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# Guide to Understanding Mucolipidosis II (ML II)

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## What is ML II?

Mucolipidosis Type II (ML II) is one of the lysosomal storage disorders known collectively as Mucolipidoses. These disorders are closely related to Mucopolysaccharidosis.

ML II is sometimes referred to as 'I-Cell Disease'. This term is derived from the observation of changes within a cell known as the fibroblast. A healthy fibroblast cell has a specific shape but in individuals affected by ML II this shape changes as a result of the accumulation of storage materials.

Dr. Jules Leroy from Belgium was one of the first doctors to write about the condition in the 1960's and his name is sometimes used to refer to ML II.

Whilst there is no cure for individuals affected by ML II, this fact sheet explores the disease's presentation and clinical management.

This fact sheet is produced by the MPS Society and draws upon the experiences of parents and doctors with reference to medical literature.

## What Causes ML II?

In the course of normal life there is a continuous recycling process of building new materials and breaking down old ones ready for disposal. This activity takes place in a special part of the body's cells called the lysosome. The process requires a series of biochemical tools called enzymes. Enzymes can only reach the lysosomes after a special signal has been attached to them.

In children with ML II the signal is not attached so the enzymes are unable to get to the right place and are therefore lost outside the cell.

Babies may show little sign of the disease but symptoms start to appear as more and more cells become damaged by the accumulation of unwanted deposits.



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## How Common is ML II?

The MPS Society, which co-ordinates the 'Registry for MPS and Related Diseases' has shown that ML II is a rare condition, for example, between 1989 and 1999 22 babies were born with ML II in the UK.

## Does ML II Affect Individuals Differently?

This disease encompasses a spectrum of clinical symptoms which, at the severe end of the spectrum are labelled ML II. Less severely affected individuals are considered to have ML III. A separate fact sheet on ML III can be obtained from the MPS Society.

## How is ML II Inherited?

ML II is an autosomal recessive disease; both parents must carry the same defective gene and each pass this same gene on to their child.

Where both parents are carriers of the ML II gene there is a 25% (1:4) chance of having an affected child with each pregnancy. There is a 50% (1:2) chance of a child receiving only one copy of the defective gene and therefore being a carrier.

A carrier will not be affected but can pass the defective gene to his/her offspring. The remaining 25% (1:4) will be neither affected nor a carrier. Using information from an affected individual's DNA, it may be possible to determine whether brothers and sisters are carriers of, or affected by ML II.

For further information on the inheritance pattern of MPS and related diseases contact the MPS Society for a specialist booklet.

## Can You Test for ML II in Pregnancy?

For each pregnancy the chances of a baby inheriting ML II are totally independent of whether a previous child was affected by the disease.

Prenatal tests can be arranged early on during a pregnancy for those families who have already had a child with ML II.

Both Amniocentesis and Chorionic Villus Sampling (CVS) can be used to diagnose the disease in utero. Most laboratories do prenatal tests on cultured cells. It may take three to four weeks for a result.

## Genetic Counselling

All parents of children with a lysosomal storage disease should consider asking for genetic counselling before having other children.

The counsellor will be able to advise on the risk to close relatives and to suggest whether the wider family should be informed.

## Clinical Presentation of ML II

### Growth

Children with ML II will be severely restricted in growth. The majority will stop growing by the age of three and are unlikely to be taller than about three feet (90 cms).

### Physical Appearance

The neck is short, cheeks are often rosy and the nose may be broad with a flattened bridge and upturned nostrils. The mouth may be wide with very prominent gums. Eyebrows may be bushy and meet in the middle and the eye sockets are shallow which makes the eyes appear prominent.

The hair on the head often has a lighter colour than that of brothers or sisters and can gradually turn white.

The head shape of children with ML II may be changed by the early closing of the soft part of the baby's skull.

### Intellectual Ability

Children are likely to be restricted in what they learn but some have learnt to talk, sing and do simple sums. Parents emphasise that it is important to help even severely affected babies to learn as much as they can.

Even if your child does not speak, you may be surprised by how much he or she understands. Some children use their hands to sign, thereby communicating their needs effectively.

### Mouth & Teeth

The gums are often overgrown and swollen. Teeth may be late and troublesome coming through. They may not come down much below the edge of the gum and are often widely spaced and poorly formed with fragile enamel.

It is important that teeth are well cared for as tooth decay could be a cause of pain. The tongue may be enlarged and the roof of the mouth has a high arch.

## Dental Hygiene

Teeth must be well cared for to avoid the need for extractions. If the water in your area has not been treated with fluoride, your child should have fluoride tablets or drops daily. Cleaning around the mouth with a small sponge, or a stick soaked in mouthwash, will help keep the mouth fresh and avoid bad breath. Dribbling is a common problem and a plastic backed bib under the clothes may help prevent soreness.

