



from an early stage. To get a blue disability vehicle badge, which is valid throughout the E.U., the child would usually have to qualify for mobility allowance i.e. be 3 or older although it is sometimes possible to get one sooner. Mobility allowance can sometimes be used for the Motability scheme to fund a vehicle. The High Rate Motability component of your DLA can sometimes be used to lease or hire a vehicle through the Motability Vehicle Scheme see www.motability.co.uk and www.direct.gov.uk or 0845 456 4566.

It is important to realise that DLA criteria apply to the level of disability and the level of help and supervision needed over and above that which a healthy child of the same age would need. Just because a child has a particular disease does not mean that the application will automatically be successful, each case is judged on its merits. There is an appeals process if the claim is unsuccessful.

If a parent has to care for the child for more than 16 hours per day and the child receives DLA then the parent may be entitled to **Invalid Carers Allowance**.

Further advice can be obtained from a social worker, the citizens' advice bureau or the benefits agency.

Equipment

As the illness progresses, various kinds of equipment and aids become needed:-

- Car seats
- Pushchairs / wheelchairs
- Seating for in the home
- Protective headwear for when the child is still mobile but falling frequently
- Postural splints for the torso or limbs
- Feeding related - feed pumps and consumables (feed, containers and syringes)
- Suction for pharyngeal secretions
- Incontinence pads ["nappies"]



- Hoisting equipment or even lifts
- Bath aids
- Later stages - possibly Oxygen or nebulizer machines
- Bed with safe sides
- Specialist mattress.

The ease or difficulty of obtaining these items and resources varies greatly around the country, but all should be available without any cost to the family. Very expensive equipment provision may be means tested to a degree.

Education

In the early stages of the illness, often before the correct diagnosis has been made, it is recognised that there is going to be some help needed with schooling. Most families find this very difficult and upsetting. At a time when the realisation is sinking in that their son or daughter isn't going to be "OK" and will need a lot of extra help to make progress at school, they often find many bureaucratic obstacles to overcome to get the help they feel their child needs. In trying to get through the process of "statementing", parents need a lot of guidance, understanding and support.

"Statementing" is the process where the child becomes the subject of a **Statement of Educational Needs**. This is a formal document drawn up by the local education authority, based on advice from the health professional and other professionals involved – usually at least a community paediatrician and an educational psychologist. It describes the child's educational needs and makes recommendations for the appropriate educational provision and allocation of resources. Unfortunately the resources provided often fall short of the resources needed. Adequate schooling is a field where considerable experience exists with BDF.



Late Infantile Batten Disease

Introduction and Terminology THE IDEA BEHIND PRODUCING THIS LEAFLET IS TO PROVIDE FAMILIES AND THE PEOPLE AROUND THEM WITH AN OVERVIEW OF THE ILLNESS. OUR UNDERSTANDING OF WHAT CAUSES THE ILLNESS IS GROWING RAPIDLY AND THIS LEAFLET TRIES TO EXPLAIN THE SCIENCE IN AN EASY TO COMPREHEND WAY.

The terminology is confusing, this is mainly because what we call Batten Disease is in fact several different genetic illnesses each with a different gene defect. They do however, have a lot of similar features. Traditionally, the different types of "Batten Disease" were classified according to the age of the child when the illness began, so we have Infantile, Late Infantile and Juvenile Batten disease for example - with the illness seeming to start at around 1, 3 and 7 years of age respectively.

As our understanding at the level of molecular genetics has increased, things have become more complex. The Batten Disease group of illnesses now tend to be referred to as the **Neuronal Ceroid Lipofuscinoses (NCLs)**. This term describes the abnormal appearance of affected cells as seen down a microscope. We also now recognise that there are more types of the illness than the Infantile, Late Infantile and Juvenile types etc, there are some less common "variant" types. Some of these are quite rare and only occur in significant numbers in certain parts of the world.

Molecular Genetics

Our chromosomes contain thousands of genes, all of which code for proteins. Nine different genes causing different varieties of NCL have been identified so far. They are called CLN1 to CLN10. (CLN4 is the gene name given to a theoretical gene causing adult onset Batten disease. It has not yet been identified.) The nine genes are different and so are the abnormal proteins, but all result in similar disturbances of cell function and lead to similar clinical symptoms. All the Batten

disease proteins seem to be involved with the function of the lysosome – this is a tiny part of a cell that is involved in breaking down and recycling certain chemicals in the cell. When this process doesn't work properly, there is a build up of substances that aren't being broken down properly.

