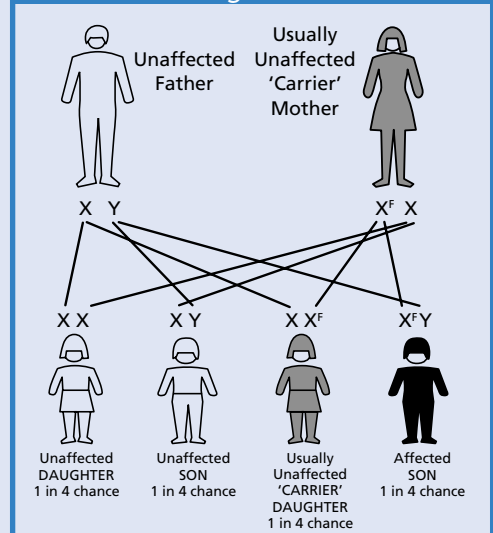
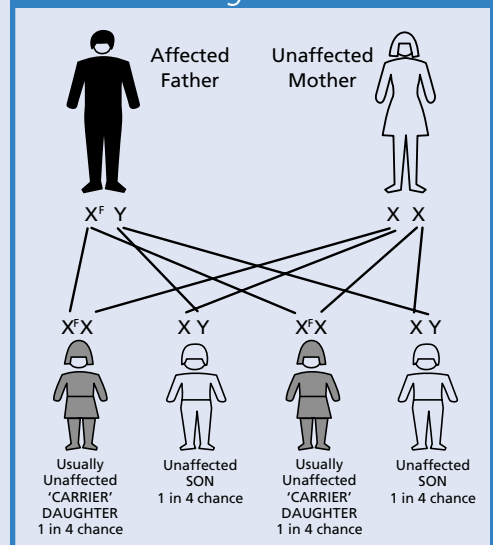


Diagram 2



Reproduced courtesy of the NSW Genetic Education Programme. X^F denotes affected chromosome.

