

## *Organic Acidurias*

### **A guide for patients, parents and families**

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[www.e-imd.org](http://www.e-imd.org)

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## Introduction

You or your child have/has been diagnosed with an organic aciduria

Initially any information regarding these types of condition is hard to understand, especially at a time when you are naturally very worried and suddenly provided with lots of medical information.

By describing this condition in booklet format, you will be able to read it at your leisure, and then write down any important questions that you may want to ask your specialist doctor, nurse or dietitian.



## Metabolic function

To be a fit healthy individual, we have to feed our body regularly with food to provide energy and repair tissues.

The foods that we eat are broken down into small packages and either used for growth and repair, stored to be available for periods of starvation, or disposed of as waste. Although, this explanation describes the basic process, it is of course much more complex.

## How the body deals with protein

Foods containing protein are eggs, milk, fish, meat, cheese bread etc. During digestion, protein is broken down into smaller molecules or “building blocks” to be transported in the blood and used for growth and tissue repair.

What started as a healthy steak or a glass of milk will have now been broken down into 20 individual “building blocks” known as amino acids. These amino acids travel in the blood stream and are supplied to the cells where they are needed. Generally speaking, we consume much more protein than the body needs. Therefore once we have finished with using what is needed, the excess is broken down by enzymes into smaller products, including ammonia and organic acids. The body is unable to tolerate large amounts of ammonia and organic acids; therefore a process in the liver converts these into harmless forms that can then be disposed of.

## Organic acids

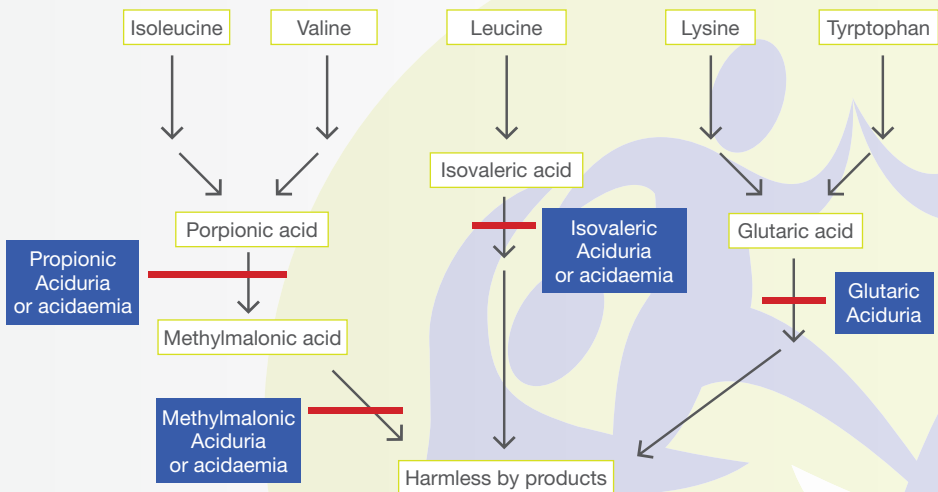
To understand your child's condition it is helpful to look in more detail at how certain amino acids (such as Isoleucine, Valine, Leucine, Lysine and Tryptophan) are broken down. Each amino acid has its own pathway using a series of enzymes. Each enzyme is essential to convert one substance to another.

If an enzyme is faulty it results in the build up of harmful products before the block, much in the same way that traffic builds up when there is a hold up on a busy road.

If you have been told that your child has an organic aciduria, this will mean that one of the enzymes is not functioning properly. The organic acids that build up before the block in the pathway give the name to each condition:

- Propionic acid – propionic aciduria or acidemia
- Methylmalonic acid – methylmalonic aciduria or acidemia
- Isovaleric acid – isovaleric aciduria or acidemia
- Glutaric acid – glutaric aciduria

The diagram shows the position of the faulty enzyme in these disorders



## What are the symptoms?

Symptoms vary from individual to individual, and may present at different ages.