CLN1, CLN2 and CLN10 are genes coding for lysosomal enzymes, responsible for breaking down and recycling proteins in the lysosomes. Enzymes are often able to move inside and between cells. Some of the other genes code for proteins which are stuck in cell membranes and cannot move between cells, for example CLN3 and CLN5.

How are NCLs inherited?

Apart from some very rare types, the NCLs are inherited in an "Autosomal Recessive" fashion. *Autosomal* means that the abnormal gene is carried on the normal chromosomes as opposed to the "sex" chromosomes – this means that the illness has nothing to do with gender. (Some illnesses are carried on the sex chromosomes and are said to be sex-linked and principally affect either males or females - such as colour blindness or haemophilia).

Recessive means that the abnormal gene does not lead to an affected individual if he or she has a normal gene as well, we each have a pair of genes – one from each parent. If both genes are normal the individual would clearly not have the disease, if a person has one normal gene and one abnormal gene, that individual would not have the disease (but would be a carrier and could pass the gene on to his or her child) but if a person has two abnormal genes he or she will have symptoms of the disease eventually.

The above diagram (Fig 1) tries to illustrate the various ways parental genes come together at conception when both parents are carriers of the disease. Child A has 2 normal genes so does not have the disease,

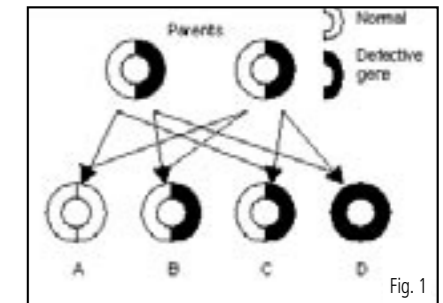
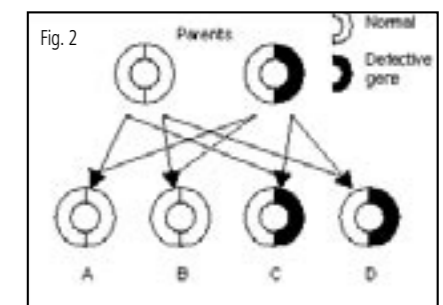


Fig. 1

child D has 2 abnormal genes so does have the disease, children B and C have one normal and one abnormal gene – they do not have the illness but will be carriers. On average one in four (25%) of these parents' children will be normal, one in four (25%) will have the disease and two in four (50%) will not have the disease but will be carriers.



If only one of the parents is a carrier as in Fig 2, there are no diseased children but 50% will be carriers (on average), this explains how the gene can be passed down family trees from our ancestors for many generations without it being expressed as an affected individual until **bad luck** brings two carriers together. When this happens (as shown in Fig. 1) **each child** this couple has will have a **one in four chance** of being affected by Batten Disease.

This leaflet is for basic information only; any decisions regarding an individual child should be done through the appropriate medical services. Some of the information in this leaflet is based on the chapter on Classic Late Infantile NCL by Dr RE Williams et al in *The Neuronal Ceroid Lipofuscinoses*, Goebel, Mole & Lake (Eds), IOS Press 1999 and 2008 and is used with permission.

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c/o Heather House, Heather Drive, Tadley, Hampshire RG26 4QR Tel: 0115 965 4815
email: BDFA.info@btinternet.com www.bdfa-uk.org.uk
Updated by R Griffith RGN and Dr R E Williams



Classical Late Infantile Onset NCL
Mutations in *CLN2*, - the gene responsible for LINCL - which is located on chromosome 11, are known to cause almost all cases of classic late infantile NCL (LINCL). The mutation in this gene causes a deficiency of an enzyme (a kind of protein) in the cell (Tri-peptidase-1, TPP1). This enzyme is involved in breaking down small proteins within the lysosome. The lack of TPP1 leads to a build up of waste products in the cell. Eventually the cells die. This accumulation of this material in cells can be seen with a powerful electron microscope and are known as curvilinear bodies (CVB).

Classic LINCL is thought to occur world-wide although it appears to be more common in northern European populations than elsewhere. The incidence of late infantile NCL has been calculated in several different populations and is of the order of 1 in 30,000 births.

