

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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