If your child is severely effected it may be safer for any treatment to be carried out in hospital. The dentist should be informed if your child has a heart problem and you will probably be advised that s/he should be given antibiotics before any treatment. This is because certain bacteria in the mouth may get into the blood stream and cause an infection of the heart valves. If teeth need to be removed under anaesthetic, this should be carried out in hospital with an experienced anaesthetist and never in a dental surgery.

## Ears

Some degree of deafness is common in individuals suffering from ML II. It may be Conductive Deafness, Nerve Deafness or both (Mixed Deafness) and can be made worse by frequent ear infections. It is important that children with ML II have their hearing checked regularly so that problems can be identified and treated at an early stage.

Conductive Deafness is concerned with impaired transmission of sound waves through the ear canal, the drum and the middle ear.

Correct functioning of the middle ear depends on the pressure behind the ear drum being the same as that in the outer ear canal and the atmosphere. This pressure is equalised by the Eustachian Tube, which runs from the middle ear to the back of the nose. If the tube is blocked, the pressure behind the eardrum will drop, the drum will be drawn in and the transmission of sound waves will be impaired. If this negative pressure persists, fluid from the lining of the middle ear will build up and in time become thick like glue, hence the condition is known as 'glue ear'.

## Conductive Deafness (Glue Ear)

Under general anesthetic a small incision behind the eardrum can be made (myringotomy) and the fluid sucked out. A small ventilation tube called a 'grommet' may be inserted to keep the hole open and allow air to enter from the outer ear canal until the Eustachian Tube starts to work properly again. Grommets will eventually fall out.

If the Conductive Deafness recurs T-tubes may be used. This is a type of grommet which stays in place longer. Due to the anesthetic risks for children with ML II, the surgeon may decide to use T-tubes on the first occasion.

## Sensorineural Deafness (Nerve Deafness)

In most cases the cause of Nerve Deafness is damage to the tiny hair cells in the inner ear. It may accompany Conductive Deafness in which case it is referred to as Mixed Deafness. Nerve Deafness is managed by the fitting of hearing aids. Some children may keep pulling out their hearing aids at first but it is important to persevere at wearing them so that communication can be maintained.

## Eyes

Clouding of the cornea caused by storage of waste products may be seen in children with ML II, however this rarely interferes with vision and is not particularly noticeable.

## Skin

The skin is often thickened and lacking elasticity. Occasionally, there may be more body hair than normal. This is called hirsutism.

## Infections

Children with ML II are prone to frequent chest and ear infections and tend to have runny noses. The shape of the chest is abnormal and it cannot move freely to allow the lungs to take in a large volume of air.

The tissue of the lungs becomes thickened by storage material and stiffer than usual, almost like a balloon that has never been blown up before and therefore needs greater force to expand.

There is an increase in secretions which are harder to clear as the restricted lungs make it difficult for sufferers to take a deep enough breath to cough properly. When the lungs are not fully cleared there is an increased risk of infection which can lead to scarring of the airways causing further obstruction.

Due to the high risk of infection, children with ML II should be protected from drafts and be kept warm at all times. Their environments, such as their nursery schools, should be clean. In particular any toys and objects with which they play.

## Chest Infections

Medication may affect individuals with ML II differently so it is essential to consult your doctor rather than using over-the-counter medication. Medication for controlling mucus production may not help. Medication such as antihistamines may dry out the mucus making it thicker and harder to dislodge.

Decongestants usually contain stimulants that can raise blood pressure and narrow blood vessels, both undesirable for children with ML II. Cough medicines that have a sedating effect may cause more problems with sleep apnoea by depressing muscle tone and respiration. Children with ML II commonly end up with secondary bacterial infections which should be treated with antibiotics.

## Heart

Some children may develop problems with one of the heart valves. 'Heart murmurs' will occur if the valves become damaged by stored Mucopolysaccharides.



Joseph

In order to stop blood flowing back in the wrong direction, the heart valves are designed to close tightly as blood passes from one chamber of the heart to another. If a valve is weakened or changed in shape it may not shut firmly enough and a small amount of blood may leak back. In time this can put a strain on the heart. This condition can be treated. Children with ML II frequently develop the more serious problem of thickening and weakening of the heart muscle (cardiomyopathy) often as a result of the damaged heart valves. In some cases drugs may be prescribed to try and help the problem.

## Heart Problems

Some children with ML II may develop problems with the aortic or mitral valve, having slowly progressive valvular heart disease for years without any apparent clinical effects. An ECG (electrocardiogram) should be carried out annually (or as often as your doctor thinks necessary) to show whether any problems are starting. This test is painless and similar to the ultrasound screening of babies in the womb. It can identify problems with heart muscles, function and valves.

