Will there be an impact on the child's education?

Sadly, due to the early onset of infantile CLN1 disease and its rapid progression, consideration of a school education is not likely to be a priority amongst the many other challenges that will be faced. However, holistic aspects surrounding development, socialisation and stimulation will continue to be important for the infant and family. There will be many associated elements that require consideration and significant assistance from those around them.

The Children and Families Act (September 2014) introduced major reforms in provision for children and young people with Special Educational Needs (SEN). Many SEN services have Early Years and Childcare teams who can help identify and provide advice regarding the provision needed to support infants with complex needs. Local sensory services and organisations such as SENSE should be able to lend additional support.

The BDFA has expertise in this field and can be approached by any parties seeking information or help.

The **BDFA Educational Advisor** may be able to provide specific support and can be contacted via **0800 046 9832** email: **admin@bdfa-uk.org.uk**

In what other ways can families be supported?

The realities of caring for a child who has variant late-infantile CLN1 disease can place enormous strain on a family, both physical and emotional. It will impact upon all members in numerous ways and so being made aware that support is available to groups and individuals to help with the challenges that will be faced is important. This support extends to wider family members and step-relatives.

There are several options to consider should families wish to explore ways of maximising the limited time available to share with their children. Contacting a charitable wish-granting organisation may lead to them being able to create some valuable and significant memories.

Where can I get additional information and support?

The BDFA offers support to any family member, friend, professional or organisation involved in caring for a child with CLN1 disease or any other form of NCL throughout the UK. We provide informed guidance and assistance as well as seeking to actively increase awareness of the disease and facilitate future research to identify potential therapies and ultimately a cure.

We organise conferences, workshops and are able to arrange connections with other affected families. The BDFA also coordinate a Small Grants Scheme that can provide assistance for a range of needs.

The BDFA has a Support and Advocacy Partner who is able to assist with many of the issues highlighted in this document and can discuss each of them in greater detail and on a more personal basis.

The BDFA family folder can also provide further specific information on CLN1 disease. The folder is free for all families and available to professionals at a cost of £25.

Please contact the **BDFA Family Support and Advocacy Partner** via our **Freephone Helpline: 0800 046 9832** or email: **support@bdfa-uk.org.uk** for further information and to order a copy of the family folder.

There are a number of local and national organisations that are also able to offer various forms of support and information that will be relevant to families. The BDFA can provide details and information about them.

It may also be appropriate for a referral to be made to a local children's hospice service, as this can offer an additional experienced and skilled source of holistic support.

Some of the information contained in this leaflet is based upon chapters in "The Neuronal Ceroid Lipofuscinoses (Batten Disease) 2nd Edition" by Mole, Williams & Goebel (Eds), Oxford University Press 2011 and is used with permission.

Contributors: BDFA Harriet Lunnemann QSW, Heather Band MSc, Barbara Cole QTVI, Matt Hobbs RN.
Advisors: Professor Paul Gissen, Scientific and Medical Advisor, Professor Sara Mole, Scientific Advisor, Clare Beesley PhD, Scientific Advisor. With support from Bluepepper Designs.

BDFA, The Old Library, 4 Boundary Road, Farnborough, Hants. GU14 6SF
Freephone Helpline: **0800 046 9832** Email: **support@bdfa-uk.org.uk** Website: **www.bdfa-uk.org.uk**

CLN1 Disease, Infantile

BATTEN DISEASE FAMILY ASSOCIATION
Together we WILL make a difference
Registered Charity In England and Wales 1084908 - Scotland SC047408

Are there any alternative names?

CLN1 disease, infantile may also be referred to as infantile CLN1 disease. It has previously been called Santavuori-Haltia Disease and referred to as Infantile Neuronal Ceroid Lipofuscinosis (INCL).

What are Neuronal Ceroid Lipofuscinoses (NCLs)?

These refer to several different genetic life-limiting neurodegenerative diseases that share similar features. Although the different forms of NCL are sometimes described according to the age of the child at the onset of the disease, they are now better classified according to the gene identified as the cause e.g. CLN1 (gene) disease, infantile (age of onset), CLN3 (gene) disease, juvenile (age of onset).

What causes NCL?

Since the first genes causing NCL were identified in 1995, over 400 mutations in 14 different genes have been described that cause the various forms of NCL disease. Our cells contain thousands of genes that are lined up along chromosomes. Human cells contain 23 pairs of chromosomes (46 in total). Most genes control the manufacture of at least one protein. These proteins have different functions and include enzymes that act to speed up molecular chemical reactions. The NCLs are caused by abnormal genes, which are unable to produce the required proteins. As a result, the cells do not work properly and this leads to the development of symptoms associated with these diseases.

What specifically causes CLN1 disease?