During the first weeks of life a baby can become very unwell, as it can no longer rely on the mother's placenta for clearing these harmful products. Once the baby is feeding protein, the harmful acids build up. Babies in this situation usually present with drowsiness, rapid breathing and vomiting and they can become seriously ill. A spell in hospital will therefore be necessary. Once your baby is stable you will be given information, support and guidance on how to manage your child's condition.

In some instances, the harmful acids emit a certain odour from the child. Children who have isovaleric aciduria have been known to emit an odour that smells like "cheesy feet". Once treatment has started, these smells disappear.

However parents sometimes notice odd smells when their children are slightly unwell with a cold or something similar; these can be an early indicator to start emergency regimen treatment. (Emergency regimen is described later in this brochure).

Occasionally children may not develop any symptoms until they are older. They may be considered to have a milder variation of the condition; however careful management is just as important.

## Treatment

### Aims of treatment

The main aim of treatment is to keep the level of harmful acids in the blood down at safe levels. Several things may cause the blood ammonia to rise; these include infections or sudden increase in the amount of protein eaten. During periods of illness and infection, the body's response is to break down body stores to supply energy. As a result of this, protein is also broken down and released back into the blood stream, which in turn leads to the ammonia level going up.

### Emergency treatment during acute illnesses

If your child is feeling unwell, they should be treated with an emergency regime. An emergency regimen is necessary for every patient who has an organic aciduria, including those who may be mildly affected. This treatment varies from one individual to the next.

An emergency regimen is given as a high glucose energy drink e.g. Maxijul. It must be taken if your child is unwell and is unable to tolerate normal diet. It is a harmless solution, therefore, if you have commenced your child on the emergency regimen and recovery is immediate it will not have caused any side effects. By consuming these additional calories the body is prevented from breaking down its own tissues to release energy and protein as discussed above and prevent the build up of harmful organic acids. Delay in starting can be dangerous. If you are unsure in any way, you should liaise with your local metabolic team.

The emergency regimen is prescribed to suit your child as an individual, it is regularly revised and the strength of solution increased with the child's age and weight. It is important that the instructions are followed rigidly during illness and the child is able to tolerate the right strength glucose solution given at regular intervals throughout the day and night.

Your dietitian will advise you on the emergency regimen and provide some written instructions for you.

If whilst on the emergency regimen, your child continues to vomit and it is apparent that he/she is not recovering, you must either:

- contact your local doctor and arrange for hospital admission,
- or go to casualty
- or telephone your paediatric unit (if you have an access facility that allows arranged admission).

On admission, the emergency regime that has been given orally will be converted to a glucose drip directly into the vein. This will give the stomach a rest from vomiting and allow the important glucose solution to be continued into the vein. The glucose solution can then be re-introduced orally followed by diet and drinks, according to recovery rate. With the support of the glucose drip, there is no need to be too hasty in encouraging large volumes of drink. Once things start to get better, the usual diet and drinks can be reintroduced gradually.

Whilst in hospital, it will be necessary to take blood tests, to ensure that the blood chemistry is becoming normal again, and to decide if any extra treatments are needed.

If during hospital admission, your child is not responding well to the glucose drip, further treatments will be needed. If organic acid levels rise to very high levels, drowsiness, irritability and confusion occurs, warning us that the brain is being affected. In order to prevent this occurring it may become necessary to treat with medicines through the vein. Your child may already take these medications by mouth or via a tube. If after all these medications have been introduced, your child continues to remain very sick it may become necessary to transfer to intensive care where further intensive treatment measures may be necessary.



## Long term treatment

### Diet

Patients that are diagnosed with an organic aciduria often have their dietary protein restricted, or they are advised to be a little cautious with the amount of protein they eat.

Restriction of protein is important as it reduces the build up of harmful organic acids. The aim is to provide the body with sufficient protein to allow for growth and repair of tissue but at the same time reducing quantities to a level your child can tolerate. There is a tendency for the amount of protein tolerated to decrease with time because as you get older the growth rate slows.