Clinical Features

The onset of symptoms that reach the attention of doctors is often between 2 and 4 years of age. Prior to this many parents recognise delayed speech and some children may have been referred for speech therapy. The major symptoms that bring children to medical attention are seizures, ataxia [clumsiness] and myoclonus [jerks, drop attacks]. The epileptic seizures usually herald the onset of further symptoms. Seizures may be varied and include Myoclonic jerks which may cause the child to fall, absence attacks when the child becomes vacant or full "grand mal" convulsions with loss of consciousness.

Alongside these seizures is a deterioration in mental functions, there is developmental regression [loss of skills e.g. speech, coordination, continence] and this becomes apparent around this time or within a few months. Ataxia increases as motor skills decline. Abnormal limb and body movements can occur and lead to spasticity (continued muscle contraction and exaggerated reflexes). Sometimes the muscle spasticity can cause joint contractures.

The examination findings do vary with the age of the child and the stage of the disease. Initially the children have an ataxic gait [clumsy, unsteady walk]. As the disease progresses, the ataxia worsens and children develop frequent myoclonic jerks. Late in the course of the disease children are unable to walk or sit unsupported (generally around

the age of 4 - 6 years). They lose language and vision (blindness is usually by 5 or 6 years), although many are able to recognise their parents' voices. They respond to their parents and siblings with smiles. Feeding becomes more difficult with resulting poor weight gain and frequent symptoms of aspiration [difficulty coordinating swallowing with subsequent coughing or choking as food & drink "goes down the wrong way"]. Most children now receive nutritional support using a nasogastric or gastrostomy tube and this may prolong life. Death usually occurs in middle childhood between the ages of 5 and 14 years depending on the speed of disease progression.

Investigations

Usually children present to a paediatric neurologist because the seizures are frequent and becoming difficult to control with anticonvulsants, or because additional features have emerged. By this time, the diagnosis lies between NCL with a late infantile onset and other causes of developmental regression and seizures. Often the child is beginning to have myoclonic jerks and is less able to walk because of worsening ataxia. The diagnosis of one of the NCLs is then straightforward and only a limited number of investigations are required. It is however of great importance to make a specific diagnosis of the type of NCL, based on a combination of histological and genetic tests in order to counsel families appropriately.

Investigations may include neurophysiology (EEG, ERG, etc), samples for microscopy (biopsy - usually skin [taken from perhaps the arm under local anaesthetic]) and genetic analysis. Blood samples may now also be collected for enzyme assay, this can now give the diagnosis without the need for a biopsy. Whilst the list of biopsy samples does not include a rectal biopsy, this may be preferred by some pathologists in place of the skin biopsy.

1. Neurophysiology

These tests involve measuring "brain waves" with electrodes on the scalp, this is not painful and doesn't usually cause any distress. There are various tests in this area and include an electro-encephalogram (EEG), electro-retinogram (ERG) and visual evoked potentials (VEP).

2. Neuroradiology

Brain imaging (CT or MRI scanning) is performed as part of the investigation

of children with multiple seizures and developmental regression. The changes found in classic late infantile NCL are relatively non-specific, and the value of imaging lies mainly in excluding other causes. Magnetic Resonance brain imaging (MRI) may be helpful in differentiating between classic and variants of late infantile NCL. Early in the course of the disease there is mild cerebral atrophy [generalised shrinkage or loss of brain tissue], but a normal scan does not exclude the diagnosis.

3. Biochemical tests

We now have a blood test enzyme assay, which measures the amount of the deficient enzyme (tri-peptidyl peptidase-1). This is low in children with LINCL.

Treatment

Therapy for children with classic LINCL is essentially supportive. Psychological support around the time of diagnosis, and as the disease progresses for both parents and healthy siblings is important. Families should be given contact addresses for local parent support groups.

Attention to posture, seating, skin and mouth care is essential, with professional guidance from physiotherapists and occupational therapists. Chest physiotherapy may be needed intermittently to help clear infections. Most children will require nutritional support at some stage, and parents often find that the use of a nasogastric tube or gastrostomy tube makes life much easier. Gastro - oesophageal reflux can often be troublesome and may require medication or surgery (eg Nissan's fundoplication).