TABLE: A summary of LSD and therapies

Disease	Clinical Phenotype	Enzyme Deficiency	Chromosome Location	Bone Marrow Transplantation	Animal Model	Human Enzyme Replacement Therapy	Australian Prevalence	Carrier Frequency
Aspartylglucosaminuria		Aspartylglucosaminidase	4q32 - 33		mouse		1 in 2,111,000	1 in 726
Cholesterol ester storage disease	Wolman disease	Acid lipase	10q24-25				1 in 528,000	1 in 363
Cystinosis		Cystine transporter	17				1 in 192,000	1 in 219
Fabry disease	Fabry disease	α -Galactosidase A	Xq22		mouse	Trials in progress	1 in 117,000	1 in 117,000
Farber Lipogranulomatosis	Farber disease	Acid ceramidase	8p21.3-p22	Not helpful in severe forms				
Fucosidosis		α -L-Fucosidase	1p34	Benefit in dog model	dog		> 1 in 2,000,000	
Galactosialidosis types I / II		Protective protein	20q13.1		sheep			
Gaucher disease types I / II / III	Gaucher disease	Glucocerebrosidase (β -glucosidase)	1q21	May benefit in type I; uncertain other types	mouse	Type I in clinical practice; Trial in Type III in progress	1 in 57,000	1 in 119
Globoid cell leucodystrophy	Krabbe disease	Galactocerebrosidase	14q31	May benefit presymptomatic patients	mouse, sheep, dog, monkey		1 in 201,000	1 in 188
Glycogen storage disease II	Pompe disease	α -Glucosidase	17q25.2-25.3	Not helpful	dog, cattle, quail,	Trials in progress	1 in 146,000	1 in 191
GM1-Gangliosidosis types I/II/III		β -Galactosidase	3p21-3pter	No benefit in dog	cat, dog, sheep, cattle		1 in 384,000	1 in 310
GM2-Gangliosidosis type I	Tay Sachs disease	β -Hexosaminidase A	15q23-24	No benefit	mouse		1 in 201,000	1 in 224
GM2-Gangliosidosis type II	Sandhoff disease	β -Hexosaminidase A & B	5q13	No benefit	mouse		1 in 384,000	1 in 310
GM2-Gangliosidosis		GM2-activator deficiency	5q32-33		dog			
α -Mannosidosis types I / II		α -D-Mannosidase	19p13.2-q12		mouse, cat, cattle, guinea pig		1 in 1,056,000	1 in 514
β -Mannosidosis		β -D-Mannosidase	4q22-q25		goats, cattle			
Metachromatic leucodystrophy		Arylsulphatase A	22q13.3-qter	May benefit presymptomatic patients	mouse		1 in 92,000	1 in 152
Metachromatic leucodystrophy		Saposin B	10q2	May benefit presymptomatic patients				
Mucopolipidosis type I	Sialidosis types I / II	Neuraminidase	6p21.3					1 in 1027
Mucopolipidosis types II / III	I-cell disease; pseudo-Hurler polydystrophy	Phosphotransferase	4q.21-23	Benefit reported for one MIII patient	cat			1 in 285
Mucopolipidosis type IIIC	pseudo-Hurler polydystrophy	Phosphotransferase γ -subunit	16p					
Mucopolipidosis type IV		Unknown	19p13.2-p13.3					
Mucopolysaccharidosis type I	Hurler syndrome Scheie syndrome	α -L-Iduronidase	4p16.3	May benefit presymptomatic patients	cat, dog, mouse	Trials in progress	1 in 88,000	1 in 148
Mucopolysaccharidosis type II	Hunter syndrome	Iduronate-2-sulphatase	Xq27-28	May benefit presymptomatic patients	mouse, dog	Trials planned	1 in 136,000	1 in 136,000
Mucopolysaccharidosis type IIIA	Sanfilippo syndrome	Heparan-N-sulphatase	17q25.3	Not helpful in symptomatic patients	mouse, dog		1 in 114,000	1 in 169
Mucopolysaccharidosis type IIIB	Sanfilippo syndrome	α -N-Acetylglucosaminidase	17q21	Not helpful in symptomatic patients	mouse, emu		1 in 211,000	1 in 230
Mucopolysaccharidosis type IIIC	Sanfilippo syndrome	AcetylCoA:N-acetyltransferase	unknown	Not helpful in symptomatic patients			1 in 1,407,000	1 in 593
Mucopolysaccharidosis type IIID	Sanfilippo syndrome	N-Acetylglucosamine 6-sulphatase	12q14	Not helpful in symptomatic patients	goat		1 in 1,056,000	1 in 514
Mucopolysaccharidosis type IVA	Morquio syndrome	Galactose 6-sulphatase	16q24.3	Not helpful			1 in 169,000	1 in 206
Mucopolysaccharidosis type IVB	Morquio syndrome	β -Galactosidase	3p21-3pter	Not helpful				
Mucopolysaccharidosis type VI	Maroteaux-Lamy syndrome	N-Acetylgalactosamine 4-sulphatase	5q11-13	May benefit	cat, rat, dog, mouse	Trials in progress	1 in 235,000	1 in 242
Mucopolysaccharidosis type VII	Sly syndrome	β -Glucuronidase	7q21.1.11		dog, mouse, cat		1 in 2,111,000	1 in 726
Mucopolysaccharidosis type IX		hyaluronoglucosaminidase-1	3p21.3-p21.2					
Multiple sulphatase deficiency		Multiple sulphatases	unknown				1 in 1,407,000	1 in 593
Neuronal Ceroid Lipofuscinosis, CLN1	Batten disease	Palmitoyl protein thioesterase	1p34					
Neuronal Ceroid Lipofuscinosis, CLN2	Batten disease	Tripeptidyl peptidase I	11p15.5					
Neuronal Ceroid Lipofuscinosis, CLN3	Vogt-Spielmeyer disease	Protein function not known	16p12.1		mouse, dog, sheep			
Neuronal Ceroid Lipofuscinosis, CLN5	Batten disease	Protein function not known	13q22					
Neuronal Ceroid Lipofuscinosis, CLN8	Northern Epilepsy	Protein function not known	8pter-p23					
Niemann-Pick disease types A / B	Niemann-Pick disease	Acid sphingomyelinase	11p15.1-p15.4	Not helpful for type A		Trials planned	1 in 248,000	1 in 249
Niemann-Pick disease type C1	Niemann-Pick disease	Cholesterol trafficking	18q11-12		cat, mouse		1 in 211,000	1 in 230
Niemann-Pick disease type C2	Niemann-Pick disease	Cholesterol trafficking	unknown					
Pycnodysostosis		Cathepsin K	1q21					
Schindler disease types I / II	Schindler disease	α -Galactosidase B	22q13.1-13.2					
Sialic acid storage disease	Sialuria, Salla disease	Sialic acid transporter	6q14-15				1 in 528,000	1 in 363