## Liver, Spleen & Abdomen

The liver and spleen are not usually enlarged in children with ML II, however the abdomen may protrude due to weakness of the muscles and the limited space available to internal organs. There is a possibility that part of the abdominal contents may push out behind a weak spot in the wall of the abdomen. This is called a hernia.

## Hernias

A hernia can come from behind the navel (umbilical hernia) or from the groin (inguinal hernia). Inguinal hernias can be repaired by an operation.

Umbilical hernias are not usually treated unless they cause entrapment of the intestine, or are very large and problematic. Recurrence of an umbilical hernia is common even after repair.



Abigail

## Bones & Joints

There is a wide variation in the severity of problems, even between affected brothers and sisters.

Skeletal problems are usually evident at birth. In some severe cases babies may be born with fractures.

The hips are sometimes dislocated and the knees may become 'knocked' (genuvalgum). The bones of the feet are sometimes deformed.

Joint stiffness is also common in ML II. All joints become stiff and their movement may be limited. Later in life this can cause pain which may be relieved by warmth and the prescribing of analgesics. Limited movement in the shoulders and arms may make dressing difficult.

### Knocked Knees

Our joints are held in place by strong bands or protein fibre known as ligaments. Individuals with ML II have ligaments which are often very lax. If this is the case, surgery may not lead to any improvement.

As a child with ML II grows older the knees gradually become more 'knocked' (genuvalgum). It is sometimes possible for the legs to be straightened by an operation but it is best to wait until the child has stopped growing.

## Spine

The bones of the spine are poorly formed and there is often a kyphosis (hump back) in the lower spine.

The neck may be fragile, due mainly to underdevelopment of the second vertebrae, but there are no reports of this causing serious problems.

## Hands

The shape of the hands of those affected by an MPS or related diseases is very noticeable and has been used as the symbol of the MPS Society. They are short and broad, with stubby fingers which gradually become curved over or 'clawed'.

## General Management of ML II

### Diet

There is no scientific evidence that a particular diet has any beneficial effect. Symptoms such as diarrhoea tend to come and go naturally. Some parents, however find that a change in their child's diet can ease such problems. Cutting down on milk, dairy products and sugar and avoiding foods with too many additives have all been said to help individual children. It would be advisable to consult your doctor or a dietician if you plan major changes to ensure that the proposed diet does not leave out any essential items.

If your child's problems are eased you could try re-introducing foods one at a time to test whether any particular one appeared to increase your child's symptoms.

### Feeding

Most children with ML II are unable to feed themselves but enjoy their food, although some are reluctant to try anything new. Due to the poor formation of teeth, chewing may be difficult and food may have to be liquidised or mashed. It is important that children are supported at all times when feeding and that the diet is regularly reviewed by a dietician.

### Drugs

Children with ML II may be affected differently by drugs so it is essential to consult your doctor, rather than purchase over-the-counter medication. Drugs may be tried for controlling mucus production, but some may make the mucus thicker and harder to dislodge and may make the child more irritable. The use of sedatives can increase the problem of sleep apnoea by depressing respiration.

Frequent use of antibiotics may make them less effective when really needed. Repeated use can also cause thrush (a fungal infection which commonly affects the mouth or vagina and produces a white curd-like deposit). Thrush causes irritation and discomfort and will need to be treated. Your doctor may, therefore wish to limit the number of times when antibiotics are prescribed for coughs and colds.

### Anaesthetic

Giving an anaesthetic to a child with ML II requires skill and should always be undertaken by an experienced paediatric anaesthetist. In some cases, it is difficult to remove the breathing tube after surgery is completed. There is a more detailed explanation of this complex subject in the specialist anaesthetic booklet published by the MPS Society.

### Physiotherapy and Hydrotherapy

Children should be as active as possible to improve their general health, and a physiotherapist may be able to suggest ways of achieving this. For children, the best forms of physiotherapy are exercises that are introduced through play.

## **Management of Body Temperature**

Due to the metabolic nature of the disease, children with ML II are unable to maintain a constant body temperature. Hands and feet can become very cold. This should be monitored regularly.

## **Pain**

When a child cannot express themselves it is very hard to know whether crying is from pain or frustration. Children may have ear infections, toothache, aches and pains in their joints or feel discomfort from a full stomach.

As with small babies, parents have to learn by trial and error. Sometimes screaming episodes are put down to behavioural problems. Do not hesitate to ask your GP to check whether there is a physical cause for your child's distress.

## **Life Expectancy**

Sadly, most children with ML II may die before the age of three or four. Some who are less severely affected have lived to the age of ten or twelve.

## **Living with a Child with ML II**

ML II children are usually happy, friendly children who enjoy the company of other people. They are much loved by all who know them and many are very easy to manage. They are usually very contented.

