It is likely that changes will be needed in the home environment to enable the family to appropriately care for a child with late-infantile CLN2 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.

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

Education will continue to be important for the child and family and there will be many aspects that require consideration and significant assistance from those around them.

Education, Health and Care Plans have now replaced statements. All children and young people with an NCL diagnosis will require an Education, Health and Care Plan. These plans are personalised plans that should meet the education health and care needs of the child or young person.

It remains probable that many parents will continue to need guidance, understanding and support when trying to navigate the process of statutory assessment and the drawing up of the EHC Plan.

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: **education@bdfa-uk.org.uk**

In what other ways can families be supported?

The realities of caring for a child who has late-infantile CLN2 disease can place great physical and emotional strain on a family. This will impact upon everyone in numerous ways so awareness that support is available from the BDFA and other sources to help with these challenges is vitally important. This support extends to wider family members.

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 any NCL disease throughout the UK. We provide informed guidance and assistance as well as seeking to 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 & Advocacy Partner who is able to assist with many of the issues highlighted in this document and can discuss each in greater detail and on a more personal basis.

They can be contacted via our Freephone Helpline:
0800 046 9832 or email: **support@bdfa-uk.org.uk**.

There are a number of local and national organisations who 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.

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.

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BATTEN DISEASE FAMILY ASSOCIATION
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CLN2 Disease, Late-Infantile

Are there any alternative names?

CLN2 disease, late-infantile may also be referred to as late-infantile CLN2 disease. It has previously been called Jansky-Bielschowsky Disease and Late-Infantile Neuronal Ceroid Lipofuscinosis (LINCL), though was more commonly known as Late-Infantile Batten Disease.

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 classified according to the gene identified as the cause e.g. CLN2 (gene) disease, late-infantile (age of onset) and 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, which 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 cannot work efficiently and this leads to the symptoms associated with these diseases.

What specifically causes CLN2 disease?

The gene called CLN2 was discovered in 1998 and lies on chromosome 11. The CLN2 gene normally directs production of a lysosomal enzyme, which breaks down cellular waste materials and is called tripeptidyl peptidase1 or TPP1.

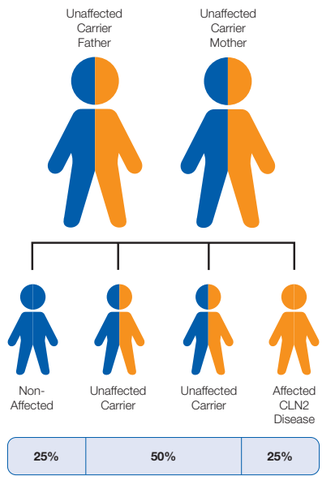
A deficiency in TPP1 results in abnormal storage of proteins and lipids (fats) in neurons (nerve cells) and other cells. The cells cannot function properly, causing the symptoms associated with CLN2 disease.

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 possibility of being born with the disease does not depend upon the gender of an individual.

CLN2 disease is inherited as an autosomal recessive disorder, which means that both chromosomes carry mutations in the CLN2 gene. Therefore both biological parents, of a child with this diagnosis, will be carriers of the disease yet physically unaffected by it.

What are the chances of inheriting CLN2 disease?



A child born to parents, who both carry the autosomal recessive mutation in the CLN2 gene, has a 25% (1 in 4) chance of inheriting the abnormal malfunctioning genes from both parents and developing CLN2 disease.

They will have a 50% (1 in 2) chance of inheriting one abnormal gene, which would make them a carrier yet unaffected by the disease. There is a 25% (1 in 4) chance of the child being born with two normal genes, therefore being unaffected and 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 the status of any sibling.

How is it diagnosed?

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

The diagnosis of late-infantile CLN2 disease is usually confirmed by enzyme (TPP1) and genetic (CLN2) tests on blood samples. Occasionally it is necessary for a skin biopsy to be taken.

How common is it?

Approximately 5 or 6 children are diagnosed with late-infantile CLN2 disease each year in the UK. We estimate there are currently between 30 - 50 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 developing normally for the first few years of life. Towards the end of the second year, developmental progress may begin to slow down and some children will be delayed in the development of language skills.

The first significant sign of the disease is usually the onset of epilepsy. The seizures may be varying in nature and include drops, vacant spells (absences) or motor seizures with violent jerking of the limbs and loss of consciousness. Initially, seizures may be successfully managed with medication for several months, yet they will always recur and often become difficult to control.