The gene called CLN1 was discovered in 1995 and lies on chromosome 1. CLN1 normally directs production of a lysosomal enzyme called Palmitoyl Protein Thioesterase 1 (PPT1). A deficiency in PPT1 results in abnormal storage of proteins and lipids (fats) in neurons (nerve cells) and other cells. The cells cannot function properly and this leads to the development of the symptoms associated with CLN1 disease.

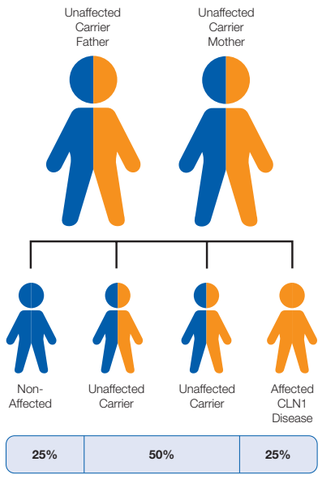
Although rarer in occurrence, CLN1 disease may also present with later ages of onset (late-infantile, juvenile and adult).

How are NCLs inherited?

Most forms of NCL are inherited as "autosomal recessive" disorders. This is one of several ways that a trait, disorder, or disease can be passed down through families. An autosomal recessive disorder means that both copies of the gene are abnormal (one inherited from each parent) with neither working properly. The disease does not depend on the sex of an individual.

What are the chances of inheriting CLN1 disease?

CLN1 disease is inherited as an autosomal recessive disorder, which means that both chromosomes carry mutations in the CLN1 gene. Therefore both biological parents of a child with this diagnosis will be carriers of the disease but physically unaffected by it.



A child born to parents who both carry the autosomal recessive mutation in the CLN1 gene has a 25% (1 in 4) chance of inheriting the abnormal malfunctioning genes from both parents and developing CLN1 disease.

They will have a 50% (1 in 2) chance of inheriting one abnormal gene, which would make them a carrier who is unaffected by the disease. There is a 25% (1 in 4) chance of the child being born with two normal genes and therefore being non-affected (not a carrier).

When it is known that both parents are carriers of the abnormal gene, we refer to there being a 2 in 3 chance of a child being a carrier, once it is established that they are unaffected by the disease.

With any pregnancy, the probability of a child inheriting one or both genes from their parents is the same each time, irrespective of any sibling's status.

How is it diagnosed?

Children will probably have been seen by a paediatrician and paediatric neurologist because of symptoms such as seizures, deteriorating motor skills and visual failure. A number of investigations may have been undertaken to look for the cause of these.

The diagnosis of infantile CLN1 disease is usually made by enzyme (PPT1) and genetic (CLN1) tests on blood samples. When viewed with an electron microscope, blood samples will usually show abnormal storage bodies in the cells. These products can have characteristic patterns, depending on the type of NCL.

Genetic testing is recommended to look for the exact mutation or mistake in the CLN1 gene. A blood or saliva sample will be taken to extract DNA from the cells for the test.

How common is it?

Approximately 1 - 2 children are diagnosed with CLN1 disease each year in the UK. We estimate there are currently less than 10 affected children in the UK. Children have been diagnosed with this condition in many countries and from a variety of ethnic backgrounds.

What are the symptoms and how does the disease progress?

Children appear to be healthy and develop normally for the first few years of life. Towards the end of the first year, developmental progress begins to slow down. Infants may have difficulty sleeping through the night and perhaps become more restless and irritable during the day. Some infants develop repetitive hand movements and often appear to be " fiddling".

Their physical tone often becomes floppy, whilst developmental skills such as walking, standing and speech are lost. Children become less able and increasingly dependent during their toddler years. By the age of two years, most will have epileptic seizures and present with "jerking" movements. Vision progressively deteriorates until they are no longer able to see. By the age of three years, children are completely dependent, unable to play, feed themselves, sit independently or communicate.

In order to ensure they receive adequate nutrition, they may require a specialist feeding tube (gastrostomy). There may be noticeable stiffening of their arms and legs, whilst some children become prone to frequent chest infections. Sadly most children who have CLN1 infantile disease die in early to mid-childhood.

Are there any treatments?

Currently there is no cure for CLN1 disease and therefore specialist symptom management and therapy is essential to assist in maintaining a good quality of life for children and their families. Holistic support for parents, siblings and wider family members is extremely important throughout their journey.

Epilepsy can be difficult to treat and therefore attaining complete control of seizures is not always possible. Antiepileptic medications, commonly lamotrigine and sodium valproate, will be necessary from the early stages of the disease process.

Myoclonic jerks (involuntary muscle spasms) are common, though should not be confused with epileptic seizures. They can interfere with rest and sleep as well as being distressing for children and their families. Along with spasticity (unusually tight or stiff muscles), these symptoms can be managed with baclofen and tizanidine, which are often used in combination with one another. In order for medication to be sufficient, the responsible doctor may need to prescribe frequent, higher dosages than are usual for those who do not have CLN1 disease.