Your dietitian will teach you how to measure protein. Using this you will be able to control and measure the amount of protein you are allowed in the diet. Measuring foods will only relate to protein-containing foods, all other foods can be eaten freely and will not need weighing.

In many instances food aversion becomes so severe that it is difficult to provide sufficient calories by mouth. In this instance use of a tube for feeding becomes essential.

Tube feeds can be given by passing a very fine tube down the nose and into the stomach. These are referred to as naso-gastric tubes. Naso-gastric tubes are not recommended for long term use. If it becomes obvious that long term tube feeding will be required, insertion of a gastrostomy tube may become necessary. A gastrostomy tube is inserted directly into the stomach and is performed under anaesthetic as a minor surgical procedure. A small plastic disc that sits just under the skin secures the gastrostomy tube. When the child is not connected to a feed, the tube is clamped and clothes are worn over the tube covering the site.

## Medication

Some children will be on medicines, whilst others may not. Listed below are the medications that may be used, and what the action of the drug is:

**Carnitine:** This helps to mop up the toxic organic acid from the blood allowing it to be cleared in the urine.

**Glycine:** this works in the same way as carnitine. In some conditions it can be given as a stand-alone therapy when well.

**Metronidazole:** this is an antibiotic but is given in a very low dose rather than a dose to fight infection. Normal bacteria that live in the gut make organic acids. Metronidazole is used to reduce the amount of gut bacteria and so decrease the amount of organic acid made and absorbed from the gut.

Besides these, there are a wide variety of medications that may be used for patients with organic acidurias. The ones described here are the most commonly used.

It is very important that you take all your medication as prescribed by your doctor.

## How has my child got this condition?

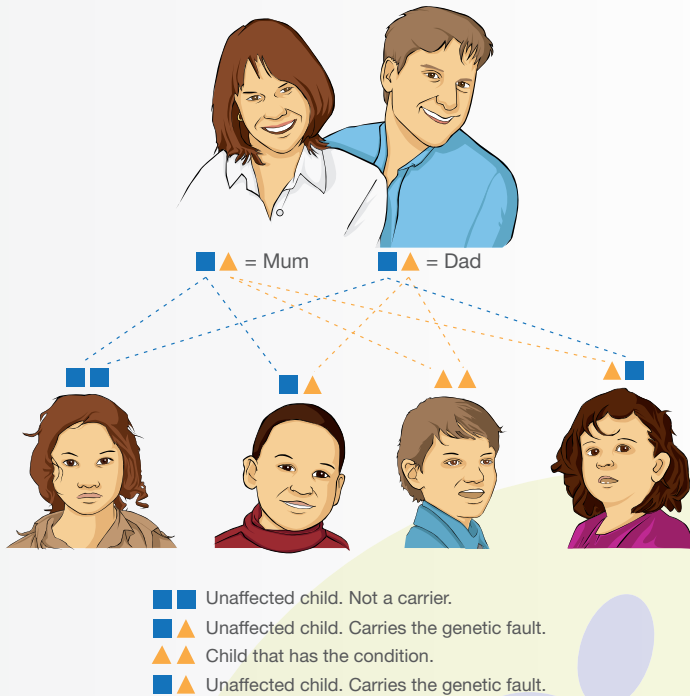
Organic acidurias are genetic. This means that they are not brought about by anything that may have occurred during pregnancy. Genetic disorders are inherited and the pattern in which your child may have developed the condition will now be described.

If the gene is inherited from both mum and dad it is described as autosomal recessive.

In the human body, every person carries approximately seven defects in their genetic information. If you and your partner both carry the same genetic fault, each time you get pregnant, there is a one in four chance that your baby will be born with a urea cycle disorder.

## How does this occur?

The diagram shows you how this happens.



When a child is conceived, there is no way of predicting which sperm and which egg will unite to make the baby. At conception one egg from mum and one sperm from dad is brought together to develop the foetus.

It is within the nucleus of each cell of the egg and the sperm that information called the DNA is stored on strands called chromosomes. It is this information that predicts the colour of the child's eyes, hair etc and will also carry any information that relates to a genetic disease.