Children become unsteady on their feet and may frequently fall. Gradually, skills related to walking, playing and speech are lost with children becoming less able and increasingly dependent.

By 4 - 5 years of age, children with late-infantile CLN2 disease usually have myoclonic (rapid involuntary muscle spasm) jerks of their limbs and are prone to erratic movements of their head (nods). They may have difficulty sleeping and often become distressed around this time, usually without obvious reason. Their vision gradually deteriorates, with its loss being ultimately inevitable.

By the age of 6 years, most children will be completely dependent on families and carers for all of their daily needs. In order to ensure they receive adequate nutrition, they will 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.

Children and young people affected by Batten disease will develop childhood dementia, resulting in increasing learning difficulties, difficulties with short term memory, unusual behaviours, poor concentration, difficulties in sleeping, mood swings, hallucinations, confusion and anxiety. Although short term memory skills decline, long term memory remains largely intact and remains a strength.

Although there is a general progression of symptoms associated with late-infantile CLN2 disease, it is impossible to state the exact rate or pattern of this as each child and situation is unique. Sadly most children who have late-infantile CLN2 disease die between the ages of 6 and 12 years, though there are exceptions.

Are there any treatments?

Currently there is no cure for CLN2 disease. Therefore, appropriate and effective symptom management 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 vital throughout the journey.

Epilepsy can be difficult to treat and therefore attaining complete control of seizures is not always possible. Anticonvulsant medications (e.g. sodium valproate) will be necessary from the early stages of the disease process. It is recommended that drugs such as carbamazepine, phenytoin and vigabatrin are avoided.

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. Levetiracetam has demonstrated positive effects in a combined action against myoclonic jerks and seizures. Spasticity (unusually tight or stiff muscles) can be managed with baclofen and/or trihexyphenidyl. In order for medication to be sufficient the responsible doctor may need to prescribe higher dosages than are usual for those who do not have CLN2 disease.

A multidisciplinary team of professionals including doctors, nurses, physiotherapists, occupational therapists, sensory specialists, speech and language therapists should be involved in the care of children and young people with CLN2 disease at all stages of the disease. Although their required levels of input may vary at various periods, they should work collaboratively and in conjunction with the family to appropriately meet the needs of the child and those caring for them.

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

Referral for support from local Continuing Care Nursing Teams, Children's Hospice and Community Palliative Care teams are recommended. These teams can provide a variety of services supporting the child and other family members.

What research is being done?

Research into possible methods for slowing the progression of the disease and potentially curative treatments are ongoing, both in the UK and worldwide. These mainly focus on methods that may replenish the activity of the PPT1 enzyme. Several promising therapeutic approaches are being investigated for CLN2 late-infantile disease, which include gene therapy and enzyme replacement.

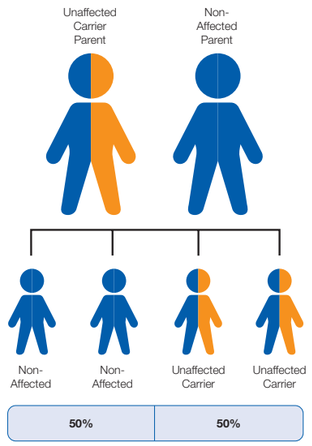
The Department of Genetic Medicine at Weill Cornell Medical School, New York, USA is conducting a gene therapy study for the CLN2 gene. The purpose of this study is to determine whether gene transfer surgery, to the brain, is safe and if the procedure will slow down or halt the progression of the disease.

A Phase I/II study by BioMarin, (a US pharmaceutical company) is ongoing in the UK and in Europe to determine the safety and efficacy of BMN190, a recombinant Human TPP1 enzyme, as an enzyme replacement therapy for CLN2 disease.

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?

The age that late-infantile CLN2 disease is usually diagnosed in a child means that some families will have younger siblings who may be affected yet have not displayed any symptoms.



It is also possible that unaffected siblings will be carriers of the disease. When they reach an appropriate age, genetic counselling can be offered to support them in understanding how this could affect their future life and family choices.

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

Parents considering having more children should ask to be referred to a local clinical genetics service by their GP. Prenatal testing may be possible in the early stages of any future pregnancy.

Is support available to families?

Following the diagnosis, families should be offered support from various professionals attached to their local health, social, sensory services and the BDFA Support and Advocacy Partner. Ideally a "Team Around the Child" will be formed, with one professional 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 ongoing 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, regular planned review meetings should be arranged by the keyworker and a system established to enable additional reviews when 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 late-infantile CLN2 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 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.