

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. Specialist Visual Impairment services exist to support both children and the education professionals working with them and these will play an important role in facilitating the appropriate quality of access to education for those affected by CLN3 disease. Communication is often another aspect that may need to be focused on should individuals begin to have difficulties with their speech.

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

The **BDFFA 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 young person who has CLN3 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 time available to share with their children, particularly in the earlier stages of the disease progression. 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 BDFFA offers support to any family member, friend, professional or organisation involved in caring for a child with CLN3 disease or any other form of NCL 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 BDFFA also coordinates a Small Grants Scheme that can provide assistance for a range of needs. The BDFFA has a Support & 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.

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

The BDFFA can provide information on 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. 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.

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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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CLN3 Disease, Juvenile

Are there any alternative names?

CLN3 disease, juvenile may also be referred to as juvenile CLN3 disease. It has previously been called Spielmeyer-Sjogren-Vogt disease and Juvenile Neuronal Ceroid Lipofuscinosis (JNCL); though was more commonly known as Juvenile 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 better classified according to the gene identified as the cause e.g. CLN3 (gene) disease, juvenile (age of onset) and CLN1 (gene) disease, infantile (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 do not work properly and this leads to the development of symptoms associated with these diseases.

What specifically causes CLN3 disease?

The gene called CLN3 was discovered in 1995 and lies on chromosome 16. This gene codes for a transmembrane protein and mutations (mistakes) in the CLN3 gene cause deficiencies that result in abnormal storage of proteins and lipids (fats) in neurons (nerve cells) and other cells. The most common mutation is a deletion of part of the gene, which is present in 85-95% of all CLN3 disease. The cells then cannot function properly and this leads to the development of the symptoms associated with CLN3 disease.

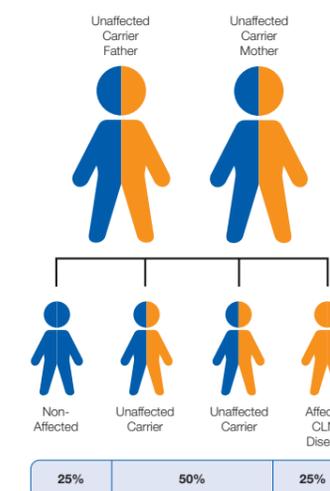
How are NCLs inherited?

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 disease does not depend on the sex of an individual.

What are the chances of inheriting CLN3 disease?

CLN3 disease is inherited as an autosomal recessive disorder, which means that both chromosomes carry mutations in the CLN3 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 CLN3 gene, has a 25% (1 in 4) chance of inheriting the abnormal malfunctioning genes from both parents and developing CLN3 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 ophthalmologist due to a progressive loss of vision. A number of investigations will often have been undertaken to look for the cause of the presenting visual impairment. The diagnosis of CLN3 disease is usually made by tests on blood samples, though a skin biopsy may also be necessary.

How common is it?

Approximately 3 - 4 children are diagnosed with CLN3 disease each year in the UK. We estimate there are currently between 30 - 40 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. The first sign of the disease usually presents as a gradual loss of vision between 4 and 7 years of age, which may first be noticed in a nursery or school environment. Each child's level of vision will change rapidly over a 6 - 12 month period initially, however it is likely that some awareness of colour along with variations between light and dark will be retained until later. By the end of their attendance at primary school, children tend to begin showing some difficulties with concentration, short-term memory and learning. Many are still able to attend a mainstream school though may require additional learning support in the classroom. Changes in behavioural patterns can become apparent at various stages of the disease and may prove particularly challenging to those around the child or young person. Professional and specialist support in addressing and managing this symptom is often required, though may not immediately be connected to the disease by those around the family.

The next stage of the disease begins with the onset of epileptic seizures (average age of onset is at 10 years old). Often, motor seizures are the first to present with violent jerking of the limbs and loss of consciousness. Seizures may be controlled by medicines for several months or years, yet will always recur, eventually becoming difficult to control completely. The pattern of seizures may change over time and other seizure types may evolve, such as vacant spells and episodes of partial awareness that may occur alongside episodes of "fiddling" behaviour and muddled speech.

During the teenage years, children slowly become more unsteady on their feet. At around the same period their speech becomes repetitive then gradually more difficult to understand. Not uncommonly, children demonstrate anxiety and may demonstrate a tendency to worry about a wide range of things. Some may even hear voices and sense or see things that are unreal. Teenagers are likely to become less able and increasingly dependent, yet the course of the disease is extremely variable even for those affected within the same family. Individual teenagers and young adults may present as much more able on some days as opposed to others. This can be particularly evident in terms of mobility, communication and feeding skills. The disease progresses with periods of stability that may last months or years. These tend to alternate with phases of deterioration lasting several months, which may sometimes be triggered by an intercurrent illness.

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.

Sadly most children who have CLN3 disease die between the ages of 15 and 35 years, though there are exceptions.