## What does the future hold for my child?

As previously described, the severity of organic acidurias is very variable. In some cases, the condition is so mild that the specialist needs only to see the child on an annual basis. With this group of patients an annual check up allows the doctor to keep up to date with any changes that may be occurring as the patient gets older. With increasing age it may become necessary to reduce protein intake and start medication.

For those children that are more severely affected, it is important to be seen and assessed regularly by a metabolic team. It is likely that the more severely affected child will need the support of the local community service in order to have access to specialist teams in addition to the metabolic doctor. This will include special needs social workers, speech therapy, physiotherapy, community paediatricians, paediatric nurse etc.

Children that are severely affected may have learning difficulties and may therefore need assessing to ensure the education he/she receives is suitable to the child's learning ability.

## Pregnancy

Whilst organic acidurias are regarded as fairly serious diseases, treatments are constantly being refined, and ongoing research means that the long term outcome for patients is improving. Of course this will always depend on the type and severity of the organic aciduria which the individual person has.

Having a baby as a fit and healthy individual imposes a significant amount of stress and fatigue on the body. As a patient with an organic aciduria, the effect of a pregnancy will increase this stress level and can cause problems to both mother and child if not cared for appropriately.

It is advised that all females involved in sexual relationships be adequately protected with suitable contraception. Where possible all pregnancies should be planned and care provided pre-conceptually with your Specialist Consultant.

During your pregnancy your care will be shared between your specialist consultant and your local obstetric team. This ensures that throughout pregnancy both mother and baby are provided with the maximum support available. It is likely that you will be monitored more closely and some of the treatment, maybe the diet or medication, will be changed.



## Travelling

Travelling is so much part of everyday life and this should provide no barriers to the person with an organic aciduria. It is wise to take sensible precautions if planning an extended trip or if going abroad.

It might be sensible to just check that your destination has suitable medical facilities locally should you become ill whilst away.

It is absolutely necessary to continue with your diet and medication whilst away and to ensure that you have adequate supplies to last you for your trip.

You should carry some information regarding the nature of your illness this can be provided by your clinical team and there are some emergency cards produced for this purpose which contain specific information about your condition and treatment. For longer periods abroad your medical team may be able to suggest a local doctor that could supervise your care.

## Glossary

**Acute:** sudden onset, severe

**Amino acids:** the building blocks of proteins

**Ammonia:** toxic by-product of the breakdown of protein in the body

**Chronic:** long term

**Decompensation:** a metabolic term describing onset of illness resulting in the body reverting to the breakdown of stored protein within the cells and tissue. Usually it is brought about by diarrhoea and vomiting or mild infection.

**Elimination:** the way in which the body gets rid of waste materials in urine or faeces

**Enzyme:** a chemical in the body that makes the chemical reactions proceed more quickly

**Gastrostomy:** a feeding tube which is placed directly through the stomach wall

**Intravenous:** into the blood vein

**Organic Acids:** Acids that are made naturally by the body; formed as breakdown products of amino acids.

**Naso-gastric tube:** a feeding tube which goes via the nose into the stomach

**Orally:** by mouth

**Paediatrician:** a doctor who trains specifically in the care of children

**Urea:** ammonia is converted into urea it is less toxic and can be passed in the Urine

For more information and contacts of patient organisations [www.e-imd.org](http://www.e-imd.org)

If you have any queries regarding your treatment, or any other aspect of organic acidiurias, please contact your consultant, clinical nurse specialist, dietitian or doctor.

This leaflet arises from the project E-IMD which has received funding from the European Union, in the framework of the Health Programme.

For more information: [http://ec.europa.eu/health/programme/policy/index\\_en.htm](http://ec.europa.eu/health/programme/policy/index_en.htm)

E-IMD would like to offer special thanks to the Eurowilson network for kindly sharing the illustrations used in this booklet [www.eurowilson.org](http://www.eurowilson.org).