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 initially likely to be focused on 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 or young person's needs.

It is likely that changes will be needed in the home environment to enable the family to appropriately care for a child or 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.

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 or young person 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 young people 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 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 or 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 BDFA offers support to any family member, friend, professional or organisation involved in caring for a child or young person 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 BDFA also coordinates 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 CLN3 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.

The BDFA can provide information on 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. 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.

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CLN3 Disease (Juvenile Batten Disease)

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

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 or young person at the onset of the disease, they are now better classified according to the gene identified as the cause e.g. CLN3 disease, juvenile and CLN1 disease, infantile.

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.

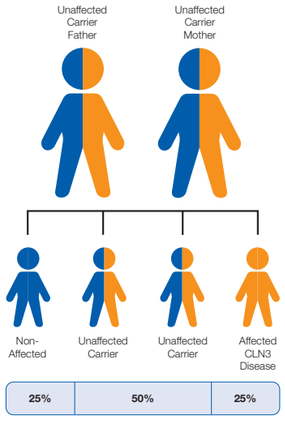
How are NCLs inherited?

Most forms of NCL are inherited as "autosomal recessive" disorders. This is one of several ways that a genetic disorder 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 or young person 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 or young people 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. 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 CLN3 gene. A blood or saliva sample will be taken to extract DNA from the cells for the test.

How common is it?

Approximately 3 - 4 children or young people are diagnosed with CLN3 disease each year in the UK. We estimate there are currently between 30 - 40 affected children and young people in the UK. Children and young people 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. 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 and young people 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 and young people 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 and young people who have CLN3 disease die between the ages of 15 and 35 years.

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 young people and their families. Holistic support for parents, siblings and wider family members is extremely important throughout their journey.

Epileptic seizures start on average at age 10. The most common type are tonic-clonic seizures where limbs can jerk and loss of consciousness occur. Other types of seizure include partial seizures where only one part of the body is affected by abnormal movement and altered consciousness may not be very obvious. A consultant neurologist's guidance is essential for managing seizures. The monitoring of effectiveness of medication on seizure control and checking for side-effects needs to be done as a collaboration between families of affected children or young people and their neurologist often working with other professionals such as GPs and specialist nurses.

Drug treatment of seizures depends on their severity and frequency. Anti-epileptic medications such as sodium valproate and lamotrigine, sometimes needed in combination, are often the first treatments introduced. Other medications used in addition include clobazam, clonazepam, levetiracetam, phenobarbital and phenytoin.

The anti-epileptic drugs carbamazepine and gabapentin have been found to be of no use in CLN3 disease.

In the later stages of CLN3 disease combinations of anti-epileptic drugs may be needed. For clusters of seizures drugs from the benzodiazepine group such as midazolam, diazepam and lorazepam given either orally, bucally or rectally may be needed. Paraldehyde is a drug given rectally in cases where clusters of seizures are resistant to other medications.

Emotional, behavioural and psychological difficulties are common in all stages of CLN3 disease with the potential for psychotic episodes to appear in the later 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).

Sometimes medication is of use in dealing with behavioural problems, hallucinations and agitation. Drugs from the benzodiazepine family such as diazepam or lorazepam can be helpful. Other drugs that have been used for hallucinations and agitation in CLN3 disease include risperidone, olanzepine and chlorpromazine. All of these types of medication can cause drowsiness which has to be considered and monitored if they are to be used.

Sleep disturbance can be a problem in CLN3 disease. This is best managed by attention to sleep routine and making every effort to help with strategies that help a child or young person relax. If medication is needed then options include melatonin or one of the drugs from the benzodiazepine family.

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 for which Occupational Therapy input is invaluable.

At some stage a child or young person with CLN3 disease is likely to develop difficulties with chewing and swallowing. It can become a challenge to maintain adequate nutrition and hydration which can lead to weight loss and problems giving medication. Symptoms of reflux can occur and may lead to distress and pain so causing behavioural disturbance. There may be difficulty with swallowing saliva leading to excessive dribbling. Difficulties in swallowing can sometimes cause choking and put a person at increased risk of chest problems.

Professionals including dieticians, speech and language therapists, physiotherapists, doctors and nurses should be involved to help with these problems. Medications such as antacids and omeprazole or lanzoprazole to suppress excess stomach acid can be of use. Attention to correct consistency of food and correct positioning whilst being fed are important. Correct head support whilst sitting may help with dribbling.

Ultimately it may well be that insertion of a gastrostomy (feeding tube into the stomach) is the best way to make sure a child or young person can get enough food and drink and can be given their medication safely.

Various professionals including doctors, nurses, physiotherapists, occupational therapists, dieticians, ophthalmologists and 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.

What research is being done?

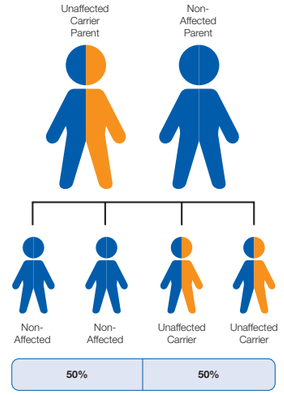
Research into possible methods for treating the disease is on going with various theoretical approaches being considered and investigated. Researchers in the UK and worldwide are investigating potential drugs which may alleviate some of the symptoms of the disease or slow its progression.

Gene therapy for CLN3 disease is being investigated, which aims to introduce a copy of the defective gene into the cells so that they can then produce a correct functioning protein within the brain and the eye. This forms part of the on-going BATCure project however it is still in the early stages of development.

For updates and information regarding developments in research please visit the BDFA website: **www.bdfa-uk.org.uk**, BATCure website: **www.batcure.eu** 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 or young person 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 and Advocacy Partner. Ideally a "Team Around the Child or Young Person" will be formed, with one of the professionals appointed as a Keyworker for the family.

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

A child or young person and their 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 or young person 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 or young person 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.