As they remain small they tend to continue as the baby of the family who is loved and spoiled by everyone.

Babies may be of low weight and rather floppy. Most learn to sit without support and some manage to stand on their own. Some learn to walk with a little help.

The children smile, laugh and show pleasure and some learn to say a few words. They often have a good understanding and have the ability to communicate without speech.

They enjoy playing with simple toys. Some have progressed further and have learnt to read simple books and do easy sums. Some learn to sing songs, although the voice is often rather hoarse. Most do not become toilet trained. Children with ML II will require support for bathing and dressing.

Particular care should be taken with the arms due to joint stiffness and pain.

Once a diagnosis of ML II disease is confirmed, families may find it a very difficult and painful process coming to terms with the news that their child's life will be so very different from what they had expected.

Over the years their child will lose skills that they have learnt. Sight and hearing will deteriorate and any control over bodily functions will gradually be lost.

## **Education**

In many cases children with ML II will benefit from the social stimulation and interactive setting of playgroups, nursery and/or primary school.

Children with ML II are often very sociable and well liked by their peers and should be encouraged to develop skills through play and learning according to their level of ability.

Depending on the child's needs, integration into play and learning activities should be achieved in consultation with the child's parents. Issues to be addressed can include appropriate seating and equipment, dedicated 1:1 support and special individual projects which the child can achieve at their own pace.

The majority of children with ML II will have the support they need detailed in a Statement of Special Educational Needs. Once again, it is important that the risk of infection in classroom environments is minimised.

## **Home Adaptations**

Children with ML II will only have very limited mobility and will become increasingly dependent on their parents and carers to meet their everyday needs in areas of incontinence, personal hygiene and nutrition.

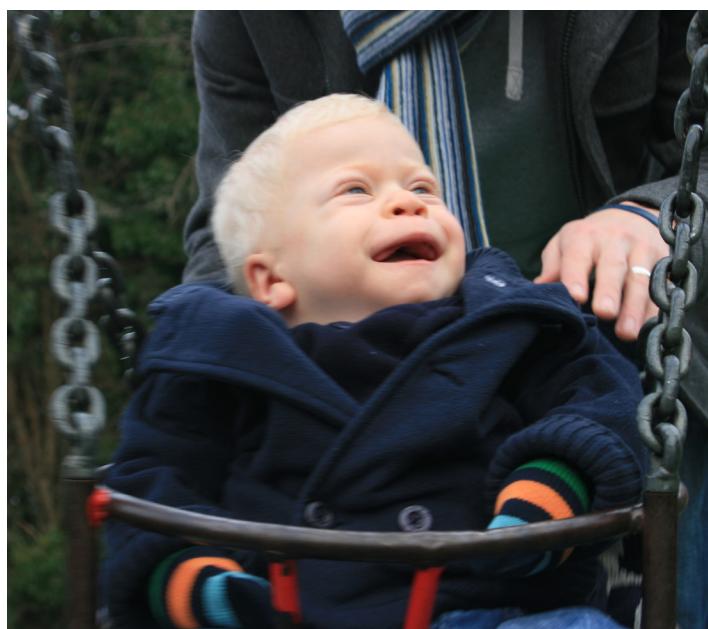
It is important to give thought early on with regards to the ways in which the families and carers will deal with these changing needs. Adaptations can often take a long time, so it is prudent to plan ahead as far as possible.

The MPS Society has considerable experience of the options available to families caring for a child with ML II.

## **Having a Break**

Caring for a child with ML II is usually hard work and parents or carers need a break to rest and enjoy activities which may not be possible when in their caring role.

Many families use local children's hospices, social services, respite care or have someone regularly to help out at busy times. Further details of hospices throughout the UK offering respite care to families are available from the MPS Society.



Joseph



Joseph

### Palliative Care

Palliative Care is provided to the family and the child affected by a life-limiting disease in situations where curative treatment is not an option.

This support encompasses aspects such as respite care, symptom management and bereavement support and may extend over a long period of time. Considerable personal care may also be required which may include feeding and personal hygiene. This can take up a large amount of time and the stress involved can put a family under immense strain.

An assessment of medical needs and care plans should lead to an approved package of support being provided to both the child and the family and enable both to experience a better quality of life.

### Treatment of ML II

At present there is treatment for symptoms as they arise but there is no cure for the underlying disease.

Bone Marrow Transplantation (BMT) has been tried in a small number of cases of ML II but this had little effect on the progress of the disease. BMT is not recommended for children with ML II. Cord blood transplant is also not usually recommended.

### About the MPS Society

The Society for Mucopolysaccharide Diseases (MPS Society) was founded in 1982 and represents over 1200 children and adults suffering from MPS and related diseases, their families, carers and professionals throughout the UK.



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### Society for Mucopolysaccharide Diseases

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