Prevalence figures quoted from Meikle et al., JAMA 281:249-254 (1999). Prevalence and ratio of lysosomal storage disorders may vary from country to country

About LDA

LDA was established in December 1998 as a non-profit company limited by guarantee. Its activities are regulated by a Board of Management, which comprises:

Mr. Ken Hatton (Treasurer) (NSW)



Ken is a retired businessman who is still involved with building and vineyard developments, and has been a long-time supporter and benefactor of genetic disorder

groups. Ken is also involved with Rotary and is a Past President of the Rotary Club of Brookvale.

Professor John Hopwood (Chairman) (SA)



John heads the Lysosomal Diseases Research Unit at the Women's and Children's Hospital in Adelaide. Over the last 20 years, he and his group have researched methods to achieve diag-

nosis at birth and effective therapy for patients affected by lysosomal storage disorders.

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Peter is a general medical practitioner and was an Independent Member of Parliament in the New South Wales legislature between 1991 and 1998. He has been a member

and chairman of a number of parliamentary committees dealing with health and social issues.

Dr. Jim McGill (QLD)



Jim is a metabolic physician and clinical geneticist at the Royal Children's Hospital and Mater Children's Hospital in Brisbane. He has

many years' experience with managing the care of patients affected by lysosomal storage disorders.

Phone: (07) 3636 8176

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Ms. Margaret Sahhar (VIC)



Margaret is a social worker at the Victorian Clinical Genetics Service. She has extensive involvement in the establishment of a number of

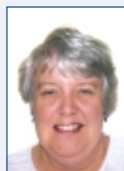
support groups throughout Victoria. In 1998, she established the Genetic Support Network of Victoria, an umbrella group for all the genetic support groups.

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Mrs. Ros Smith (Deputy Chairman) (NSW)



Ros had a child affected by a lysosomal storage disorder and has been involved with the Mucopolysaccharide and Related Diseases

Society of Australia since its inception in 1983. Her commitment to families affected by genetic disorders is demonstrated by her continued involvement with umbrella organisations such as The Association of Genetic Support of Australasia.

Patron



Dr Peter Doherty is a well-respected Australian scientist who was awarded the Nobel Prize for Physiology or Medicine in 1996 for his work on the immune system.

The discoveries have had an impact on the development of vaccine design and organ transplantation, and have led to further understanding of the mechanisms involved in immunity.

Dr. Doherty is Chairman of the Department of Immunology at St. Jude Children's Research Hospital in Memphis, USA

LYSOSOMAL DISEASES AUSTRALIA

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Enquiries about LDA and its activities can be directed to any Board member at the contact points provided above.

If you would like to be placed on our mailing list, please contact the Public Officer.

Our newsletters are posted on our website at

www.lda.org.au