Are there any treatments?

Currently there is no cure for CLN3 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 will not likely be a presenting symptom if a diagnosis is made before the child is 10 years old; however generalised tonic-clonic seizures are the type most commonly experienced, though any form of seizure may occur through the course of the disease. Treatment will depend on the severity of the epilepsy and seizures may initially appear infrequent. Antiepileptic medications sodium valproate and lamotrigine (individually or in combination) are generally the first drug treatments to be introduced when required. Both topiramate and levetiracetam have also recently been shown to be effective with the latter appearing to improve the parkinsonian tremor that some affected by CLN3 disease experience.

These newer options need to be properly monitored and evaluated to assess if there may be any long-term side-effects though. Benzodiazepines such as clobazam and clonazepam can be useful in combination therapy as singular drug therapy is likely to become less effective as the disease progresses. However, they can also create issues with excessive bronchial secretions.

Once CLN3 disease is at a more progressed state, epilepsy can be difficult to treat and therefore attaining complete control of seizures is not always possible. Clusters of seizures tend to be managed with rectal or oro-buccal benzodiazepines (e.g. diazepam and midazolam), whilst rectal paraldehyde may also be effective.

It is generally agreed that carbamazepine, gabapentin and phenytoin can potentially worsen myoclonic seizures in CLN3 disease so their use is usually refrained from.

Emotional, behavioural and psychological difficulties are common in all stages of CLN3 disease with the potential for psychotic episodes to appear in the latter phases of the disease. These include restlessness, anxiety, panic attacks, aggressive behaviour, hallucinations, delusions and depression. Familiar supportive environments that are peaceful and structured can make a significant difference in managing these challenges along with a focus on promoting self-esteem and flexibly adapting activities to each individual's abilities (acknowledging that these can sometimes vary rapidly depending on fatigue, underlying illness etc.).

Anxiety (oxazepam); extreme restless and/or aggressive behaviour, delusions and hallucinations (risperidone, olanzapine, sulpiride, pipamperone) may all require treatment with medications depending on the individual. Sleep disturbance is often evident throughout the disease, usually worsening as the young person ages. Chloral hydrate or benzodiazepines may be prescribed for short periods when it has been suggested that melatonin has little effect. Clonazepam can be helpful if sleep disturbance is linked to epileptic activity.

Deteriorating motor skills e.g. problems with balance and walking can be first addressed through promoting various activities such as walking, swimming, cycling and riding. Regular physiotherapy and other similar input should be utilised as the disease progresses with a focus on maintaining mobility for as long as possible and, although there can be great variation in each individual, there will ultimately be a need for mobility aids and other specialist equipment.

Various professionals including doctors, nurses, physiotherapists, occupational therapists, ophthalmologists, speech and language therapists should be involved in the care of children and young people with CLN3 disease at various stages of the disease. They will work collaboratively and in conjunction with the family to provide a holistic approach to care.

At certain points 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, seating, skin and mouth care is essential and young people may ultimately require additional nutritional support that could include consideration of a gastrostomy.

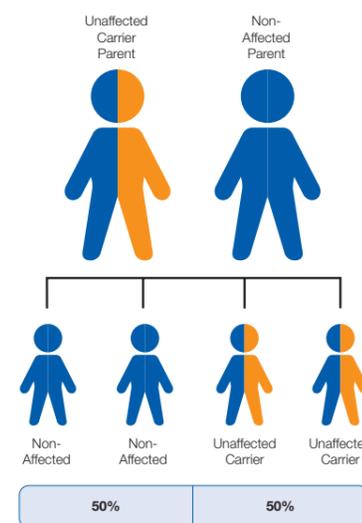
What research is being done?

Research into possible methods for treating the disease is ongoing with various theoretical approaches being considered and investigated.

Current strategies being examined include modulating the immune system, blocking classes of glutamate receptors, and targeted eye therapy. However there are many scientific questions yet to be answered and all are currently at very early stages of development.

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 CLN3 disease is usually diagnosed in a child means that some families will have younger siblings who may be affected but have not displayed any symptoms.

It may also be possible that older unaffected siblings are carriers of the disease and may want to understand how CLN3 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 CLN3 disease, families should be offered support from various professionals attached to their local health, social, educational, visual impairment services and the BDFA Support & 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 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, 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 CLN3 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 particular example.

What are the practical implications for the family?

As the illness progresses, specialist equipment and aids will become necessary and this is another area where the family will need help. Items are initially likely to be focused in addressing challenges associated with living with a visual impairment, though will ultimately include specialist seating, 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 young person with CLN3 disease. These may initially include particular adaptations to promote independence for living with a visual impairment e.g. specialist lighting, tactile labelling, introducing contrasting colours for objects and areas, as well as installing suitable floor surfaces. In the latter stages of the disease it may be necessary to install ramps, widen doorways or invest in a purpose-built wet room with a specialist bath or shower, whilst there are various other aspects that will require consideration.