What is leukodystrophy?

The word "leukodystrophy" is an old word that was coined to describe a genetic disease of the white matter of the brain. The term comes from the Greek language – leuko "white"), dys "abnormal", and trophy "thrive or grow". Put together, this describes a deteriorative process of the white matter in the brain. Before the gene abnormalities that cause leukodystrophies were identified, the term "leukodystrophy" referred to a genetic disease of the white matter of the brain usually following a deteriorating or degenerative course. As myelin is one of the major components of white matter and as abnormalities in myelin are striking in leukodystrophies, for many years it was thought that leukodystrophies were primarily diseases of myelin or myelination. In the past two decades there has been a revolution in the understanding of the causes of white matter diseases with the identification of the gene abnormalities that cause the diseases to develop. This has led to increased understanding of the many different ways in which the white matter of the brain may be affected and a recognition that these were not exclusively diseases of myelin. It was also recognised that not all leukodystrophies followed a degenerative course.

Leukodystrophies may also be referred to as Inherited (or genetic) White Matter Disorders (IWMDs) meaning that the affected person has been born with a genetic abnormality that causes the disease. This may happen because a genetic abnormality occurs for the first time in the affected person at conception, or may have been inherited from one or both parents who "carry" the genetic abnormality.

The current definition of leukodystrophy is a genetic disorder primarily affecting central nervous system (brain or spinal cord) white matter. Many different processes can affect the white matter e.g. trauma, infection, drug abuse, vascular disease. These conditions are not leukodystrophies. Similarly, acquired demyelination such as that which occurs in Multiple Sclerosis and similar conditions is not regarded as a leukodystrophy. Another word that is often used in medical literature when discussing white matter diseases is "leukoencephalopathy". This simply means abnormal white matter in the brain and does not imply a genetic cause.

Sometimes the same disease is referred to as a leukodystrophy and a leukoencephalopathy e.g. adult onset autosomal dominant leukodystrophy (ADLD) can also be referred to as autosomal dominant late-onset leukoencephalopathy. Due to this terminology, there is often confusion surrounding what is and is not a leukodystrophy. As such there is no universally-agreed definition within the medical profession. For the purposes of clarifying the conditions supported by Alex TLC, our definition of leukodystrophy is based on those conditions classified as inherited or genetic. This remit is based on guidance from UK specialists in paediatric and adult Inherited White Matter Disorders alongside three clinical papers:

- Update on Leukodystrophies: A Historical Perspective and Adapted Definition. Neuropediatrics. 2016 Dec;47(6):349-354. Epub 2016 Aug 26.
- Case Definition and Classification of Leukodystrophies and Leukoencephalopathies.
- A practical approach to diagnosing adult onset leukodystrophies

There are over 100 identified inherited or genetic leukodystrophies, with some so rare they are yet to be named. The majority of these conditions cause progressive neurodegeneration and are largely untreatable. Individual conditions and their symptoms are described here. Alex TLC focuses on the similarities between these conditions, bringing together all affected within a community of Tender Loving Care. Some of the less rare leukodystrophies already have established and reputable support groups and, where applicable, we have signposted to these organisations and endeavour to work in partnership with them.

For more information please visit www.alextlc.org or contact info@alextlc.org