Anticonvulsants are necessary from quite early in the course of the disease and many children eventually require more than one drug to control seizures. Even then control is not always achieved and myoclonic jerks can be very troublesome. Sodium Valproate, topiramate, levetiracetam and clonazepam are often prescribed either as monotherapy or in combination with varying success. In the very later stages of the disease Benzodiazepines (Lorazepam, Clonazepam, Clobazam) sometimes cause problems due to increased secretions in the mouth and throat but may be useful as add-on therapy because of their sedative, anti-jerk and muscle-relaxant properties.

Carbamazepine, phenytoin, lamotrigine and vigabatrin may exacerbate myoclonus

and are therefore best avoided. There are no reported trials of antioxidant or PUFA (polyunsaturated fatty acids) therapy in the literature. Bone marrow transplantation has been attempted in one case and possibly slowed down development of the disease for a while but did not prevent the illness eventually progressing.

Research is continuing into ways to treat or slow down the disease, e.g. gene therapy where the normal gene is reintroduced back into the cells & tissues and enzyme therapy where the defective or missing enzyme is reintroduced.

Genetic Considerations

Because the diagnosis of classic late infantile NCL is usually made when children are 3 or 4 years old, there are often younger siblings who may also be affected but presymptomatic [before the onset of symptoms but destined to get the disease]. In addition, the question of future pregnancies and prenatal diagnosis may arise. Once the diagnosis is certain, presymptomatic testing can be performed for siblings using blood samples. Prenatal diagnosis is usually available and based on genetic testing of the baby very early in pregnancy. The idea of prenatal testing is that if the test shows that the baby would be affected by Batten Disease then a termination of pregnancy [abortion] can be considered. Early advice from Local Clinical Genetics Service should be sought.

Family Aspects

From the time parents detect that their son or daughter is not developing properly, the family will need support. Sadly - probably because of the vagueness of the early clinical features - parents are often reassured that there isn't a problem and their worries are minimised, they are left feeling that they are worrying too much. This seems to be quite common and can be quite damaging in terms of the relationship between the family and health professionals.

The level of support and the personnel involved will vary between cases and depend on many variables such as the needs of the child and family at any one time, the rate at which the illness is progressing, the level of existing care and support from family and friends. The professionals usually involved would include; GP and members of the primary health care team - health visitor, district nurse; paediatrician (and / or paediatric neurologist), specialist paediatric

community nursing, children's hospice staff, social worker, agencies such as Crossroads etc. There will be important involvement with education personnel from special schools and input from specialist teachers for the visually impaired.

Given the appropriate level of professional support around the family - it is important that parents should be encouraged to take some control of their situation; for the services around to include them in decisions and plans of action; and for the families' wishes to be of paramount importance. This is not about families fitting into packages of care provided by the authorities, and parents should be encouraged and supported thoroughly, by appropriate giving of information - to follow their intuitions, and to decide themselves what they want and need for their child or children. Following diagnosis it is important that parents can feel empowered - and able to provide quality of life for the little time they have left with their child. This kind of situation needs the full support, implemented sensitively and carefully, by the surrounding professional team.

Respite needs introducing at an appropriate stage and plenty of time needs to be given for parents to come to terms with needing this. It takes time and sensitive care to bring families to a stage where they can feel safe handing over the care of their child even for a short period of time. Paediatric health facilities and or children's hospices may be available locally or in the home for the families. Hospices - both adult and children's can still carry a stigma associated with use only at the end stages of life, however, most children's hospices are able to offer specialised and earlier respite and emotional support to families than this.

Financial Support

Finances often become much tighter as one or both parents often have to sacrifice their career to care for their child. Some benefits are available, these include the following. **Disability Living Allowance (DLA)** is a benefit that is available to people if they need help with mobility and/or are being cared for at home. It comprises of two benefits; care allowance and mobility allowance, which is applicable from the age of 3 years. A child with the classic form of LINCL will usually qualify for the care component Disability Living Allowance (DLA)



MUMMY'S LITTLE ANGEL

You've just walked on ahead of me
And I've got to understand
I had to release the boy I loved
And let go of your hand.

It broke my heart to let you go
Although the end I knew
Not a day from now will pass
When I won't think of you.

I'll try and cope the best I can
But I'm missing you so much
If I could only see you
And once more feel your touch.

You've just walked on ahead of me
Don't worry I'll be fine
But now and then I'm sure I'll feel
Your hand slip into mine.

Good night, God Bless Sweetheart.

With Love Mummy

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