In some individuals during the advanced phase of the disease, the use of fentanyl patches and orally administered morphine derivative medications have provided good effects, in addition to baclofen and tizanidine. Various professionals including doctors, nurses, physiotherapists, occupational therapists and sensory specialists should be involved in the care of children with infantile CLN1 disease. They will work collaboratively and in conjunction with the family to provide a holistic approach to care.

Support and treatment will be needed for a range of issues including progressive difficulties with chewing and swallowing, constipation, hydration, respiratory function, oral secretions, motor disorder and sleep disturbance. Attention to posture, skin and mouth care is essential and infants will require additional nutritional support that may include consideration of a gastrostomy.

What research is being done?

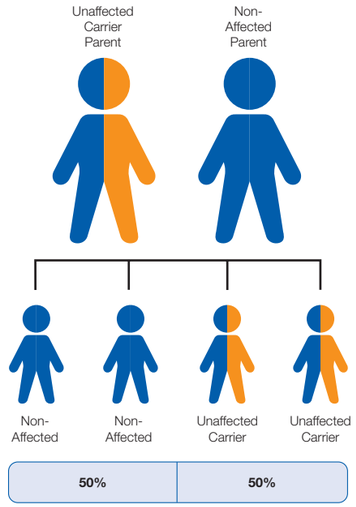
Research into possible methods for treating the disease is ongoing with current consideration of several possible therapeutic strategies being investigated. These focus mainly on methods that may replenish the activity of the PPT1 enzyme or compensate for its loss of function. These include the use of gene therapy directed to the Central Nervous System (CNS).

Gene therapy is an experimental treatment where the aim is to introduce a healthy copy of a defective (abnormal) gene into the patient cells. As PPT1 is an enzyme, research is also being undertaken into Enzyme Replacement Therapy (ERT) administered to the CNS. Small molecule therapies are also being investigated using compounds, or drugs, which may mimic the function of the enzyme.

For updates and information regarding developments in research please visit the BDFA website: **www.bdfa-uk.org.uk** or contact the **BDFA Scientific Officer** via **0800 046 9832**, email: **research@bdfa-uk.org.uk**

What are the genetic considerations?

It may also be possible that older unaffected siblings are carriers of the disease and may want to understand how CLN1 disease may affect their family choices when they are older.



When only one parent is a carrier of the abnormal gene, and the other is non-affected, there is a 50% (1 in 2) chance that any child will be an unaffected carrier.

If parents are considering having additional children, they can access specialist advice and support from their local clinical genetics service following a referral from their GP. Prenatal testing may be possible in the early stages of any future pregnancy.

Is support available to families?

As soon as possible following a diagnosis of CLN1 disease, families should be offered support from various professionals attached to their local health, social, educational services and the BDFA Support and Advocacy Partner. Ideally a "Team Around the Child" will be formed, with one of the professionals appointed as a Keyworker for the family.

The child's needs should be discussed with the parents and assessed by the team. The team will work together to ensure that the child and family receive the on-going care and support they need and that their choices are taken into account.

A child and family's needs will inevitably change as the disease progresses. As such, it is often helpful if a clear process for regular planned reviews is identified and that a system is established for enabling additional reviews as and when they are deemed necessary. As the rate or pattern of the progression of the disease for each child remains uncertain, an individualised plan of care and support is essential.

The BDFA is able to provide various forms of holistic support and can be contacted via **0800 046 9832** email: **support@bdfa-uk.org.uk**

How can families manage the financial challenges?

Caring for a child with CLN1 disease will bring additional financial challenges. It is vital that families are well informed about the full level of economic assistance available and the support that they are entitled to. They may well need help and guidance in accessing benefits and other sources of assistance. The professionals and services supporting the family should provide advice and guidance. The BDFA can also support families with these issues in various ways, the Small Grants Scheme being one example.

What are the practical implications for the family?

As the disease progresses, specialist equipment and aids will become necessary and this is another area where the family will need help. Items are likely to include specialist seating, buggies/wheelchairs, bathing and toileting aids, hoisting equipment and a specialist bed/mattress. Professionals will play a key role in ensuring that these and other items are provided in a timely manner following proper assessment of the individual child's needs.

It is likely that changes will be needed in the home environment to enable the family to appropriately care for a child with CLN1 disease. These may include installing ramps, widening doorways and providing suitable floor surfaces. A purpose-built wet room with a specialist bath or shower is commonly needed and there are various other aspects that will require consideration.

There are grants and funds available to ensure that the work involved is affordable. An occupational therapist will consult on all aspects of any adaptations and assist the family in undertaking this process.

Freephone Helpline: 0800 046 9832 www.bdfa-uk.org.uk