TEMPLE (Tools Enabling Metabolic Parents LEarning) are a set of teaching slides and booklets that provide essential information about different inherited metabolic disorders that require special diets as part of their management. These teaching tools are aimed at parents who may have an infant or child that has been recently diagnosed with a disorder. They are also useful when teaching children, extended family members, child minders, nursery workers and a school team. They have been developed by a team of experienced clinical and research metabolic dietitians from the UK who are members of the British Inherited Metabolic Disease Group (BIMDG).

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Each module produced is reviewed by a consultant clinician who is a member of the BIMDG.

This teaching tool is not designed to replace dietary information that may be given by a dietitian in clinic.
Citrullinaemia

Information for families following a new diagnosis

ADAPTED BY THE DIETITIANS GROUP

BIMDG
British Inherited Metabolic Diseases Group

BASED ON THE ORIGINAL TEMPLE WRITTEN BY BURGARD AND WENDEL
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Supported by NUTRICIA as a service to metabolic medicine
What is Citrullinaemia?

It is an inherited metabolic condition.
What is protein?

Many foods contain protein.
The body needs protein for growth and repair.
Many people eat more protein than the body needs.
How do we remove waste protein from the body?

• Firstly, the body converts waste protein to a toxic chemical called **ammonia**

• Ammonia is then converted into a non-toxic chemical (**urea**) in the liver

• This process occurs via the **urea cycle**

• In the urea cycle, several steps have to take place. Each step needs an enzyme (like chemical scissors) for it to work

• Urea is then removed by the kidneys
What happens in Citrullinaemia?

In Citrullinaemia, the body lacks an enzyme called **argininosuccinate synthetase**.

This means the liver cannot convert waste protein into urea as fast as normal. It can lead to high ammonia levels, particularly at times of increased protein breakdown.
When does Citrullinaemia cause high ammonia levels?

Ammonia levels can rise when there is an increased break down of protein. This may happen if too much protein is eaten.

It commonly results from break down of the body’s own protein. This is often triggered by infections, particularly if there is vomiting.

This causes **catabolism** which is a break down of body protein and can lead to a metabolic crisis.
What are the symptoms in Citrullinaemia?

Some babies become ill in the first few days of life.

Signs and symptoms:

- Poor feeding
- Vomiting
- Floppiness
- Excessive sleepiness
- Rapid breathing
- Dehydration (lack of body fluids)
- Seizures

The effects of high ammonia can quickly become life-threatening if unmanaged.
What are the long term effects of Citrullinaemia?

It may cause learning difficulties.

It may also cause delays to normal development like walking and talking.
Protein balance is needed in Citrullinaemia

In Citrullinaemia it is important that enough protein is given to grow... but not too much as it will make waste protein causing high ammonia levels.
How is Citrullinaemia diagnosed?

The diagnosis is suspected in a patient with high ammonia levels because of the pattern of chemicals in the blood and urine.

The diagnosis is confirmed by finding the mutation in the citrullinaemia gene.
How is Citrullinaemia managed day to day?

Citrullinaemia is managed with the following:

- A protein restricted diet
- Sometimes a special amino acid supplement may be needed
- Sufficient energy supply from food and feeds
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How is Citrullinaemia managed day to day?

- Regular feeding
- Arginine supplements
- Vitamin and mineral supplements
- Other medications to control the level of ammonia in the blood
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Is tube feeding needed?

Tube feeding may be necessary to give regular feeds. This will ensure energy, nutrient and fluid needs are met.
How is Citrullinaemia managed during illness?

- During any childhood illness, an emergency regimen is given
- This will reduce the break down of protein and the build-up of ammonia
How is Citrullinaemia managed during illness?

Stop all protein in food & drink

Start the emergency regimen.
This is made up of glucose polymer

Continue medication as prescribed
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- Start the emergency regimen. This is made up of glucose polymer
- Continue medication as prescribed
Checklist for illness

Always take full amounts of emergency feeds as prescribed

If symptoms continue and/or you are worried, go immediately to the hospital

Regularly update your metabolic team
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Key message

It is imperative that emergency feeds are started *promptly* and there are *no delays* in management.
How is Citrullinaemia monitored?

- Frequent blood tests to check amino acids, nutrient and chemical levels
- Height and weight
- Developmental checks

Diet and medications are adjusted according to age, weight and blood chemical levels.
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Chromosomes, genes, mutations

Humans have chromosomes composed of DNA

Genes are pieces of DNA that carry the genetic instruction. Each chromosome may have several thousand genes

The word mutation means a change or error in the genetic instruction

We inherit particular chromosomes from the egg of the mother and sperm of the father

The genes on those chromosomes carry the instruction that determines characteristics, which are a combination of the parents
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The genes on those chromosomes carry the instruction that determines characteristics, which are a combination of the parents
Inheritance

Citrullinaemia is an inherited condition. There is nothing that could have been done to prevent your baby from having Citrullinaemia.

Everyone has a pair of genes that make the argininosuccinate synthetase enzyme. In children with Citrullinaemia neither of these genes work correctly. These children inherit one non-working Citrullinaemia gene from each parent.

Parents of children with Citrullinaemia are carriers of the condition.

Carriers do not have Citrullinaemia because the other gene of this pair is working correctly.
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Inheritance – Autosomal recessive (carriers of Citrullinaemia)

Mother is a carrier of Citrullinaemia

Father is a carrier of Citrullinaemia

Female egg cells

Male sperm cells
Inheritance – Autosomal recessive – possible combinations

Mother is a carrier of Citrullinaemia

Child will not be a carrier of Citrullinaemia

Child will be a carrier of Citrullinaemia

Child will have Citrullinaemia

Father is a carrier of Citrullinaemia
Future pregnancies

When both parents are carriers, in each pregnancy the risk to the baby is as follows:

- 25% chance (1 in 4) of Citrullinaemia
- 50% chance (1 in 2) for the baby to be a carrier of Citrullinaemia
- 25% chance (1 in 4) for the baby to have two working genes and neither have Citrullinaemia or be a carrier
Take home messages

Citrullinaemia is a serious inherited metabolic disorder that can lead to severe problems.

The condition is managed with a protein restricted diet, regular feeding and medications.

Remember, during illness, it is imperative that emergency feeds are started promptly, followed strictly and there are no delays in management.
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Take home messages

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- The condition is managed with a protein restricted diet, regular feeding and medications

- Remember, during illness, it is imperative that emergency feeds are started promptly, followed strictly and there are no delays in management
Always ensure you have a good supply of your dietary products and medicines and that they are in date

Your dietary products and medications are prescribed. These are obtained via a pharmacy or home delivery.

Always ensure you have your emergency feed products and a written emergency plan.

Medications to control fever should be given as normally recommended – always keep supplies available.
Helpful hints

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Who’s who

- My dietitians
- My nurses
- My doctors
  - Contact details, address, photos
Visit www.lowproteinconnect.com and register to get access to support and practical advice for those living on a low protein diet.

The site also provides information on upcoming events and personal stories from others on a low protein diet.